To investigate the effect of the simultaneous administration of Homoeopathic low potencies (4 CH) of phosphocreatine and glycogen on the anaerobic work capacity of human thigh muscle.

Dissertation submitted in compliance with the requirements for the Masters Degree in Technology in the Department of Homoeopathy at the Technikon Natal.

By

Wayne Stuart Naude

I hereby declare that this dissertation represents my own work, in conception as well as execution.

Approved for final submission

Dr A. Gerber Ph.D (UOFS)
Supervisor

27-03-97
Date

W. S. Naude

To my wife,

Catherine

I would like to acknowledge the contribution of the following persons and institutions towards the completion of this dissertation:

Dr. Gerber	Supervisor
Dan Grobler	Biokineticist
Mariane Pienaar	Subject Librarian (Life Sciences)
Technikon Natal	Funding
Dr. F. Burger	Advice

ABSTRACT

The purpose of this study was to investigate the effect of the administration of homoeopathic dilutions of phosphocreatine and glycogen on the anaerobic work capacity of human thigh muscle. It was hypothesized that there would be an increase in the anaerobic work capacity after one week, and that this effect would persist for a further four weeks.

The experiment was performed according to the protocol of a double - blind clinical trial. The subjects were male caucasians between 17 and 23 years of age, all in good health for the duration of the test period. Sixteen subjects took doses of Phosphocreatine 4 CH and Glycogen 4 CH three times daily for 7 days (the experimental group). Twenty one different subjects took a placebo preparation at a similar dosage. The placebo preparation was 20 % ethanol in water, making it impossible to distinguish it by taste from the experimental preparation.

Tests were performed on the Akron isokinetic tester. Three tests were performed by each subject: an initial test, and follow - up tests on days 7 and 35. The tests were in the form of explosive flexion and extension of the leg, with a maximum displacement of 195 degrees per second, for 30 seconds. The accumulated work done in flexion and extension was calculated.

The subjects were instructed to continue in their normal lifestyle for the duration of the test period.

Statistical analysis was carried out, using the Wilcoxon signed - rank test to test for intra - group variation, and the Mann - Whitney U test to test for inter - group variation.

Intra - group analysis of the variance revealed statistically significant increases in work done in the first and second follow - up tests for both the experimental and placebo groups. Inter - group analysis revealed that the groups were not statistically different in any of the parameters tested.

Because the anaerobic work capacity increased in both the experimental and placebo groups, we conclude that the preparation was not the cause of the increase. We speculate that the increase could be due to psychological factors, such as differing responses to motivation, and familiarity with the procedure in the follow - up tests, and physiological factors such as meals eaten or missed before the tests were performed.

Table of Contents

List of Tables

Table of Figures

Page No.

Page No.

CHAPTER 1 . Introduction

In order to stimulate muscle hypertrophy, a sportsperson must exert forces while training that are close to their maximal output (Evans 1995).

When performing such exercise, the ATP or energy demands of the muscle cannot be supplied by oxidative pathways alone. The majority of the ATP required is produced via anaerobic pathways.(Kemp et al. 1995.)

The two major sources of ATP from these anaerobic pathways are glycolysis, by which glycogen is consumed and ATP and lactate produced, and phosphocreatine degradation, by which ADP is phosphorylated to ATP, and creatine is released (Radda et al. 1995).

It is in order to support these two pathways, as well as aerobic metabolism, that various sports supplements and nutrients have been developed, and are being used daily by sports people all over the world. These products range from simple protein and carbohydrate shakes to scheduled and banned substances such as stimulants and anabolic steroids.

These products are claimed to increase muscle glycogen levels and supply nutrients consumed during exercise, among other things. Unfortunately, some of these products also have side effects, ranging from hypervitaminemia to liver cancer.

For competitive sports people, being able to increase the rate of ATP production through the anaerobic pathway would clearly be advantageous, especially those participating in event involving bursts of maximal or near - maximal output, such as javelin throwing, shot - putting, sprinting, power lifting and bodybuilding. An increase in the rate of ATP production leads, in effect, to an increase in strength.

Homoeopathy is a medical system that operates according to several laws, discovered and laid out over the past 200 years by homoeopaths and physicians. Homoeopathic medicines serve as a specific stimulant to the body. (Jouanny 1991:81.)

Because we are attempting to influence the anaerobic work capacity of human thigh muscle, we are using glycogen in homoeopathic potency (4CH) to stimulate glycogen storage, and phosphocreatine (4CH) to maximise the amount of phosphocreatine in the muscles before each follow - up test is performed.

The aim of this study is to investigate the effect of the simultaneous administration of phosphocreatine and glycogen in homoeopathic potency (4CH) on the anaerobic work capacity of human thigh muscle.

