THE IMMEDIATE EFFECT OF LOW BACK MANIPULATION ON SERUM CORTISOL LEVELS IN ADULT MALES WITH MECHANICAL LOW BACK PAIN

by

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I, Keseri Padayachy,
do hereby declare that this dissertation represents my own work
in both conception and execution, except where specific assistance is
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DEDICATION

It is with immense pleasure that I dedicate this dissertation to:

The Supreme Lord of the Universe: thank you for your wisdom and guidance, especially through the difficult times.

My parents: thank you for your continued sacrifice, support and encouragement. You have given me the greatest gifts of a wonderful upbringing and an excellent education. I am eternally grateful.

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ABSTRACT

Objectives:

To determine if serum cortisol levels are increased following Spinal Manipulation Therapy (SMT) to the low back region and to determine the effect of a short rest interval on the cortisol levels.

Project Design:

The research project was in the form of a randomised, clinical trial using human subjects.

Setting:

Patients presenting with low back pain to the Chiropractic Day Clinic at the Durban Institute of Technology and the Community Health and Indigent Programme Services clinic.

Subjects:

Adult, male patients, aged between 18 and 35 years of age, diagnosed with mechanical low back pain.

Outcome measure:

Daytime, serum cortisol levels.

Results:

A decrease in serum cortisol levels following SMT. Serum cortisol levels decreased significantly following a short rest interval.

Conclusions:

The results of this study support the previous finding that a neuroendocrine effect can be stimulated by SMT, albeit, a decrease in serum cortisol levels. A short-term rest period also influenced the serum cortisol levels. However, the mechanism of these effects is not established and requires further investigation as this was not within the scope of the present study.

TABLE OF CONTENTS

CHAPTER   **PAGE**

LIST OF TABLES

LIST OF FIGURES

LIST OF FIGURES, CONTINUED

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.1. INTRODUCTION

Mechanical low back pain (LBP) is one of the most common clinical disorders that more people are seeking help for (Browning, 2003). The prevalence of LBP increases with age and the magnitude depends on the population surveyed (Docrat, 1999).

The options for management of LBP are vast, as there is no consensus amongst health care professionals as to the best possible form of intervention (Browning, 2003). With respect to spinal manipulation, literature reveals that it is a common form of intervention that is widely used in the treatment of LBP (Giles and Muller, 1999; Kirkaldy-Willis and Bernard, 1999). The outcome of most of the studies on LBP and spinal manipulative therapy (SMT) support the view that SMT results in a greater improvement in mechanical LBP.

Kirkaldy-Willis and Bernard (1999) suggest that mechanical LBP is possibly caused by a repetitive rotational and compressive motion to the lumbar facet joint. This will in turn cause trauma to the facet joint resulting in a synovitis of the facet joint. There are various chiropractic theories on the alleviation of mechanical LBP, such as Korr's theory, Sandoz's theory, somatovisceral theory, Dvorak's theory and the neuroendocrine physiological mechanism (Leach, 1994). One theory, which is under the ambit of neuroendocrine physiological mechanism that has been inadequately explained, is the stress effect of SMT on serum cortisol levels (Will, 1978). The researcher extrapolated this theory further, proposing that SMT causes an increase in serum cortisol levels by an unconfirmed yet hypothetically possible neuroendocrine mechanism and since cortisol is an anti-inflammatory hormone, the increased cortisol levels will have an anti-inflammatory effect on the inflamed lumbar facet and sacroiliac joints, thus reducing LBP.

One of the major hormones secreted by the adrenal gland is a glucocorticoid, called cortisol. Cortisol follows a circadian rhythm of activity. The rhythm consists of the highest cortisol levels shortly after awakening (9am-10am) and progressively falling until they are lowest during the first several hours of sleeping (Guyton and Hall, 2000). Acute physical and psychological stress activates the hypothalamic-pituitary-adrenal axis, resulting in increased plasma adrenocortico-trophic and cortisol levels (Wilson and Foster, 1992; Greenspan and Gardner, 2001).

There is little documented literature stating that SMT can, in fact, cause a stress effect on the body hence increasing cortisol levels and thus resulting in an anti-inflammatory effect. To date, there are only two studies that have attempted to determine, the effect of SMT on salivary cortisol levels. The findings of these studies are discussed in detail in Chapter 2, however, both these studies have methodological flaws in their design.

1.2. AIM AND OBJECTIVES

1.2.1 AIM
The aim of this study is to determine if serum cortisol increases immediately after SMT.

1.2.2. OBJECTIVES
- To determine if serum cortisol levels increase immediately post-SMT to the low back region
- To determine the effect of a short rest interval on serum cortisol levels

1.3. HYPOTHESES
- Serum cortisol levels should significantly increase after SMT.
- Short-term rest does not influence serum cortisol levels.

Data was analysed using the Wilcoxon signed rank test for intra group analysis and Mann-Whitney-U test for inter group analysis using the SPSS version 11.5 package.

CHAPTER 2
LITERATURE REVIEW

2.1. INTRODUCTION

LBP is one of the most common and costly medical conditions confronting health care providers and medical insurers today (Browning, 2003; Perina, 2005). Despite the magnitude of the problem, no general consensus exists concerning an appropriate treatment for this condition (Browning, 2003). The traditional allopathic methods of treating this condition undoubtedly have demonstrated inadequacies, therefore alternative treatment methods are often considered. Manipulative therapy has been shown to be an efficacious method of treating mechanical LBP (Pustaver, 1994; Hendler *et al.,* 1995; Giles and Muller, 1999; Cooperstein *et al.,* 2001). LBP has a lifetime prevalence of between 60% to 90% for any general population (Kirkaldy-Willis and Bernard, 1999; Hills, 2004).

2.2. MECHANICAL LOW BACK PAIN

The majority of LBP is mechanical i.e.: it exists without overt structural pathologies (Kirkaldy-Willis and Burton, 1992; Hills, 2004). Mechanical LBP is caused by:

1) Joint dysfunction i.e. joint mechanics showing area disturbances of function without structural change (Bergmann *et al*., 1993) and

2) "Soft tissue" syndromes (e.g. myofascial pain dysfunction syndromes) which involve nociceptive processes (pain sensitive processes) rather than nerve injury (Waddel, 1995).

Mechanical LBP conditions include lumbar facet syndrome, sacroiliac syndrome, Maignes' syndrome, disc herniation, facet and disc degeneration, central and lateral canal stenosis, myofascial pain and dysfunction syndromes (Kirkaldy-Willis and Burton, 1992; Hills, 2004).

For the purpose of this study, the focus was on acute lumbar facet and sacroiliac joint syndrome. Acute was defined as the subjects presenting

within 4 weeks of initial onset of LBP (Bigos *et al.,* 2004). According to Kirkaldy-Willis and Burton (1992), acute lumbar facet syndrome is the result of rotation or compressive strain sometimes due to a major, but more often is due to a minor episode of spinal trauma. The mechanism they propose is that the trauma to the lumbar region results in lumbar facet joint sprain, i.e.: small capsular tears resulting in a minimal degree of joint subluxation. Joint subluxation is defined as an aberrant relationship between two adjacent articular structures that may have functional or pathological sequelae, causing an alteration in the biomechanical and or body systems that may be directly or indirectly affected (Bergmann *et al.*, 1993). The various pathological changes that occur subsequent to this regional trauma often lead to synovitis. This inflammation can stimulate pain sensitive receptors and also affect blood supply to surrounding musculature, by intense protective spasm, thus increasing joint dysfunction and decreasing mobility (Kirkaldy-Willis and Bernard, 1999; Seaman and Cleveland, 1999).

An earlier study by Cavanaugh and Ozaktay (1997), laid the foundation for evidence of this proposed mechanism. In this study, adult male, white rabbits weighing 3 to 4 kg were anaesthetised, and neurophysiological studies were performed on the lumbar facet joints as well as the surrounding tissues.

A lumbar laminectomy was performed in the rabbits to expose the lumbar dorsal roots under study. The L3/L4 or L4/L5 facet joints were kept intact, and recordings were made from the appropriate dorsal roots on (L4 or L5). A ventral ramus rhizotomy was performed at the appropriate level so that nerve discharge from peripheral tissues would not be recorded. They showed that inflammatory mediators could produce ongoing background discharge in sensory nerves of joints and sensitise the nerves to mechanical stress. Thus, facet joint pain fibres that would normally fire only when mechanical stress is clearly noxious, can fire at much lower stresses and hence thresholds in the presence of these chemicals and maintain a background discharge even without mechanical stress. With respect to the current study, we extrapolate that noxious mechanical stress in humans

may lead to the production of inflammatory mediators which would sensitise the nerves of the facet joints. It is this peripheral nerve sensitisation that may be contributing to the ongoing episodes of LBP.

2.3. CORTISOL

Cortisol, biochemically known as 17 hydroxycorticosterone, is the primary endocrine secretory product of the adrenal gland, present in the peripheral blood of humans (DeGroot *et al.*, 1989). A steroid hormone, it is secreted by the *zona glomerulosa* of the adrenal cortex and is regulated by the hypothalamic-pituitary axis (HPA) (Guyton and Hall, 2000).

2.3.1 DIURNAL NATURE OF CORTISOL SECRETION

Cortisol is not synthesised continuously during the day. It has a diurnal variation, which is characterised by the plasma levels being elevated in a cyclical manner throughout the day. This diurnal pattern results from a series of discontinuous bursts of secretory activity during the early part of the day, with virtual cessation of secretion for several hours just before and after midnight (Kacsoh, 2000; Briegel *et al.*, 1994).

Cortisol secretion is increased by physical and emotional stress. Such stress-related stimuli override the baseline regulatory mechanism, mediated as a biofeedback in the hypothalamus. The resultant increments are superimposed on the usual diurnal pattern. Both the stress response and the baseline cortisol secretory pattern depend on adreno-cortico-trophic hormone (AcTH) released by the anterior pituitary under the influence of the hypothalamic corticotrophin releasing factor (CRF). It is documented that cortisol concentrations are highest at 8am to about 10am and steadily decreases throughout the rest of the day (Guyton and Hall, 2000). Cortisol should spike immediately after a stress is placed on the body and should thereafter decrease. The rate at which cortisol decreases will depend on body clearance i.e.: renal function and the amount of circulating cortisol in the body (Naidoo, 2004)[1]. Gray and James (1983), DeGroot *et al.* (1989), and Besser and Thorner (2002) also mention that cortisol is released in response to stress but are uncertain as to exactly how soon cortisol is

released following a stressor. Normal values for male serum cortisol range between 190nmol/l - 690nmol/l in the mornings and 55nmol/l - 250nmo/l in the evening (Naidoo, 2004)[1]. These laboratory values are based on King Edward VIII Hospital values. Currently, despite an exhaustive literature search (books, Internet, journals) there appears to be no studies determining serum cortisol variation amongst the different ethnic populations.

