THE RELATIVE EFFECTIVENESS OF A NON-STEROIDAL ANTI-INFLAMMATORY MEDICATION (MELOXICAM) VERSUS MANIPULATION IN THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE

By

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A dissertation submitted to the faculty of health at Technikon Natal in partial compliance with the requirements for the Masters Degree in Technology: Chiropractic.

I, Mark Lawrence Tucker do hereby
declare that this dissertation is representative of my own work

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Dedication

This work is dedicated to my parents. To my father, who unfortunately is not with us to share this moment, wish you were here. To my mother, the most unselfish, loving and supportive person I have ever had the privilege of knowing, I couldn't have done it with out you...

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Abstract

The purpose of this study was to evaluate the relative effectiveness of manipulation versus meloxicam (a Non-Steroidal Anti-Inflammatory Drug) to determine which is more beneficial in treating osteoarthritis of the knee. This was a prospective, randomized clinical trial consisting of a population of sixty voluntary subjects, diagnosed as suffering from osteoarthritis of the knee. The patients were divided equally into two groups of thirty, with Group A receiving chiropractic manipulative therapy on eight consultations over three weeks, and Group B receiving meloxicam 7,5mg tablets once daily for three weeks. Capturing of the subjective and objective data for both groups took place on the first, fourth and eighth consultations. Subjective data was captured using the Numerical Pain Rating scale-101, the Visual Analogue scale, as well as the Patient-Specific functional scale. Objective data was gathered from goniometric and pressure algometer measurements.

Statistical Analysis was completed under the guidance of a statistician from Technikon Natal, using the Two-Sample Paired T-test, and the Independent Samples T-test, comparing the intra-group and inter-group data respectively at a 95% level of confidence. It was evident from the intra-group comparison, that Group A showed a greater statistically significant improvement than Group B objectively. However, both groups showed significant improvements subjectively. The inter-group comparison showed that there was no statistically significant difference between the two groups objectively or

subjectively. Power analysis of the goniometric results was low, indicating the possibility of a Type II error.

It was therefore concluded that both manipulation and meloxicam are equally effective in treating osteoarthritis of the knee.

Further studies using greater specificity with larger sample sizes are warranted. Insight into the long-term efficacy of these treatments using long-term follow-up consultations is also recommended.

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List of Abbreviations

- B.M.I. - Body Mass Index
- C.I. - Confidence Interval
- C.O.X. - Cyclo-oxygenase
- Cm - Centimeters
- Ft - Foot
- G.I. - Gastrointestinal
- H_1 - Alternative Hypothesis
- H° - Null Hypothesis
- Kg - Kilograms
- M.E.L.L.I.S.S.A. - Meloxicam Large Scale Internet Study Safety Assessment
- Mg - Milligram
- N.S.A.I.D.'s – NonSteroidal Anti-inflammatory Drugs
- N.R.S. - Numerical Pain Rating Scale
- O.A. - Osteoarthritis
- P.F. - Patellofemoral
- P.F.J. - Patellofemoral Joint
- P.F.J.R. - Patellofemoral Joint Reaction
- P.R.O.M. - Passive Range of Motion
- P.R.S. - Pain Resistance Sequence
- P.S.F.S. - Patient-specific Functional Scale
- P.U.B. - Perforations, Ulcers, Bleeding

- R.I.L. - Repetitive Impulse Loading
- R.O.M. - Range of Motion
- S.E.L.E.C.T.- Safety and Efficacy Large-Scale Evaluation of COX Inhibiting therapies
- T.F. - Tibiofemoral
- T.F.J. - Tibiofemoral Joint
- T.x. - Treatments
- V.A.S. - Visual Analogue Scale
- α - Alpha
- β - Beta

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Definitions of terms

- **Kinematics**: Division of mechanics that daels with the geometry of the motion of bodies, displacement velocity, and acceleration without taking into account the forces that produce the motion (Gatterman 1990: 408).

- **Biomechanics**: Application of mechanical laws to living structures. The study and knowledge of biological function from an application of mechanical principles (Gatterman 1990: 406).

- **End feel**: Discrete, short range movements of a joint, independent of the action of voluntary muscles, determined by springing each vertebra at the limit of its passive range of motion (Gatterman 1990: 407).

- **Homogeneity**: of the same kind; of the same consistency throughout (Churchill & Livingstone 1987: 130).

- **Joint play**: Discrete, short range movements of a joint, independent of the action of voluntary muscles, determined by springing each vertebra in the neutral position (Gatterman 1990: 409).

- **Manipulation**: Passive maneuver in which specifically directed manual forces are applied to vertebral and extravertebral articulations of the body, with the object of restoring mobility to restricted areas (Gatterman 1990: 410).

- **Manual therapy**: Therapeutic application of amnual force. Spinal manual therapy broadly includes all procedures in which the hands are used to mobilize, adjust, manipulate, apply traction, massage stimulate, or otherwise influence the spine and paraspinal tissues with the aim of influencing the patients health (Gatterman 1990: 410).

- **Mobilization**: Process of making a fixed part movable. A form of manual therapy applied within the physiological passive range of motion, characterized by nonthrust increase in passive joint play (Gatterman 1990: 411).

- **Subluxation**: A subluxation occurs in a motion segment in which alignment, movement integrity, and/or physiologic function are altered although contact between the joint surfaces remains intact. A manipulable subluxation is a subluxation in which altered alignment, movement, or function can be improved by manual thrust procedures. (Gatterman 1995:1

CHAPTER ONE

1.0 INTRODUCTION

1.1 The problem and its setting.

Osteoarthritis (O.A.) is the most common joint disease in humans, with knee O.A. resulting in more disability than any other form of O.A. (Brandt 1995: 1057). Thirty three percent of persons 63 to 94 years of age are affected by O.A. of the knee (Deyle et al. 2000: 173). McAlindon et al. (1996:332) wrote that this condition accounts for the majority of the 95000 total knee replacements per year in the United States. Recent evidence suggests that in the elderly, knee O.A. accounts for as much lower extremity disability as any other disease (Felson et al. 1995: 1500). Most people over the age of 65 have some radiographic evidence of knee O.A., the prevalence of which increases with age and is higher in women than men, especially in the elderly (Oliveria et al. 1995: 1134).

Osteoarthritis is a degenerative pathology primarily affecting the articular cartilage that leads to periodic acute inflammation (Morraele et al. 1996: 1385). Yochum and Rowe (1996: 802) consider the term osteoarthritis to be no longer accurately descriptive, as in reality it represents a misnomer since the suffix "itis" implies an inflammatory condition, which is not substantiated by the observed pathologic alteration.

Knee O.A. is characterised by joint pain and mechanical disruption due to pathologic alterations in articular and meniscal cartilage, synovium, bone, tendons, ligaments,

muscles and nerves. Mechanical stresses are likely to play a critical role in the onset and/or the subsequent progression of the pathophysiology and symptomatology of degenerative joint disease of the knee. (Pai et al. 1994: 1297.)

Hertling & Kessler (1996: 48) wrote that if O.A. may be caused by a loss of normal joint mechanics, then primary treatments should be aimed at restoration of normal mechanics. In the cases of capsular tightness or capsular adhesion, treatment must consist of specific mobilization aimed at restoration of normal accessory movements at the joint. The approach to treatment of joint problems that appear to be mechanical should have a biomechanical basis. (Hertling & Kessler 1996: 48.)

Physical therapists frequently use manual therapy procedures as part of comprehensive rehabilitation programs to help patients regain joint mobility and function (Deyle et al. 2000: 174). Chiropractic treatment of O.A. includes a plethora of conservative techniques and therapies aimed at arresting and/or reversing the arthropathy. Central to chiropractic treatment is the restoration of joint motion and function. Chiropractic manipulation improves range of motion, improves coordinated movement, relaxes hypertonic muscles and reduces pain through complex neurophysiological pathways. (Gottlieb 1997: 408.)

N.S.A.I.D.'s continue to be the mainstay of drug therapy for patients with O.A., with both prescription and over the counter N.S.A.I.D.'s being aimed at palliating the symptoms of O.A., however, inflammation is a relatively minor and transient component of degeneration (Gottlieb 1997: 404).

The prolonged use of N.S.A.I.D.'s for O.A. is controversial, and there is recent evidence that some of these anti-inflammatory agents may depress the synthesis of essential proteoglycans in cartilage. Since O.A. occurs with increasing frequency in older individuals, and since this is the group with the highest incidence of adverse effects from N.S.A.I.D.'s, many physicians are now reluctant to prescribe N.S.A.I.D.'s in O.A. (Walker 1996: 71.)

Gottlieb (1997: 404) wrote that adverse effects from these medications are reported to the Food and Drug Administration more frequently than any other medication class. He continues that there is little evidence to suggest the efficacy of N.S.A.I.D.'s for the treatment of O.A; in fact, there is evidence to the contrary, which suggests that the use of N.S.A.I.D.'s may actually increase the progression of the disease process (Gottlieb 1997: 402).

The newer specific, selective, or preferential C.O.X.-2-selective drugs have been developed on the premise that those side effects that are related to the inhibition of the production of physiologically important prostaglandins through C.O.X.-1 enzyme systems may be avoided. Drugs like meloxicam have minimal effects on this enzyme. (Rainsford 1999: 27s.)

Clinical trials have shown that, in doses of 7.5 and 15 mg daily, meloxicam is comparable in efficacy to standard N.S.A.I.D.'s, such as piroxicam, diclofenac and naproxen, in both O.A. and R.A.. While G.I. adverse events will not be eliminated with meloxicam, it does

appear to offer the distinct advantage of superior G.I. tolerability compared with other, established N.S.A.I.D.'s at equipotent doses. (Barner 1996: 29.)

Clinical experience suggests that the treatment of osteoarthrosis with anti-inflammatory drugs does not alter the progression of the arthrosis. This is to be expected if one remembers that the arthritis (inflammatory joint reaction) is secondary to the mechanical reaction in osteoarthrosis. Thus one is obliged to approach the prevention of osteoarthrosis mechanically. (Radin 1986: 63.)

1.2 Aims and objectives of the study:

The aim of the investigation is to evaluate the relative effectiveness of Meloxicam to manipulation using subjective and objective measures in order to determine which is more beneficial in treating osteoarthritis of the knee.

The first objective will be to evaluate the relative effectiveness of Meloxicam and manipulation in terms of subjective clinical findings.

The second objective will be to evaluate the relative effectiveness of Meloxicam and manipulation in terms of objective clinical findings.

1.3 Benefits of the study:

Osteoarthritis has for too long been regarded as a degenerative dead end, uninspiring, unimportant and as a result uninvestigated. This is beginning to dramatically change as a result of a revolution in methodology and a reappraisal of existing approaches to its research. (Hutton 1994: 85.)

The medical management of O.A. currently involves reducing the symptoms of pain with drugs and does not focus on increasing function or inhibiting the progression of the disease (Gottlieb 1997: 402).

This study will attempt to bring focus to the mechanical origin of degenerative joint disease and to help to determine if chiropractic manipulation is a safe, equally effective form of treatment for this condition.

CHAPTER TWO

2.0 REVIEW OF THE RELATED LITERATURE

2.1 Introduction:

The following is an overview of the related literature concerned with the basic clinical, etiological and epidemiological aspects of osteoarthritis of the knee. The theoretic basis for the action and effects of Meloxicam and manipulation are also discussed.

2.2 Osteoarthritis synonyms

Berkson (1991: 356) wrote that Tarnopolsky collected 54 terms applied to this disease. The most common terms include osteoarthritis, osteoarthrosis, degenerative arthritis, degenerative arthrosis, and degenerative joint disease (Yochum & Rowe 1996: 802). The term O.A. was coined by Spender in 1889 while the presently popular name, degenerative joint disease, was first coined by Bennett et al. in 1942, at the Massachusetts General Hospital (Berkson 1991: 356).

2.3 The incidence, prevalence and gender distribution

O.A. is the most common joint disorder found in man, affecting over 25 million Americans. O.A. of the knee and hip have the greatest effects, resulting in impaired mobility and lower extremity physical dysfunction and more than 250,000 joint replacements each year. Population surveys indicate that 10% to 13% of men and women

aged 65 years and older have symptomatic knee O.A.; nearly one third have radiographic findings. (Nevitt & Lane 1999: 632.) Arthritis is the leading cause of disability in the United States with associated direct and indirect costs of $65 billion in 1992 (Grubber et al. 1998: 959).

Van Baar et al. (1998: 2432) wrote that the incidence in general practice in the Netherlands is 3.6/1000 per year and a patient is referred to physiotherapists 22.4% of the episodes of care for O.A. of the knee and prevalence increases with age. They continued that in the 4 years after consulting their general practitioner, 40% of the patients are referred to the physiotherapist.

The Framingham Osteoarthritis Study performed by Felson et al. (1995: 1500), was aimed at determining the incidence of radiographic knee O.A. and symptomatic O.A., as well as the rate of progression of pre-existing radiographic O.A. in a population-based sample of elderly persons. Rates of incident disease were 1,7 times higher in women than in men (95% confidence interval [C.I.] 1,0-2,7), and progressive disease occurred slightly more often in women (relative risk = 1,4; 95% C.I. 0,8-2,5) but rates did not vary for age in this sample. Among women, approximately 2% per year developed incident radiographic disease, 1% per year developed symptomatic knee O.A., and about 4% per year experienced progressive knee O.A. They concluded that in elderly persons, the new onset of knee O.A. is frequent and is more common in women than in men. However, among the elderly, age may not affect new disease occurrence or progression. (Felson et al.1995: 1500).

Oliveria et al. (1995: 1134) performed a study to quantify the incidence of symptomatic hand, hip, and knee O.A. among the members a health maintenance organization located in central Massachusets. Among women, the incidence rates for knee O.A. ranged from a low of 0/100,000 person-years among those ages 20-29 to a high of 1,082/100,000 person-years for those aged 70-79. The age- sex-standardized incidence rates for knee O.A. was 240/100,000 person-years (95% C.I. 218,262). They concluded that O.A. incidence increased with age and that women had higher rates than did men, especially after the age of 50. The incidence of knee O.A. was twice that of hand or hip O.A. The annual incidence of clinical knee O.A. was >1%/year in women ages 70-89. (Oliveria et al. 1995: 1134.) There is no reason to believe that this would be different for South Africans, however this statement cannot be substantiated due to there being no information available to this date on the incidence or prevalence of knee O.A. in the South African population.

2.4 Osteoarthritis

2.4.1 Definition

O.A. is defined as a progressive, non-inflammatory disease characterized by degenerative pathologic changes in articular cartilage and its related components (Yochum & Rowe 1996: 802). Inflammation is a relatively minor and transient component of degeneration (Gottlieb 1997: 402), therefore the term degenerative joint disease has gained the most universal acceptance (Yochum & Rowe 1996: 802). Radin (1986: 6089) preferred to

differentiate between the terms osteoarthrosis (joint deterioration from mechanical causes) and osteoarthritis (joint deterioration from inflammatory causes).

2.4.2 Anatomy

Cailliet (1991: 1) wrote that the knee joint is probably the most complicated joint in the human body. Its intricacy lies in the fact that it comprises two structurally and functionally different yet inter-related joints: the tibiofemoral and patellofemoral joints.

The knee joint is a diarthrodial joint which is a load-bearing unit that consists of two or more skeletal surfaces, the subchondral bone covered with hyaline (articular) cartilage, and united by a fibrous capsule (Walker & Helewa 1996: 20).

Cailliet (1991: 1) continued that the tibiofemoral joint is formed by the distal end of the femur and the proximal surfaces of the tibia. The distal aspect of the femur has two surfaces, which are convex, asymmetrical, saddle-shaped condylar surfaces that are coated with cartilage. They are seperated by a deep U-shaped notch, the intracondylar fossa. These femoral articular surfaces correspond to similar articular surfaces of the opposing tibial condyles. Cartilage covers a small part of the anterior curvature and the entire posterior surface of the inferior and posterior portion of the femoral condyles. The tibial surface has two concavities, which are shallower than the convex femoral condyles, and these opposing articular surfaces are asymmetrical and incongruent and thus, even though they are directly opposed and are in contact, they do not constitute a stable joint.

The intrusion of the menisci improves static stability but has no effect on the kinetic component, of which only the ligaments impart stability. (Cailliet 1991: 1.)

The patella, a sesamoid bone contained "within" the quadriceps tendon, has assymetrical facets on its inferior surface that are separated by a central incongruous manner with the femoral condyles, which are coated with hyaline cartilage (Cailliet 1991: 144).

Knee ligaments: Internal to the joint are the cruciate ligaments, arranged in opposing directions, providing anterior to posterior as well as medial to lateral stability to the knee. They also prevent excessive medial rotation of the tibia and help to maintain contact between the articular surfaces of the tibia and femur. The anterior cruciate ligament resists anterior displacement of the tibia and checks extension movements. In contrast the posterior cruciate ligament checks posterior displacement of the tibia and resists internal rotation of the tibia. The collateral ligaments provide medial and lateral stability and support for the knee while also preventing excessive external rotation of the tibia. (Bergmann et al. 1993: 659.)

Articular cartilage: Hyaline articular cartilage covering the subchondral bone plate functions to distribute and transmit loads and shear forces to the underlying bone, protecting the underlying bone, and permiting synovial joints to have a wide range of almost frictional movement. It is aneural, largely avascular, and only sparsely cellular: it is up to 80% water. Cells called chondrocytes are responsible for the synthesis of the proteoglycans and collagen fibres that comprise the cartilage matrix. Proteoglycans and

glycosaminoglycans are hydrophyllic (water-loving) and play an important role in regulating the movement of water within the matrix, thereby influencing the mechanical and lubricant properties of cartilage. Articualr cartilage, bone, fibrous capsule, tendons and ligaments are all comprised of a high proportion of collagen constituting the extracellular matrix of these tissues. Articular cartilage differs from bone, capsule, tendon and ligament in that it is chiefly comprised of type II collagen as opposed to type I in the other tissues. (Walker & Helewa 1996: 21.)

Joint capsule: Surrounding the external aspect of the joint is the fibrous joint capsule attaching at the margins of the articular cartilage (Bergman 1993: 663). The capsule is a type of regular white connective tissue similar to that of tendons and ligaments (Walker & Helewa 1996: 25). The capsule is redundant and essentially acts to contain the nutrient synovial fluid, but the capsule adds little support to the joints stability (Cailliet 1991: 13). The extent of redundancy in the fibrous capsule and its associate synovial tissue, or lack thereof, has important consequences to the mobility of the joint, especially when involved in an inflammatory process (Walker & Helewa 1996: 25).

Synovial membrane: The synovial membrane borders the joint cavity and covers all intra-articular structures except for the load-bearing surfaces of the joint. It consists of vascular fibrous tissue and superficial branching synovial cells. Synovial fluid nourishes articular structures and provides joint lubrication. It has a very low coefficient of friction, as it is non-Newtonian, i.e. the faster the joint moves the less viscous the fluid becomes.

Fluid becomes Newtonian (like water) when less viscous, in inflammatory conditions. (Golding 1989: 3.) The author continues that fluid film lubrication may be:

a) Hydrodynamic: a thick synovial film separates articular cartilage; the surfaces are at an angle to each other, a gap is produced and fluid drawn into the gap produces a pressure which separates the surfaces.

b) Fluid film lubrication: the cartilage is separated by a fluid film.

c) Hydrostatic lubrication: pressure on cartilage causes interstitial fluid to weep-out, to be re-imbibed when pressure becomes normal.

d) Boosted lubrication: under loads, the plasma dialysate portion of synovial fluid is squeezed out to form trapped pools in undulations which act as reservoirs and hyaluronic-acid-protein complexes form a 'sticky' skin over rough areas.

Bursae: Because the knee is exposed to a variety of demands in human locomotion, numerous bursas are located in relationship to the knee joint and to the synovial cavity (Bergmann et al. 1993: 665). Bursae facilitate gliding and provide a low-friction movement of one tissue over another (Walker & Helewa 1996: 26).

Menisci: Lying between the femur and the tibia are two semilunar cartilages called menisci. The menisci are shaped such that the more peripheral portions are thicker than

the central part. This serves to deepen the articular surface on the tibial plateau, which provides additional stability to the joint. The periphery of each meniscus attaches to the joint capsule, while the inner edge remains free. The medial meniscus is C-shaped, with a posterior portion being larger than the anterior. The anterior horn inserts on the intercondylar area of the tibia, while the posterior horn inserts just anterior to the attachment of the posterior cruciate ligament. The lateral meniscus is almost a complete circle, with the tips of each horn quite close to one another. The lateral meniscus is more mobile than the medial meniscus. (Bergmann et al. 1993: 664.)

Vascular supply: There are five branches of the popliteal artery that supply vasculature to the knee joint. The femoral artery originates from the iliac artery in the femoral triangle of the groin and descends anteriorly into the profundus femoral artery, which branches further into four perforating arteries of which the popliteal artery is one. The popliteal artery has five branches in the area of the knee joint: the middle and inferior genicular branches supply the menisci, which are mostly avascular. Only the outer one third of the menisci has any significant blood supply and its this vascularity that plays a major part in the recovery from any injury that may be sustained by the meniscus. (Cailliet 1991: 11.)

2.4.3 Biomechanics of the knee

The knee joint must provide a broad range of motion while maintaining its stability. The knee must react to rotational forces as well as absorb shock and then immediately prepare for propulsion. The knee functions as a modified hinge joint, with knee flexion and

extension being its primary motions. Because the opposing articulating surfaces of the femoral condyles and the tibial plateau are incongruent or asymmetrical (Cailliet 1991: 6), these movements are a combination of roll, slide and spin movements (Bergmann et al. 1991: 666). This spin of the articulating joint surfaces combined with rotation, results in an arc-slide movement as the knee moves from extension to flexion (Cailliet 1991: 6).

The total range of knee flexion-extension in the healthy knee is from about 5-10 degrees of hyperextension to about 140-150 degrees of flexion. Extension is terminated by locking of the joint in its close-packed position, as the capsule and ligaments draw tight and become twisted. (Hertling & Kessler 1996: 320.)

Hertling & Kessler (1996: 320) stated that the femorotibial joint is markedly incongruent in positions of flexion, but becomes progressively more congruent as the knee extends. They continued that the fibrocartilaginous menisci reduce joint surface incongruency. The anterior segments of the menisci are somewhat mobile, whereas the posterior horns are comparatively fixed, thus as the knee extends and the contacting surface of the femoral condyle increases, the anterior aspects of the menisci glide forward. Conversely, as the knee flexes, the anterior segments of the menisci recede to conform to the smaller surface area of the contacting femoral condyles. By reducing joint surface incongruency, the menisci help distribute the compressive loading over a greater area, thus reducing compressive stresses to the joint surfaces of the knee. (Hertling & Kessler 1996: 320.)

Menisci also aid in the lubrication and nutrition of the joint and, coupled with their shock-absorbing capabilities, help to decrease cartilage wear (Bergmann et al. 1991: 664).

The patellofemoral joint plays an active role in flexion and extension of the knee joint; it has a gliding motion, moving caudally approximately 7 cm when going from full flexion to full extension. The articular surface of the patella never makes complete contact with the femoral condyles. (Bergmann et al. 1991: 667.)

Joint play is an accessory motion necessary for normal active and passive range of motion, and represents the amount of capsular laxity within a joint. When assessing joint play, the following accessory motions are checked: long axis distraction, translatory glide and axial spin. Joint play should not be confused with end feel (end play), which is the assessment of the resistance supplied at the end of passive range of motion and tests the integrity of the capsular and ligamentous fibers. (Gatterman 1990: 98.)