CHAPTER 2. Review of the related literature

2.1 Biochemistry and Physiology

The purpose of the review of the biochemistry and physiology is to illustrate the rationale for the choosing of the particular substrates used in this study, and to give the reader an understanding of the biochemical and physiological mechanisms that we are attempting to influence.

2.1.1 *Anaerobic Metabolism*

Anaerobic metabolism is the production of ATP (adenosine triphosphate) without the consumption of oxygen. In the human body, this occurs mainly through the process of glycolysis, by which glucose or glycogen is metabolized to lactate, and ATP released. The classical pathway of glycolysis is the production of two ATP molecules from every molecule of glucose. In the muscle, however, it is the conversion of glycogen, rather than glucose, to lactate, resulting in three ATP molecules, that is the chief anaerobic pathway in operation. To place these figures in the proper perspective, however, it is important to remember that aerobic or oxidative metabolism yields more than 10 times the quantity of ATP molecules per molecule of glucose. (Reynolds et al. 1995.)

2.1.2 *The Physiological Importance of Anaerobic Glycolysis in Skeletal Muscle*

Anaerobic glycolysis is constantly continuing within the tissues of the body. Glycolysis yields the substrate necessary for oxidative metabolism - pyruvate. Under resting conditions, or mild effort, most tissues rely on ATP production from the oxidative pathway for their energy needs. However, in tissues that are under perfused with blood, or lack mitochondria, or under conditions (eg. maximal exertion) where the demand for ATP cannot be met by the oxidative processes, glycolysis and the degradation of phosphocreatine are the only pathways capable of supplying the ATP necessary for work. In skeletal muscle, glycolysis and ATP from phosphocreatine are also important when vigorous exercise is initiated- before the exercise induced increase in blood supply occurs, and also in the more anaerobic type of muscle fibre (Type IIB). (Kemp et al. 1995.)

2.1.3 *Classification of skeletal muscle fibres*

Human muscle fibres have been classified into two (Saltin et al.1977) main types:

a) Type I fibres

These are known as the slow-twitch oxidative fibres (Wank et al. 1994).

They are identifiable histologically by their small size compared with the other fibre types, except type IIA fibres, which are of a similar size. They contain myosin heavy chain (MHC) isoform I. The type I and type IIA fibres also contain the most succinate dehydrogenase (SDH), and type I fibres contain the least actomyosin ATPase. They contain high levels of triacylglycerol, and have high activities if the enzymes of the tricarboxylic acid cycle, of fatty acid oxidation, and of the electron transfer chain. (Sieck et al. 1995.)

It has also been observed that the deeper portions of skeletal muscle contain more type I fibres than the superficial portions (Travnik et al. 1995).

Type I fibres are also known as fatigue resistant (Guyton 1992:646).

b) Type II fibres

Type II fibres are classified into three types according to their MHC isoforms and their ATP producing characteristics.

Type IIA fibres contain the MHCIIA isoform (Hamalainen and Pette 1995).

They are also termed fast - twitch oxidative (Wank et al. 1994).

Type IIA fibres have high oxidative and glycolytic capacities, and contain an intermediate amount of triacylglycerol. Along with type I fibres, they are the smallest fibre type and have the highest concentration of SDH. They have less actomyosin ATPase than type I fibres, but more than the other fibre types. (Sieck et al. 1995.)

Type IIB fibres are known as fast - twitch glycolytic fibres (Wank et al. 1994).

They have a high glycolytic and low oxidative capacity. They contain a large amount of endogenous glycogen (in man, approximately 80 micromol.g-1 fresh weight). The fibres contain only a small amount of triacylglycerol. (Newsholme and Leech 1983: 212,213.)

Type IIB fibres are the largest of all muscle fibre types (Sieck et al. 1995).

Since the glycolytic capacity is large, it is possible that the degradation of glycogen to lactate could occur in a matter of seconds. Thus these muscle fibres are the ones used in violent exercise of short duration. The rate of endogenous glycogen utilization during anaerobic (short - term maximal effort) tests has been shown to be between 20 and 40 times greater than that measured during aerobic (sustained sub - maximal effort) tests. It may seem surprising that the energy used is derived from the relatively inefficient process of glycolysis, rather than the oxidative pathway with its high yield of ATP. (Reynolds et al. 1995.)

There are two suggested explanations for this:

First, vasodilation and changes in the distribution of blood within the body take several minutes to establish, and so getting oxygen to the fibres sufficiently rapidly to support oxidative metabolism may be difficult (Pittman 1995).

The second point is that accommodating more myofibrils in a muscle fibre is possible if the mitochondria are omitted. Mitochondria perform oxidative functions and so are not required in fibres reliant on glycolysis for ATP. (Tseng et al. 1995.)