2.3.2. ANTI-INFLAMMATORY EFFECTS OF CORTISOL

Cortisol's potent anti-inflammatory effects are thought to maintain endothelial integrity (Oppert *et al.,* 2000). This anti-inflammatory effect is brought about by cortisol interfering with the actual synthesis of inflammatory components (Guyton and Hall, 2000).

Cortisol has two basic anti-inflammatory effects:-

1. Cortisol blocks the early stages of the inflammation process before inflammation even begins (Guyton and Hall, 2000).

2. If inflammation has already begun, cortisol causes rapid resolution of the inflammation and increases the rapidity of the healing process (Guyton and Hall, 2000).

These effects are explained further as follows: cortisol prevents the development of inflammation by the following effects:

- Cortisol stabilises the lysosomal membranes.
- Cortisol decreases the permeability of the capillaries.
- Cortisol decreases both migration of white blood cells into the inflamed area and phagocytosis of the damaged cells.
- Cortisol suppresses the immune system, causing lymphocyte proliferation to decrease markedly.
- Cortisol lowers fever mainly because it reduces the release of interleukin-1 from the white blood cells.

Thus cortisol has an almost global effect in reducing all aspects of the inflammatory process (Guyton and Hall, 2000).

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[1] Verbal communication Dr P. Naidoo, senior chemical pathologist (February 2004)

2.4. SPINAL MANIPULATION

SMT is a specific form of articular manipulation, using either long or short leverage techniques, with specific contacts. It is characterised by a dynamic thrust of controlled high velocity, amplitude and direction (Bergmann *et al.,* 1993). SMT has been documented to be efficacious in the treatment of mechanical LBP (Shekelle *et al.,* 1992; Opperman, 1997; Kruger, 1999; Whelan *et al.*, 2002; Smith, 2003), as it results in improved flexibility, reduced pain and increased joint mobility (Gatterman, 1990).

There are many hypotheses on the effects of spinal manipulation on the body e.g. neural and endocrine effects, (Leach, 1994), but the one of interest to this study is Dvorak Inflammatory Model. Dvorak (1985) proposed that segmental dysfunction or local joint dysfunction creates both a mechanical and the chemical stimulation necessary for the activation of nociceptors and spinothalamic tract activity. His model proposed that segmental dysfunction would have reflex effects on the muscle thus increasing the muscle spindle discharge of alpha motor neuron fibres post-muscle contraction. If this effect occurs for prolonged periods, it will lead to local muscle spasm. This spasm will result in a sensory discharge, leading to the same muscle contracting i.e. shortening of postural slow-twitch muscle fibres, which can then either result in inflammatory histochemical changes or cause relative local hypoxaemia. These effects result in damage to the muscle causing muscular pain and muscular imbalance, which in turn results in disturbed joint movement. This theory could be considered as the foundation for Kirkaldy-Willis' and Burton's (1992) explanation of joint inflammation (synovitis) found in mechanical LBP syndrome.

Selye (1956) determined that the nervous system is also involved in the hypophyseal-adrenocortical response to stress by a number of pathways. Experiments with animals showed that a neurogenic stressor triggers a neural response through the hypothalamus to the anterior lobe of the pituitary where AcTH is secreted into the systemic circulation. Thus the interaction between the neuroendocrine and central nervous system was demonstrated (Selye, 1956).

However, there appears to be little documented literature whether SMT *per se* has any anti-inflammatory or neuroendocrine effects (Christian *et al.*, 1988).

2.5. STUDIES CONCERNING SALIVARY CORTISOL AND SMT

To date, there are two documented studies regarding salivary cortisol and SMT (Tuchin, 1998; Whelan *et al.,* 2002). The study by Tuchin (1998) was conducted to assess if spinal manipulation has the potential to effect salivary cortisol levels. This may also have some implications in the prevention of stress-related medical conditions such as hypertension, coronary artery disease, migraines, peptic ulcers, rheumatoid arthritis, inflammatory bowel disease and other significant disease conditions that are known to have a correlation with stress. Both these studies utilised Selye's definition of stress as "the non-specific response of the body to any demand" (Selye, 1956).

Nine subjects, six male and three females participated in Tuchin's study. Subjects acted as their own controls and were informed they were receiving a therapeutic treatment to the area of spine that was affected. Saliva specimen was collected at 12 noon on Wednesdays and Saturdays. These days have been shown to be the most and least stressful periods of the week, respectively (Bassett, 1982). The procedure required a minimum of 2ml of saliva to be collected in a centrifuge tube and stored immediately, on ice. The study consisted of establishment of each individual's baseline cortisol level, a 2 week pre-experimental evaluation of the subject's cortisol levels, 2 week's of experimental evaluation in conjunction with pre-treatment and post-treatment evaluation of the salivary cortisol levels and 1 week of post-experimental re-evaluation of the subject's salivary cortisol levels. The subjects were not restricted from their usual daily activities during the course of this study.

The results of Tuchin's study showed statistically significant reduced levels ($p<0.001$) of salivary cortisol over the complete five-week study period. There was no apparent change in the salivary cortisol levels immediately

preceding and 15 minutes after the spinal manipulation. This study however, did not include control for gender bias on cortisol measurement, because both men and women were used as subjects. The relatively small sample size and the lack of a control group, make conclusions drawn from this study somewhat limited.

The objective of the study conducted by Whelan *et al.,* (2002) was to determine if basal salivary cortisol levels can be properly detected and whether manipulation of the cervical spine had any direct effect on basal salivary cortisol levels in humans. Subjects were thirty, asymptomatic adult male, students attending a chiropractic college. The subjects where divided into three groups; namely, a control group, the "sham" group and the chiropractic cervical manipulation group. The control group received no manipulation or vertebral positioning, the sham group received spinal positioning without being taken to the end-range of motion and the spinal manipulation group received a high velocity low amplitude manipulation to the cervical spine. No reason has been given as to why a cervical spine manipulation was chosen for this study. Salivary samples were collected for 5 weeks. Subjects were requested to refrain from eating, exercising, using tobacco, and consuming any drinks other than water for 1hour before the test sample collection. This was presumably done to prevent any of these activities from affecting the cortisol levels. Disposable, plain cotton salivettes were used for the quick and hygienic collection of the saliva sample. Chewing on the cotton-wool swab for 30 to 60 seconds collected saliva. During Week I, samples were collected by the students at home, upon waking and stored in their personal freezers until the final day of the testing. Home samples were transported to the laboratory on ice on the final day of testing. During Weeks 2 through 5, home samples were collected upon waking and were followed by an additional time course of samples collected in laboratory settings before and after manipulation. All laboratory testing occurred between 8am and 10am, each test day, were collected on ice and stored at $-80^{\circ}c$ until biochemical analysis.

The results of the study showed that cervical spinal manipulation did not significantly change basal salivary cortisol levels. The time course of acute changes to cortisol levels was independent of the testing week and group. A decrease in salivary cortisol was detected over time on each trial-testing day. The results of the study suggest that the physical component of manipulation of the cervical spine is not a potent enough stressor to disrupt homeostatic mechanisms and override the hypothalamic-pituitary-adrenal axis.

However, in the study by Whelan *et al.,* (2002), a difference in temperature between the personal freezers and laboratory freezers added another variable that has not been considered in the study. Furthermore, it is possible that the transport of the samples on ice to the laboratory could also have affected the results, depending on the quantity of ice used for the transportation process. Considering these shortcomings, the results of the study could be questioned.

2.6. POSSIBLE EXPLANATION OF EFFECTS OF SMT ON CORTISOL

To explain how SMT may affect cortisol release from the adrenal cortex, it is necessary to briefly introduce and discuss the mechano-sensitive units (also known as mechanoreceptors i.e. they detect mechanical deformation of the receptor or of the tissues adjacent to the receptor) found in the facet joints of the lumbar spine. An assumption is made that mechano-sensitive units found in the lumbar facets of rabbits represent those of humans (Yamashita *et al.,* 1990).

Yamashita *et al.* (1990) conducted a study with the purpose of characterising mechano-sensitive units of the lumbar facet joint in rabbits, which may play a central role in LBP. In these rabbits, twenty-four units were identified (by means of laminectomy) in the region of the facet joint: ten, in the capsule of the joint; twelve, in the border regions between capsule and muscle or tendon; and two in the ligamentum flavum. Of these units, two had a conduction velocity that was slower than 2.5 meters per second (mps) (Group IV), fifteen had a velocity ranging from 2.5 to twenty

mps (Group III), and seven had a velocity faster than twenty mps. Fourteen other mechano-sensitive units were found in the muscle, tendon, and interspinous ligaments. Seven units in the facet joint responded to movement of the joint when stimulated electrically with a bipolar electrode. Grigg *et al.,* (1986) reported that inflammation of the joint sensitised Group-III and Group-IV units and increased their responsiveness to movement under an inflammatory condition, thus increasing pain threshold. The clinical relevance of the finding of the study of Yamashita *et al.* (1990), is that the facet joint contains Group-III and Group-IV mechano-sensitive units with low to high thresholds and that several units responded to movement of the joint.

A study by Pickar and McLain (1995) tested the hypothesis that Group III and Group IV afferents with receptive endings in the lumbar spine respond to passive manipulation of the lumbar facet joint in cats. They noted that sensitive afferents were found in all tissues of the lumbar spine, including tissues of the facet joint, connective tissue immediately surrounding the facet joints, para-spinal muscle, and fascia distant from the facet joint. Distraction of the facet activates these sensory receptors. A hemilaminectomy approach was developed that permitted physiologic loading of the lumbar facet without disturbing its overlying musculature. Recordings of single unit afferent activity were made from filaments teased from the L5 dorsal root. This study showed that Group III and Group IV afferents located in tissues throughout the low back respond to forces applied through the lumbar facet.

These findings indicate the presence of a complex network of small diameter neural elements in the low back area capable of responding to movements of the lumbar spine. This network may play an important role in the normal function of the spinal column and may contribute to somatic and autonomic reflexes. In addition, stimulation or modulation of this system may explain the beneficial effects many patients receive through physical therapy, bracing as well as spinal manipulation.