2.4.4 Risk factors, mechanisms and pathophysiology

O.A. has been essentially classified as primary (idiopathic) or secondary, that is, a process related to infection, trauma, inflammation, metabolism or aging (Cailliet 1991: 191). Primary O.A. is termed when there is no known causative factor (Hertling & Kessler 1996: 363), although it is often hereditary (Golding 1989). Genetic studies have

suggested that genetic factors may account for 40-60% of the disease (Hart et al. 1999: 17).

Golding (1989: 144) described that both sexes are affected, but primary degenerative arthritis is more common in women, especially after menopause. He continued that previous fracture or dislocation as well as accumulated microtrauma (occupational O.A., obesity and occupational trauma) can also predispose joints. Secondary O.A. may follow previous joint disease such as inflammatory joint disease (rheumatoid arthritis, gout), endocrine disorders (acromegaly, diabetic neuropathy, hypothyroidism), metabolic disorders (haemochromatosis, ochronosis, chondrocalcinosis, gout, Wilsons disease), Pagets disease of bone, developmental disorders (Perth's disease of the hip, slipped femoral epithesis), neuropathic joints, avascular necrosis and haemophylic arthritis. Climatic factors play a role as more frequent symptoms are seen in populations exposed to cold air and damp weather. (Golding 1989: 144.)

2.4.4.1 Risk factors

Ageing and sex predisposition: Knee O.A prevalence increases with age and is more common in women than in men, especially after the age of 50 (Felson & Radin 1994: 181). Hart et al. (1999: 21) found that 3% of middle-aged women will develop new knee osteophytes and joint space narrowing each year, and a 2-fold increase in risk is seen in older women compared with women 20 years younger. They concluded that 3% of middle-aged women will develop radiographic knee O.A. every year. Clinical studies

have described a "menopausal arthritis" and observations suggest that estrogen deficiency may play a role in the development of O.A. in women (Zhang et al. 1998: 1867). Hart et al. (1999: 23) provided evidence to support the notion of a protective effect of estrogen replacement therapy.

Obesity: Obesity is a risk factor for both the development and progression, of knee O.A. (Sharma et al. 2000: 568). In a study performed by Spector et al. (1994: 565), obesity was the most important factor related to incident disease, with 47% of women in the top body mass index (B.M.I.) tertile developing knee O.A., compared with 10% in the lowest tertile. Greater body mass index in young men aged 20-29 years is associated with an increased risk of subsequent knee O.A. (Gelber et al. 1999: 542). In addition, obesity may increase the risk of O.A. because adiposity is associated with abnormal levels of hormones and growth factors, greater bone mineral density, and other metabolic intermediaries (Nevitt & Lane 1999: 632).

Structural malalignment: Sharma et al. (2000: 568) stated that varus malalignment increases medial tibiofemoral compartment load; valgus malalignment increases lateral compartment load. They performed a study, which showed that B.M.I. was related to O.A. severity in those with varus knees, but not those with valgus knees. Eckhoff et al. (1994: 608) showed that O.A. of the knee correlates with decreased tibial torsion as well as femoral anteversion.

Level of activity: Heavy physical activity is an important risk factor for the development of knee O.A. in the elderly, especially among obese individuals (McAlindon et al. 1999: 151). However, Hannan et al. (1993: 704) found that habitual physical activity does not increase the risk. Cooper et al. (1994: 90) performed a study to determine the risk factors of occupational physical activities and found the risk for knee O.A. increased in jobs that entailed prolonged or repeated knee bending, kneeling or combined knee bending with mechanical loading. The highest incidence of knee O.A. in sporting activities was found to be in soccer players and weight lifters (Kujala et al. 1995: 539).

Metabolic factors: Hart et al. (1995: 1118) studied the association between metabolic risk factors and knee O.A.in women in the general population. They found the data suggesting that hypertension, hypercholesterolemia and high blood glucose levels are associated with both unilateral and bilateral knee O.A., independent of obesity, and supports the concept that O.A. has an important systemic and metabolic component in its aetiology.

Mechanical derangement: Cooper et al. (1994: 307) confirmed the importance of significant knee injury as a risk factor for the development of medial tibiofemoral joint (T.F.J.) O.A. Surgical removal of a meniscus following knee injury also represents a significant risk factor for radiographic T.F.J. O.A. (Roos et al. 1998: 687). Varus-valgus laxity may increase the risk of knee O.A. and cyclically contribute to progression (Sharma et al. 1999: 861).

Knee O.A. studies have focussed on the T.F.J compartment only. However, according to

autopsy studies and recent epidemiological investigations, patellofemoral joint (P.F.J.) O.A. may be as common as T.F.J. O.A. (Felson & Radin 1994: 181.) Cooper et al. (1994: 307) found that mechanical and constitutional factors differ in between tibiofemoral (T.F.) and patellofemoral (P.F.) compartments. Felson & Radin (1994: 182) agree that these risk factors differ because, from a biomechanical point of view, the P.F. and T.F. joints are different. They continue that the clinical and epidemiological splitters and those who would define O.A. as primarily a mechanically caused joint failure seem the victors in the continuing etiological debate.

2.4.4.2 Mechanisms

Manek & Lane (2000: 1795) wrote that biomechanical and biochemical forces are involved in cartilage destruction, which is at the core of osteoarthritis. Cytokines and growth factors are thought to play a role in the pathophysiology of the disorder. Interleukin-1 and tumour necrosis factor-B may function to activate enzymes involved in proteolytic digestion of cartilage. Growth factors such as tissue growth factor-B and insulin growth factor-1 may play a role in the body's attempts to repair cartilage through cartilage synthesis. When catabolism exceeds cartilage synthesis, O.A. develops. Collagenolytic enzymes are thought to contribute to the breakdown of cartilage. (Manek & Lane 2000: 1795.)

Hertling & Kessler (1996: 44) stated that it is generally accepted that changes in the articular cartilage trigger a cycle leading to the progression of degenerative joint disease.

Cartilage damage may occur after a single traumatic incident, causing a tension or compression strain sufficient to interfere with the structural integrity of the cartilage. More common is cartilage wearing from fatigue, or the cumulative effects of abnormal stresses, neither of which is sufficient in itself to cause structural damage. Cartilage may be susceptible to fatigue in part because it is aneural; any other musculoskeletal tissue is relatively immune to fatigue because protective reflex inhibition occurs with abnormal stress. This inhibitory response requires intact innervation. Cartilage is also susceptible to damage because it is avascular. It lacks the normal inflammation and repair response that would replace damaged parts of the tissue. If a lesion is sufficient to penetrate the subchondral bone, it immediately fills with blood and a clot is formed. This clot is invaded with new blood vessels that apparently bring in undifferentiated mesenchymal cells, which proceed to fill the defect with fibrocartilage, not hyaline cartilage. Hyaline articular cartilage partly makes up for the fact that it is aneural and avascular by its considerable ability to deform when loaded in compression. (Hertling & Kessler 1996: 44.)

Mechanisms of hyaline articular cartilage breakdown involve multiple factors and imbalance between extracellular matrix degradation and synthesis. Repetitive impulse loading (R.I.L.) is considered to be a major factor. Other factors are stress deprivation (immobilisation, bed rest, weightlessness), excessive loading (body weight, obesity), developmental etiologies (hip dysplasia, Perthes disease, coxa valga), joint surface incongruity, and joint instability (cruciate ligament trauma, generalised ligamentous laxity). The type of load and manner of loading is more important than the actual load on

joint surfaces. The more rapid the loading, the higher the tensile and shear rates and the greater the potential for damage. (Walker & Helewa 1996: 32.)

Articular cartilage tends to deform, causing resultant tension at its periphery. A constant clinical finding is the presence of cartilage degeneration in the load-bearing areas, implying that compression and shear play a vital role in degeneration. Cartilage, albeit resilient because of its viscoelastic properties, is too thin to be an effective shock absorber. Cartilage absorbs most of its shock at its bony union, which deforms on compression, and through the muscular ligamentous reaction to its external stresses. Although loads borne by the joint come from weight bearing, most of the force on joints results from muscular contraction about the joint. The muscles acting across the knee joint are alternatively used for acceleration and deceleration, which places compressive stress and impact on the knee. The cartilage absorbs some portion of these forces, but the subchondral bone probably absorbs most of it. (Cailliet 1991: 194.)

2.4.4.3 Pathophysiology

Articular cartilage: The essence of O.A. is a noninflammatory degeneration of articular cartilage. Initial changes are in the cartilage, which becomes soft and less resilient due to a loss of proteoglycans in the ground substance (Golding 1989: 145). There is an increased water content and increased turnover of the chondroid matrix (Walker & Helewa 1996: 66). The collagen meshwork breaks up at the surface and the cartilage loses its glistening appearance and becomes roughened (Golding 1989: 145).

Fracturing of these fibres causes a "softening" of the surface layers of the cartulage; the cartilage becomes less able to withstand stresses in this region, with resultant death of local chondrocytes. The death of chondrocytes is believed to allow the release of proteolytic enzymes that have a further degradative effect on chondroitin sulphate. The adjacent areas of cartilage, peripheral and deep to this damaged area, must now absorb stresses, so the process tends to spread. Added to this mechanical factor in spreading is the chemical factor due to destructive enzyme release. (Hertling & Kessler 1996: 45.)

Perpendicularly orientated fissures appear in the superficial zone of the cartilage and gradually extend deeper. These fissures promote detachment of small articular cartilage fragments into the joint space, where they are eventually degraded. Progressive thinning of the cartilage occurs and the end stage is full-thickness loss of articular cartilage. (Walker & Helewa 1996: 67.)

Bone: Concurrent with the loss of articular cartilage is a profound remodeling of the juxta-articular bone, which gradually leads to thickened (sclerotic) bone. A characteristic of this remodeling is the formation of new bone at the joint margin (osteophyte or a bony spur). (Walker & Helewa 1996: 67.) Exposed bone undergoes pressure necrosis and microfractures occur (Golding 1989: 145).

Synovial membrane: In the acute stages, the synovial membrane may undergo villous hypertrophy and synovial effusion (Golding 1989: 146). The effusion is the result of synovial irritation caused by the release of proteolytic enzymes and other cartilagenous

debris, and further irritation may result from altered joint mechanics (Hertling & Kessler 1996: 45).

Capsule: Low-grade inflammation, if chronic, will result in capsular fibrosis, or thickening. The result is that which occurs with any scarring process: reduced extensibility from loss of elasticity, gradual contracture, and adherence to adjacent tissues. Such a lack of mobility of the joint capsule will contribute significantly to the cycle of degeneration because of the resultant alteration of normal joint mechanics. (Hertling & Kessler 1996: 45.)

Loose bodies: Microfractures also result in bone debris being dislodged into the joint space (Walker & Helewa 1996: 67), as well as calcified cartilage (Golding 1996: 146). Such debris can induce a secondary synovitis that is usually mild, and this secondary synovial response is often referred to as a "detritus synovitis" (Walker & Helewa 1996:67).

2.4.5 Knee osteoarthritis and inflammation

Osteoarthritis literally means inflammation of a bony joint; the term is usually applied to the process involved in degenerative joint disease, understood as a noninflammatory process that primarily involves breakdown of cartilage (Gottlieb 1997: 401). Radin (1986: 60) wrote that arthrosis (joint deterioration from mechanical causes) must be separated from arthritis (joint deterioration from inflammatory causes). He continued that

the difficulty in distinguishing between the two types of conditions rests primarily on the fact that the debris from mechanical wear, particularly from articular cartilage, provokes a significant inflammatory response within the synovium. Thus all arthroses provoke a secondary arthritis in the same joint. The opposite is true for arthritis because the inflammatory degradation of the tissues causes a disruption of even stress distribution, provoking secondary mechanical deterioration. (Radin 1986: 60.)

British writers prefer the term osteoarthrosis in recognition that O.A. is essentially noninflammatory (Walker & Helewa 1996: 66). For convenience, the term osteoarthritis will be used in this study.

Walker & Helewa (1996: 30) stated that the typical protective reaction of the body tissues to injury, pathologic insult and microbes is one of inflammation. The classic inflammatory process, as seen in wound repair, is characterized by redness, swelling, heat and pain. The process involves increased vascular permeability, vasodilation, cell proliferation, neovascularization and fibroplasia. The ability of a tissue to exhibit the classic inflammatory response is strongly related to its vascularity. Hence in arthritis, synovial lining tissues invariably demonstrate a degree of inflammation, while hyaline articular cartilage, being avascular, does not. Similarly, strong fibrous, less vascular structures such as tendons and ligaments demonstrate a poor inflammatory response. Healing and restoration of the original tissue is dependant on the intrinsic ability of the tissue to regenerate and the complexity of the tissue. When regeneration does not occur, there is replacement by fibrous tissue, which organizes into a firm scar. In ligaments and

tendons, which are poorly vascularized, healing times are long. An inflammatory process involving these structures results in extensive fibrosis. Extensibility, tensile strength and loading characteristics are compromised. (Walker & Helewa 1996: 30.)

An acute inflammatory response consists of:

1) Vascular dilatation, increased permeability, endothelial stickiness causing cell adhesion.
2) Fluid exudation of protein rich fluids into tissues
3) Cellular exudation, dominated by polymorphs
4) Results: thrombosis, microhaemorrhages and tissue destruction. (Golding 1989: 12)

Cell membrane phospholipids of injured cells and inflammatory cells may release arachidonic acid. Two enzyme pathways (lipoxygenase and cyclooxygenase) are critical in the conversion (oxygenation and hydrolysis) of arachidonic acid into other acids and metabolites (eg. prostaglandins, thromboxane). Varieties of prostaglandins enhance vascular permeability as they produce vasodilatation; effusion is increased. (Walker & Helewa 1996: 31.)

2.4.6 Clinical features and diagnostic criteria

Pain: This the major complaint (Hertling & Kessler 1996: 364), which varies from mild to severe and can be due to many causes such as:

Patellofemoral arthritis, tense popliteal cysts, medial ligament strain, worn internal structures, painful bone cysts, trabecular fractures, tender fat pads, synovitis, capsular contraction, loose bodies and super-added crystal deposition (Golding 1989: 148). Pain may also be mediated through the activation of pain receptors by hystamine and bradykinin, products of the arachidonic acid pathway in the inflammatory cascade (Golding 1989: 12).

Hertling & Kessler (1996: 364) wrote that pain could have muscular, capsular or perhaps venous origins.

Pain is aggravated by activity or weight bearing, but may also be aggravated by rest, particularly if the knee is held in one position for a prolonged time (Hertling & Kessler 1996: 364). Pain associated with O.A. of the knee will often be worse on activities involving climbing or prolonged standing. This is especially so if the patellofemoral compartment is involved, as it undergoes a major compressive force when the body is raised from a kneeling or squatting position and on climbing stairs and hills. Parellofemoral O.A. may precede other manifestations in the knee joint. (Walker & Helena 1996: 69.) The patellofemoral joint reaction (P.F.J.R.) force during walking is 0.5 times body weight (B.W.), but during deep knee bends (squatting) it rises to 7.6 times B.W., and during stair climbing or descending can reach a level of 3.3 times B.W. (7 times greater than when walking) (Scuderi 1995: 30). Abnormal anatomic and biomechanical relationships between the patella and the femoral condyles can predispose the knee to chondromalacia and ultimately osteoarthritic changes (Cailliet 1991: 149).

Stiffness: Morning stiffness is a common complaint, which is relieved after motion, but the knee becomes painful again once the weight-bearing tolerance of the joint is exceeded by prolonged standing or walking (Hertling & Kessler 1996: 364). Moderate stiffness can be aggravated by rest, which is a form of elastic (as opposed to frictional or viscous) stiffness in which the patient complains of difficulty in getting going after sitting for a while (Golding 1989: 148).

Swelling: Synovial swelling or effusions occur in episodes of acute O.A. (Golding 1989: 148).

Limitation of movement: Range of movement may be decreased by capsular fibrosis, osteophytes, irregularity of articular surfaces or impaction of loose bodies. Fine or coarse crepitus may occur on motion. (Golding 1989: 148.)

Muscle wasting: Weakness of the quadriceps muscle is common and it is generally believed to be the result of disuse atrophy, due to a decrease in loading of the limb because of pain (Brandt et al. 1999: 2431).

Deformity: Malalignment may result from irregularities of articular surfaces (Goulding 1989: 149). Degenerative changes in the medial compartment are associated with a varus deformity, and those in the lateral compartment are associated with valgus deformities (Hertling & Kessler 1996: 363).

Instability: Episodes of giving way occur secondarily to muscle fatigue, transient severe pain or secondarily to minor trauma which may be the result of impingement of degenerated menisci, the presence of loose bodies, or a misstep (Hertling & Kessler 1996: 36).

2.4.7 Radiographic evidence

There are eight essential roentgen signs of degenerative joint disease: asymmetric distribution, nonuniform loss of joint space, osteophytes, subchondral sclerosis, subchondral cysts, intraarticular loose bodies, intraarticular deformity, and joint subluxation. These roentgen signs closely parallel the underlying pathogenetic sequence involving the joint components. All signs will not necesssarily be present in every case of degenerative joint disease. (Yochum & Rowe 1996: 804.)

Most people over the age of 65 have some radiographic evidence of O.A., although many do not have symptoms (Oliveria et al. 1995: 1134). Data from the Framingham cohort indicate that only 40% of persons with radiographic evidence of O.A. are symptomatic, and those with radiographic disease who are asymptomatic report less disability than those who are symptomatic (Rejeski et al. 1995: 1124). McAlindon et al. (1993: 258) elaborates that by the age of 65 years, 30% of men and 40% of women have radiographic changes of knee O.A. They continued that traditionally the severity of O.A. has been assessed using a system which scores radiographic features believed to be characteristic of the disorder.

Concordance of radiographic O.A. with pain and clinical signs is poor, particularly in the knee. Discordance between symptoms and radiographic appearances suggests that there may be determinants of functional impairment in this disorder other than radiographic evidence. They proposed an alternative hypothesis that radiographic features reflect outcome and tell us little about the disease process, or more provocatively, that the radiopathological changes believed to constitute O.A. do not represent a disease entity and are not a cause of disability. (McAlindon et al. 1993: 258.)

Hannan et al. (1993: 707) similarly stated that increased rates of asymptomatic osteophytosis in men suggest that habitual physical activity may predispose men to the development of osteophytes but not more advanced structural or symptomatic disease. Other studies have noted that osteophytes may be a function of aging and not related to the pathology of knee O.A. (Hannan et al. 1993: 707.)

In a more recent study performed by Lanyon et al. (1998: 595), they evaluated radiographic features of O.A. to determine which is more closely associated with knee pain and hence might be used as a radiographic definition of O.A. in the community. They concluded that among men and women, osteophytes are the radiographic feature that associates best with knee pain. Radiographic assessment of both T.F. and P.F.J.'s should be included in all community studies. Their results showed that joint space loss is not a feature of asymptomatic aging. This finding that joint space does not necessarily decrease with age among asymptomatic subjects is in keeping with the concept that O.A. is a specific process and not an inevitable part of aging or "wear and tear". There is not a

biological cut off for joint space width below which the likelihood of knee pain markedly increases. (Lanyon et al. 1998: 595.)

2.5 Manual therapy

2.5.1 Introduction

Gatterman (1990: 410) defines manual therapy as a therapeutic application of manual force. Spinal manual therapy broadly includes all procedures in which the hands are used to mobilize, adjust, manipulate, apply traction, massage stimulate, or otherwise influence the spine and paraspinal tissues with the aim of influencing the patients health (Gatterman 1990: 410).

Gatterman (1990: 106) wrote that the goals of manual therapy are as follows:

Mechanical effects: manual therapy is thought to produce changes in:

- Joint alignment
- Dysfunction of motion
- Spinal curvature dynamics
- Entrapment or extrapment of a synovial fold

Soft tissue effects:

- Changes in the tone and strength of supporting musculature

- Influencing the dynamics of supportive capsuloligamentous connective tissue (viscoelastic properties of collagen)

Neurological effects:

- Reduction in pain
- Altering motor and sensory function
- Influencing autonomic nervous system regulation

Psychological effects:

- Laying on of hands
- Placebo factor
- Patient satisfaction

Bergmann et al. (1993: 124) classify manual therapies into two classes:

1. Joint manipulation procedures: mobilizations, adjustments, manual traction/ distraction
2. Soft tissue manipulation procedures: point pressure techniques, massage, therapeutic muscle stretching, visceral manipulation

2.5.2 Mobilization

Mobilization is the process of making a fixed part movable. It is a form of manual therapy applied within the physiological passive range of motion, characterized by non-thrust increase in passive joint play. (Gatterman 1990: 411.)

2.5.3 Manipulation

Manipulation is defined as a passive maneuver in which specifically directed manual forces are applied to vertebral and extravertebral articulations of the body, with the object of restoring mobility to restricted areas (Gatterman 1990: 410).

The terms' manipulation and adjustment have created much friction among chiropractors. Some practitioners believed that adjustments are a more skilled form of osseous manual thrust techniques, whereas others believed that manipulations are a more accomplished form of treatment. Most of these practitioners basically perform similar types of osseous manual thrust procedures, but call them by different names. (Gatterman 1990: 91.) In this study, the term manipulation will be used.

Bergmann et al. (1991: 124) defines the chiropractic adjustment as a specific form of articular manipulation using either long- or short-leverage techniques with specific contacts. It is characterized by a dynamic thrust of controlled velocity, amplitude, and direction.

1. Direct (short lever): specific joint contact, high velocity, low amplitude thrust
2. Semidirect: combination of a specific joint contact with a long-lever contact: high-velocity low-amplitude thrust
3. Indirect (long lever): Nonspecific contact at points of leverage: high-velocity, low-amplitude thrust
4. Characteristics of an adjustment:

a. Specific contact (exception, indirect method)
b. Dynamic thrust of controlled depth and speed
c. The thrust is delivered within the boundaries of the joints anatomic integrity
d. Usually associated with an audible articular click and subsequent improved joint mobility. (Bergmann et al. 1991: 124.)

2.5.4 Subluxation : the articular lesion

A subluxation occurs in a motion segment in which alignment, movement integrity, and/or physiologic function are altered although contact between the joint surfaces remains intact. A manipulable subluxation is a subluxation in which altered alignment, movement, or function can be improved by manual thrust procedures. (Gatterman 1990: 11.)

2.5.5 Indications for manipulation

If osteoarthritis may be caused by loss of normal joint mechanics, then primary treatments should be aimed at restoration of normal mechanics. Currently, treatment tends to be directed at physiologic changes, including various modalities for pain relief and pharmaceutical agents for controlling inflammation. Efforts to restore joint mechanics too often consist only of range-of-motion exercises and muscle strengthening, carried out without regard for the possible deleterious effects to the joint and without regard for abnormal reflex activity accompanying joint movement in the absence of normal arthrokinematics. (Hertling & Kessler 1996: 48.)

Bergmann et al. (1993: 139) stated that in the mechanical arena, manipulation is directed toward reversing or mitigating the soft tissue pathology and mechanical dysfunction associated with disorders or injuries of the neuromusculoskeletal system. Disorders or injuries often result in soft tissue fibrosis, adaptational shortening, loss of flexibility, and altered joint mechanics. If tissue damage is marked, the issuing fibrous repair may result in a scar, which has matured to fill the injured area, but lacks the resilience, strength, and durability of the original tissue. Such an asymmetric scar, produced either by injury, degenerative disease or surgical trauma, may produce severe disturbances of biomechanical performance. Therefore, when injury or degenerative disease results in contracture, stiffness, joint hypomobility, and chronic pain or impairment, therapies shift toward a more vigorous approach and are directed toward the restoration of mobility and function. (Bergmann et al. 1993: 139.)

Joints undergo arthrokinematic movement, which is motion between two articulating surfaces without reference to the forces being applied to that joint. Arthrokinematic motion in each joint also is characterized by a specific number of degrees of freedom. This is determined by the amount of accessory motion present in a particular articulation. Accessory motion, or joint play, is joint motion that is not under voluntary control, yet is necessary for pain-free, unrestricted voluntary movement to occur. (Edmond 1993: 2.)

Joint play is an accessory motion necessary for normal active and passive range of motion. Joint play represents the amount of capsular laxity within a joint, and if reduced, active motion will be decreased, restricted, or abnormal, and may be painful. The muscles that move a joint do not function efficiently with decreased joint play and become hypertonic, resulting in muscle spasm, trigger points, myotogenous pain, articular pain, or decreased or abnormal active range of motion. Voluntary motion or exercise cannot restore joint play. Joint play can be restored only through manipulations or adjustments. (Gatterman 1990: 98.)

Determining whether accessory motion is available involves placing the joint in a specific position and attempting passively to move one bone on another. If end feel is springy, then the joint play is available. If there is a perceived restriction, however, movement at the joint may be restricted. (Souza 1997: 13.)

The goal of manipulation is to restore maximal, pain-free movement to a musculoskeletal system (Edmond 1993: 2). Joint manipulation accomplishes this goal in the following ways:

1. Increasing joint extensibility: Joint manipulation promotes optimal, pain-free movement by maintaining extensibility of joint and other periarticular structures or by increasing extensibility in the presence of periarticular restrictions. Restrictions in the joint capsule usually are accompanied by a corresponding limitation in joint range of motion. Restrictions are usually the result of either immobilization or inflammation of articular and surrounding structures. Immobilization results in an increase in fiber cross-link formation, which produces adhesions in the joint capsule, as well as between synovial folds. Joint manipulation is thought to reverse these changes by promoting movement between capsular fibers. More aggressive manipulation techniques are thought to break adhesions in the joint capsule and synovial folds. It also increases the length of capsular fibers and breaks fibrofatty adhesions. Although the one structure affected is the joint capsule, all periarticular tissue, including muscles, tendons, and fascia, are affected by joint manipulation techniques.

2. Correcting positional faults: Joint surfaces can alter their position in relation to one another. Even minimal displacement can place abnormal stress on periarticular structures and thus can be a source of pain. Manipulation of one of the directions consistent with realigning it into the proper position is thought to normalize the static positioning of one joint surface in relation to the other, thus reducing pain.

3. Nutrition: Because articular surfaces are avascular and receive their nutrition from the synovial fluid, the synovial fluid must circulate within the capsule to allow nutrients to be in contact with the articular surface. Joint manipulation techniques are thought to produce movement of fluid within the synovium. If functional mobility is also a goal of the manipulation technique being performed, the restoration of functional range of motion will aid in delivering nutrients to intracapsular tissue on a more permanent basis through active movement.

4. Pain control/ Muscle relaxation: Manipulation decreases pain in joint and periarticular structures by stimulating joint receptors. This reduces pain perception by blockage of pain impulses through the gate control mechanism and by producing reflexive muscle relaxation.

5. Meniscoid impingement: (only applicable to vertebrae)

6. Reduction of disc herniation: (only applicable to vertebrae)

7. Psychological benefits: In a medical system in which few practitioners remain who heal by touch, one must not discount the psychological benefit to a patient of a treatment composed of techniques requiring touch. (Edmond 1993: 2.)

2.5.6 Chiropractic and Osteoarthritis

The progression of degenerative changes is discussed within a three-part model based on the three phase degenerative theory proposed by J.H. Wedge and Kirkaldy-Willis (Berkson 1991: 356). Berkson continued that this three-phase model is superimposed upon a newly proposed three-part subluxation model for the science of chiropractic. Spinal and other joint subluxations have pathological and histological correlates that overlap with the cascading events of O.A. Since research is proving that cartilage can heal and thus joints have the capacity to heal, this suggests that there may be measures to help reverse cartilage erosion and cause resorption of osteophytes. If the initial abnormal factors that lead to the cartilaginous defects could be improved, if joint motion dynamics and biochemistry could be moved toward normal once again, then arresting and reversing the osteoarthritic deterioration should be possible. (Berkson 1991: 356.)

Kirkaldy-Willis (1983: 75) divided the stages of spinal degeneration into three phases; Dysfunction, Unstable Phase and Stabilization. Dysfunction, the earliest stage: where minor dysfunctions begin to affect the joint and disc. This would be equivalent to the beginning erosion of the hyaline cartilage in the O.A. model. Phase 2 the Unstable phase, is intermediate: where progressive degeneration, ongoing trauma and stress produce weaker collagen or scar tissue and produces laxity of the posterior joint capsule and the annulus (of the spine). This is equal to synovial proliferation and active synovitis. Phase 3, Stabilization, is the final stage: where fibrosis of the posterior joints and capsule,

destruction of the articular cartilage, loss of disc material, and osteophyte formation create substantial fixation. (Berkson 1991: 359.)

Berkson (1991: 359) points out that all the tissues involved in O.A. are capable of repair. In fact, much data suggests that O.A. is the body's inept cellular and tissue response aimed at repair. If O.A. is the body's poor repair attempt, then methods that alter the original stresses may repair or halt degeneration. Improved joint play and circulation through manipulation should move the joint away from factors that may have initially contributed to hyaline surface erosion. Normal joint motion promotes proper joint environment, which should promote reparative histologic change and improved cartilage dynamics. (Berkson 1991: 359.)

Fritz et al. (1998: 1046) performed a study to examine whether there is evidence to support 2 elements of the passive-range-of-motion (P.R.O.M.) portion of Cyriax's selective tissue tension scheme for patients with knee dysfunction: a capsular pattern of motion restriction and the pain-resistance sequence. A capsular pattern of motion restriction is a proportional motion restriction unique to each joint that indicates irritation of the entire synovial membrane or joint capsule, as occurs with an active inflammatory process (arthritis) or degenerative joint changes (arthrosis). According to Cyriax, motion restrictions in proportions other than the capsular pattern are supposed to occur in lesions that are capable of restricting motion, but that are localized in such a way that the whole joint is not involved. Cyriax defined the capsular pattern of the knee as "great limitation of flexion and slight limitation of extension." (Fritz et al. 1998: 1046.)

Fritz et al. (1998: 1047) continued that in the assessment of passive range of motion (P.R.O.M.), Cyriax contended that the examiner should assess the available P.R.O.M., the nature of the end-feel for the motion, and the relationship of the onset of pain with the onset of resistance during P.R.O.M. (pain resistance sequence [P.R.S.]). The P.R.S. reflects the acuity of the inflammatory process. Cyriax contended that pain occurring prior to resistance to movement indicates an acutely inflamed joint, that pain that is synchronous with resistance indicates a less acutely inflamed joint, and that pain occurring after resistance indicates a non-inflamed joint. By evaluating the P.R.S., the clinician can judge the acuity of the patient's condition and can determine how aggressively to proceed with treatment.

The study performed by Fritz et al. (1998: 1046) provided evidence to support the concept of a capsular pattern of motion restriction in persons with inflamed knees or evidence of osteoarthrosis. According to Cyriax, joint mobilization would be indicated for the patient with a capsular pattern, with aggressiveness dictated by the acuity of the inflammatory status, as determined by the P.R.S. It would be reasonable to assume that manipulation, too, would be indicated. (Fritz et al. 1998: 1048.)

Sims (1999: 136) wrote a paper on the assessment and treatment of hip osteoarthritis. Because the hip is a synovial, diarthrodial joint, it is assumed that parallels with knee osteoarthritis can be drawn. In the early stages of degeneration, the accessory motions may help the clinician to identify the pattern of hip O.A. If the hip O.A. is relatively advanced or severe, then all accessory motions may be very limited. Local treatment

includes the restoration of normal joint glides, the stretching of capsular and muscular restrictions and the restoration of normal neuromuscular function. Manual therapy causes a physical loading and unloading of joint cartilage, which facilitates the flow of synovial fluid within the joint, ensuring adequate nutrition to the articular cartilage. In the early stages of O.A., simply improving cartilage nutrition may be a very important rationale behind the use of manual therapy techniques. (Sims 1999: 136.)

The author continues that manual therapy techniques should also facilitate improvements in joint range of motion, by restoring the normal accessory joint glides associated with movement. Capsular tightness is recognized as an important predisposing factor in hip O.A., and many clinicians believe that early stretching of a tight capsule may prevent joint damage or at least slow further progression. It is important to acknowledge that manual therapy procedures have wide-ranging effects that are not purely biomechanical. Gentler techniques may be very useful for pain modulation, or to facilitate lubrication within the joint, and may be equally effective as stronger belt or stretching techniques. (Sims 1999: 139.)

In an article by Wiles (1979: 93) on the management of O.A. of the knee, he performed a retrospective study of 25 cases of clinically diagnosed O.A. of the knee. He divided their complaints into three main groups: 1) pain; 2) stiffness and loss of mobility; 3) instability.

He continued that treatment should consist of consideration of these three main groups of presenting complaints:

1) Pain relief should comprise of avoidance of weight bearing during periods of acute discomfort; application of moist heat; intermittent, pulsed ultrasound; myofascial therapy and cryotherapy.

2) Stiffness and "tightness" can result from a loss of normal joint play and manipulation can be greatly beneficial in restoring this joint play and thereby relieving stiffness. Joint play movements should all be present and normal before exercise therapy is instituted. He includes lateral and medial, rotational and anterior-posterior joint play movements as well as patellar mobility assessment (in all four planes of movement). He added that the patello-femoral joint may be severely fixed and may require many manipulative treatments.

3) Instability should be treated with quadriceps isometric "setting" exercises initially as well as later active flexion-extension exercises.

Treatment of these patients in this retrospective study using the above mentioned stategy obtained excellent results in 60% of patients, moderate relief in 20% and minimal or no relief in the remaining 20%. Treatment duration was 5-6 weeks (7-8 treatments). (Wiles 1979: 96.)

2.5.7 Contraindications to manipulation:

The following contraindications are related to the knee. Any contraindications related to the spine have been omitted.

Edmond (1993: 8) lists the following conditions to which joint manipulation is contraindicated:

a) any undiagnosed lesion
b) joint ankylosis
c) joint hypermobility
d) any infection in the area
e) malignancy in the area
f) unhealed fracture in the area
g) inflammatory arthritis
h) metabolic bone disease
i) any debilitating disease that compromises the integrity of the periarticular tissues, such as diabetes
j) considerable joint effusion
k) considerable pain or joint irritability
l) protective muscle spasm

2.5.8 The effectiveness of manipulation:

Edmond (1993: 21) wrote that little research has been done on the efficacy of joint manipulation techniques. Much of the research that has been performed has been on spinal manipulation. Most of the studies that have been performed on extremity joints have centered on the efficacy of manipulation under anesthesia, and response to treatment

with manipulation was compared with the patient's status before manipulation. (Edmond 1993: 21.)

An internet search of Medline, Grateful Med, Pub Med and Mantis web sites revealed no articles of studies performed on chiropractic manipulation of osteoarthritic knees. Very few studies on manual therapies of osteoarthritic knees were found, and thus the author has drawn parallels with studies performed on other osteoarthritic joints.

Deyle et al. (2000: 173) performed a study to evaluate the effectiveness of manual physical therapy and exercise in O.A. of the knee. Eighty-three patients were randomly assigned into two groups; the treatment group received a combination of manual physical therapy and supervised exercise and the placebo group received ultrasound at sub-therapeutic levels. The manual physical therapy treatment techniques consisted of passive physiologic and accessory joint movements, muscle stretching, and soft-tissue mobilization to the knee. The same treatments were also administered to the lumbar spine, hip or ankle if these areas showed limitation in active or passive movement, were symptomatic or were contributing to overall lower limb dysfunction. The treatment group also performed a closely supervised standardized knee exercise program at each of the eight treatment sessions. (Deyle et al. 2000: 173.)

Patients who received the manual physical therapy and exercise experienced clinically and statistically significant improvements in self-perceptions of pain, stiffness, and functional ability and the distance walked in 6 minutes. The beneficial effects of

treatment persisted at 4 weeks and 1 year after the conclusion of the clinical treatment. (Deyle et al. 2000: 178.)

The effects of the manual therapy procedures cannot be separated from either the clinical or home exercise programs. However, a recent randomized clinical trial found that a combination of manual therapy and clinical exercise provided greater improvements in strength, pain, and function than did clinical exercise alone for impingement syndrome of the shoulder, another chronic inflammatory joint condition. (Deyle et al. 2000: 179.)

Patients frequently reported 20-40% relief of symptoms after only two to three clinical treatments of manual therapy and exercise. This rapid reduction of symptoms implies that the structures responsible for at least part of the pain are not the most fixed or unchangeable aspects of the pathology of O.A. Periarticular connective and muscular tissue could be implicated as symptom sources. Perhaps the repeated challenge to the end range movement, as occurs with closed-chain strengthening exercises, manually applied passive movement, and active range-of-movement exercises, provides a strong stimulus to connective tissue, resulting in pain relief. Of note, unweighting of the knee joint during walking has not been demonstrated to relieve pain in patients with O.A. of the knee. It seems logical that if articular surfaces or subchondral bone were the primary pain generators, walking under decreased loads would decrease pain. (Deyle et al. 2000: 179.)

Vaux (1998: 17) wrote a case report on chiropractic intervention of hip osteoarthritis. The paper presents two cases of hip O.A.: one in which the replacement surgery was not

currently indicated; the other, more severe case where the patient was awaiting surgery. Both patients were affected by severe pain, which caused a deleterious effect on their quality of life. Both patients were treated in a similar manner, using the gentlest active muscular relaxation technique (post-isometric relaxation, to stretch the hypertonic muscles, followed by mobilization of both hips with long axis distraction. In addition, the drop technique (a manipulative procedure) was applied to the right proximal femur in order to stretch the capsule around the hip in the first patient. Dysfunction of the sacroiliac joints was also addressed using prone blocking and drop technique. Both patients were given stretches and cryotherapy techniques. Both patients responded well to chiropractic care, demonstrating the potential for this approach to a wide spectrum of sufferers. (Vaux 1998: 17.)

2.6 Nonsteroidal Anti-inflammatory Drugs (N.S.A.I.D.'s)

2.6.1 Introduction

N.S.A.I.D.'s are the most common pharmacological treatment for rheumatic disease. A wide range of N.S.A.I.D.'s are available, however, clinical response and undesirable effects resulting from their use vary enormously between patients (Linden et al. 1996: 35). Over the past quarter century, many non-aspirin N.S.A.I.D.'s have come on the market, gradually replacing aspirin as the main treatment for many different aches and pains. This market now amounts to >$6 billion annually worldwide, with more than a third in the United States. (McCarthy 1999: 37s.)

N.S.A.I.D.'s were developed in response to the need for aspirin like drugs without the toxicity of aspirin (Walker & Helewa 1996:152). Most N.S.A.I.D.'s are also powerful analgesics and may effectively relieve the symptoms of O.A. without necessarily influencing its progression (Gottlieb 1997: 404). They do this by their inhibitory effect on the arachidonic acid cascade. For most of the N.S.A.I.D.'s, the dose required to reduce inflammation is double that needed for analgesia. (Walker & Helewa 1996: 156.)

N.S.A.I.D. use however, is limited by the associated high incidence of side-effects, particularly in the gastrointestinal tract. Although serious events such as perforation, ulceration and bleeding are associated with N.S.A.I.D. use, the most common side-effects are less serious, with symptoms being described as dyspeptic in about half of affected patients. (Distel et al. 1996: 68.)

The N.S.A.I.D. used in this study was Meloxicam under the trade name Mobic®.

2.6.2 Meloxicam

Meloxicam [4-hydroxy-2-methyl-*N*-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide; U.H.A.C. 62 XX, Boeringer Ingelheim], is a new enolic acid class N.S.A.I.D. (Turck et al. 1996: 13).

2.6.2.1 Pharmacological properties

Although the efficacy of the N.S.A.I.D.'s in the treatment of O.A. is well established, their main limitation is the relatively high incidence of gastrointestinal (G.I.) adverse events associated with their use, due to inhibition of the cyclooxygenase (C.O.X.) enzyme involved in prostaglandin biosynthesis (Hosie et al. 1996: 39).

It has not been clear why there are differences between agents in terms of their potential to cause gastrointestinal side effects, while displaying similar anti-inflammatory potency. The discovery of two isoforms of the C.O.X. enzyme, C.O.X.-1 and C.O.X.-2, has gone some way to explaining this. Recent findings have suggested that the anti-inflammatory actions of N.S.A.I.D.'s are primarily mediated through the inhibition of the inducible enzyme C.O.X.-2, whereas unwanted adverse effects, such as gastric and renal toxicity, are due to inhibition of C.O.X.-1. C.O.X.-1 activity is thought to be necessary to protect the stomach, kidney and possibly other organs against damage. (Distel et al. 1996: 68.) Meloxicam's good tolerability, particulary in the G.I. tract, is believed to be due to its preferential inhibition of C.O.X.-2 over C.O.X.-1 (Turck et al. 1996: 13).

Most N.S.A.I.D.'s are highly protein bound to albumin; meloxicam is no exception, being 99% bound. Meloxicam is almost exclusively eliminated by metabolic degradation. The drug undergoes more or less equal renal and fecal elimination, with roughly <0,25% excreted unchanged in urine and 1,6% of the parent compound present in the feces. Oral meloxicam has a total clearance of 0.42-0.48 l/h. In comparison with other N.S.A.I.D.'s

of the same class, meloxicam has a relatively short elimination half-life ($T_{1/2}$) of ~20 hours. This value allows for a once-a-day dosage without the need for a slow release formulation. The values for piroxicam are ~53 hours and for tenoxicam ~65-70 hours. Additionally, steady state is achieved within 3-5 days with meloxicam whereas 1-2 weeks is necessary for other N.S.A.I.D.'s. The absolute bio-availabilty of meloxicam is 89% for oral capsules after a single 30mg dose, and maximum plasma concentrations are achieved after 5-6 hours when administered after breakfast. The pharmacokinetics of N.S.A.I.D.'s may be affected by hepatic or renal insufficiency. For meloxicam there was no relevant influence of hepatic insufficiency or renal dysfunction on the drug's pharmacokinetics. (Turck et al. 1996: 13.)

2.6.2.2 Indications and therapeutic uses

Meloxicam is indicated for:

- the symptomatic treatment of rheumatoid arthritis
- the symptomatic treatment of osteoarthritis
- the symptomatic treatment of ankylosing spondylitis (Mobic® package insert: Appendix A)

Clinical trials have shown that, in doses of 7.5 and 15 mg daily, meloxicam is comparable in efficacy to standard N.S.A.I.D.'s, such as piroxicam, diclofenac and naproxen, in both O.A. and R.A. The drug has a half-life which is ideal for once daily dosing. While G.I. adverse events will not be eliminated with meloxicam, it does appear to offer the distinct

advantage of superior G.I. tolerability compared with other, established N.S.A.I.D.'s at equipotent doses. (Barner 1996: 29.)

2.6.2.3 Toxicity of N.S.A.I.D.'s

The major side effects of N.S.A.I.D.'s include G.I. ulceration and bleeding, hepato-renal dysfunction and organ failure, and skin reactions. In the last decade there has also been much concern about the possibility that some N.S.A.I.D.'s (indomethacin, aspirin and the more potent prostaglandin inhibitors) may accelerate the process of cartilage destruction in O.A. (Rainsford 1999: 27s.)

It is now clear that most N.S.A.I.D.'s can damage the esophagus, stomach, duodenum, small and large intestine, and can impair platelet function systematically, with a consequent increase in bleeding from a variety of G.I. lesions (McCarthy 1999: 37s). The overall risk of hospitalization or death due to an N.S.A.I.D.-related G.I. event has been estimated to be 0.4%/year for patients with O.A. and such figures would suggest 3200 deaths in the U.S.A. per year (Hawkey et al. 1998: 937). Large case-control studies have examined the risk of G.I. perforation and bleeding with different N.S.A.I.D.'s and in different patient groups. The studies showed that there are differences in G.I. toxicity between N.S.A.I.D.'s, and the risk increases with higher doses. The risk is greatest in the elderly, patients with a previous history of such events and those treated with concomitant corticosteroids. (Distel et al. 1996: 68.)

The complications include G.I. bleeding resulting from platelet dysfunction and its effects on various types of lesions, regardless of their etiology but including erosions and ulcers. Some of the ulcers that bleed significantly may be caused by N.S.A.I.D.'s, but many are undoubtedly peptic ulcers not caused by N.S.A.I.D.'s, but caused to deteriorate, bleed, or perforate by the injurious effects of N.S.A.I.D.'s on the ulcer, including impairment of healing. It has been estimated that there are 10,000-20,000 deaths per year attributable to N.S.A.I.D.'s in the United States. (McCarthy 1999: 44s.)

Cartilage destruction is a major concern with N.S.A.I.D.'s. A major part of the actions of these drugs in promoting cartilage degradation has been traditionally ascribed to their potential to inhibit the biosynthesis of proteoglycans in cartilage (Rainsford 1999: 32s). Huskisson et al. (1995: 1941) performed a study to compare the rate of radiographic progression in knee O.A. between indomethacin with placebo and tiaprofenic acid with placebo, and concluded that indomethacin increased the rate of radiological deterioration of joint space in patients with O.A. of the knee.

More recent studies have indicated that other potent prostaglandin synthesis inhibitors may also have the same effects as indomethacin. However, the inhibition of proteoglycan synthesis does not occur with the C.O.X.-2 inhibitor, meloxicam. This drug and other oxicams did not inhibit proteoglycan synthesis in human or porcine cartilage explants in the presence or absence of interleukin-1 (which was added to stimulate cartilage destruction seen in O.A.). It remains to be seen if this translates into any beneficial

actions on the progression of joint changes in O.A. observed radiologically or from magnetic resonance imaging. (Rainsford 1999: 33s.)

The newer specific, selective, or preferential C.O.X.-2-selective drugs have been developed on the premise that those side effects that are related to the inhibition of the production of physiologically important prostaglandins through C.O.X.-1 enzyme systems may be avoided. Drugs like meloxicam have minimal effects on this enzyme. (Rainsford 1999: 27s.)

2.6.2.4 Toxicity of meloxicam

The most commonly occurring adverse events are dyspepsia, abdominal pain, nausea and diarrhoea. Serious adverse events include upper G.I. perforations, ulcerations and bleedings, which frequently require hospitalization. (Hawkey et al. 1998: 937.)
G.I. adverse events occur in roughly 12.9% and 12.7% of meloxicam 7.5 mg and 15mg patients respectively. Patients discontinue therapy prematurely due to adverse events 5% and 6.7% for 7.5mg and 15mg respectively. (Barner 1996:30.)

Other side-effects that can occur as a result of meloxicam administration include: anaemia; skin rashes and pruritis; acute asthma; light headedness and headaches; oedema; abnormal renal function parameters (Mobic® package insert: Appendix A.)