Neuroanatomically, the lumbar facet joint receives sensory and postganglionic sympathetic fibres, which ipsilaterally and segmentally innervated by the sensory nervous system. Suseki *et al.*, (1997) support the hypothesis that sensory pathways from the L4-L5 facet joint to L1 or L2 dorsal root ganglia pass through the sympathetic trunk. The lumbar segment of the sympathetic trunk may therefore transmit afferent impulses monitoring LBP caused by lumbar facet lesions.

Once action potentials in the dorsal column-medial lemniscal system (Suseki *et al.,* 1997) are initiated by administered SMT, it is possible that they travel up the dorsal column-medial lemniscal system to the thalamus from which inter-neurons stimulate the hypothalamus to secret corticotrophin-releasing hormone (CRH). This causes the anterior pituitary to secrete adreno-corticotrophic hormone (AcTH), which causes the adrenal cortex to release cortisol (Guyton and Hall, 2000). Cortisol then functions as an anti-inflammatory agent (Guyton and Hall, 2000) and thus prevents further injury to joint complex, enhancing the recovery phase.

The proposed mechanism for cortisol release is summarised in the flow diagram: -

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┌─────────────────────────────┐
│   Patient with acute low    │
│    back facet syndrome      │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│    Spinal Manipulation      │
│      Therapy applied        │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│  Stimulation of articular apophyseal │
│  mechanoreceptors and muscle spindles in │
│         paraspinal muscles           │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│     Neurons in network stimulated    │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│  Action potentials travel up the dorsal column- │
│  medial lemniscal system to thalamus where │
│  interneurons stimulate the hypothalamus. │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│  Hypothalamus secretes corticotrophin- │
│      releasing hormone (CRH)         │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│  CRH causes the anterior pituitary to secrete │
│   adenrocorticotrophic hormone (AcTH) │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│   AcTH causes the adrenal gland to   │
│      increase cortisol levels        │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│        Effect on inflamed tissue:    │
│         Decreases inflammation       │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────────┐
│  Preventing further injury to joint complex │
│     and enhancing recovery phase.    │
└─────────────────────────────────────┘
```

2.7. SUMMARY

Mechanical LBP is a common condition; however there exists a disagreement amongst researchers on the aetiology and treatment protocols. Most authors agree that there is some degree of inflammation that occurs in the muscles and joints of the affected areas. SMT utilised for treating mechanical LBP has been documented to be of therapeutic value.

How exactly SMT eliminates or reduces LBP is not known. A possible explanation may lie in the neuroendocrine theory. This theory supports the idea that SMT may trigger neural and endocrine effects. One hypothesis proposed in this study states that lumbar SMT may lead to a release of cortisol, a known anti-inflammatory agent, and this may lead to a decrease in inflammation of the affected area, hence a decrease in the symptom of pain.

CHAPTER 3

MATERIALS AND METHODS

3.1 INTRODUCTION

This chapter includes a detailed description of the study design, patient inclusion criteria to participate in this study and the interventions used. The measurements obtained and the statistical procedures used in the analysis of the data are also discussed.

3.2 RESEARCH DESIGN

The research design was in the form of a randomised clinical trial where the effect of SMT was tested for its proposed anti-inflammatory effect by means of an immediate increase in serum cortisol level in subjects with mechanical LBP, particularly those with acute lumbar facet syndrome or sacroiliac syndrome, following SMT.

3.3 STUDY DESIGN PROTOCOL

3.3.1 OBJECTIVES

The aim of the study was to determine if serum cortisol increases immediately after lower back manipulative therapy. For the purpose of this study immediately was defined as occurring within five minutes of the first blood specimen drawn and assayed for serum cortisol level.

It was hypothesised that if SMT increases cortisol levels, then it is possible to initiate an anti-inflammatory cascade which may result in a decrease in joint inflammation thereby leading to relief of LBP.

3.3.2 THE SUBJECT DEMOGRAPHICS

3.3.2.1 SUBJECT RECRUITMENT

Subjects had to be residents of the greater Durban functional region and were selected from those people who responded to advertisements (Appendix 9) placed in public places (e.g. gymnasia), pamphlet distribution

and newspaper advertisements. There were no restrictions on ethnicity, cultural or socioeconomic background. The subjects had to present with acute mechanical lumbar facet or sacroiliac syndrome. For the purpose of this study, acute was defined as the subject presenting within 4 weeks of initial onset of LBP (Bigos *et al.*,1994).

3.3.2.2 SAMPLING AND GROUP ALLOCATION

Convenience sampling was utilized in this study. Subjects who responded to the advertisements were selected and randomly allocated into two groups of fifteen by drawing the group code, (1 or 2). This code was written on a piece of paper, folded and placed in a box which was shaken to mix the pieces of paper. Subjects in Group 1 were phlebotomised, received a low back spinal manipulation and then immediately (within 5 minutes) re-plebotomised. Subjects in Group 2 were phlebotomised, rested for 5 minutes, re-phlebotomised, then received a low back spinal manipulation and immediately thereafter re-phlebotomised. In Group 2, the subjects were phlebotomised thrice, through the butterfly venous catheter, to obviate repeated punctures.

3.3.3 INCLUSION AND EXCLUSION CRITERIA
3.3.3.1 INCLUSION CRITERIA

1) The study was limited to male subjects who were between the ages of 18 and 35. Males younger than 18 years of age would need parental consent and according to DeGroot *et al.,* (1989) older males are more likely to have unstable cortisol levels which could have affected the final results.

2) Subjects diagnosed with acute facet or sacroiliac syndrome of the low back as described by Kirkaldy-Willis and Bernard (1999)

3) Subjects with a Numerical Pain Rating Scale (NRS) of 5 to 10. This was used to homogenise the sample size, based on similar pain ratings.

3.3.3.2 EXCLUSION CRITERIA

1) Subjects with LBP of non-mechanical origin or other mechanical conditions e.g. disc herniation and other serious pathological conditions (excluded by means of case history and physical examination findings).

2) Subjects apprehensive of needles.

3) Subjects with contact allergies to disinfectant used in the research.

4) Hypertensive subjects i.e.: patients with a blood pressure of 140/90 mmHg or greater (Longmore *et al.,* 2001)

5) Subjects with any haematological disorders e.g. haemophilia and anaemia.

6) Subjects with any cortisol abnormality e.g.: Cushing's syndrome / Addison's disease.

7) Subjects with contra-indications to SMT including: joint ankylosis, joint hypermobility, infection in the area that will be receiving treatment, malignancy in the area that will be receiving treatment, fractures, inflammatory arthritis, metabolic bone disease (Bergmann *et al.,* 1993; Kirkaldy-Willis and Bernard, 1999)

8) Female subjects due to their menstrual cycles which affect cortisol levels (DeGroot *et al.*,1989).