2.6.2.5 Safety of meloxicam

Distel et al. (1996: 75) performed the first global analysis of the safety data from a clinical trial program for meloxicam. They explored the safety and tolerability of meloxicam in therapeutic doses of 7.5 and 15 mg in 4175 patients, including 1379 patients >65 years old, with the majority of patients having O.A. or R.A.. The data shows that meloxicam 7.5 and 15 mg have a better G.I. safety profile in comparison with diclofenac 100 mg, piroxicam 20 mg and naproxen 750-1000mg. When considering all G.I. adverse events, and specific categories of G.I. events, both doses of meloxicam were significantly better than the comparator N.S.A.I.D.'s in most cases. Discontinuation due to adverse events was least common with meloxicam 7.5mg, followed by meloxicam 15mg. Both doses of meloxicam showed a statistically significant decrease in the incidence of perforations, ulcers and bleeding (P.U.B.) over piroxicam and naproxen. There was a significant difference in favour of meloxicam 7.5mg and diclofenac 100mg with respect to P.U.B.'s which were reported as serious adverse effects. (Distel 1996: 76.)

A multicentre, double blind, randomized study was conducted by Hosie et al. (1996:39) on patients with O.A. of the hip or knee to compare efficacy and safety of meloxicam with diclofenac sodium. Adverse events were reported by 59.8% of patients in the meloxicam group and 60.5 % in the diclofenac group. G.I. system disorders were reported in 26,6% of meloxicam and 27.7% of diclofenac patients. Severe events were reported by 22% of diclofenac patients compared to 15.8% of meloxicam patients. Similarly, 18.7% of diclofenac patients and 12.4% of meloxicam patients were

withdrawn due to adverse events. Thus meloxicam demonstrated a trend towards an improved safety profile compared to diclofenac. (Hosie et al. 1996:39.)

A more recent study was performed by Hawkey et al. (1998: 937) using MELISSA (the Meloxicam Large-scale International Study Safety Assessment) comparing meloxicam with diclofenac. MELISSA was a large-scale, double-blind, randomized, international, prospective trial, conducted over 28 days and using 9232 patients with O.A. Significantly fewer adverse events were reported by patients receiving meloxicam. This was attributable to fewer G.I. adverse events (13%) compared to diclofenac (19%; P <0.001). Of the most common G.I. adverse events, there was significantly less dyspepsia (P <0.001), nausea and vomiting (P <0.001) and diarrhoea (P <0.001) with meloxicam compared to diclofenac. Adverse events caused withdrawal from the study in 5.48% of patients receiving meloxicam compared to 7.96% on diclofenac (P <0,001). (Hawkey et al. 1998: 937.)

Dequeker et al. (1998: 946) performed a large-scale, prospective, international, multi-center, double-blind, double-dummy, randomized, parallel-group trial comparing meloxicam to piroxicam in 8656 patients with O.A. The incidence of adverse events was significantly lower in the meloxicam group (22.5%) compared with the piroxicam group (27.9%; P <0.001), mainly due to the significantly lower incidence of G.I. adverse events in the meloxicam than in the piroxicam group (10.3% *vs* 15.4%; P <0.001). Individual G.I. events occurred significantly less often with meloxicam than piroxicam: dyspepsia (3.4% *vs* 5.8%; P <0.001), nausea/vomiting (2.5% *vs* 3.4%; P <0.05) and abdominal pain

(2.1% *vs* 3.6%; P <0.001). The relative risk for P.U.B.'s was piroxicam: meloxicam=1.4. (Dequeker et al. 1998:946.)

2.6.2.6 The efficacy of meloxicam

Lund et al. (1998: 32) performed a double-blind, randomized, placebo-controlled study of efficacy and tolerance of meloxicam treatment in patients with O.A. of the knee. Five hundred and thirteen patients were treated in a double-blind trial comparing meloxicam 7.5mg, 15mg, 30mg, or placebo. Both doses of meloxicam 7.5mg and 15mg were significantly more effective than placebo with respect to pain on movement (P <0.01 and P <0.03, respectively). Both doses of meloxicam compared favourably with placebo with respect to pain at rest, although only the 15mg dose achieved statistical significance (P <0.02). Global efficacy showed a significant difference for both doses of meloxicam (P <0.05 and P <0.02 for meloxicam 7.5mg and 15mg doses, respectively). They concluded that meloxicam 7.5 and 15mg is effective and well tolerated in the short-term symptomatic treatment of O.A. of the knee. (Lund et al. 1998: 32.)

Hosie et al. (1996: 42) demonstrated that meloxicam 7.5mg once daily and diclofenac 100mg slow release once daily showed comparable efficacy in the treatment of O.A., although diclofenac was associated with somewhat higher incidence of severe adverse events, treatment withdrawals and laboratory test abnormalities.

In a more recent study comparing meloxicam to diclofenac, Hawkey et al. (1998: 937) found that although meloxicam has a significantly improved G.I. tolerability profile than diclofenac, differences in efficacy, as assessed by visual analogue scales, consistently favoured diclofenac. In all instances, 95% confidence intervals did not cross zero, suggesting a statistically significant effect. However differences were small (4.5-9.0% difference) and did not reach pre-determined levels of clinical significance. Nevertheless, significantly more patients discontinued meloxicam because of a lack of efficacy (80 out of 4635 *vs* 49 out of 4688: $P < 0.01$). (Hawkey et al. 1998: 937.)

Dequeker et al. (1998: 946) compared meloxicam to piroxicam in a SELECT study (Safety and Efficacy Large-scale Evaluation of COX-inhibiting Therapies), and concluded that all efficacy assessments were comparable, with no significant statistical differences between them. However, it was shown that meloxicam induced significantly fewer G.I. adverse events than an equi-effective dose of piroxicam. (Dequeker et al. 1998: 946.)

2.6.3 Comparison of treatments

There are no documented trials involving a comparison between N.S.A.I.D.'s and manual therapies for the treatment of O.A. of the knee. In order to compare the two forms of treatment under discussion, it is important to summarize the processes involved in O.A. and therefore where in these processes the two treatments take their effect. One must also bear in mind the role that placebo plays as an extraneous variable in a study of this

nature. Wiles (1979: 94) wrote that in the management of O.A. of the knee, three major concerns should be given consideration: 1) pain relief, 2) relief of stiffness and restoration of mobility or function, and 3) correction of instability and weakness.

It is reasonable to assume that each of the signs and symptoms of pain, stiffness, inflammation, loss of function and weakness is directly linked to one another and thus treating one will have an indirect, beneficial effect on the other. Pain is a well recognized as a key symptom in the decision to seek professional medical care, and the pain associated with progressive degenerative diseases such as O.A. of the knee has been shown to be an important antecedant to disability (Rejeski et al. 1995: 1124). However, alleviation of pain does not alter the underlying disease (Manek et al. 2000: 1795). Pain may be mediated through the activation of pain receptors by hystamine and bradykinin, products of the arachidonic acid pathway in the inflammatory cascade (Goulding 1989: 12). This would explain why N.S.A.I.D.'s are effective pain relievers. However, Manek et al. (2000: 1800) stated that the pain in O.A. is not necessarily due to inflammation. Hertling & Kessler (1996: 364) wrote that pain can have muscular, capsular or perhaps venous origins.

Gottlieb (1997: 410) argued that pain is not a good indicator of the treatment that is needed. He continued that because there is no correlation between pain levels and the extent of the degeneration detected by radiographic examination, conservative management should be initiated and sustained based on functional, objective findings and not strictly on how the patient feels. Because of the absence of pain receptors in articular

cartilage, considerable degeneration may take place before symptoms bring the problem to the attention of the patient (Hertling & Kessler 1996: 45).

In a study performed by Deyle et al. (2000: 179) on manual physical therapy and exercise in the treatment of O.A. of the knee, patients reported 20%-40% relief of symptoms after only 2-3 treatments. This rapid reduction of symptoms implies that the structures responsible for at least part of the pain are not the most fixed or unchangeable aspects of the pathology of O.A. Periarticular connective and muscular tissue could be implicated as symptom sources. Perhaps the repeated challenge to the end range of movement, as occurs with closed- chain strengthening exercises, manually applied passive movement, and active range-of-movement exercises, provided a strong stimulus to connective tissue, resulting in pain relief. They continued that of note, unweighting of the knee joint during walking has not been demonstrated to relieve pain in patients with O.A. of the knee. It seems logical that if the articular surfaces or subchondral bone were the primary pain generators, walking under decreased loads would decrease pain. (Deyle et al. 2000: 179.)

Edmond (1993: 5) explained that manipulation decreases pain in joint and periarticular structures by stimulating joint receptors. This reduces pain perception by producing blockage of pain impulses through the gate control mechanism and by producing reflexive muscle relaxation. The author continues that minimal displacement of joint surfaces can cause abnormal stress on periarticular structures and thus can be a source of pain. Manipulation realigns joints into proper positions and normalizes the static

positioning of one joint surface in relation to another, thus reducing pain. (Edmond 1993: 5.)

Effusion is a result of synovial irritation caused by the release of proteolytic enzymes and other cartilagenous debris. (Hertling & Kessler 1996: 45.) However, effusions usually occur during acute inflammatory exacerbations (Golding 1989: 146) which are transient and relatively minor (Gottlieb 1997: 402). The anti-inflammatory effect of N.S.A.I.D.'s is mediated through their ability to inhibit the activity of the cyclooxygenase enzyme (Walker & Helewa 1996: 152). The newer specific, selective, or preferential C.O.X.-2-selective drugs have been developed on the premise that those side effects that are related to the inhibition of the production of physiologically important prostaglandins through C.O.X.-1 enzyme systems may be avoided. Drugs like meloxicam have minimal effects on this enzyme. (Rainsford 1999: 27s.)

It has been shown by Lund et al. (1998: 32) that meloxicam is effective in alleviating pain and inflammation in patients suffering from O.A. of the knee. They concluded that meloxicam 7.5 and 15mg is effective and well tolerated in the short-term symptomatic treatment of O.A. of the knee. Distel et al. (1996: 75) showed that meloxicam 7.5 and 15 mg have a better G.I. safety profile in comparison with diclofenac 100 mg, piroxicam 20 mg and naproxen 750-1000mg. When considering all G.I. adverse events, and specific categories of G.I. events, both doses of meloxicam were significantly better than the comparator N.S.A.I.D.'s in most cases. (Distel et al. 1996: 75.) However, G.I. adverse events occur in roughly 12.9% and 12.7% of meloxicam 7.5 mg and 15mg patients

respectively. Patients discontinue therapy prematurely due to adverse events 5% and 6.7% for 7.5mg and 15mg respectively. (Barner 1996:30.) Thus it can be seen that meloxicam is an effective anti-inflammatory, however, O.A. generally does not have an inflammatory component, except in advanced disease (Manek et al. 2000: 1796). As stated by Lund et al. (1998: 32), meloxicam is effective and well tolerated in the short-term symptomatic treatment of O.A. of the knee. Thus it would be indicated during times of acute exacerbation, or when the condition is advanced and unresponsive to other forms of care.

Radin (1986: 63) wrote that the clinical experience suggests that the treatment of O.A. with N.S.A.I.D.'s does not alter the progression of the arthrosis. This is to be expected if one remembers that the arthritis (inflammatory reaction) is secondary to the mechanical reaction in osteoarthrosis. Thus one is obliged to approach the prevention of osteoarthrosis mechanically. (Radin 1986: 63.) Maitland (1991: 11) explained that it is common for a patient to have O.A. producing an inflammatory reaction, superimposed upon a mechanical factor provoking further inflammatory reaction. He continues that when this is so, passive movement treatment can have a degree of improvement commensurate with the extent of the mechanical cause.

Gottlieb (1997: 402) stated that loss of joint function and movement occurring from O.A. is attributable to stiffness and use-related pain. He continued that the medical management of O.A. currently involves reducing the symptoms of pain with drugs and does not focus on increasing function or inhibiting the progression of the disease.

Edmond (1993: 3) described that inflammation produces hypertrophy of the synovial lining of the joint, due to invasion of connective tissue fibers. She continued that this results in fibrosis of the synovial lining, which produces joint contractures. Similarly, immobilization produces adhesions in the joint capsule, as well as fibrofatty proliferation within the joint forming scar tissue. (Edmond 1993: 3.) Such a lack of mobility of the capsule will of course contribute significantly to the cycle of degeneration because of the resultant alteration of joint mechanics (Hertling & Kessler 1996: 46).

Gottlieb (1997: 409) stated that a joint that loses the ability to move properly also loses the ability to nourish itself, maintain tissue integrity and consequently begins to degenerate. All types of manipulation techniques are thought to produce movement of fluid within the synovium (Edmond 1993: 3), and thus improve nutrition.

Joint manipulation breaks adhesions within the capsule and synovial folds, increases the length of capsular fibers, breaks intracapsular fibrofatty adhesions and increases the amount of arthrokinematic motion of the joint (Edmond 1993: 3). Thus one can deduce that although N.S.A.I.D.'s would be able to halt fibrosis, they have no mechanism of reversing it.

It is the authors' opinion that because N.S.A.I.D.'s cannot reverse scar tissue formation and thus reintroduce vital biomechanical function, the improvement in function and stiffness experienced by patients receiving this medication is attributable to the reduction of pain and \or synovial effusion. This amelioration of symptoms may have long-term

detrimental effects as the loss of the pain protection mechanism may cause the patient to over-use the knee in daily activity or through prescribed exercise programs. Hertling & Kessler (1996: 48) elaborate by saying that efforts to restore joint mechanics (without passive manual procedures) too often only consist of range of motion exercises and muscle strengthening. These are carried out without regard for the possible deleterious effects to the joint and without regard for the abnormal reflex activity accompanying joint movement in the absence of normal arthrokinematics.

The act of the chiropractic manipulative thrust is in effect treating the dysfunctional biomechanics of the joint, affecting histological change, and is thus contributing to the treatment and perhaps reversal of O.A. (Berkson 1991: 357).

2.6.4 Conclusion

The review of the literature reveals that there are many causative factors involved in the pathogenesis of osteoarthritis. This implies that a clinician is required to address all of these factors to arrive at a complete treatment strategy. The alleviation of symptoms is thus not sufficient to halt the progression of this disease.

N.S.A.I.D.'s are the most common pharmaceutical treatment for rheumatic disease (Distel et al. 1996: 68). However, use of N.S.A.I.D.'s can lead to gastric complications, increased risk of hospitalization and death (Deyle et al. 2000: 173). Because O.A. usually affects the elderly, they are the greatest at risk for complications. Manek et al. (2000:

1801) wrote that the risk of N.S.A.I.D. induced renal and hepatic toxicity is increased in the older patients and with patients exhibiting preexisting renal and hepatic insufficiency. The authors recommended that liver function tests and serum hemoglobin, creatine and potassium measurements be performed before N.S.A.I.D. therapy is initiated and again after 6 months. Drugs like misoprostol (Cytotec) and omeprazole (Prilosec) were said to be effective for healing N.S.A.I.D. induced ulcers and erosions, while ranitidine (Zantac) can prevent duodenal ulcers in patients receiving chronic N.S.A.I.D. therapy. However, in a developing country such as South Africa, the average elderly arthritis sufferer will be hard pressed to afford such additional medical expenditure. Manek et al. (2000: 1802) also mentioned a new preferential C.O.X.-2 inhibitor on the market called celecoxib (Celebrex), which showed a low risk of G.I.T bleeding but still showed side-effects of dyspepsia, diarrhea and abdominal pain. This medicine, including meloxicam, will also be difficult for the average elderly South African to afford. They will in all probability, be prescribed the cheaper, more available C.O.X.-1 inhibitors, with their associated G.I.T., liver and renal side-effects as well as potential deleterious cartilage effects (eg. indomethacin).

N.S.A.I.D.'s should be limited to the treatment of gross inflammation and effusion and analgesics should only be used in the short term when absolutely necessary (Gottlieb 1997: 410). Knowledge of normal kinematics, ability to detect changes in joint mechanics through joint-play movements, and ability to restore normal component movements to a joint are necessary in the successful management of patients with joint problems that are

of a mechanical etiology or in which mechanical dysfunction is a prime factor (Hertling & Kessler 1996: 48).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Introduction

This chapter gives a detailed description of the design, primary and secondary data, the subjects and interventions used. An overview of each questionnaire and the validity of each measurement parameter is discussed. Statistical analysis and data evaluation methods are also discussed.

The objective of this study was to compare the relative effectiveness of a N.S.A.I.D (meloxicam) to manipulation, in terms of subjective and objective findings, to determine which is more beneficial in treating osteoarthritis of the knee.

3.2 The data

The data consisted of primary and secondary data.

3.2.1 The primary data

The primary data consisted of:

- The case-history, physical examination (including recording of vital signs), knee regional examination and radiographic findings of the patients used in this study.
- The patient's perception of their disability (The Patient-Specific Functional Scale [P.S.F.S.]).

- The patient's perception of pain intensity (Visual Analogue Scale [V.A.S.]).
- The patient's perception of their worst and least levels of pain (Numerical Pain Rating Scale-101 [N.R.S.-101]).
- The patient's knee ranges of motion (Goniometer).
- The patient's pressure threshold in terms of pain (Wagner Algometer).
- The reaction of the N.S.A.I.D. group in terms of pain and disability and range of motion.
- The reaction of the manipulation group in terms of pain and disability and range of motion.

3.2.2 The Secondary Data

- Relevant literature was obtained from various sources, including journal articles, books, pharmaceutical research, Internet Medline, Mantis and Grateful Med search engines.

3.3 The subjects

Patients were notified of this study through advertisements placed on notice boards in the Technikon Natal Chiropractic Day Clinic, in local newspapers and radio stations. Upon reply, patients were telephonically interviewed to assess their eligibility for the study, with questions pertaining to the history and progression of their complaint and to explain the nature of the study to the prospective participants. Patients were immediately

excluded if they were pregnant females, below the age of 18 or over the age of 85, or had any history of surgery to the knee.

Sixty patients were consecutively selected from those that responded, with no discrimination against gender, racial group, occupation or economic factors. If the patient was deemed likely to be acceptable for the study, he or she underwent a case history (Appendix B), a physical examination (Appendix C) and a knee regional examination (Appendix D). Therefore, non-probability sampling was utilized in order to attract the most suitable candidates.

3.4 Inclusion and exclusion criteria

The criteria were as follows:

1. Patients between the ages of 18 and 85 were to be accepted.
2. Patients with any of the following conditions were immediately excluded from the study: asthma, nasal polyps, active peptic ulceration, severe hepatic insufficiency, non-dialysed severe renal insufficiency. Patients were also excluded if they had any known hypersensitivity to meloxicam or any excipient of the drug, or developed angioedema or urticaria following the administration of acetyl acetic acid or other N.S.A.I.D.'s. (Mobic® package insert: Appendix A.)
3. Pregnant or lactating women were also excluded.
4. Patients taking aspirin, anticoagulants, lithium, methotrexate, diuretics, antihypertensive medicines, cyclosporin, digoxin and oral anti-diabetics were not

included in the study due to potentially harmful interactions with meloxicam (Mobic® package insert: Appendix A).

5. Patients who were currently taking N.S.A.I.D.'s before entering the study, were required to undergo a two week washout period.
6. Patients receiving any other form of therapy in the duration of the study were excluded.
7. Any patient who developed signs or symptoms of side effects that could be related to meloxicam was to be immediately excluded.
8. Patients were instructed not to change their everyday routine, and compliance was ensured through the researcher at each consultation.
9. Radiographs were taken on certain patients when there was a suspicion of contraindication to manipulation, or when the diagnosis was unclear, or to rule out pathology outside of osteoarthritis.
10. Rheumatoid factor blood tests were performed to rule out rheumatic diseases.
11. In order for a diagnosis of O.A. to be made, the signs and symptoms should include:

- pain in the effected knee
- pain that is worsened with activity and relieved by rest
- morning stiffness lasting less than 30 minutes
- stiffness after disuse
- joint crepitus on passive and active motion
- tenderness upon motion
- decreased range of motion
- instability/ malalignment

12. The evidence of radiographic O.A. should include (Yochum & Rowe 1996: 803):

- joint space narrowing of either the medial or lateral tibiofemoral compartments seen on a standing A.-P. radiograph
- osteophyte formation
- subchondral sclerosis
- evidence of varus or valgus malalignment

13. If a patient was diagnosed as having O.A. of the knee, they were to be excluded from the study if they showed any evidence of contraindication to manipulation such as (Edmond 1993: 8):

- severe joint ankylosis
- ligamentous instability or joint hypermobility
- severe osteoporosis
- considerable knee pain or joint irritability
- considerable knee effusion
- concomittant joint infection, malignancy, periarticular tissue disease (eg. diabetes), metabolic bone disease or unhealed fracture

14. Due to the fact that severe, end stage osteoarthritis exhibits the features that are contraindicated to manipulation, this study focussed on mild to moderate stage osteoarthritis of the knee.

3.5 Ethics

All patient information was treated as confidential. Each patient, upon acceptance to the study, was required to complete and sign an informed consent form (Appendix E). Each patient was informed of the possible side-effects of manipulation and the N.S.A.I.D. used. Patients were free to withdraw from the study at any time.

3.6 The sample group

A sample group size of sixty patients was chosen by recommendation of the chiropractic research committee of Technikon Natal. Sixty patients who met the inclusion criteria were randomly assigned into two groups using the "gold fish bowl technique" (Willemse 1990: 274). Sixty pieces of paper with the numbers one through sixty written on them were placed in a box. Patients were required to look away and draw a single piece of paper from the box. Patients who drew numbers 1-30 were assigned to the manipulation group and patients who drew numbers 31-60 were assigned to the meloxicam group. After drawing a number, the piece of paper was discarded, and the process was repeated until all 60 patients were assigned to a group, with the last patient being automatically allocated the last remaining number.

3.7 Assessments

Subjective information was obtained using the N.R.S.-101 (Jenson et al. 1986 [Appendix F]), the V.A.S. (Jenson et al. 1986 [Appendix G]) and the P.S.F.S. (Chatman et al.1997 [Appendix H]). Objective information included knee range of motion, obtained using a goniometer (Appendix I), and pain threshold readings using an algometer (Wagner FX2 model [Appendix J]). The subjective questionnaires and objective measurements were performed at the initial, fourth and eighth treatment sessions. These were completed at the beginning of the consultation, prior to the commencement of the examination or treatment.

3.8 Interventions

Each patient accepted into the study underwent a total of eight consultations over a three-week period, equating to one consultation every second day. If a patient became asymptomatic during that period, the patient continued to be assessed for the remainder of the treatment period.

3.8.1 Knee Manipulative Therapy

The involved tibiofemoral and patellofemoral joints were motion palpated according to the method described by Schafer & Faye (1990: 393-396). A low amplitude, high velocity thrust was used to restore movement in the directions of these motion palpation

findings. Manipulations were of the method described by Schafer & Faye (1990: 393-396).

3.8.2 Medication

The N.S.A.I.D. used in this study was meloxicam 7.5mg with the trade name of Mobic®. Meloxicam was chosen because of the following reasons:

- Lund et al. (1998: 32) showed that a once daily dose of meloxicam 7.5mg is effective and well tolerated in the short-term symptomatic treatment of O.A. of the knee.
- With respect to all G.I. adverse events, meloxicam 7.5mg was significantly better than piroxicam 20mg, diclofenac 100mg slow release and naproxen 750-1000mg in a pooled analysis of double-blind studies on O.A. This is thought to be due to meloxicams' preferential inhibition of the C.O.X.-2 enzyme over the C.O.X.-1 enzyme. (Distel et al. 1996: 68.)
- Meloxicam diffuses into and out of synovial tissue.
- Meloxicam comes in convenient blister packs and can be taken on an empty stomach, or after food which can increase patient compliance.
- Meloxicam is an over-the-counter medication, which is freely available.

Patients in the meloxicam group were required to take one 7.5mg tablet once a day, after their main meal, with a full glass of water, to increase patient compliance. They were required to take the medication for the duration of the eight treatments over three weeks

unless they became asymptomatic (in which case they remained on the study for observation) or if they showed signs of side-effects or intolerance (in which case they were discontinued from the study).

3.9 Measurements

3.9.1 Objective measurements

Objective measurements were obtained using a goniometer (Appendix I) and an algometer (Appendix J). Both readings were recorded prior to examination and treatment on the first, fourth and eighth treatments.

3.9.1.1 The Goniometer

The procedure for assessing the knee R.O.M. was as follows:

- The patient was placed supine on the examining table with the involved knee placed flat in extension
- The goniometer was placed with the center binding ring placed over the "middle" of the knee (ie. Over the central aspect of the lateral femoral condyle)
- The two arms of the goniometer were extended in such a way that the inferior, distal portion was in line with the lateral malleolus of the ankle, and the superior, proximal portion was in line with the trochanteric notch of the femur.

- The patient was asked to fully extend the knee, and the reading was measured and written on Appendix I.
- The patient was then asked to fully flex the knee and again the measurement was recorded.

3.9.1.2 The Algometer

The algometer readings were used to quantify any changes in the patients' pressure-pain threshold and pressure-pain tolerance objectively. The algometer used in this trial was the FDK20 Force Dial, a product of Wagner Instruments.

Fischer (1986: 863) reported that an algometer could be utilized to reliably quantify the tenderness in hypersensitive spots. These areas of focal tenderness may be due to pain originating from ligaments, joint capsules, tendons and periosteum (Fischer 1987: 207).

Measurements were taken over the most tender/painful point in the involved knee. Force readings were measured in kilograms per square centimeter. The algometer had a square rubber disc attachment by which pressure from the algometer was transmitted. The procedure for assessing the pressure-pain threshold with the algometer was as follows:

- The dial was reset to zero by depressing the reset button
- The disc was placed on the tender spot perpendicularly to the skin and pressure applied at a rate of one kilogram per second.

- The patient was instructed to say "now" at the point at which they first experienced discomfort, and then the pressure was released.

3.9.2 Subjective Measurements

Subjective information was obtained through the use of the Numerical Pain Rating Scale-101 (Appendix F), the Visual Analogue Scale (Appendix G) and the Patient-Specific Functional Scale (Appendix H). Patients were required to complete these forms prior to the commencement of examination or treatment on the first, fourth and eighth visitations.

3.9.2.1 The Numerical Pain Rating Scale (101 Scale) (Appendix F)

The N.R.S.-101 is a questionnaire used to evaluate the intensity of pain a patient is experiencing. The patient is presented with two lines marked with 0 at the beginning and ending with 100. The patient is informed that 0 represents "no pain at all", and the 100 represents "pain as bad as it could be". On the first line, the patient is asked to identify the number which best represents the level of pain they are experiencing when the pain is at its worst. On the second line, they are asked to identify the number which best represents the level of pain when it is at its least. The average between these two figures was then taken as the percentage intensity of pain they were experiencing prior to the treatment session.

Bolton & Wilkinson (1998: 1) conducted a study to compare the responsiveness of three pain scales, and found the N.R.S. to be the most responsive of the measures (Effect size = 0.86, as opposed to 0.77 for the V.A.S. and 0.76 for the Verbal Rating Scale).

3.9.2.2 The Visual Analogue Scale

The Visual Analogue Scale (V.A.S.) is normally used to evaluate the overall severity of pain (McDowell & Newell 1996: 341). The scale consists of a straight line, 10cm long, that is marked at each end with labels that indicate the range of pain intensity to be measured. On the beginning of the scale is the range "no pain at all" and at the end of the scale is the range "pain as bad as it could be". The patients were instructed to indicate where on the line they believed the level of pain at that point in time to be. This level was then measured using a ruler and documented.

Visual analogue scales are more sensitive to change than verbal rating scales, and show good reliability and validity (McDowell & Newell 1996: 343).

3.9.2.3 The Patient-Specific Functional Scale

Chatman et al. (1997: 820) performed a study on the P.S.F.S. on patients with knee dysfunction. The results of the study provided further evidence supporting the reliability, validity, and efficiency of the P.S.F.S.

The P.S.F.S. was developed by Stratford and colleagues to provide a method for eliciting, measuring and recording descriptions of patients disabilities and to be used to guide treatments and asses patient outcome (Chatman et al. 1997: 822).

Patients were asked to identify up to five important activities that they were having difficulty with or were unable to perform as a result of their condition. In addition to identifying these activities, patients were asked to rate, on a point scale, the current level of difficulty associated with each activity. The scale anchors were 0 ("unable to perform activity") to 10 ("able to perform activity at same level as before injury or problem"). At each subsequent visit, the patient was reminded of the activities that were listed at the last visitation and reevaluated, and any new difficulty was documented.

3.10 Specific treatment of the subproblem

3.10.1 The First Subproblem

The first subproblem was to evaluate the relative effectiveness of meloxicam and manipulation in the treatment of osteoarthritis of the knee, in terms of subjective clinical findings.

3.10.2 The Second Subproblem

The second subproblem was to evaluate the relative effectiveness of meloxicam and manipulation in the treatment of osteoarthritis of the knee, in terms of objective clinical findings.

3.11 Statistical analysis

3.11.1 Treatment of the data

3.11.1.1 Subjective Data

The subjective data were examined in the following way:

- The information was tabulated.
- The raw data from the three questionnaires was statistically analyzed using a 95% level of confidence.

3.11.1.2 Objective Data

The objective data were examined in the following way:

- The algometer readings, measured in Kg/cm^2, were recorded separately for the two groups.
- The knee ranges of motion (flexion and extension), recorded in degrees, were also recorded separately for the two groups.
- The data was the statistically analyzed using a 95% level of confidence.

3.11.2 Statistical analysis of the data

A statistician from Technikon Natal was consulted for advice on how to statistically analyze the data.

Due to the sample size used in this study (N_1 and N_2=30), parametric tests were used to analyze the data. All data analysis used a 95% level of confidence.

3.11.2.1 Two-Sample Unpaired T-Test

In order to determine whether there was any significant change in the data from the first, fourth and eighth treatments between the two groups (inter-group analysis), the Two-Sample Unpaired T-Test was used.

A 95% level of confidence was used (Alpha = 0.025).

3.11.2.2 Two-Sample Paired T-Test

In order to determine whether there was any significant change in the data from the first, fourth and eighth treatments within each respective treatment group (intra-group analysis), the Two-Sample Paired T-Test was used.

A 95% level of confidence was used (Alpha = 0.025).

3.11.2.3 Hypothesis Testing

The null hypothesis (H°) for subproblem one and two stated that within each group there was no significant improvement of the patients in terms of subjective and objective clinical findings. The alternative hypothesis (H_1) for subproblem one and two stated that within each group there was a significant improvement of the patients in terms of subjective and objective clinical findings.

The null hypothesis (H°) for subproblem three was that there was no statistical significant difference (alpha = 0.025) between groups one and two in terms of subjective and objective clinical findings. The alternative hypothesis (H_1) for subproblem three was that there was a statistical significant difference (alpha = 0.025) between groups one and two in terms of subjective and objective clinical findings.

CHAPTER FOUR

4.0 THE RESULTS

4.1 Introduction

This chapter discusses the data collected using the methodology outlined in chapter three. Also presented is the interpretation of the results with the relevant tables and bar charts.

Group A- manipulation group.

Group B- meloxicam group

4.2 Recruitment

Eighty-one people were screened, of which sixty-three were accepted onto the study. The nineteen who were not accepted did not meet the selection criteria (Table 4.1). Three of the sixty-three patients dropped out of the study during the course of the treatment (Table 4.2).

Table 4.1 Reasons for patients not meeting selection criteria.

Reason	**No. of patients and percentage**
History of adverse reaction to NSAIDS	6 (32%)
History of G.I. ulcer	5 (26%)
History of knee surgery	6 (32%)
Knee too degenerated	1 (5%)
Rheumatoid factor test positive	1 (5%)
Total	**19 out of 81 = 24%**

Table 4.2 Reasons for patients not completing study.

Reason	No. of patients and percentage
Dyspepsia/ Nausea	1 (33%)
Allergic reaction	1 (33%)
Lack of transport	1 (33%)
Total	**3 out of 63 = 8%**

4.3 DEMOGRAPHIC DATA

Table 4.3 Age prevalence.

Age	Group A	Group B	% Patients
35-44	2	1	5%
45-54	5	6	18.33%
55-64	8	12	33.33%
65-74	11	10	35%
75-85	4	1	8.33%

The average age (mean) for group A: 61.2.

The average age (mean) for group B: 57.4.

The average age (mean) for group A and B: 59.3.

Table 4.4 Gender distribution.

Gender	Group A	Group B	Total
Male	12	11	23
Female	18	19	37

Table 4.5 Racial distribution.

Patients Racial Group	Group A	Group B
Black	0	2
White	24	25
Indian	6	2
Coloured	0	1

Table 4.6 Average pain duration.

Average no. of Years	Group A	Group B
	2.71	2.8

Table 4.7 (a) Occupation of patients.

GROUP A	Number of Patients	Percentage
Retired	13	43.33%
Clerk	1	3.33%
Home Executive	9	30%
Technical Manager	1	3.33%
Security Officer	1	3.33%
Restaurant Owner	1	3.33%
Salesman	1	3.33%
Driver	1	3.33%
Book Keeper	1	3.33%
Company Director	1	3.33%

Table 4.7 (b) Occupation of patients.

GROUP B	Number of Patients	Percentage
Retired	16	53.33%
Home executive	5	16.66%
Manager	1	3.33%
General Assistant	1	3.33%
Book Keeper	1	3.33%
Chef	1	3.33%
Clerk	1	3.33%
Unemployed	1	3.33%
Reverend	1	3.33%
School Principal	1	3.33%
Image Consultant	1	3.33%

Table 4.8 Average height and weight.

Average Ht and Wt	Group A	Group B
Height	5 ft 3"	5 ft 5"
Weight	78.66 kg	86.16 kg

Overall mean height: 5 ft 4".

Overall mean weight: 82.41 kg.

Table 4.9 Percentage of knees affected.

Knee Affected	Number	Percentage
Left	18/60	30%
Right	28/60	46.6%
Both	14/60	23.3%

4.4 Manipulation data

Table 4.10 Number of adjustments for 30 patients over 8 consultations according to motion palpation findings.

Adjustment	Number	Percentage
Anterior- Posterior	238	26%
Posterior- Anterior	187	20%
Medial- Lateral	113	12%
Lateral- Medial	96	10%
External Rotation	36	4%
Internal Rotation	22	2%
Long Axis Distraction	240	26%

Table 4.11 Total and average number of adjustments.

Total no. of adjustments for 30 patients	932
Ave. no. of adjustments per pt. over 8 tx.'s	31
Ave. no. of adjustments per patient per tx.	4

Twenty-two out of the thirty patients (73.33%) in the manipulation group received patellofemoral manipulations according to motion palpation findings.

4.5 N.S.A.I.D. data

Table 4.12 Number of patients reporting adverse symptoms.

Symptom	No. of Patients	Discontinued Treatment
Nausea	1 (3.33%)	No
Diarrhea	1 (3.33%)	No
Allergic reaction	1 (3.33%)	Yes

4.6 The analyzed data

4.6.1 P- Value

The data was analyzed at the $\propto = 0.05$ level and the decision rule was as follows:

- Reject the null hypothesis if the P- value is less than or equal to $\propto / 2$, and accept alternative hypothesis.
- Accept the null hypothesis if the P- value is greater than $\propto / 2$, and reject the alternative hypothesis.
- As $\propto / 2 = 0.025$, the P- value must be equal to or less than 0.025 in order to reject the null hypothesis (there is a significant difference).

4.6.2 Power Test

The power- value assesses the sensitivity of the statistical tests by assessing the probability of a particular test to detect a difference between the groups. The smaller the power of a test, the larger becomes the likelihood of a type II error (incorrectly accepting the null hypothesis). The power should be as close to one as possible, therefore with the probability of a Type II error being $\propto$, the power of a statistical test is $(1- \propto)$.

4.6.3 Two- sample paired t- test (Intra-group analysis)

Table 4.13 Statistical results of the subjective and objective data, comparing the 1st and 4th consultations in Group A.

	CONSULTATION 1			CONSULTATION 4	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	127.8000	9.5787	**0.008**	129.2333	9.2127
Extension	-5.1667	8.8399	0.647	-5.0667	8.7373
Algometer	4.8700	1.6176	0.081	5.1967	1.6904
NRS 101	35.9000	11.6066	**0.000**	26.1333	12.0537
VAS	33.8333	15.3513	**0.000**	22.8333	15.6295
PSFS	17.4667	4.9947	**0.000**	21.2000	5.8156

When comparing the subjective and objective data between consultation 1 and 4 for Group A, it can be seen that with the exception of extension and the algometer, there was a statistically significant improvement for all other readings. The null hypothesis is therefore rejected for all the readings except extension and the algometer

Table 4.14 Statistical results of the subjective and objective data, comparing the 1st and 4th consultations in Group B.

	CONSULTATION 1			CONSULTATION 4	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	126.0333	11.4002	0.212	127.1667	8.5544
Extension	-5.9667	7.9719	0.794	-5.9000	8.3018
Algometer	4.4433	1.3469	0.666	4.6000	1.9064
NRS 101	37.1667	13.0439	**0.000**	25.8333	12.5123
VAS	32.8333	19.9863	0.140	26.6667	21.4288
PSFS	17.7667	4.9458	**0.000**	22.3667	7.6586

When comparing the results of the subjective and objective data between consultation 1 and 4 for Group B, it can seen that there was a statistically significant improvement for the NRS-101 and PSFS only, with the others having no statistically significant improvement. The null hypothesis is therefore accepted for the above values except for the NRS-101 and PSFS values.

Table 4.15 Statistical results of the subjective and objective data, comparing the 4th and 8th consultations in Group A.

	CONSULTATION 4			CONSULTATION 8	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	129.2333	9.2127	0.291	129.6000	9.4781
Extension	-5.0667	8.7373	0.081	-4.5333	8.7286
Algometer	5.1967	1.6904	**0.002**	5.8667	1.7036
NRS 101	26.1333	12.0537	**0.000**	17.6000	12.7701
VAS	22.8333	15.6295	**0.000**	11.5000	13.5284
PSFS	21.2000	5.8156	**0.000**	27.7667	7.2952

When comparing the results of the subjective and objective data between consultation 4 and 8 for Group A, it can be seen that except for flexion and extension, there was a

statistically significant improvement in all other readings. The null hypothesis is therefore rejected for the above readings except for flexion and extension.

Table 4.16 Statistical results of the subjective and objective data, comparing the 4th and 8th consultations in Group B.

	CONSULTATION 4			CONSULTATION 8	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	127.1667	8.5544	0.035	128.2000	7.8714
Extension	-5.9000	8.3018	**0.019**	-5.4000	8.5847
Algometer	4.6000	1.9064	0.055	5.1167	1.6377
NRS 101	25.8333	12.5123	**0.000**	18.8000	13.3168
VAS	26.6667	21.4288	**0.000**	12.5667	15.4154
PSFS	22.3667	7.6586	**0.000**	26.5667	8.8383

When comparing the results of the subjective and objective data between consultation 4 and 8 for Group B, it can be seen that except for flexion and the algometer, there was a statistically significant improvement for all other readings. The null hypothesis is therefore rejected for the above readings except for flexion and the algometer.

Table 4.17 Statistical results of the subjective and objective data, comparing the 1st and 8th consultations in Group A.

	CONSULTATION 1			CONSULTATION 8	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	127.8000	9.5787	**0.001**	129.6000	9.4781
Extension	-5.1667	8.8399	**0.018**	-4.5333	8.7286
Algometer	4.8700	1.6176	**0.000**	5.8667	1.7036
NRS 101	35.9000	11.6066	**0.000**	17.6000	12.7701
VAS	33.8333	15.3513	**0.000**	11.5000	13.5284
PSFS	17.4667	4.9947	**0.000**	27.7667	7.2952

When comparing the results of the subjective and objective data between consultation 1 and 8 for Group A, it can be seen that there was a statistically significant improvement for all the readings. The null hypothesis is therefore rejected for the above readings.

Table 4.18 Statistical results of the subjective and objective data, comparing the 1st and 8th consultations in Group B.

	CONSULTATION 1			CONSULTATION 8	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	126.0333	11.4002	0.034	128.2000	7.8714
Extension	-5.9667	7.9719	0.064	-5.4000	8.5847
Algometer	4.4433	1.3469	0.054	5.1167	1.6377
NRS 101	37.1667	13.0439	**0.000**	18.8000	13.3168
VAS	32.8333	19.9863	**0.000**	12.5667	15.4154
PSFS	17.7667	4.9458	**0.000**	26.5667	8.8383

When comparing the results for the subjective and objective data between consultation 1 and 8 for Group B, it can be seen that except for flexion, extension and algometer, there was a statistically significant improvement in the NRS-101, VAS and PSFS. Those values were close to the P-value of 0.025, showing there was some improvement, however not being statistically significant. The null hypothesis is therefore rejected for the subjective readings and accepted for the objective readings.

4.6.4 Independent samples t- test (Inter-group analysis)

Table 4.19 Statistical results comparing Group A and Group B in terms of subjective and objective data from the initial consultation.

	GROUP A CONSULTATION 1			GROUP B CONSULTATION 1	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	127.8000	9.5787	0.518	126.0333	11.4002
Extension	-5.1667	8.8399	0.714	-5.9667	7.9719
Algometer	4.8700	1.6176	0.271	4.4433	1.3469
NRS 101	35.9000	11.6066	0.693	37.1667	13.0439
VAS	33.8333	15.3513	0.829	32.8333	19.9863
PSFS	17.4667	4.9947	0.816	17.7667	4.9458

When comparing the results for the subjective and objective data from the first consultation of Group A and B, it can be seen that there was no statistically significant difference between the two groups. The null hypothesis is therefore accepted for the above results.

Table 4.20 Statistical results comparing Group A and Group B in terms of subjective and objective data from the fourth consultation.

	GROUP A CONSULTATION 4			GROUP B CONSULTATION 4	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	129.2333	9.2127	0.372	127.1667	8.5544
Extension	-5.0667	8.7373	0.706	-5.9000	8.3018
Algometer	5.1967	1.6904	0.205	4.6000	1.9064
NRS 101	26.1333	12.0537	0.925	25.8333	12.5123
VAS	22.8333	15.6295	0.432	26.6667	21.4288
PSFS	21.2000	5.8156	0.509	22.3667	7.6586

When comparing the results of the data between Groups A and B for consultation 4, it can be seen that there was no statistically significant difference between the two groups. The null hypothesis is therefore accepted for the above results.

Table 4.21 Statistical results comparing Group A and Group B in terms of subjective and objective data from the eighth consultation.

	GROUP A CONSULTATION 8			GROUP B CONSULTATION 8	
Goniometer	**Mean**	**Std. Dev.**	**P-Value**	**Mean**	**Std. Dev.**
Flexion	129.6000	9.4781	0.536	128.2000	7.8714
Extension	-4.5333	8.7286	0.700	-5.4000	8.5847
Algometer	5.8667	1.7036	0.087	5.1167	1.6377
NRS 101	17.6000	12.7701	0.723	18.8000	13.3168
VAS	11.5000	13.5284	0.777	12.5667	15.4154
PSFS	27.7667	7.2952	0.569	26.5667	8.8383

When comparing the results of the data between Groups A and B for consultation 8, it can be seen that there was no statistically significant difference between the two groups. The null hypothesis is therefore accepted for the above results.

Table 4.22 Power analysis for continuous variables.

Continuous Var.	Consultation 1	Consultation 4	Consultation 8
Algometer	0.1896	0.2384	0.3968