9) Subjects who were medicated or received any other forms of treatment for LBP between the first and second consultation.

10) Subjects who received any form of treatment for a condition that may have arisen between the first and second consultation e.g. paracetamol for headaches.

11) Subjects who part-took in any kind of exercise between the first and second consultation.

12) Subjects who arrived 10 minutes after the stipulated time of 07:30 hours.

3.3.4 PATIENT PROCEDURE

At the initial consultation, once the subjects were randomly assigned to their groups, subjects were given an information sheet (Appendix 1or 2) outlining the research procedure, which was personally explained to them by the

researcher. Each subjects signed an informed consent form (Appendix 3 or 4) allowing the researcher to begin the research with the subjects understanding that they were able to withdraw from the study at any stage, with no constraints or repercussions. Each subject was informed not to take any pain-relief medication or perform any strenuous physical activity, including exercise, between Days I and 2 of the study. Each patient underwent a complete case history (Appendix 5), physical examination (Appendix 6) and lumbar regional examination (Appendix 7). Subjects were also required to fill in a NRS (Appendix 8). Subjects with an NRS score of less than 5 were excluded from this study. This was done on Day 1 of the study.

3.3.5 RESEARCH PROCEDURE

Day 1- Case history, physical and regional examinations were done for both Groups 1 and 2 at the Durban Institute of Technology's Chiropractic Day Clinic. During this consultation subjects were also required to complete an NRS form. Subjects received explanations that the substance (cortisol) being tested has circadian rhythm (changes at different times of the day) therefore it was imperative that they arrived at the times stipulated by the researcher on Day 2. The times at which the subjects were phlebotomised were crucial to the final results of the study due the circadian nature of cortisol (Guyton and Hall, 2000)

Day 2- Subjects were required to arrive before 7:30am to the Community Health and Indigent Programme Services clinic. On arrival, subjects were questioned on the use of any medication for their LBP or participation in any exercise on Day 1 of the study. Subjects who had taken medication or any other form of treatment, or engaged in strenuous exercise were excluded from the study.

The subjects of both groups had their weights and heights recorded by the researcher and were motion palpated.

Figure 3.1: Subject being motion palpated

Motion palpation is described as that aspect of palpation, which assesses the physiological range of motion possible in the different axes of motion, both generally and specifically for the joints of the spine (that is, a dynamic evaluation of the spine). This evaluation determines if a joint or motion unit of the lumbar spine/sacroiliac area has natural movement or if this movement is relatively increased or decreased (Ames, 1991). The evaluation continues until a joint fixation is found. Joint fixation is described by Haldeman (1992) as the state whereby the joint has become temporarily immobilized in a position that it may normally occupy during any phase of a physiological range of movement. This means that an affected motion unit of the spine may become hypomobile.

The subject was then rested supine, on a chiropractic examination bed for 10 minutes at normal room lighting, without the interference of sunlight due to the fact that sunlight has an effect on the biochemical pathway of cortisol (DeGroot *et al.,* 1989).

Figure 3.2: Subject resting supine

After the 10 minutes had elapsed, blood pressure was measured on the subject's dominant arm. Blood pressure was determined on the dominant forearm side due to blood pressure being higher on this side of the patient (Vawda, 1995). Subjects were then rested for a further 5 minutes and blood pressure was re-measured on the selected side. Blood pressure was measured to prevent undiagnosed hypertensive or hypotensive subjects from participating in the research. Co-supervisor, Professor G.H.M. Vawda, phlebotomised the subjects, as described below.

Figure 3.3: Instruments used for phlebotomy

Subject's dominant hand was cleansed on the dorsal aspect for catheterising a suitable superficial vein.
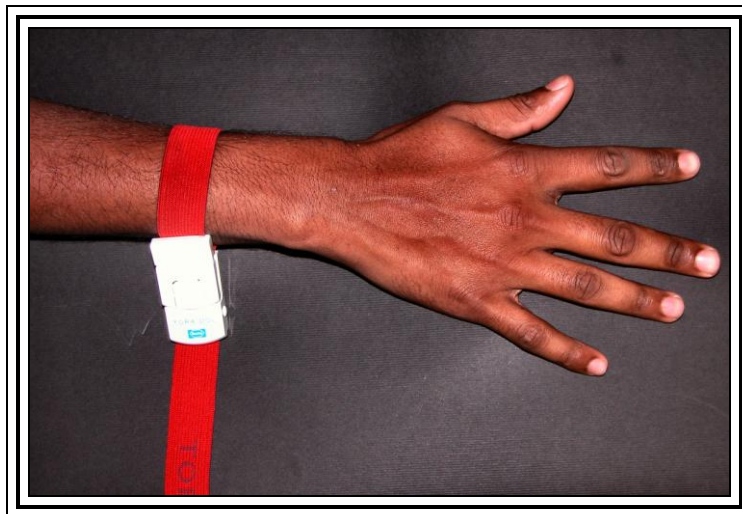
Figure 3.4: Tourniquet placed about 4cm proximal to the wrist

The dominant upper limb was slightly flexed and supported by the chiropractic couch. A tourniquet was placed and appropriately tightened at about 4 cm proximal to the wrist joint.
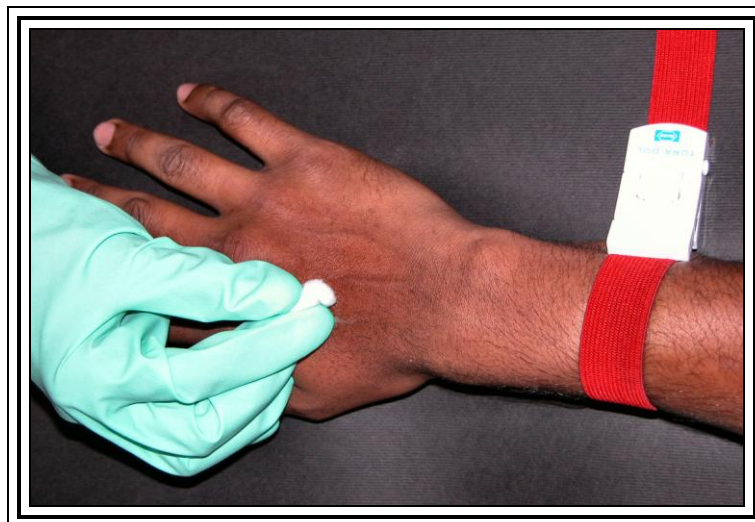
Figure 3.5: Dorsal surface of hand being cleansed

An appropriate sized, but easily accessible, vein was punctured with a disposable sterile 21 gauge Vacutainer systems butterfly catheter.
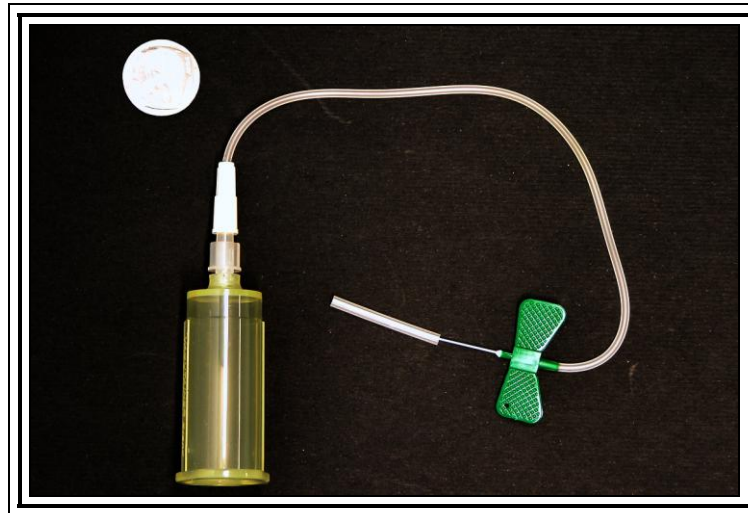
Figure 3.4: Butterfly catheter attached to sharp gauge
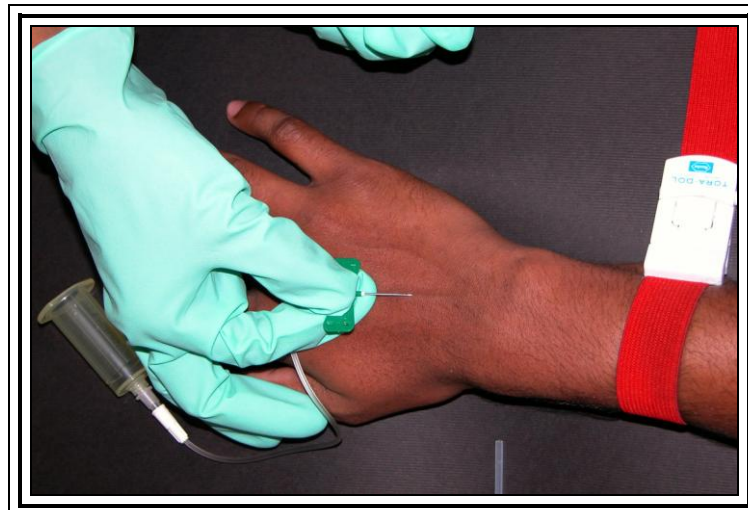
Figure 3.7: Butterfly catheter being inserted into a prominent vein

In the absence of this catheter (21 gauge Vacutainer systems butterfly catheter), a 21 gauge Venisystems butterfly catheter was used. The butterfly catheter was removed from a needle guard after being angled at about 30°. The plastic end of the needle was attached to a clear plastic holder called the sharp gauge that had a plastic tube clipped on its free end.
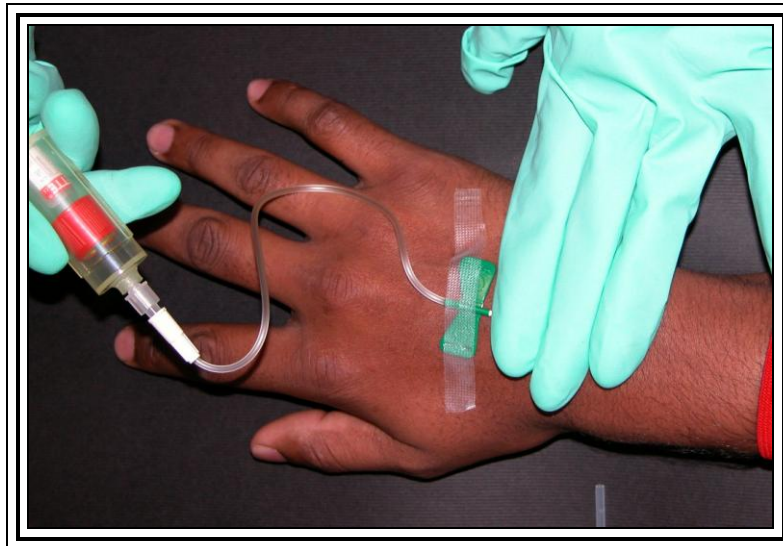
Figure 3.8: Plastic tube being pushed into sharp gauge

Once the collection tube was pushed into the sharp gauge it filled with blood from the patient due to the vacuum the tube contains. This tube did not contain any anticoagulant substances.
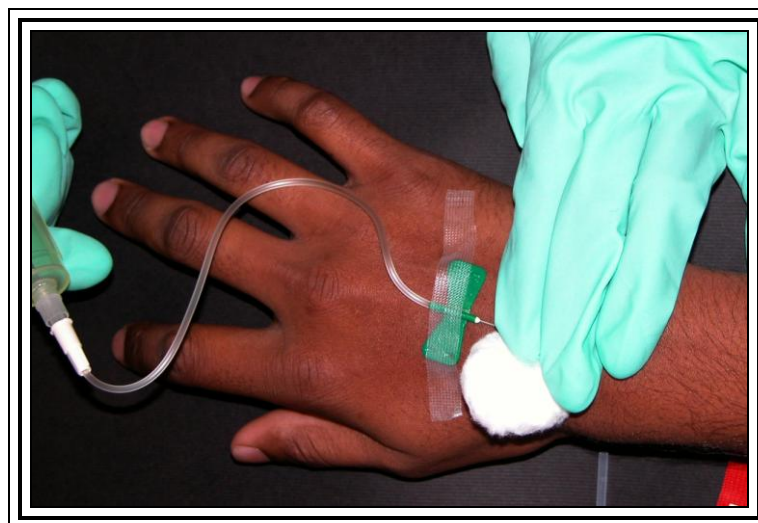
Figure: 3.9: Cotton wool being placed over the catheter before being removed from the vein

Once 8 -10 ml of blood had been drawn, the tube was removed. The tube was labeled as either Group 1 or 2, Pre-Treatment X (X was the number allocated to the subject in the group of 15, selected subjects).

The subjects of Group 1 were first manipulated in the low back region according to the technique described by (Bergmann *et al.,* 1993). The subjects were then re-phlebotomised; this sample being labeled Post-Treatment X.

A typical low back manipulation may be described as follows: the subject lies in the lateral position with the headpiece elevated, for comfort. The subject's lower arm is tractioned laterally, folded over the shoulder of the opposite arm and stabilised with the indifferent hand, while cephalad traction is provided.
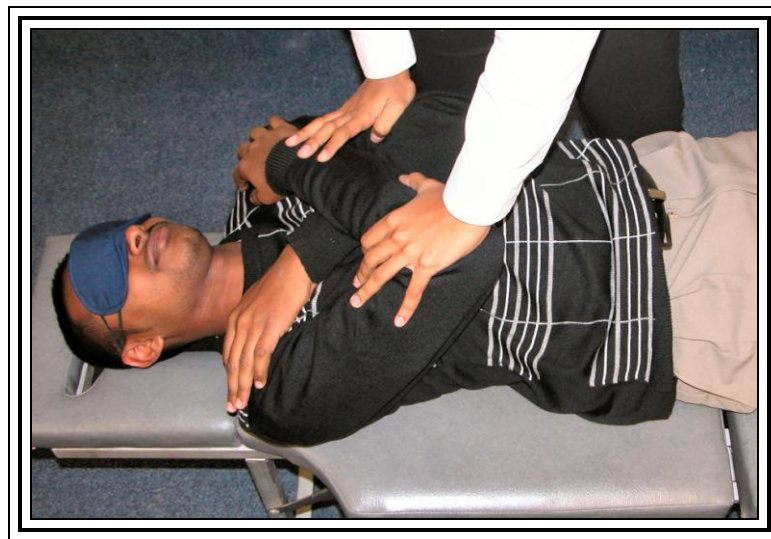
Figure: 3.10 Subject's forearms being crossed over to opposite shoulders

The subject's leg is bent at the knee while the thigh is flexed at the hip, with the foot placed into the popliteal fossa of the opposite leg.

Figure 3.11: Subject's upper leg being flexed at the hip and knee joints

Figure 3.12: Foot of upper limb being placed in the region of the popliteal fossa of the lower limb

The doctor takes up the "Fencer" stance and places the subject's upper bent knee between manipulator's thighs.

Figure 3.13: Doctor takes up a "Fencer" stance