Median Values Represented Graphically

Figure 4.1

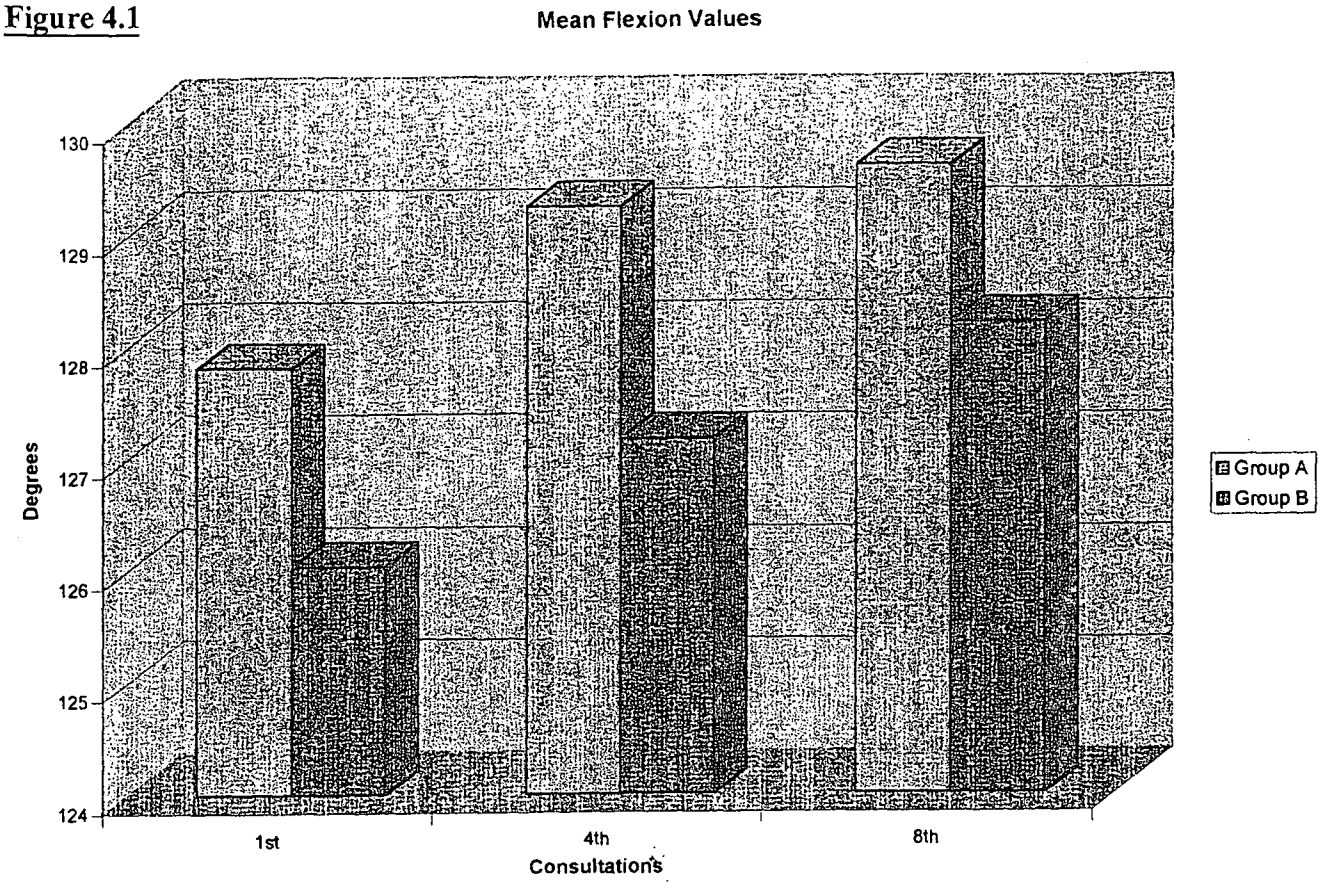


Figure 4.2

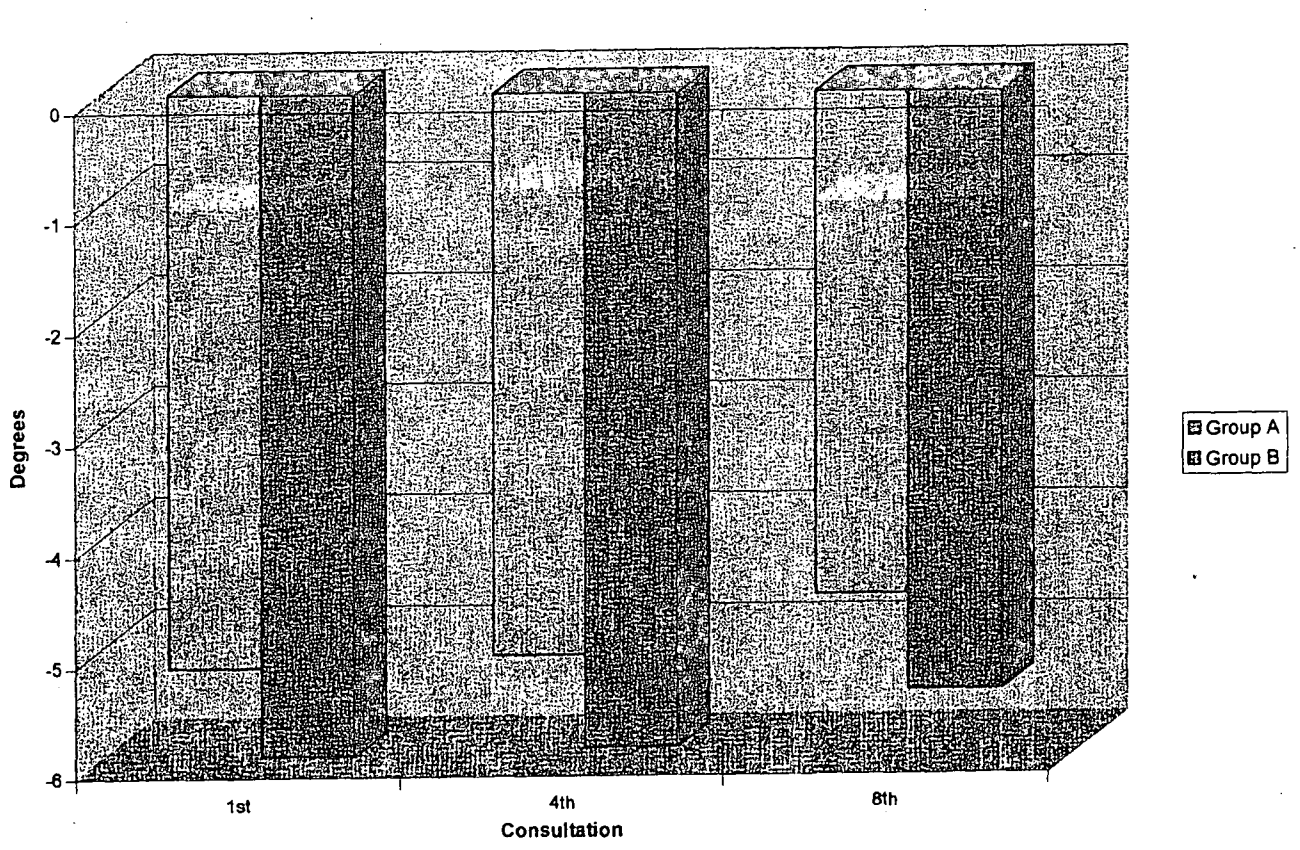


Figure 4.3

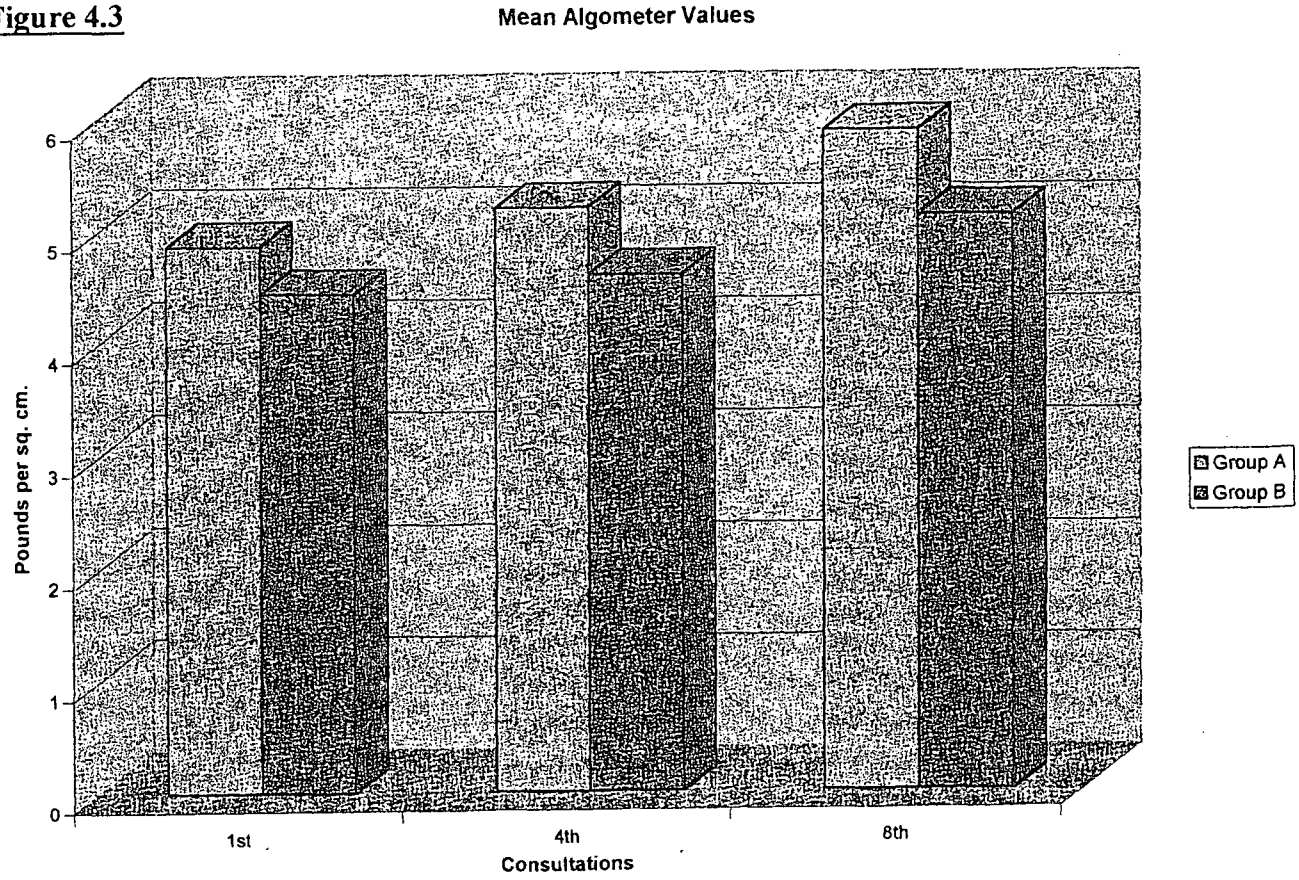


Figure 4.4

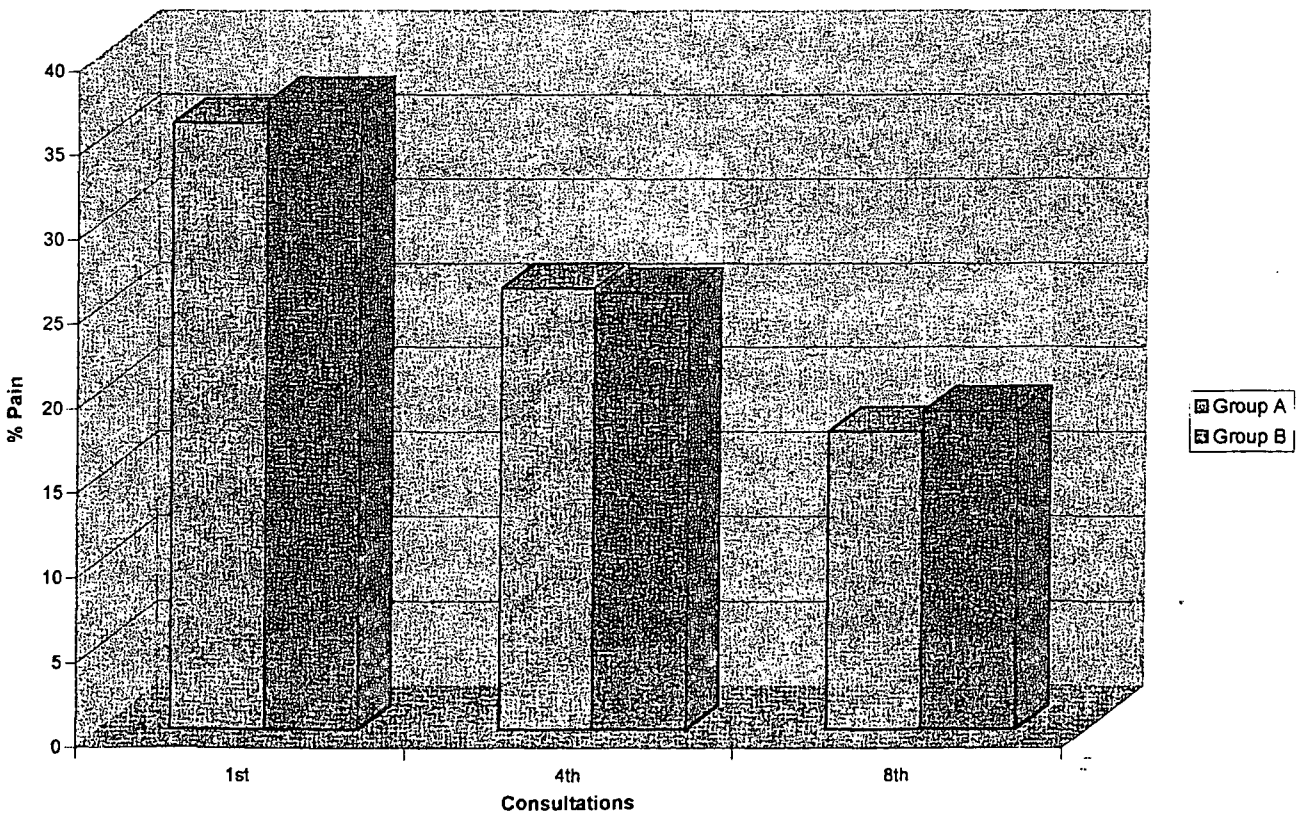


Figure 4.5

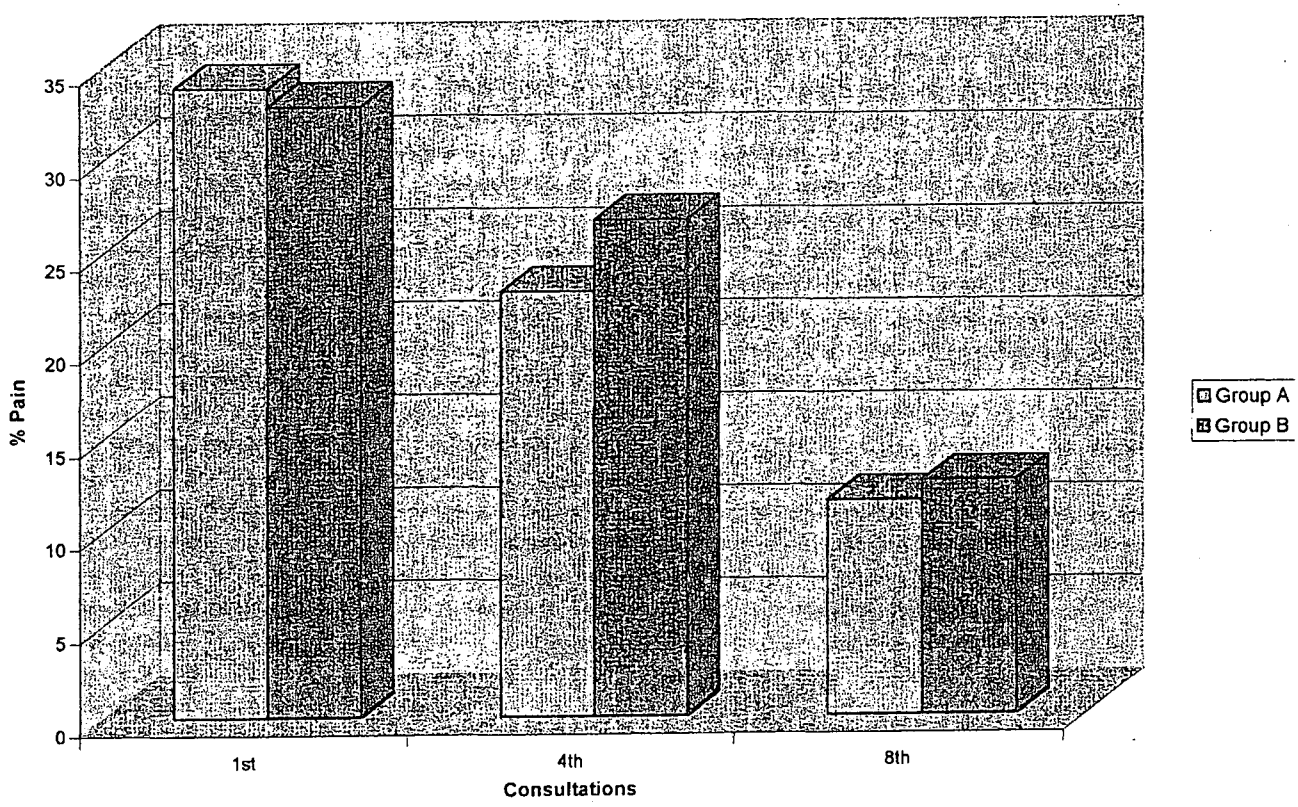
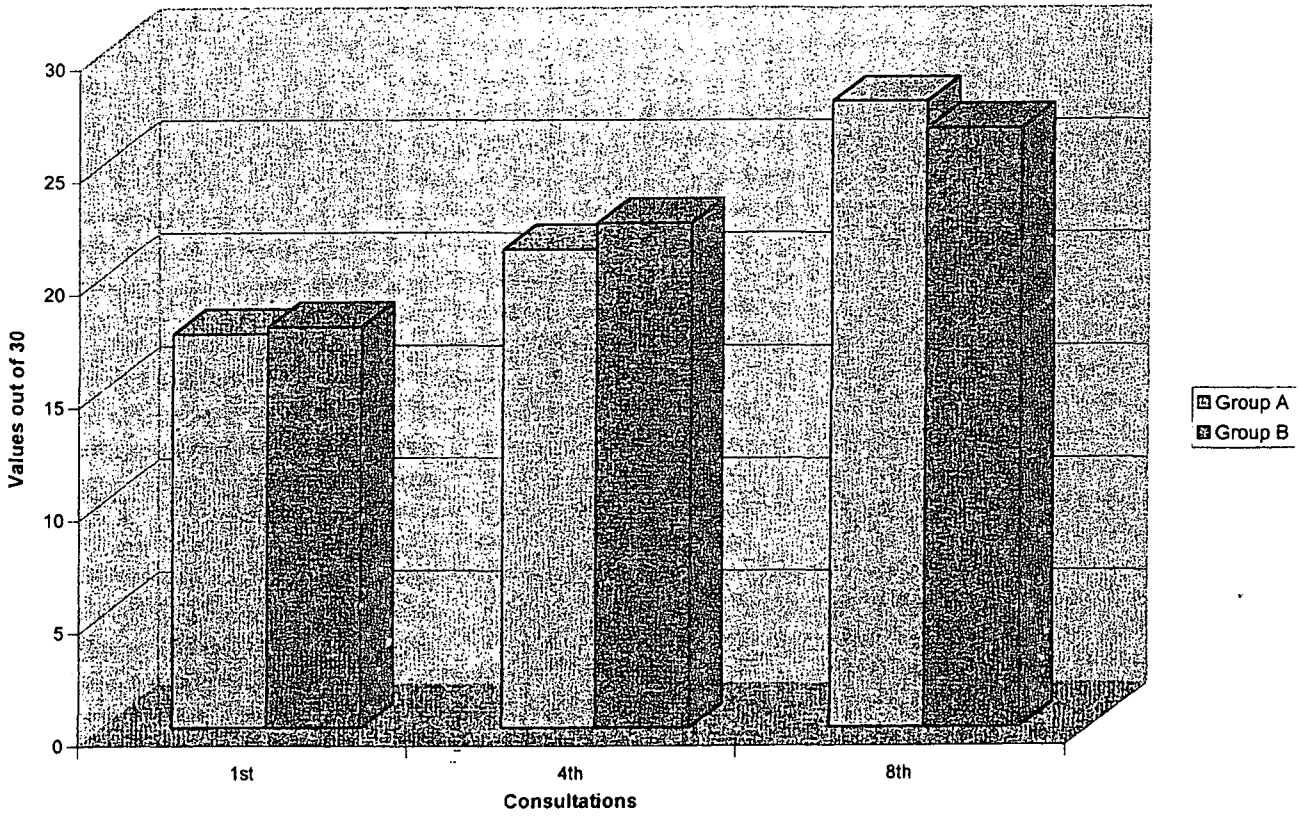


Figure 4.6



CHAPTER FIVE

5.0 DISCUSSION

5.1 Introduction

This chapter deals with the discussion of the objective and subjective data obtained from the first, fourth and eighth treatments.

- The objective data: algometer and goniometer
- The subjective data: Numerical Pain Rating Scale-101, Visual Analogue Scale and the Patient Specific Functional Scale.

The results are discussed in two sections:

Intra-treatment results: The evaluation of the data comparing the first and fourth consultations represents the initial efficacy of each treatment regime. An evaluation of the data comparing the fourth and eighth consultations represents the end- stage efficacy. Finally, an evaluation of the data comparing the first and eighth consultations indicates the extent to what the clinical condition has returned to baseline values, within each group evaluated.

Inter-treatment results: A comparison of the initial consultation from both groups is assessed in order to determine if there was any difference between the two groups in terms of signs and symptoms of the condition. A comparison of the fourth consultations from both groups is assessed in order to determine which treatment is more effective at this intermediate point. A comparison of the eighth consultations from both groups is

assessed in order to determine which treatment is more effective, at the end of the management protocol.

5.2 Intra-group comparison

5.2.1 Objective Data

5.2.1.1 Goniometer Readings.

The range of motion data for intra-treatment comparisons can be found in tables 4.13-4.18.

The manipulation group demonstrated a statistically significant improvement in results for flexion between the first and fourth and first and eighth consultations, demonstrating that manipulation was effective in improving flexion over the duration of the study. For extension, the manipulation group only showed a statistically significant improvement overall (between the first and eighth consultations), but not significantly between the first and fourth and fourth and eighth consultations. The meloxicam group only demonstrated a statistically significant improvement for extension between the fourth and eighth consultations. There was no statistically significant change for flexion or extension for any of the other consultations. Therefore meloxicam did not significantly improve the ranges of motion overall.

The intra-treatment results suggest that with regard to range of motion, manipulation produced better short-term results than N.S.A.I.D.'s. However, this statement was not supported by the inter-group comparison, which is covered further on.

5.2.1.2 Algometer Readings.

The algometer readings for the manipulation group showed no statistically significant improvement between the first and fourth consultations, however between the fourth and eighth and first and eighth consultations, there was a statistically significant improvement. This demonstrates that over the entire treatment period, manipulation significantly raised the patients pain threshold. The meloxicam group failed to show any statistically significant improvement between any of the consultations.

The results suggest that treatment with manipulation will result in the patient's pain threshold being higher over a longer period than with N.S.A.I.D.'s. However, this statement was not supported by the inter-group comparison, which is covered further on.

5.2.2 Subjective Data

5.2.2.1 The Numerical Pain Rating Scale-101.

Both the manipulation and meloxicam groups demonstrated a statistically significant improvement between all the data capturing consultations. These results indicate that over the same treatment period (three weeks), both treatment protocols were successful in significantly reducing pain.

5.2.2.2 The Visual Analogue Scale.

The manipulation group demonstrated a statistically significant improvement between all the data capturing consultations. The meloxicam group demonstrated that there was a statistically significant improvement between all the data capturing consultations except for between the first and fourth. These results indicate that both treatment protocols are effective in significantly reducing pain.

5.2.2.3 The Patient-Specific Functional Scale.

Both the manipulation and meloxicam groups demonstrated a statistically significant improvement in the P.S.F.S. readings between each of the data capturing consultations. This means that both treatment protocols are effective in improving function for patients over a three week period.

5.3 Inter-group comparison

Inter-group comparison of the subjective and objective data suggests that patients from Group A and Group B experienced relatively the same restricted range of motion (goniometer), pressure pain threshold (algometer), disability (P.S.F.S.) and pain intensity (N.R.S.-101, V.A.S.) at the first consultation.

5.3.1 Objective Data

5.3.1.1 Knee Range of Motion.

Statistical analysis revealed that after the fourth and eighth treatments, there was no statistically significant difference between Group A and Group B for flexion or extension. This indicates that at a 95% level of confidence, the two treatment protocols are equally effective in improving the range of motion of osteoarthritic knees.

5.3.1.2 Algometer.

Statistical analysis revealed that after the fourth and eighth consultations, there was no statistically significant difference between the two groups with respect to pressure pain thresholds.

Power analysis for all three assessments was weak, indicating the possibility of a type II error.

5.3.2 Subjective Data

5.3.2.1 Numerical Pain Rating Scale-101.

As mentioned previously, baseline values for both groups were very similar. Statistical analysis revealed that after the fourth and eighth consultations, there was no statistically significant difference between the two groups with respect to pain intensity. This means that both treatment protocols were effective in decreasing pain in osteoarthritis of the knee.

5.3.2.2 Visual Analogue Scale.

As mentioned previously, baseline values for both groups were very similar. Statistical analysis revealed that after the fourth and eighth consultations, there was no statistically significant difference between the two groups with respect to pain intensity. This means that both treatment protocols were effective in decreasing pain in osteoarthritis of the knee.

5.3.2.3 Patient Specific Functional Scale.

As mentioned previously, baseline values for both groups were very similar. Statistical analysis revealed that after the fourth and eighth consultations, there was no statistically significant difference between the two groups with respect to disability.

This means that both treatment protocols were effective in increasing function for osteoarthritis of the knee.

5.3.2.4 Standard deviation of Measurement.

The standard deviation is a measure of central tendency. Chapter Four of this study indicated that several of the results were not well centered around the mean. This could be due to the fact that there was a large dispersion of subjects leading to poor homogeneity within the study, as well as the study using a small sample size.

5.4 Outcome Commentary.

Although this study could not demonstrate any significant difference between the two groups, it has demonstrated that manipulation is effective in treating osteoarthritis of the knee. It can be concluded from the intra-group data analysis that both manipulation and N.S.A.I.D.'s effectively treat the subjective clinical aspects of osteoarthritis of the knee. However, only manipulation proved effective with regards to the objective clinical measurements. This however is not evident in the inter-group analysis as this study used a 95% level of confidence, and thus this assumption was not statistically supported.

The null hypothesis for the inter-group data analysis was that there would be no statistical difference between Group A and B in terms of subjective and objective clinical findings.

The null hypotheses for all three data collecting consultations were accepted as there was no statistical difference between the two groups for subjective and objective clinical findings. Thus it can be concluded that both manipulation and meloxicam are equally effective in the treatment of osteoarthritis of the knee.

5.5 Power Analysis

The power values for the continuous variables were low, indicating the possibility of a Type II error. However, there is a close connection between sample size and the power of a statistical test (Bailar III and Mosteller 1992: 359,387). The smaller the sample size the greater the risk of Type II error and thus a weaker power will probably be reflected. However, a larger sample size was not practical for this study due to financial and time constraints.

5.6 Discussion of the demographic data

The age distribution of patients in both groups was very similar, with both groups having the majority of patients falling into the 65-74 year old category, with the next highest age ratio falling into the 55-64 year old category (Table 4.3). The average age distribution was fairly similar between the two groups (Group A= 61.2; Group B= 57.4). The gender distribution was almost exactly equal between the two groups with a higher ratio of females (Table 4.4). There were surprisingly few black patients in this study, with the majority of patients being white (Table 4.5). This was possibly due to the fact that the

newspaper adverts were published in English, and distributed in a majority white area. It may also be due to the fact that chiropractic is a relatively unknown profession in the black community. This may have had a negative effect on the outcome of the study, as demographically, blacks make up a significant portion of O.A. sufferers. Both groups had very similar duration of pain distribution (Table 4.6). The majority of patients from both groups were retired (Table 4.7), which parallels with the average age distribution. Mean height and weight was also similar between the two groups with the exception of Group B being slightly heavier on average (Table 4.8).

The left knee was affected on average 16.6% more of the time with both knees being affected 23.3% of the time (Table 4.9)

5.7 Discussion of the manipulation and N.S.A.I.D. data

Table 4.10 discusses the type and number of adjustments per motion palpation finding. On average, the adjustment delivered the most was anterior to posterior and long axis distraction adjustments delivered to the tibio-femoral joint. The patello-femoral joint was manipulated in 73.33% of the patients. Each patient received on average 4 adjustments per consultation (Table 4.11).

Only 9.99% of patients experienced any adverse reaction to meloxicam. This compares to a multicentre, double blind, randomized study that was conducted by Hosie et al. (1996:39), in which adverse reactions were reported by 59.8% of the patients receiving meloxicam.

A large-scale, prospective, international, multi-center, double-blind, double-dummy, randomized, parallel-group trial comparing meloxicam to piroxicam in 8656 patients with O.A., showed the incidence of adverse events in the meloxicam group to be 22.5%.

5.8 Study limitations

Baseline characteristics for patients between both groups were very similar for age, gender distribution, height and weight and duration of knee pain. The baseline characteristics that were different for each group were the occupations of the patients. Although the majority of patients were retired, this did not divulge any information with regards to hobbies or activities that patients continued with in their retirement. This together with varying occupations in the remainder of the patient groups may have had an impact on the outcome of the study, as patients may have returned from the treatment to adopt a position of stress or aggravation upon the knee related to their occupation or extramural activity. This may have caused an early return of pain or disability. It was not possible to ensure absolute homogeneity in this study due to financial and time constraints.

The subjective measurements were not designed specifically for patients suffering from osteoarthritis of the knee. Patients may also have not fully understood the subjective questionnaires or may have exaggerated their improvement so as to please the researcher. The objective measurements may have the possibility of containing some error due to human error in taking the readings. The researcher also felt that the algometer readings might have been influenced by the fact that the clinic utilizes three algometers, which

apparently are re-calibrated yearly, but were not calibrated prior to the onset of the study, and which might also be susceptible to inter- algometer discrepancies. The state of some of the algometers was also questionable, as with some, the rubber disc at the point of application had become detached, and had to placed and held manually during each data capturing session.

Perhaps the biggest limitation to this study was the elimination of a long-term follow-up consultation, which might have divulged valuable information with regards to the long-term efficacy of these two treatments. An estimation as to the duration of pain relief and improvement of function whilst the patient is no longer receiving the treatment, would have been invaluable in a study of this nature.

Another obvious limitation is the sample size, which could not have been increased due to time and financial constraints.

It is also possible that an improvement in outcome in the manipulation group might have been possible, had the manipulations been performed by a practitioner of several years worth of experience and not by a student.

Whilst every effort was taken to ensure patients were compliant with taking their medication, there is the possibility that this might have not been the case.

CHAPTER SIX

6.0 RECOMMENDATIONS AND CONCLUSIONS

6.1 Recommendations.

In a study of this nature, it is always preferable to have a larger sample size, which would further more accurate results, and minimize the chances of a type II error. This was indicated by the variability of the standard deviation. Unfortunately, due to time and financial constraints, this was not possible. Of particular importance for future studies of this nature, is to include a long-term follow-up consultation of the patients after completion of the treatments. This would illicit vital information regarding the long-term efficacy of the respective treatments.

It is also recommended that patients be matched according to age, gender, duration of complaint, extent of pain and disability and occupation, in order to ensure homeogenity.

It would also be preferable for each research student to be assigned a specific, calibrated algometer at the commencement of the research study. This would prevent errors in data collection from inter-algometer variations.

6.2 Conclusion

The results of this study indicate that both manipulation and meloxicam are equally effective in treating osteoarthritis of the knee. At a 95% level of confidence neither group

showed any advantage over the other in treatment efficacy. The intra-group comparison was inclined to indicate that manipulation was more effective for the mean objective measurements, however this was not conclusive in the inter-group analysis using the statistical parameters employed in this study.

It would be of vital interest to perform a long-term follow up consultation after cessation of the treatment regimes. It is the researchers' opinion that manipulation would demonstrate greater long-term results, as this treatment addresses the biomechanical aspect of osteoarthritis. Many authors listed in this dissertation subscribe to the theory that it is this biomechanical aberration which causes the inflammation, pain and loss of function, which leads to this authors opinion that restoring biomechanical integrity, restores function to the joint and thereby prevents inflammation, reduces pain and improves function. N.S.A.I.D.'s, by nature, work through their inhibition of inflammatory mediators, thereby relieving pain and inflammation. It is this authors opinion that this reduction in inflammation and hence pain, is the cardinal reason for the patients improvement in function, however the anti-inflammatories failed to address what is causing the inflammation. Hertling & Kessler (1996: 48) propose that this amelioration of symptoms (through N.S.A.I.D.'s) may have long-term detrimental effects as the loss of pain protecting mechanism may cause the patient to overuse the knee in daily activity or through prescribed exercise programs. It is again this authors opinion that because N.S.A.I.D.'s only address reducing the inflammation, and not the cause of the inflammation, this group would experience a quicker return of pain and dysfunction, than the manipulation group.

In conclusion, this study has demonstrated that manipulation is as effective as meloxicam in the treatment of osteoarthritis of the knee. Due to the possible deleterious effects encountered with certain percentages of the population (especially the elderly when treating osteoarthritis) N.S.A.I.D.' therapy should be restricted to episodes of acute inflammation. In conjunction with the judicious use of this drug, the osteoarthritic knee should undergo an evaluation of its biomechanical integrity and appropriate chiropractic manipulative procedures administered by a qualified practitioner.

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APPENDIX H

SCHEDULING STATUS S3

PROPRIETARY NAME (and dosage form) **Mobic®**
7,5 mg tablet

COMPOSITION
Each MOBIC 7,5 mg tablet contains 7,5 mg meloxicam.
The tablets do not contain tartrazine.

PHARMACOLOGICAL CLASSIFICATION
A3.1 Antirheumatics (anti-inflammatory agents).

PHARMACOLOGICAL ACTION
MOBIC is a non-steroidal anti-inflammatory drug (NSAID) of the enolic acid class which has shown anti-inflammatory, analgesic and antipyretic properties in animals.
A common mechanism for the above effects may exist in the ability of MOBIC to inhibit the biosynthesis of prostaglandins, known mediators of inflammation.
A selective inhibition of cyclooxygenase-2 (COX-2) relative to cyclooxygenase-1(COX-1) by meloxicam has been demonstrated in vitro on various cell systems. COX-2 inhibition relates to the anti-inflammatory effects of NSAIDs whereas inhibition of constitutive COX-1 is thought to be responsible for gastric and renal side-effects.

Pharmacokinetic properties
Meloxicam is 89 % absorbed following peroral administration. The absorption is not altered by concomitant food intake. Drug concentrations are dose-proportioned for peroral 7,5 and 15 mg doses, respectively. Steady state conditions are achieved in three to five days. Continuous treatment for periods of more than one year results in similar drug concentrations to those seen once steady state is first achieved. In plasma, more than 99 % is bound to plasma proteins. Once daily dosing leads to drug plasma concentrations with a relatively small peak-trough fluctuation in the range of 0,4 – 1,0 µg / ml for 7,5 mg doses or 0,8 – 2 µg / ml for 15 mg doses, although values outside this range have been encountered.
Meloxicam penetrates into synovial fluid to give concentrations approximately half those in plasma.
Meloxicam is extensively metabolised and less than 5 % of the daily dose is excreted unchanged in faeces, while only traces of the unchanged compound are excreted in urine. The major metabolic pathway is the oxidation of the methyl group of the thiazolyl-moeity of the substance, followed by urinary or faecal excretion of the metabolites. About half of the substance is excreted in urine, the remainder in the stool.
Meloxicam is eliminated from the body with a mean elimination half-life of 20 hours. Neither hepatic, nor mild or moderate renal insufficiency do substantially affect meloxicam pharmacokinetics.

Plasma clearance is on average 8 ml / min. Clearance is halved in the elderly. Volume of distribution is low, on average 10 litres. Interindividual variation is the order of 30 – 40 %.

INDICATIONS
MOBIC is indicated for:
- symptomatic treatment of rheumatoid arthritis.
- symptomatic treatment of painful osteoarthritis.
- symptomatic treatment of ankylosing spondylitis.

CONTRA-INDICATIONS
Known hypersensitivity to meloxicam or any excipient of the drug. There is a potential for cross sensitivity to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs).
MOBIC should not be given to patients who have developed signs of asthma, nasal polyps, angioedema or urticaria following the administration of acetyl salicylic acid or other NSAIDs.

Further contra-indications for the use of MOBIC are active peptic ulceration, severe hepatic insufficiency, non-dialysed severe renal insufficiency and children and adolescents aged less than 15 years. The safe use of MOBIC during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE
Rheumatoid arthritis and ankylosing spondylitis:
15 mg / day. According to the therapeutic response, the dose may be reduced to 7,5 mg / day.
Osteoarthritis:
7,5 mg / day. If necessary, the dose may be increased to 15 mg / day.
In patients with increased risks of adverse reactions (e.g. the elderly), start treatment at the dose of 7,5 mg / day.
In dialysis patients with severe renal failure the dose should not exceed 7,5 mg / day.
The maximum recommended daily dose of MOBIC is 15 mg.

As a dosage for use in children has yet to be established, MOBIC should not be used in children and adolescents aged less than 15 years.

MOBIC tablets should be swallowed with water or other fluid in conjunction with food.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Precautions:
Caution should be exercised when treating patients with a history of upper gastrointestinal disease and in patients receiving treatment with anticoagulants. MOBIC should be withdrawn if peptic ulceration or gastrointestinal bleeding occurs.

In patients reporting mucocutaneous adverse events special attention should be paid and consideration given to discontinuing MOBIC.

Meloxicam inhibits the synthesis of renal prostaglandins which play a supportive role in the maintenance of renal perfusion in patients whose renal blood flow and blood volume are decreased. In these patients administration of meloxicam may precipitate overt renal decompensation which is typically followed by recovery to pre treatment state upon discontinuation of therapy. Patients at greatest risk of such a reaction are dehydrated patients, those with congestive heart failure, liver cirrhosis, nephrotic syndrome and overt renal disease, those receiving a diuretic or those having undergone major surgical procedures which led to hypovolaemia. In such patients the volume of diuresis and the renal function should be carefully monitored at the beginning of therapy.

Meloxicam may cause interstitial nephritis, glomerulonephritis, papillary necrosis and the nephrotic syndrome.

The dose of MOBIC patients with end-stage renal failure on haemodialysis should not be higher than 7,5 mg. No dose reduction is required in patients with mild or moderate renal impairment (i.e. in patients with a creatinine clearance of greater than 25 ml / min).

Occasional elevations of serum transaminases or other indicators of liver function have been reported. In most cases these have been small and transient increases above the normal range. If the abnormality is significant or persistent, MOBIC should be stopped and follow up tests carried out.
No dose reduction is required in patients with clinically stable liver cirrhosis.

Frail or debilitated patients may tolerate side-effects less well and such patients should be carefully supervised. Caution should be used in the treatment of elderly patients who are more likely to be suffering from impaired renal, hepatic or cardiac function.

There are no specific studies about effects on the ability to drive vehicles and to use machinery. However when adverse effects such as vertigo and drowsiness occur it is advisable to refrain from these activities.

Drug Interactions:
The concomitant administration of more than one NSAID (including salicylates) may increase the risk of gastrointestinal ulceration and bleeding through synergistic action. Plasma levels (AUC) of MOBIC are increased by 30% when MOBIC is administered in conjunction with aspirin (3000 mg/day).

An increased risk of bleeding through inhibition of platelet function and irritation of the gastroduodenal mucosa may occur when MOBIC is condministered with oral anticoagulants, parentally administered heparin, thrombolytics and ticlopidine. Interactions with coumarin-type anticoagulants have been reported with NSAIDs. If such a co-prescription cannot be avoided, close monitoring of the effects of anticoagulants is required.

NSAIDs have been reported to increase plasma lithium levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing MOBIC treatment.

MOBIC may increase the haematologic toxicity of methotrexate. In this situation, strict monitoring of blood cell count is recommended.

NSAIDs have been reported to decrease the efficacy of intrauterine devices.

Treatment with MOBIC is associated with the potential for acute renal insufficiency in patients who are dehydrated. Patients receiving MOBIC and diuretics should be adequately hydrated and be monitored for renal function prior to initiating treatment.

A reduced effect of antihypertensive medicines (ß-blockers, ACE-inhibitors, vasodilators, diuretics) by inhibition of vasodilating prostaglandins has been reported during treatment with NSAIDs.

Cholestyramine binds meloxicam in the gastrointestinal tract leading to a faster elimination of meloxicam.

Nephrotoxicity of cyclosporin may be enhanced by MOBIC via renal prostaglandin mediated effects. During combined treatment renal function should be assessed regularly.

No relevant pharmacokinetic drug-drug interactions were detected with respect to the concomitant administration of antacid, cimetidine, digoxin and furosemide.

Interactions with oral anti-diabetics cannot be excluded.

Side-effects:
Gastrointestinal symptoms are the most commonly encountered side-effects. There is a risk of peptic ulceration and gastrointestinal bleeding.

The following adverse reactions were reported in subjects treated with recommended doses of MOBIC:

Gastrointestinal:

More frequent:	dyspepsia, nausea, abdominal pain, vomiting, diarrhoea, constipation, flatulence.
Less frequent:	abnormalities of liver function parameters (e.g. raised transaminases or bilirubin) eructation, oesophagitis, gastroduodenal ulcer, occult or macroscopic gastrointestinal bleeding.
Occasionally:	gastrointestinal perforation, colitis.

PATIENT INFORMATION LEAFLET

MOBIC® 7,5 mg Tablets

Read this leaflet about MOBIC tablets before you start treatment. If any of this information causes you concern or if you need more information, contact your doctor or pharmacist.

Composition:

MELOXICAM (mel-ox-i-kam) 7,5 mg per tablet.
Lactose – caution lactose intolerant patients.

Medicine Uses:

MOBIC is used to relieve symptoms of arthritis such as joint pain and inflammation in patients over 15 years of age.
Meloxicam belongs to a class of medicines called non-steroidal anti-inflammatories.
These medicines are usually used to treat inflammation, swelling, stiffness, pain and fever

How to use this medicine:

Follow the directions for using this medicine as provided by your doctor or pharmacist.
MOBIC is usually taken in a dose of:
- *One or two tablets taken ONCE DAILY with a FULL* GLASS OF WATER or other fluid and WITH OR AFTER FOOD.
  Do not take more than two tablets a day.
  If you MISS A DOSE OF THIS MEDICINE, take it as soon as you remember. However, if it is almost time for the next dose, skip the missed dose and go back to your normal dosing schedule. DO NOT DOUBLE THE DOSE.

Before using this medicine:

- Tell your doctor and pharmacist about any **other medicines** that you are taking – both prescription medicines and medicines bought over the counter such as **aspirin** and other **anti-inflammatories**. Meloxicam *may interact with prescription medicines such as lithium,* methotrexate, cyclosporin, blood thinners and certain medicines used to treat high blood pressure and diabetes.
- Note that meloxicam may reduce the contraceptive effectiveness of the intra-uterine device (IUD).
- Check with your doctor and pharmacist if you are pregnant, intend to become pregnant or are breast-feeding while using this medicine.
- Check with your doctor if you are allergic to aspirin or have experienced asthma symptoms after taking anti-inflammatory medicines in the past. Also, check with your doctor if you have a stomach ulcer, bleeding problems, reduced liver, kidney or heart function.
- MOBIC may cause stomach irritation. To reduce this effect, take MOBIC tablets with or after food and with a full glass of fluid (e.g. water or milk).

Side-effects:

These possible side-effects may go away during treatment as your body adjusts to the medicine. If they continue or bother you, check with your doctor or pharmacist.
More common (greater than 1 % of patients)
- nausea, vomiting, heartburn, stomach upset or abdominal pain
- light-headedness or headache

Less common or rare (less than 0.1 to 1 % of patients)
- *increased sun sensitivity*
- *drowsiness or dizziness*
- hot flushes or increased sweating

Although the following side-effects are rare, if they do occur they need medical attention. Contact your doctor as soon as possible if you notice:
- any difficulty in breathing
- unusual heartbeat or palpitations
- severe, persistent abdominal pain
- any changes in urination
- bloody or black-coloured stools
- unusual bleeding or bruising
- sore throat, fever and chills
- vomiting blood or material that looks like coffee grounds
- swelling of face, feet or lower legs
- skin rash or *itching*
- yellow eyes or skin
- ringing in the ears

If you notice any other effects, contact your doctor or pharmacist.

Storage and disposal:

Store MOBIC tablets in a cool place (below 25 °C) **out of reach of children.**
Return unused medicines to your pharmacist for safe disposal.
Do not share medicines that have been prescribed for you with others.

Overdose:

In the event of an overdose or accidental ingestion, contact your doctor immediately or take the patient to the nearest hospital.

MOBIC 7,5 mg tablet
Ingelheim Pharmaceuticals (Pty) Ltd
Pine Avenue
Randburg

symptomatic treatment of rheumatoid osteoarthritis.
symptomatic treatment of ankylosing spondylitis.

[redacted] INDICATIONS
[redacted]persensitivity to meloxicam or any excipient of the drug. There is a potential for cross sensitivity to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs).
OBIC should not be given to patients who have developed signs of asthma, nasal polyps, angioedema or urticaria following the administration of acetyl salicylic acid or other NSAIDs.

[redacted]ontra-indications for the use of MOBIC are active peptic ulceration, severe hepatic insufficiency, non-dialysed severe renal [redacted]cy and children and adolescents aged less than 15 years. The safe use of MOBIC during pregnancy and lactation has not [redacted]en established.

OSAGE AND DIRECTIONS FOR USE
heumatoid arthritis and ankylosing spondylitis:
[redacted]day. According to the therapeutic response, the dose may be reduced to 7,5 mg / day.
[redacted]ritis:
[redacted]day. If necessary, the dose may be increased to 15 mg / day.
patients with increased risks of adverse reactions (e.g. the elderly), start treatment at the dose of 7,5 mg / day.
dialysis patients with severe renal failure the dose should not exceed 7,5 mg / day.
e maximum recommended daily dose of MOBIC is 15 mg.

[redacted]ge for use in children has yet to be established, MOBIC should not be used in children and adolescents aged less than 15 [redacted]

OBIC tablets should be swallowed with water or other fluid in conjunction with food.

DE-EFFECTS AND SPECIAL PRECAUTIONS
[redacted]ections:
[redacted]ould be exercised when treating patients with a history of upper gastrointestinal disease and in patients receiving treatment [redacted]coagulants. MOBIC should be withdrawn if peptic ulceration or gastrointestinal bleeding occurs.

patients reporting mucocutaneous adverse events special attention should be paid and consideration given to discontinuing OBIC.

[redacted]loxicam inhibits the synthesis of renal prostaglandins which play a supportive role in the maintenance of renal perfusion in patients [redacted]*al blood flow and blood volume are decreased. In these patients administration of meloxicam may precipitate overt renal [redacted]sation which is typically followed by recovery to pre treatment state upon discontinuation of therapy.* Patients at greatest [redacted]of such a reaction are dehydrated patients, those with congestive heart failure, liver cirrhosis, nephrotic syndrome and overt renal [redacted]ease, those receiving a diuretic or those having undergone major surgical procedures which led to hypovolaemia. In such patients [redacted]volume of diuresis and the renal function should be carefully monitored at the beginning of therapy.

[redacted]loxicam may cause interstitial nephritis, glomerulonephritis, papillary necrosis and the nephrotic syndrome.

[redacted]of MOBIC patients with end-stage renal failure on haemodialysis should not be higher than 7,5 mg. No dose reduction is [redacted]quired in patients with mild or moderate renal impairment (i.e. in patients with a creatinine clearance of greater than 25 ml / min).

[redacted]casional elevations of serum transaminases or other indicators of liver function have been reported. In most cases these have [redacted]n small and transient increases above the normal range. If the abnormality is significant or persistent, MOBIC should be stopped [redacted]up tests carried out.
[redacted]duction is required in patients with clinically stable liver cirrhosis.

[redacted]ll or debilitated patients may tolerate side-effects less well and such patients should be carefully supervised. Caution should be [redacted]d in the treatment of elderly patients who are more likely to be suffering from impaired renal, hepatic or cardiac function.

[redacted]are are no specific studies about effects on the ability to drive vehicles and to use machinery. However when adverse effects such [redacted]vertigo and drowsiness occur it is advisable to refrain from these activities.

[redacted]ractions:
Concomitant administration of more than one NSAID (including salicylates) may increase the risk of gastrointestinal ulceration [redacted]bleeding through synergistic action. Plasma levels (AUC) of MOBIC are increased by 30% when MOBIC is administered in [redacted]junction with aspirin (3000 mg/day).

[redacted]increased risk of bleeding through inhibition of platelet function and irritation of the gastroduodenal mucosa may occur when [redacted]Bcoadministered with oral anticoagulants, parentally administered heparin, thrombolytics and ticlopidine. Interactions with [redacted]type anticoagulants have been reported with NSAIDs. If such a co-prescription cannot be avoided, close monitoring of the [redacted]cts of anticoagulants is required.

[redacted]NSAIDs have been reported to increase plasma lithium levels. It is recommended that plasma lithium levels be monitored when [redacted]rting, adjusting and discontinuing MOBIC treatment.

[redacted]may increase the haematologic toxicity of methotrexate. In this situation, strict monitoring of blood cell count is [redacted]ded.

[redacted]NSAIDs have been reported to decrease the efficacy of intrauterine devices.

[redacted]tment with MOBIC is associated with the potential for acute renal insufficiency in patients who are dehydrated. Patients receiving [redacted]BIC and diuretics should be adequately hydrated and be monitored for renal function prior to initiating treatment.

[redacted]effect of antihypertensive medicines (β-blockers, ACE-inhibitors, vasodilators, diuretics) by inhibition of vasodilating [redacted]ins has been reported during treatment with NSAIDs.

[redacted]lestyramine binds meloxicam in the gastrointestinal tract leading to a faster elimination of meloxicam.