The doctor's pelvis should be at the level of the lesion. The subject's thigh is flexed while the doctor monitors the interspinous movement of the segments cranial and caudad to the lesion. The pelvis and thighs are stabilised at the point of the start of any movement of the involved spinous process by downward transfer of the doctor's weight. The doctor's forward leg carries the majority of the manipulator's body weight. Skin slack is removed by cephalad traction of the indifferent hand, while a pisiform contact is made with the caudad hand on the mamillary process of the superior segment. The fingers should be spread, facing cephalad and with the fifth digit parallel to the spinal column. The cephalad hand is placed on the subject's upper shoulder, used to stabilize the torso and prevent excessive torque. The thrust is a body drop with a sudden impulse and small amplitude. (Szaraz, 1990)
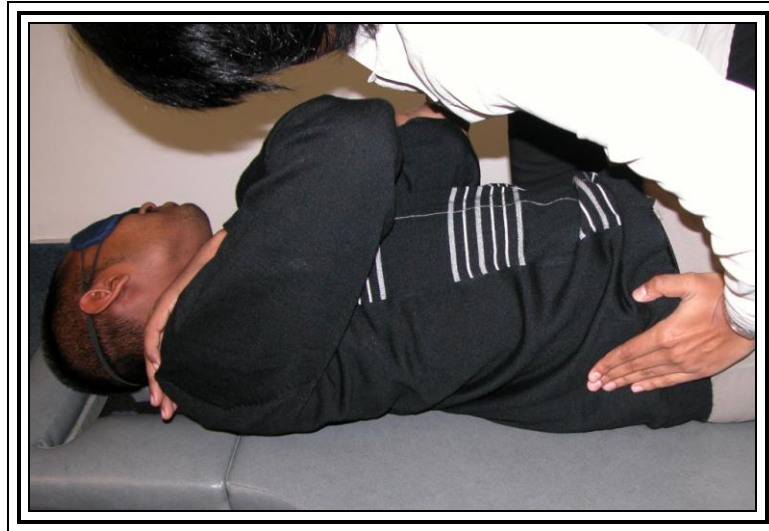
Figure 3.14: Subject being manipulated

Figure 3.15: Subject being brought back to supine position

The subjects of Group 2 rested supine for 5 minutes, then phlebotomised for the second time. They then received a low back spinal manipulation (Szaraz, 1990) and were phlebotomised for the third time. This third sample (labeled Post Treatment 2X[1]) was done as soon as it was possible after the low back manipulation. A 5-minute cut off time was used to standardise the procedure as well as to consider the immediate action of cortisol to increase after a "stressor" (Naidoo, 2004).

The tourniquet was then released, the tube removed, cotton wool placed on the site of the punctured skin, pressure applied, the needle removed and disposed in a "sharps" container, to prevent accidental needle prick injury. A strip of clear adhesive tape was placed on the cotton wool and the subject was asked to apply pressure to the area for three minutes, so as to prevent extravasation. This procedure was applied to both groups of subjects.

The researcher filled in blood test requisition form and the sample tubes were labeled appropriately. The sample request form contained the code of the research and subject's name. Identical labeling was used for the test tubes. The researcher personally took the specimens and form to the Department of Chemical Pathology laboratory on the 1st floor of the Nelson R. Mandela School of Medicine, within 5 minutes of collection. The specimens were handed to Dr. P. Naidoo [senior chemical pathologist, Nelson R. Mandela School of Medicine] (or in her absence the personnel of the laboratory on duty.) The blood samples were centrifuged and separated before freezing. Storage of the cortisol samples had no adverse effects on the final results of the study and in fact, prevented batching errors (Robertson, 2004).

The following is a flow diagram summarizing the research procedure:

Group 1 15 subjects	**Group 2** 15 subjects
Day 1 Examination	**Day 1** Examination
Day 2 Subject phlebotomised at approximately 7:50am, then manipulated and then re-phlebotomised.	**Day 2** Blood drawn at approximately 7:50am, subject rests supine for a few minutes and then phlebotomised. Subject then rests for 5minutes, is then manipulated and re-phlebotomised within 5 minutes of the manipulation.

3.4 MEASUREMENTS AND OBSERVATIONS

3.4.1 THE DATA

The data was in two forms, primary data and secondary data.

3.4.1.1 THE PRIMARY DATA

The primary data was obtained from the following:

- Height and weight of the subjects
- Serum cortisol concentrations at the different times of the research process

3.4.1.2 THE SECONDARY DATA:

The secondary data was collected from a variety of different sources as all the available literature was screened and the relevant data selected for this particular study. These sources included journal articles, textbooks and the Internet.

3.5 STATISTICAL ANALYSIS

The statistical package SPSS (as supplied by SPSS Incorporated, Marketing Department- 1999, Chicago, USA) was used to input data and for analysis of the data in this study.

3.5.1 METHODS OF DATA ANALYSIS

Intra-group analyses: the data collected on the outcome measure of cortisol levels was checked for normality of distribution using histograms and skewness statistics. For normally distributed data, paired t-tests were used for comparisons of pre- and post- (Blood 1 and Blood 2) cortisol measurements. For data that is not normally distributed, Wilcoxon signed ranks tests were used to compare pre-measurements and post-measurements. Box and whisker plots were used to graphically show distributions of data pre-manipulation and post-manipulation.

Inter-group analyses: Baseline comparisons were made between the two groups using the Mann-Whitney test. For cortisol levels that were normally

distributed, repeated measures ANOVA were used to compare the two groups over time and examined for a time by group interaction which would be indicative of a treatment effect. For cortisol levels that are not normally distributed, the difference between the Blood 1 and Blood 2 measurements and Blood 1 and Blood 3 measurements were calculated and compared between the two groups using a Mann-Whitney-U test.

Non-parametric descriptive methods and statistical tests were used due to the skewness of the data and the small sample size. Intra-group comparisons were achieved by Wilcoxon signed ranks tests for two paired groups, while inter-group comparisons were done with Mann-Whitney-U tests for two independent groups (Kirkwood and Stern, 2003). Demographic variables were compared between groups using independent samples t-tests because these variables did not show significant skewness. An alpha level of 0.05 was used to classify statistical significance.

Hypotheses:

Two sets of hypotheses were tested viz.:

1) Serum cortisol levels would be increased post-low back SMT (The Null Hypothesis (Ho)). The Alternate Hypothesis (Ha) states that serum cortisol levels would decrease or be unaffected post-low back SMT.

2) Short-term rest will have no affect on serum cortisol levels (The Null Hypothesis (Ho)). The Alternate Hypothesis (Ha) states that short-term rest will in fact increase or decrease serum cortisol levels.

CHAPTER 4

STATISTICAL ANALYSIS AND RESULTS

4.1. RESULTS

4.1.1. Demographics

Thirty male subjects between the ages of 18 and 35 years were selected by convenience sampling to participate in the study. They were randomized into two groups, Group 1 (n=15), and Group 2 (n=15). Table 1 shows that, as expected (since randomisation distributes all baseline values evenly between groups, therefore, there were no expected baseline differences) there was no significant difference in weight ($p = 0.831$) or height ($p = 0.481$) between the subjects of the two groups.

Table 1: Comparison of weight and height between participants from Groups 1 and 2 (n =30)

	Group	n	Mean	Std. Deviation	Std. Error Mean	p-value
WEIGHT (kg)	1	15	74.5	15.1	3.9	0.831
	2	15	73.5	10.0	2.6	
HEIGHT (m)	1	15	1.8	.08	.02	0.481
	2	15	1.7	.07	.02	

4.1.2 INTRA-GROUP ANALYSIS OF SERUM CORTISOL
CONCENTRATIONS (nmol/l)

4.1.2.1. Group 1

Group 1 was only measured pre-spinal manipulation and post- spinal manipulation. There were three missing values for these time points in Group 1. The missing values are due to haemolysis of serum samples prior to analysis. Results of the Wilcoxon signed ranks tests for comparison between the median cortisol levels at these two time points are shown in Figure 4.1 and Table 2. There was a non-significant decrease in the cortisol levels ($p = 0.126$). Table 2 shows that in 9 of the 12 participants the serum cortisol values decreased between pre-treatment and post-treatment, and in 3 of the participants in this group the values increased from pre-treatment to post-treatment. There were 0 participants whose values were tied at the two time points.
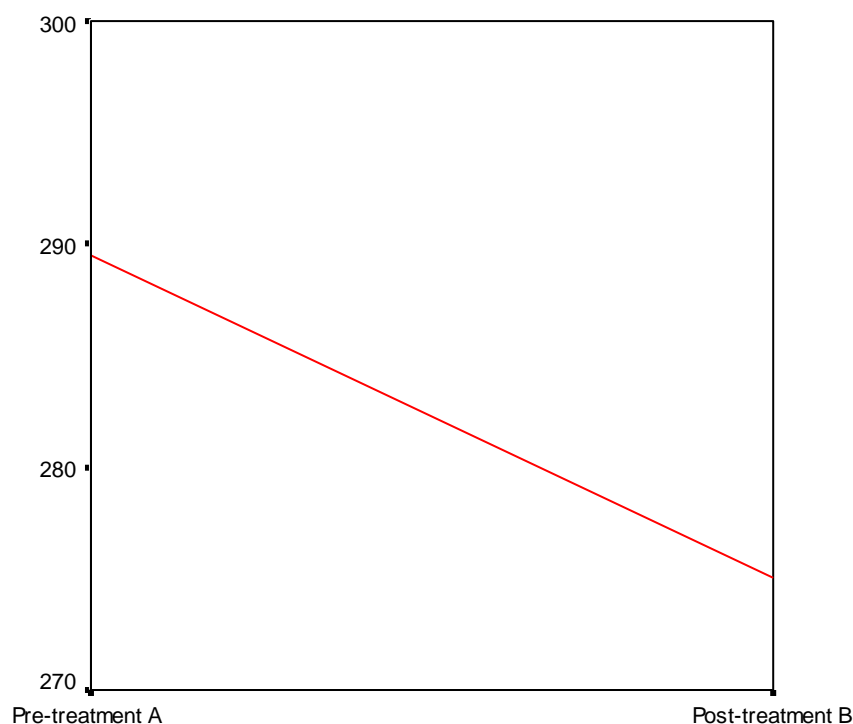

**Figure 4.1: Median serum cortisol levels (nmol/l)
at pre- and post-treatment in Group 1**

Table 2: Wilcoxon signed ranks test for paired intra-group comparison in Group 1

		n	Mean Rank	Sum of Ranks	*p*-value
Post-Treatment B Pre - Treatment A	Negative Ranks	9(a)	6.50	58.50	