[redacted]nrotoxicity of cyclosporin may be enhanced by MOBIC via renal prostaglandin mediated effects. During combined treatment [redacted]function should be assessed regularly.

[redacted] pharmacokinetic drug-drug interactions were detected with respect to the concomitant administration of antacid, [redacted]tidine, digoxin and furosemide.

[redacted]actions with oral anti-diabetics cannot be excluded.

[redacted]-effects:
[redacted]nal symptoms are the most commonly encountered side-effects. There is a risk of peptic ulceration and gastrointestinal [redacted]

[redacted]following adverse reactions were reported in subjects treated with recommended doses of MOBIC:

[redacted]rointestinal:
[redacted]frequent: dyspepsia, nausea, abdominal pain, vomiting, diarrhoea, constipation, flatulence.
[redacted]t: abnormalities of liver function parameters (e.g. raised transaminases or bilirubin) eructation, oesophagitis, gastroduodenal ulcer, occult or macroscopic gastrointestinal bleeding.
[redacted]sionally: gastrointestinal perforation, colitis.

[redacted]matological:
[redacted]frequent: anaemia.
[redacted]frequent: disturbances of blood count, including differential white cell count, leukopenia and thrombocytopenia. Concomitant administration of a potentially myelotoxic drug, in particular methotrexate, appears to be a predisposing factor to the onset of a cytopenia.

[redacted]atological:
[redacted]frequent: pruritus, skin rash.
[redacted]frequent: stomatitis, urticaria.
[redacted]: photosensitisation.
[redacted]y: onset of acute asthma has occasionally been reported in certain individuals following the administration of MOBIC.

[redacted]al nervous system:
[redacted]frequent: lightheadedness, headache.
[redacted]t: vertigo, tinnitus, drowsiness.

[redacted]ular:
[redacted]frequent: oedema.
[redacted]requent: increase of blood pressure, palpitations, flushes.

[redacted]urinary:
[redacted]: abnormal renal function parameters (increased serum creatinine and / or serum urea).

[redacted]MPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
[redacted]of overdose, the standard measures of gastric evacuation and general symptomatic and supportive treatment should be used [redacted]re is no known antidote. It has been shown in a clinical trial that cholestyramine accelerates the elimination of meloxicam.

[redacted]IFICATION
[redacted]g tablets are round, pale yellow tablets. One face is convex, has a bevelled edge and is impressed with the Company's [redacted]ther face is impressed with the tablet code 59D and is scored across its entire diameter.

[redacted]ENTATION
[redacted]s of 30 MOBIC 7,5 mg tablets packed in blister strips.

[redacted]AGE INSTRUCTIONS
[redacted]5 °C. Keep out of reach of children.

[redacted]ION NUMBER
[redacted]421

[redacted] AND BUSINESS ADDRESS OF THE APPLICANT
[redacted]im Pharmaceuticals (Pty) Ltd
[redacted]

[redacted]OF PUBLICATION OF THIS PACKAGE INSERT
[redacted]mber 1997.

C317/3

Do not take more than two tablets a day.
If you MISS A DOSE OF THIS MEDICINE, take it as soon as you remember. However, if it is almost time for the next dose, skip the missed dose and go back to your normal dosing schedule. DO NOT DOUBLE THE DOSE.

Before using this medicine:

- Tell your doctor and pharmacist about any other medicines that you are taking – both prescription medicines and medicines bought over the counter such as aspirin and other anti-inflammatories. Meloxicam may interact with prescription medicines such as lithium, methotrexate, cyclosporin, blood thinners and certain medicines used to treat high blood pressure and diabetes.
- Note that meloxicam may reduce the contraceptive effectiveness of the intra-uterine device (IUD).
- Check with your doctor and pharmacist if you are pregnant, intend to become pregnant or are breast-feeding while using this medicine.
- Check with your doctor if you are allergic to aspirin or have experienced asthma symptoms after taking anti-inflammatory medicines in the past. Also, check with your doctor if you have a stomach ulcer, bleeding problems, reduced liver, kidney or heart function.
- MOBIC may cause stomach irritation. To reduce this effect, take MOBIC tablets with or after food and with a full glass of fluid (e.g. water or milk).

Side-effects:

These possible side-effects may go away during treatment as your body adjusts to the medicine. If they continue or bother you, check with your doctor or pharmacist.
More common (greater than 1 % of patients)
- nausea, vomiting, heartburn, stomach upset or abdominal pain
- light-headedness or headache

Less common or rare (less than 0.1 to 1 % of patients)
- increased sun sensitivity
- drowsiness or dizziness
- hot flushes or increased sweating

Although the following side-effects are rare, if they do occur they need medical attention. Contact your doctor as soon as possible if you notice:
- any difficulty in breathing
- unusual heartbeat or palpitations
- severe, persistent abdominal pain
- any changes in urination
- bloody or black-coloured stools
- unusual bleeding or bruising
- sore throat, fever and chills
- vomiting blood or material that looks like coffee grounds
- swelling of face, feet or lower legs
- skin rash or itching
- yellow eyes or skin
- ringing in the ears

If you notice any other effects, contact your doctor or pharmacist.

Storage and disposal:

Store MOBIC tablets in a cool place (below 25 °C) **out of reach of children.**
Return unused medicines to your pharmacist for safe disposal.
Do not share medicines that have been prescribed for you with others.

Overdose:

In the event of an overdose or accidental ingestion, contact your doctor immediately or take the patient to the nearest hospital.

MOBIC 7,5 mg tablet
Ingelheim Pharmaceuticals (Pty) Ltd
Pine Avenue
Randburg

Version May 1996
Information in this monograph is for use as an educational aid only. It is not intended as individual advice. It does not cover all possible uses, actions, precautions, side-effects or interactions of this medicine. Consult your doctor or pharmacist for further and individual advice.

APPENDIX B

TECHNIKON NATAL CHIROPRACTIC DAY CLINIC
CASE HISTORY

Patient:_____ Date: _____
file #:_____ X-Ray#:_____
Age:_____ Sex:_____ Occupation:_____
Intern:_____ Signature:_____

FOR CLINICIAN'S USE ONLY
Initial visit clinician:_____Signature:_____

Case History:

Examination:
Previous: Current:

X-Ray Studies:
Previous: Current:

Clinical Path. lab:
Previous: Current:

Case Status:

PTT: Conditional: Signed Off: Final Sign out:

Recommendations:

Intern's Case History

1. Source of History:

2. Chief Complaint: (patient's own words)

3. Present Illness:

- Location
- Onset
- Duration
- Frequency
- Pain (Character)
- Progression
- Aggravating Factors
- Relieving Factors
- Associated S & S
- Previous Occurrences
- Past Treatment and Outcome

4. Other Complaints:

5. Past Medical History:

- General Health Status
- Childhood Illnesses
- Adult Illnesses
- Psychiatric Illnesses
- Accidents/Injuries
- Surgery
- Hospitalizations

6. Current health status and life-style:

- Allergies
- Immunizations
- Screening Tests
- Environmental Hazards (Home, School, Work)
- Safety Measures (seat belts, condoms)
- Exercise and Leisure
- Sleep Patterns
- Diet
- Current Medication
- Tobacco
- Alcohol
- Social Drugs

7. Immediate Family Medical History:

- Age
- Health
- Cause of Death
- DM
- Heart Disease
- TB
- Stroke
- Kidney Disease
- CA
- Arthritis
- Anaemia
- Headaches
- Thyroid Disease
- Epilepsy
- Mental Illness
- Alcoholism
- Drug Addiction
- Other

8. Psychosocial history:

- Home Situation and daily life
- Important experiences
- Religious Beliefs

9. Review of Systems:

- General
- Skin
- Head
- Eyes
- Ears
- Nose/Sinuses
- Mouth/Throat
- Neck
- Breasts
- Respiratory
- Cardiac
- Gastro-intestinal
- Urinary
- Genital
- Vascular
- Musculoskeletal
- Neurologic
- Haematologic
- Endocrine
- Psychiatric

APPENDIX C

TECHNIKON NATAL

TECHNIKON NATAL CHIROPRACTIC DAY CLINIC

PHYSICAL EXAMINATION

Patient:_____File#: _____Date:_____
Clinician:_____Signature:_____
Intern:_____Signature:_____

1. VITALS

Pulse rate:
Respiratory rate:
Blood pressure: R L
Temperature:
Height:
Weight:

2. GENERAL EXAMINATION

General Impression:
Skin:
Jaundice:
Pallor:
Clubbing:
Cyanosis (Central/Peripheral):
Oedema:
Lymph nodes - Head and neck:
- Axillary:
- Epitrochlear:
- Inguinal:

Urinalysis:

3. CARDIOVASCULAR EXAMINATION

1) Is this patient in **Cardiac Failure** ?
2) Does this patient have signs of **Infective Endocarditis** ?
3) Does this patient have **Rheumatic Heart Disease ?**

Inspection - Scars
- Chest deformity:
- Precordial bulge:
- Neck -JVP:

Palpation: - Apex Beat (character + location):
- Right or left ventricular heave:
- Epigastric Pulsations:
- Palpable P2:
- Palpable A2:

Pulses:
- General Impression:
- Radio-femoral delay:
- Carotid:
- Radial:
- Dorsalis pedis:
- Posterior tibial:
- Popliteal:
- Femoral:

Percussion: - borders of heart

Auscultation:
- heart valves (mitral, aortic, tricuspid, pulmonary)
- Murmurs (timing,systolic/diastolic, site, radiation, grade).

4. RESPIRATORY EXAMINATION

1) Is this patient in **Respiratory Distress** ?

Inspection
- Barrel chest:
- Pectus carinatum/cavinatum:
- Left precordial bulge:
- Symmetry of movement:
- Scars:

Palpation
- Tracheal symmetry:
- Tracheal tug:
- Thyroid Gland:
- Symmetry of movement (ant + post)
- Tactile fremitus:

Percussion
- Percussion note:
- Cardiac dullness:
- Liver dullness:

Auscultation
- Normal breath sounds bilat.:
- Adventitious sounds (crackles, wheezes, crepitations)
- Pleural frictional rub:
- Vocal resonance
  - Whispering pectoriloquy:
  - Bronchophony:
  - Egophony:

5. ABDOMINAL EXAMINATION

1) Is this patient in **Liver Failure** ?

Inspection
- Shape:
- Scars:
- Hernias:

Palpation
- Superficial:
- Deep = Organomegally:

- Masses (intra- or extramural)
- Aorta:

Percussion - Rebound tenderness:
- Ascites:
- Masses:

Auscultation - Bowel sounds:
- Arteries (aortic, renal, iliac, femoral, hepatic)

Rectal Examination
- Perianal skin:
- Sphincter tone & S4 Dermatome:
- Obvious masses:
- Prostate:
- Appendix:

6. G.U.T EXAMINATION

External genitalia:
Hernias:
Masses:
Discharges:

7. NEUROLOGICAL EXAMINATION

Gait and Posture
- Abnormalities in gait:
- Walking on heels (L4-L5):
- Walking on toes (S1-S2):
- Rombergs test (Pronator Drift):

Higher Mental Function
- Information and Vocabulary:
- Calculating ability:
- Abstract Thinking:

G.C.S.:
- Eyes:
- Motor:
- Verbal:

Evidence of head trauma:

Evidence of Meningism:
- Neck mobility and Brudzinski's sign:
- Kernigs sign:

Cranial Nerves:

I Any loss of smell/taste:
Nose examination:

II External examination of eye:
- Visual Acuity:
- Visual fields by confrontation:

- Pupillary light reflexes = Direct:
  = Consensual:
- Fundoscopy findings:

III Ocular Muscles:
Eye opening strength:

IV Inferior and Medial movement of eye:

V a. Sensory - Ophthalmic:
- Maxillary:
- Mandibular:

b. Motor - Masseter:
- Jaw lateral movement:

c. Reflexes - Corneal reflex
- Jaw jerk

VI Lateral movement of eyes

VII a. Motor - Raise eyebrows:
- Frown:
- Close eyes against resistance:
- Show teeth:
- Blow out cheeks:

b. Taste - Anterior two-thirds of tongue:

VIII General Hearing:
Rinnes = L: R:
Webers lateralisation:
Vestibular function - Nystagmus:
- Rombergs:
- Wallenbergs:
Otoscope examination:

IX & X Gag reflex:
Uvula deviation:
Speech quality:

XI Shoulder lift:
S.C.M. strength:

XII Inspection of tongue (deviation):

Motor System:

a. Power
- Shoulder = Abduction & Adduction:
  = Flexion & Extension:
- Elbow = Flexion & Extension:
- Wrist = Flexion & Extension:

- Forearm = Supination & Pronation:
- Fingers = Extension (Interphalangeals & M.C.P's):
- Thumb = Opposition:
- Hip = Flexion & Extension:
  = Adduction & Abduction:
- Knee = Flexion & Extension:
- Foot = Dorsiflexion & Plantar flexion:
  = Inversion & Eversion:
  = Toe (Plantarflexion & Dorsiflexion):

b. Tone
- Shoulder:
- Elbow:
- Wrist:
- Lower limb - Int. & Ext. rotation:
- Knee clonus:
- ankle clonus:

c. Reflexes
- Biceps:
- Triceps:
- Supinator:
- Knee:
- Ankle:
- Abdominal:
- Plantar:

Sensory System:

a. Dermatomes
- Light touch:
- Crude touch:
- Pain:
- Temperature:
- Two point discrimination:

b. Joint position sense
- Finger:
- Toe:

c. Vibration:
- Big toe:
- Tibial tuberosity:
- ASIS:
- Interphalangeal Joint:
- Sternum:

Cerebellar function:

Obvious signs of cerebellar dysfunction:
= Intention Tremor:
= Nystagmus:
= Truncal Ataxia:

Finger-nose test (Dysmetria):
Rapid alternating movements (Dysdiadochokinesia):
Heel-shin test:
Heel-toe gait:
Reflexes:
Signs of Parkinsons:

8. **SPINAL EXAMINATION:**(See Regional examination)

Obvious Abnormalities:
Spinous Percussion:
R.O.M:
Other:

9. **BREAST EXAMINATION:**

Summon female chaperon.

Inspection
- Hands rested in lap:
- Hands pressed on hips:
- Arms above head:
- Leaning forward:

Palpation
- masses:
- tenderness:
- axillary tail:
- nipple:
- regional lymph nodes:

APPENDIX D

TECHNIKON NATAL

Knee regional examination

Patient:_____ File #:_____ Date:_____
Intern:_____ Signature:_____
Clinician:_____ Signature:_____

Observation (Standing, Seated and during gait cycle).

A. Anterior view.
Genu Varum:_____
Genu Valgum:_____
Patellar position:_____
Tibial Torsion:_____
Skin:_____
Swelling:_____

B. Lateral view
Genu Recurvatum:_____
Patella Alta:_____
Patella Baja:_____
Skin:_____

C. Posterior view.
Swelling:_____
Skin:_____

Active movements:
Flexion (0 - 135°)_____
Extension (0 - 15°)_____
Medial Rotation (20 - 30°)_____
Lateral rotation (30 - 40°)_____

Passive movements:
Tissue approx_____
Bone-bone_____
Tissue stretch_____
Tissue stretch_____
Patellar movement_____

Resisted isometric movements:
Knee: Flexion:_____
Extension:_____
Internal rotation:_____
External rotation:_____

Ankle: Plantarflexion_____
Dorsiflexion_____

Ligamentous assessment:

<u>One-Plane Medial Instability</u>:
Valgus stress (abduction)
- Extended_____
- Resting Position_____

<u>One-Plane Lateral Instability</u>:
Varus stress (adduction)
- Extended_____
- Resting Position_____

<u>One-Plane Anterior Instability</u>
Lachman Test (0-30°)_____
Anterior Drawer Sign _____

<u>One-Plane Posterior Instability</u>
Posterior "sag" Sign_____
Posterior Drawer Test_____

<u>Anterolateral Rotatory Instability</u>
Slocum Test_____
Macintosh Test_____

<u>Anteromedial Rotatory Instability</u>
Slocum Test_____

Posterolateral Rotatory Instability
Jacob _____
Hughston's Drawer Sign_____
Reverse pivot shift test_____

Posteromedial Rotatory Instability
Hughston's Drawer Sign_____

Tests for meniscus injury:
McMurray_____
"Bounce Home"_____
Anderson med-lat grind_____
Apley's_____

Plica tests:
Mediopatellar Plica _____
Plica "Stutter"_____
Hughston's Plica_____

Tests for swelling:
Brush/Stroke Test _____
Patellar Tap Test_____

Tests for patella femoral pain syndrome:
Clarke's Sign _____
Waldron test_____
Passive patella tilt test_____

Other tests
Wilson's_____
Fairbank's_____
Noble Compression_____
Quadriceps Contusion Test_____
Leg Length Discrepancy_____

Joint play:
P-A movement of the tibia on the femur_____
A-p movement of the tibia on the femur_____
Medial translation of the tibia on the femur_____
Lateral translation of the tibia on the femur_____
Inf, sup, lat, + med glide of the patella_____
A-P movement of the inf. tibiofibular joint_____
A-P movement of the sup. tibiofibular joint_____
Inf-sup movement of the sup tibiofibular joint_____
Long axis distraction of the tibiofemoral joint_____

Palpation:
Tenderness_____
Joint line pain _____
Swelling_____
Nodules/exostoses_____

Reflexes and cutaneous distribution:
Patellar Reflex (L3,L4) R____L____
Medial Hamstring Reflex (L5,S1) R____L____

Dermatomes

L2	R____L____	S1	R____L____
L3	R____L____	S2	R____L____
L4	R____L____	S3	R____L____
L5	R____L____		

APPENDIX E

Dear Participant

The aim of this study is to compare the relative effectiveness of two treatment therapies in the management of osteoarthritis of the knee.

Sixty people will be required to complete the study. These participants will be randomly divided into two treatment groups of thirty patients each. Patients in both groups will receive treatment.

One group will receive manipulative treatment of the knee. Stiffness and loss of function are symptoms encountered in this condition. Manipulation of the knee restores motion in this joint and allows for greater pain-free movement.

The second group of patients will receive a once daily dose of Meloxicam tablets. Meloxicam is a non-steroidal anti-inflammatory drug which helps to control inflammation and pain. This drug may, however, produce side-effects in some patients such as gastric irritation and bleeding.

Some patients may require an X-ray of the knee in order to make a diagnosis. Patients found with severe ligamentous instability of the knee, a history of adverse reactions to anti-inflammatory drugs, peptic ulcers or gastrointestinal bleeding will be excluded from the study.

Patients will be required to return for three treatments per week over a three week period.

All treatments will be performed under the supervision of a qualified chiropractor and will be free of charge.

Thank you.

Yours faithfully

Mark Tucker

(6th year Chiropractic Resident)

APPENDIX F

NUMERICAL RATING SCALE – 101

NAME: ..... DATE: .....

PLEASE INDICATE ON THE LINE BELOW THE NUMBER BETWEEN 0 AND 100 THAT BEST DESCRIBES THE PAIN OF YOUR MAJOR PROBLEM AT THIS POINT, WHEN IT IS AT ITS WORST. A ZERO (0) WOULD MEAN "NO PAIN AT ALL", AND A HUNDRED (100) WOULD MEAN "PAIN AS BAD AS IT COULD BE."
PLEASE WRITE ONLY ONE NUMBER.

PLEASE INDICATE ON THE LINE BELOW THE NUMBER BETWEEN 0 AND 100 THAT BEST DESCRIBES THE PAIN OF YOUR MAJOR PROBLEM AT THIS POINT, WHEN IT IS AT ITS LEAST. A ZERO (0) WOULD MEAN "NO PAIN AT ALL" AND A HUNDRED WOULD MEAN "PAIN AS BAD AS IT COULD BE".
PLEASE WRITE ONLY ONE NUMBER.

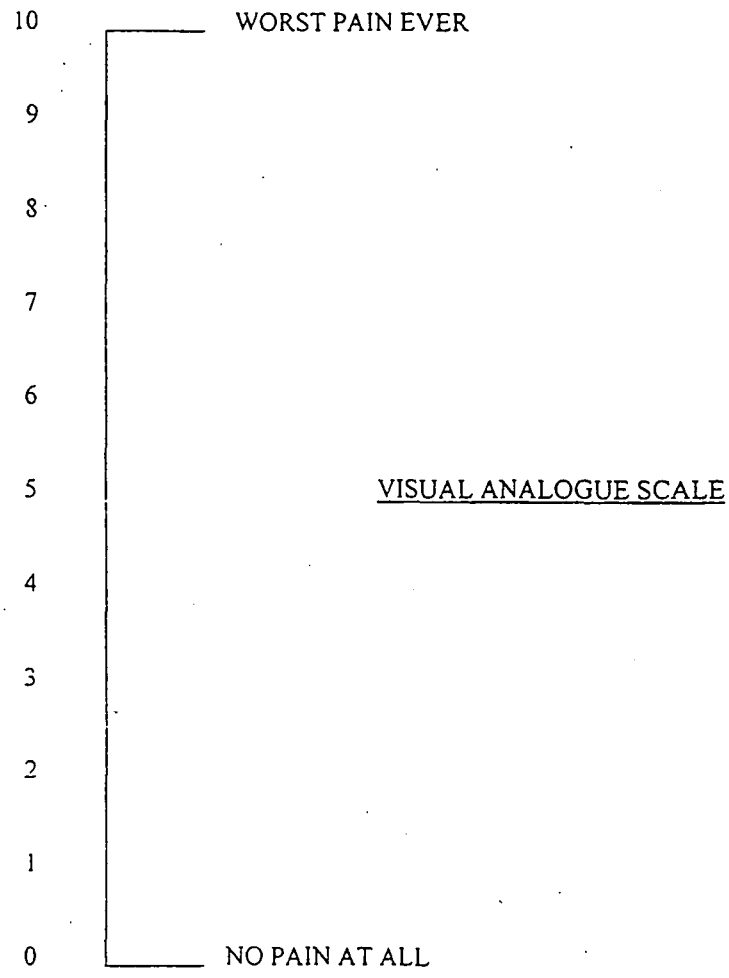
APPENDIX G

PATIENT : .....

FILE NO: .....

DATE : .....

PAIN RATING SCALES



CLINICIAN TO READ AND FILL IN: Complete at the end of the history and prior to physical

READ AT BASELINE ASSESSMENT

I'm going to ask you to identify up to 5 important activities that you are unable to do or have difficulty with as a result of your problem.

Today, are there any activities that you are unable to do or have difficulty with because of your problem (show scale)

READ AT FOLLOW-UP VISITS

When I assessed you on (state previous visit), you told me you had difficulty with (read 1,2,3,4,5 from list).

Today, do you still have difficulty with 1 (have patient score each activity); 2 (have patient score each activity); 3 (have patient score each activity); 4 (have patient score each activity); 5 (have patient score each activity).

Scoring scheme (show patient scale):

0	1	2	3	4	5	6	7	8	9	10
Unable to perform activity										Able to perform activity at pre-injury level

	Date/score								
Activity									
1									
2									
3									
4									
5									
Additional									
Additional									

APPENDIX I

GONIOMETER READINGS

PATIENT NAME: _____.

FILE No: _____.

TREATMENT No: _____.

	Treat. 1	Treat. 2	Treat. 3	Treat. 4	Treat. 5	Treat. 6	Treat. 7	Treat. 8
Flex.								
Ext.								
Int. rot.								
Ext. rot.								

APPENDIX J

ALGOMETER READINGS

PATIENT NAME: _____.

FILE No: _____.

	Date	Reading
Treatment 1		
Treatment 2		
Treatment 3		
Treatment 4		
Treatment 5		
Treatment 6		
Treatment 7		
Treatment 8		