	Positive Ranks	3(b)	6.50	19.50	0.126
	Ties	0(c)			
	Total	12			

a Post-treatment B < Pre-Treatment A

b Post-treatment B > Pre-Treatment A

c Post-treatment B = Pre-Treatment A

4.1.2.2. Group 2

Group 2 was measured pre-treatment A, pre-treatment B and post-treatment C. There was a significant decrease in cortisol levels from pre-treatment A to pre-treatment B (p = 0.018). This is shown in Table 3. There was one missing value due to haemolysis of serum samples prior to analysis. Of the 14 participants 12 showed a decrease between pre-treatment A and pre-treatment B, while 2 showed an increase.

Table 3: Wilcoxon signed ranks test for paired intra-group comparison in Group 2 between pre-treatment A and pre-treatment B

		n	Mean Rank	Sum of Ranks	*p*-value
Pre-treatment B Pre-treatment A	Negative Ranks	12(a)	7.5.00	90.00	0.018
	Positive Ranks	2(b)	7.5.00	15.00	
	Ties	0(c)			
	Total	14			

a Pre-treatment B < Pre-treatment A

b Pre-treatment B > Pre-treatment A

c Pre-treatment B = Pre-treatment A

There was a borderline decrease in median cortisol levels from pre-treatment B to post-treatment C (p = 0.064) in Group 2, as shown in Table

4.   There were two missing values due to haemolysis of serum samples prior to analysis. Eleven subjects out of 13 showed a decrease between these time points, while only two showed an increase.

Table 4: Wilcoxon signed ranks test for paired intra-group comparison in Group 2 between pre-treatment B and post-treatment C

		n	Mean Rank	Sum of Ranks	*p*-value
Post-Treatment C Pre-Treatment B	Negative Ranks	11(a)	6.55	72.00	0.064
	Positive Ranks	2(b)	9.50	19.00	
	Ties	0(c)			
	Total	13			

a Post-treatment C < Post-treatment B

b Post-treatment C > Post-treatment B

c Post-treatment C = Post-treatment B

There was also a significant decrease overall in Group 2 between pre-treatment A and post-treatment C (*p* = 0.019) (Table 5). The overall decrease is shown in Figure 4.2. There was one missing value due haemolysis of serum samples prior to analysis. Twelve of 14 participants showed a decrease while only 2 showed an increase.

Table 5: Wilcoxon signed ranks test for paired intra-group comparison in Group 2 between pre-treatment A and post-treatment C

		n	Mean Rank	Sum of Ranks	*p*-value
Post-Treatment C Pre-Treatment A	Negative Ranks	12(a)	7.50	90.00	0.019
	Positive Ranks	2(b)	7.50	15.00	
	Ties	0(c)			
	Total	14			

a Post-treatment C < Pre-treatment A

b Post-treatment C > Pre-treatment A

c Post-treatment C = Pre-treatment A
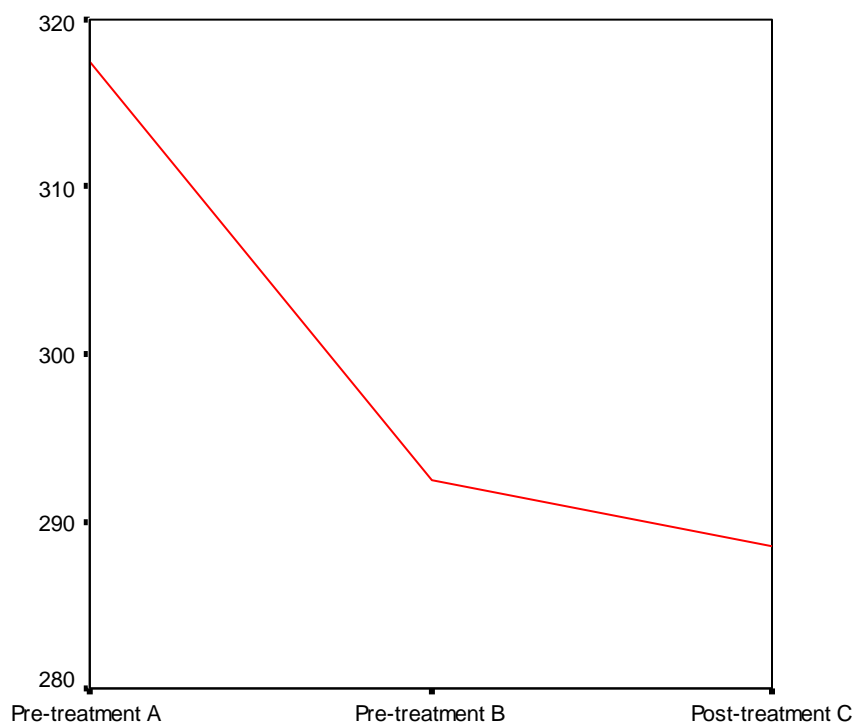
Figure 4.2: Median serum cortisol levels (nmol/l) at pre- and post-treatment in Group 2

4.1.3. INTER-GROUP ANALYSIS

There was no significant difference between the median baseline cortisol levels of the two groups (p = 0.400). This is shown in Table 6 and Figure 4.3. There was one missing value at baseline in Group 1 due to haemolysis of the serum sample. Median serum cortisol for Group 1 at baseline was 289.5 nmol/l (range 214 to 656 nmol/l). The median for Group 2 was 387 nmol/l (range 119 to 591 nmol/l).

Table 6: Mann-Whitney test for baseline (pre-treatment) serum cortisol level comparison between Group 1 and 2

	GROUP	n	Mean Rank	Sum of Ranks	p-value
Pre-treatment A	1	14	13.61	190.50	0.400
	2	15	16.30	244.50	
	Total	29			
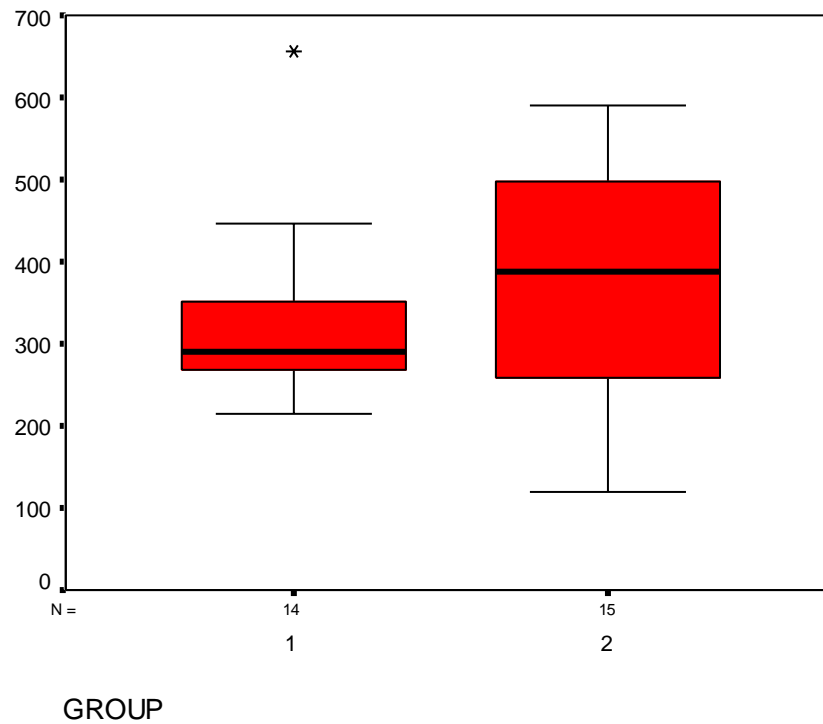
**Figure 4.3: Distribution of pre-treatment serum cortisol levels
(nmol/l) of Group 1 and 2**

There was no significant difference between the post-treatment cortisol
levels of the two groups (p = 0.981). This is shown in Table 7 and Figure
4.4.

**Table 7: Mann-Whitney test for post-treatment serum cortisol level
comparison between Group 1 and 2**

	GROUP	n	Mean Rank	Sum of Ranks	p-value
Post-treatment serum cortisol levels	1	13	14.08	183.00	0.981
	2	14	13.93	195.00	
	Total	27			
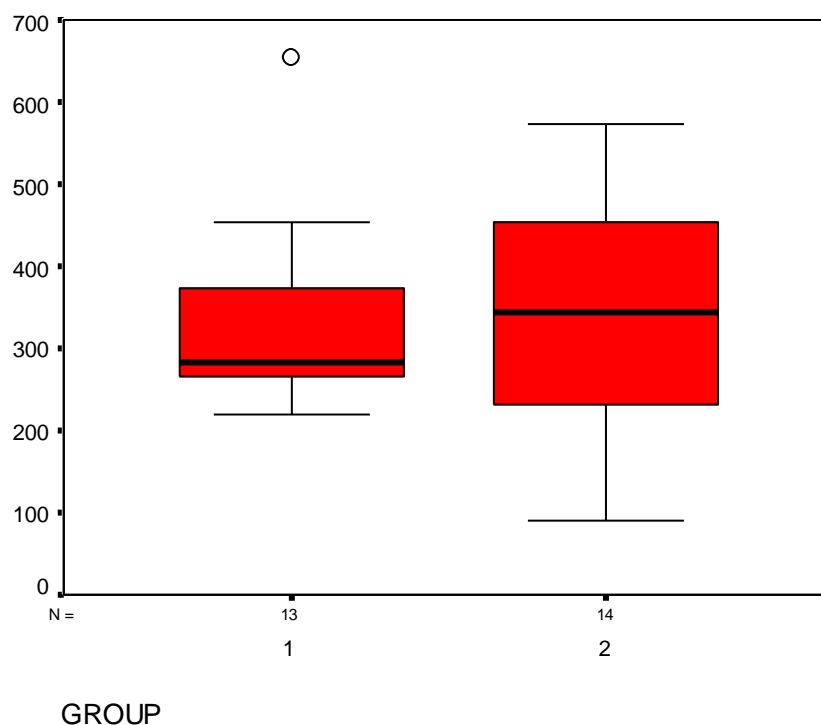
Figure 4.4: Distribution of post-treatment serum cortisol levels (nmol/l) of Groups 1and 2

The change in cortisol from baseline to final reading was calculated for each participant from both groups. Median change was compared between the groups. Table 8 shows that the median change in Group 1 was -5nmol/l and in Group 2 it was -33nmol/l. Thus Group 2 showed a larger decrease in cortisol between baseline and final measurement than Group 1. This was statistically significant, as shown in Table 9. Figure 4.5 shows the distributions of the change in cortisol, by group.

Table 8: Descriptives for change in serum cortisol levels between baseline (pre-treatment) and post-treatment reading by Groups

GROUP	Median	Minimum	Maximum
1	-5.0000	-31.00	24.00
2	-33.0000	-83.00	167.00
Total	-20.0000	-83.00	167.00

Table 9: Mann-Whitney test for comparison of change in serum cortisol by Groups

	GROUP	*n*	Mean Rank	Sum of Ranks	*p*-value
CHANGE IN SERUM CORTISOL LEVEL	1	12	17.88	214.50	0.005
	2	14	9.750	136.50	
	Total	26			
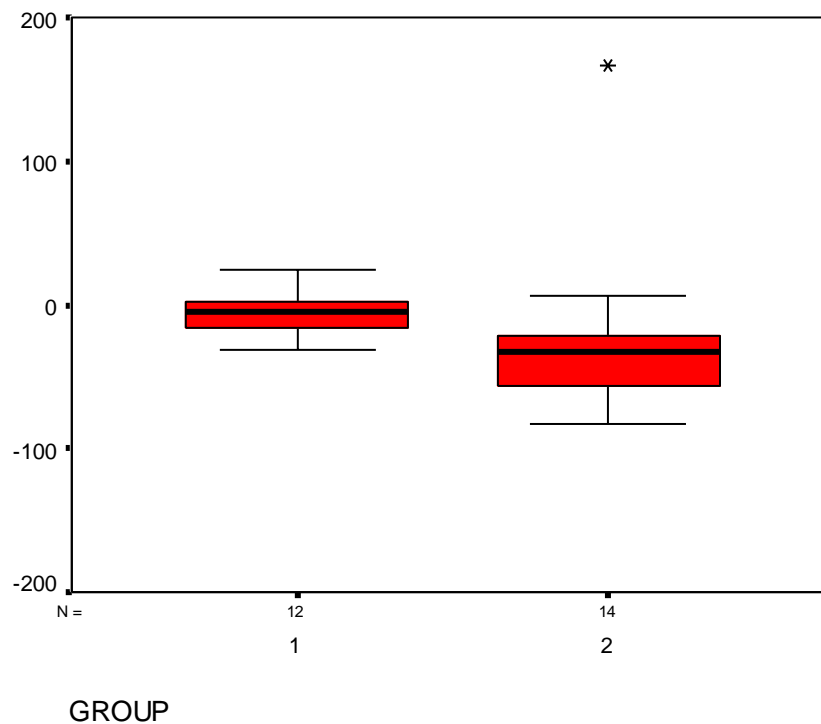
Figure 4.5: Distribution of the change in serum cortisol levels (nmol/l) of Groups 1 and 2

4.3. SUMMARY

Figure 4.6 shows the profile plot of both groups' median serum cortisol values over time. Group 2 showed the largest decrease between pre-treatment A and pre-treatment B. There was only a minor change after SMT. Thus it appears that resting between measurements had a greater impact on serum cortisol levels than the manipulation had.

Figure 4.6: Profile plot of median serum cortisol levels (nmol/l) over time by Groups

CHAPTER 5

DISCUSSION

5.1. INTRODUCTION

This chapter discusses the results obtained through the statistical analyses of the objective data.

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The sample size of the present study consisted of thirty male subjects who presented with mechanical LBP, attributable purely to acute lumbar facet syndrome or acute sacroiliac syndrome. These patients had no other diagnosed pathological problems of the lumbarsacral spine.
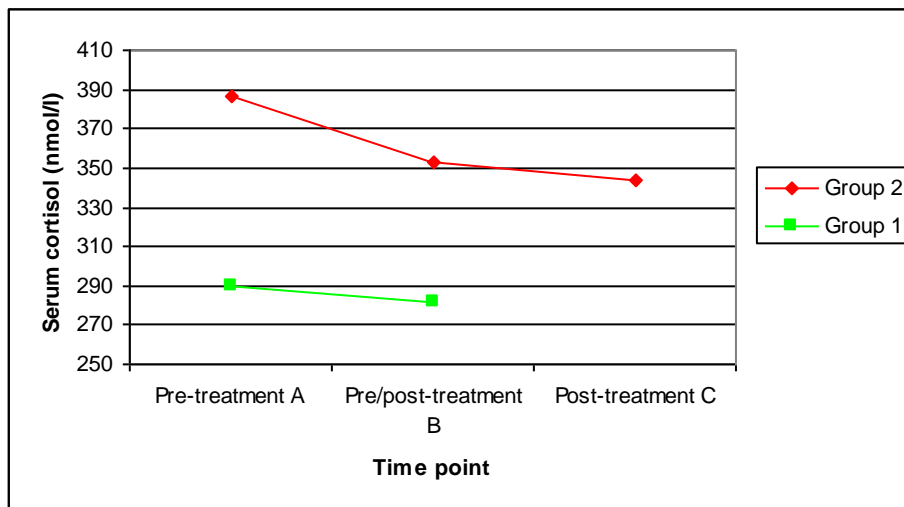
The hypothesis proposes that low back SMT may lead to a release of endogenous cortisol which effects a decrease in inflammation in the affected area. It was also hypothesised that a short-term rest period would not affect the release of cortisol.

5.2. Interpretation of Data

5.2.1. Demographical data

The demographical data pertaining to this study sample was presented in Chapter Four under 4.2.1. The study by Tuchin (1998) used a sample size of 9 subjects (3 females and 6 males). The study by Whelan *et al.* (2002) used a sample size of 30 males. Both these studies failed to report the use of any other demographic data.

The demographical data used in this present study were height and weight. The height and weight of Group 1 was compared to that of Group 2. There was no significant difference between the height and weight of both groups. The average Body Mass Index (BMI) of Group 1 was 24.3 and that of Group 2 was 24.5. These values fall in the upper part of the acceptable range (Haslett *et al.,* 1999). It is thus possible that these subjects were symptomatic with LBP as a result of being slightly overweight which is in

keeping with several studies that concluded that an increase in weight increases the incidence of LBP (Orvieto *et al.,* 1994; Van der Meulen, 1997). There is no indication in the literature that height has an effect on serum cortisol levels but there have been documented findings that over weight people generally have higher serum cortisol levels (DeGroot *et al.,* 1989).

5.2.2 Serum cortisol analyses

The thirty male subjects were randomly allocated to one of two groups i.e. Group 1 (*n*=15) or Group 1 (*n*=15). The subjects in Group 1 received pre-treatment A and post-treatment B phlebotomies. The subjects of Group 2 received pre-treatment A, pre-treatment B and post-treatment C phlebotomies, via the single phlebotomy catheter, cannulated prior to commencement of any procedures.

GROUP 1   **GROUP 2**

| Pre-SMT | Post-SMT | | Pre-Rest | Pre-SMT | Post-SMT |
| A | B | | A | B | C |
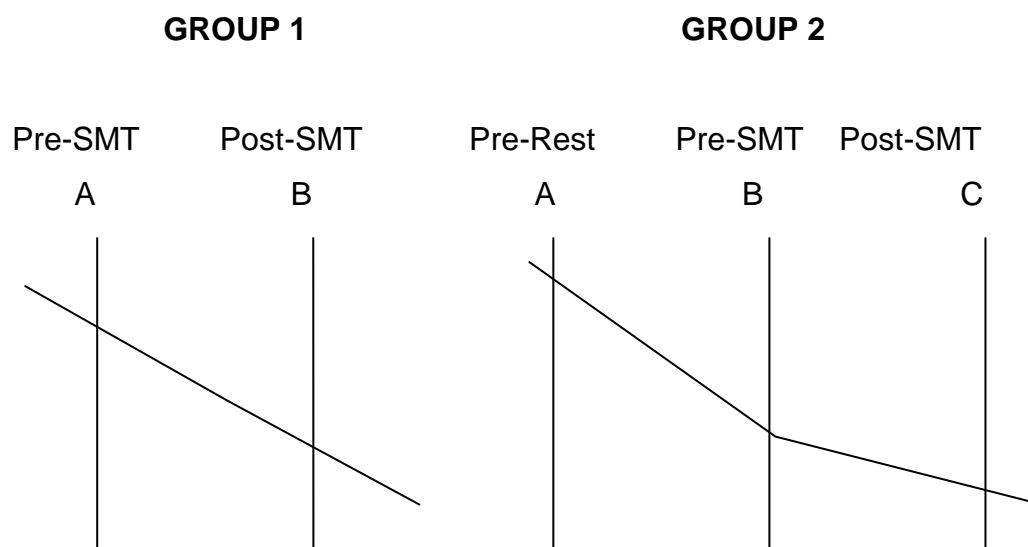
Figure 5.1: Schematic Diagram illustrating cortisol levels pre-and post-intervention

The common finding, in both intra-group and inter-group comparisons, was a decrease in serum cortisol levels. This decrease in serum cortisol levels may possibly demonstrate the natural circadian drop in basal cortisol levels. This is not in keeping with our proposed hypothesis that low back spinal manipulation would cause a stress on the body significant enough to

increase cortisol levels. It was also found that short-term rest caused a significant decrease in serum cortisol levels. It is worth noting that any activity resulting in a stress response on the body should increase serum cortisol levels (Guyton and Hall, 2000). However, short-term rest is actually a period of inactivity and as such, there is no stressor on the body and this could possibly explain the decrease in serum cortisol levels after short-term rest.

Baseline serum cortisol levels differ in individuals depending on a few factors which are mentioned below:

- Sexual dimorphism: females have more unstable serum cortisol levels due to their menstrual cycle having an influence on cortisol levels hence females were excluded from this study (DeGroot *et al.*, 1989)

- Age ranges: research has shown that the older the individual the higher the baseline serum cortisol levels hence one of the reasons this study was limited to males between the ages of 18 to 35 (Beale *et al.*, 2002).

- Occupational variations: cortisol is considered a stress hormone and is released when an individual is exposed to a stressor. Occupational factors do result in individuals experiencing large amounts of stress (Selye, 1956) and this could result in them having higher baseline cortisol levels.

- Diurnal variations: are often disturbed in individuals who work alternating day and night shifts. The diurnal cycle is based on 24hours but if the day is lengthened to more than 24hours the cycle also lengthens thus affecting baseline serum cortisol levels (Ganong, 2001).

The researcher did not investigate the occupational and diurnal variations on serum cortisol levels in this study, and therefore cannot comment on how these factors could have influenced the final results of this study and

recommend that the effect of occupational and diurnal variations be investigated in future studies.

Group 2, in fact, showed a larger decrease in serum cortisol between baseline and final measurements, than Group 1. This was statistically significant (p=0.005). This larger decrease in serum cortisol levels is possibly due to the fact that in Group 2 there was a greater time interval between baseline and final measurements of serum cortisol.

Group 1 showed a minimal decrease in serum cortisol levels after a low back spinal manipulation. Group 2 showed the largest decrease between pre-treatment A and pre-treatment B (i.e. rest interval). Thus, it appears that resting between measurements had a greater impact on serum cortisol levels than a low back spinal manipulation. These results are not in keeping with the proposed hypothesis that low back spinal manipulation may possibly cause a short-term increase in serum cortisol levels. It was possible that this could have lead to a decrease in inflammation on the affected area since cortisol is an anti-inflammatory hormone. Therefore we fail to accept the null hypothesis and accept the alternate hypothesis with respect to SMT and serum cortisol release and the affect of short-term rest and serum cortisol release. The results of the present study showed a minimal decrease in serum cortisol levels after SMT which are in keeping with the results of Tuchin (1998) and Whelan *et al.* (2002) who both showed a decrease in salivary cortisol levels after SMT. Even though the results of all three studies are the similar, each study had methodological differences which are mentioned below.

When comparing the present study to previous studies, it was found that the study by Tuchin (1998) questioned the use of blood testing due to possible rises in the cortisol levels because of the invasive nature of vein puncture required for blood sampling. He further questioned false increases in cortisol may occur due to the physical stress of sampling. It was therefore expected in this present study, due to the invasive nature of intravenous samples that

the cortisol would most certainly have risen at the least to borderline significance (p=0.005).

The results of this present study have shown the opposite, serum cortisol levels in fact significantly decreased considering intravenous sampling was used. This then suggests that the use of salivary cortisol in Tuchin (1998) should be questioned since salivary cortisol only closely reflects the plasma levels of cortisol and does not emulate serum cortisol levels (Kahn *et al.,* 1988).

The results of Whelan *et al.* (2002) should therefore also be questioned due to the use of salivary cortisol rather than serum cortisol. Whelan *et al.* (2002) concluded from their results that spinal manipulation had no significant affect on salivary cortisol level. He went on further to suggest that the physical component of spinal manipulation is not a potent enough stressor to disrupt homeostatic mechanisms and activate the hypothalamic-pituitary-adrenal axis. The results of the present study show that spinal manipulation did have an effect on serum cortisol albeit cortisol levels decreased hence the physical component of spinal manipulation is able to affect the homeostatic mechanisms and activate the hypothalamic-pituitary-adrenal axis.

The findings, although not supporting the initial hypothesis proposed, showed a decrease in short-term serum cortisol levels after low back spinal manipulation. This unexpected decrease in serum cortisol levels gives rise to numerous unexplained questions. These questions result in the formulation of the following explanations.

5.3. PROPOSED EXPLANATIONS FOR OBSERVED FINDINGS:

Explanation One

The following explanation is based on the physiology of cortisol catabolism as outlined in Ganong (2001). Cortisol is metabolised by the liver, which is the principle site of glucocorticoid catabolism. During an individual's

exposure to stress, the rate of hepatic inactivation of cortisol is depressed. It is possible that cortisol was released immediately after a subject was exposed to SMT (SMT is considered a stressor). This resulted in a depression of liver catabolism of cortisol, thus the gradient on Figure 4.1 appears shallow. However when we look at the gradient on Figure 4.2 between Pre-treatment A and Pre-treatment B, we see that is much steeper than gradient between Pre-treatment B and Post-treatment C (when the individual was exposed to SMT). The individual was resting during the interval Pre-treatment A and Pre-treatment B, was not exposed to a stressor and thus the liver metabolism of cortisol was essentially normal or possibly increased. This indicates the normal response of a body to a stressor or rest with respect to serum cortisol catabolism and not really linked to a neural pathway from the lumbar spine to the adrenal glands.

Explanation Two

After a 5 minute rest period and spinal manipulation there is an effect on the neuroendocrine system resulting in the release of serum cortisol together with another substance that for purpose of this research shall be referred to as "Substance **X**".   However, "Substance **X**", possibly a neuropeptide, secretes negative substances that have a denaturing effect on circulating cortisol, hence causing a quantitative decrease of circulating serum cortisol. The question that arises and requires further research is does a "Substance **X**" exist and if so, what is the nature and control mechanism of this endogenous chemical. This further research has a tremendous impact on clinical medicine, in the future. After an exhaustive search in the literature (books, journals, Internet and personal communication with a chemical pathologist (Naidoo, 2005)) the researcher could not find anything similar in the human body where two substances are secreted simultaneously and one denatures the other.

Explanation Three

Cortisol is metabolised rapidly, mainly by the liver, and has a plasma half-life of approximately 2 hours. The metabolic clearance rate is 200L per day. It is not known how soon after a "stressor", cortisol is expected to be

released but what is known is that there is a several minute lag time in humans between AcTH stimulation and cortisol release (DeGroot *et al.,*1989). It is also possible that the blood samples were taken too early to detect any changes in the serum cortisol levels. Due to budget constraints we were also not able to carry out renal sampling over at least one hour.

In keeping with the above, it is proposed that in patients with inflammation do in fact have their cortisol released after a spinal manipulation but the cortisol is denatured at a faster rate than in patients without inflammation. It is reasoned that the levels of cortisol in this study therefore decreased due to the analysis of the hormone levels in symptomatic patients (Ganong, 2001).

Explanation Four

Inflammation has nothing to do with cortisol release and possibly other substances are actually involved in the process. The presence or absence of such substances needs to be elucidated in future studies.

Explanation Five

Spinal manipulation interferes with microcirculation in the adrenal cortex, which may give rise to relative ischaemia and therefore temporarily decreases circulating blood levels in systemic circulation (Leach, 1994). This is proposed on the basis of the anatomical proximity of the blood supply of the adrenal gland to the lumbar spine as well as alterations in the curvature of the lumbar lordosis during the SMT (Gray, 1974).

Explanation Six

The study was conducted in a young sample population of otherwise healthy males. It is proposed that since the resting basal levels were sufficiently "high" for the anti-inflammatory needs of this study group, the SMT did not result in a further increase. It is suggested that if a similar study were conducted in an older patient group, the levels would significantly increase after SMT. The rationale for this hypothesis is that

relative and temporary arterial ischaemic processes involving the adrenal gland is much more prominent in an older age group (Beale *et al.*, 2002).

Explanation Seven

Since there are no significant reasons for the decrease in the 2 groups it therefore stands to reason that the higher the initial level, the more dramatic is the decrease and this could only be brought about by a "mass effect" of denaturing a large amount of circulating cortisol.

Explanation Eight

This study protocol catered for the analysis of the cortisol levels after a five-minute interval, post-SMT. It is proposed that the increase occurs well after this period, the exact period of time is unknown at present and further studies are indicated in this area. For this reason, in the present study, an objective increase in the cortisol level was not noted in the study group in view of the time interval elapsed between the SMT and sample collection.

5.4. Study limitations

Missing values for statistical analysis was due to haemolysis of samples prior to being analysed. These missing values could certainly have affected the final statistical analysis of the present study.

Room lighting may also have an affect on cortisol levels and therefore should also be considered (Ganong, 2001). In this study the effect of ambient lighting was minimized on the test subjects by making the subjects wear a standard airline issue eye shades prior to the collection of samples. Ideally the test subjects should be placed in a darkened room for collection of cortisol samples. However, this would not be practical and may even add to the "stressor" effect on the subjects.

Further studies could possibly include estimation of serum AcTH levels which could not be incorporated into the present study for reasons of financial constraints.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1. CONCLUSION

The aim of this study is to determine if serum cortisol increases immediately after low back SMT. Our hypothesis proposed an increased serum cortisol level post-SMT. This could have lead to a decrease in inflammation on the affected area. The following conclusions maybe drawn based on the objective laboratory tests carried out in this study:

- The cortisol assays in this study indicate that there was a non-significant decrease in serum cortisol levels post-low back spinal manipulation but there was a significant decrease in serum cortisol levels between the initial blood sample and the 5-minute rest period. These findings are contradictory to what was theoretically expected to happen.

- The results of this study support the fact that a neural and endocrine effect can be stimulated by rest and to a lesser extent low back spinal manipulation, albeit a decrease in serum cortisol occurred. This mechanism that results in the decrease of cortisol is not established and requires further investigation.

- Finally, this study has been unable to show an increase in serum cortisol levels after a low back spinal manipulation. Further research is necessary to determine what role SMT may have on decreasing facet joint inflammation and its proposed neural and endocrine affects that have been advanced based on previous studies.

6.2. RECOMMENDATIONS

The author is of the opinion that the following recommendations could improve the validity of future studies investigating the effects of low back

spinal manipulation on serum cortisol levels, which may lead to a decrease in inflammation in the affected area.

- In the present study, the sample size was limited to thirty subjects. A larger sample size would minimise the chances of a Type II error and result in the generation of valid study data.
- Future studies must correlate the salivary cortisol levels with serum cortisol assays in the study patients. Financial constraints in the present study precluded this aspect of the analysis.
- The effect of low back spinal manipulation on long term serum cortisol levels should be assessed i.e. the post-treatment blood test for cortisol assays should be done at least an hour or more after the low back spinal manipulation.
- The present study suggests that there are indication to perform serum AcTH assays in future studies involving LBP.
- Correlating laboratory results with clinical data e.g. NRS or clinical case history and examination findings.
- Studies to determine the time of cortisol release following a stressor and the time and nature of its degradation.
- Correlating serum cortisol levels and release with its effect on inflammatory markers such as C reactive proteins (CRP) and erythrocyte sedimentation rate (ESR).
- Studies to determine the effect of ethnicity, seasonal and dietary variations on baseline serum cortisol levels.

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