If the glycogen phosphorylase were fully activated, the glycogen store may be depleted in less than 20 seconds in muscles composed almost entirely of these type IIB fibres. Lactate levels in the blood peak at between five and 15 seconds in explosive exercise. (Yamamoto and Kanehisa 1995.)

Type IIX or type IIC fibres contain MHCIIX isoform. They are of intermediate size, and contain intermediate amounts of SDH and actomyosin ATPase (Sieck et al. 1995).

Apart from the pure fibre types discussed above, there do occur hybrid fibre types, containing more than one MHC isoform (Hamalainen and Pette 1995).

In rat diaphragm muscle, 86% of fibres were of the pure type. When co - expression was present, the most prevalent combination was the co - expression of the MHCIIX and MHCIIB isoforms (Sieck et al. 1995).

2.1.4 *The contraction of skeletal Muscle*

2.1.4.1 The Physiological Anatomy of Skeletal muscle

2.1.4.1.1 The Skeletal Muscle Fibre

Skeletal muscles are composed of individual, parallel - lying muscle fibres. Each muscle fibre is between 10 and 80 microns in diameter, depending on type. Muscle fibres run the entire length of the muscle, and are innervated by only one nerve ending, in all but 2 percent of fibres. (Sieck et al. 1995.)

The outer membrane of the muscle fibre (the sarcolemma) is composed of a true cell membrane (the plasma membrane) and an outer thin layer of polysaccharide material. At the ends of the muscle fibres, the surface layers of the sarcolemmas fuse with the tendon fibres, which collect to form the muscle tendons, which insert into the bones. (Guyton 1992:57.)

The functional units within the muscle fibres are the myofibrils. Myofibrils are composed of actin and myosin filaments, which lie side by side and partially interdigitate. It is the interaction between these filaments that brings about shortening of the myofibrils, and in turn, the shortening of the muscle fibre. Actin and myosin filaments are large, polymerized protein molecules. The degree of interdigitation of these actin and myosin filaments varies with the degree of contraction of the myofibril. Each myofibril contains approximately 1 500 myosin filaments, and twice that number of actin filaments. (Milligan 1996.)

The myosin filaments are thicker than the actin filaments. Protruding from the surface of the myosin filaments are globular protein cross - bridges. The physical and chemical interactions between the myosin cross - bridges and the actin filaments bring about shortening or tension development in the muscles. (Milligan 1996.)

The intracellular matrix of the muscle fibre is termed the sarcoplasm, and it contains the common organelles and constituents found in the cytoplasm of the cells of other tissues. It does contain, however, unusually high numbers of mitochondria, indicating the need of the contracting myofibrils for large amounts of ATP. It also contains an extensive endoplasmic reticulum, called the sarcoplasmic reticulum, containing Ca2+, which plays an important role in the contraction of the muscle fibre. (Fryer et al. 1995.)

2.1.4.1.2 Molecular mechanisms of muscle contraction

Action potentials from the motor nerves transmitted to the sarcolemmas of the muscle fibres, and the spreading of these action potentials along the length of the muscle fibres initiates the contraction process. As the action potential spreads into the sarcoplasmic reticulum, depolarization of the membrane occurs, releasing stored Ca2+ into the sarcoplasm. The Ca2+ initiates the chemical events of the contractile process. This mechanism is termed excitation - contraction coupling. (Jontes 1995.)

The increased concentration of Ca2+ in the sarcoplasm causes exposure of the active sites on the actin filaments. The protein cross - bridges of the myosin filaments bind to the exposed active sites. This results in a conformational change in the cross - bridge, and the development of a tension between the two filaments, causing shortening of the myofibril, and increasing the degree of interdigitation of the actin and myosin filaments. The Ca2+ remains in the sarcoplasm for a very short period (approximately 1/30th of a second) as it is rapidly pumped back into the sarcoplasmic reticulum by calcium pumps in the membrane of the sarcoplasmic reticulum. (Jontes 1995.)

The energy for muscle contraction is provided by ATP. Although the exact mechanism of ATP utilization is unknown, a possible mechanism has been suggested:

ATP is bound to the cross - bridges on the myosin filaments, and the ATP is cleaved to form ADP by the ATPase activity of the cross - bridge. The ADP remains bound to the cross - bridge. In this state the bridge extends perpendicularly towards the actin filament. When the calcium ions are released, binding of the cross - bridges to the exposed active sites occurs, pulling the actin filaments - the so - called power stroke. Energy for the power stroke is provided by the stored energy from the cleavage of ATP. Once the head of the cross - bridge has tilted, this allows release of the ADP molecule, and exposes a site on the head where a new ATP molecule may bind. Binding of the ATP molecule causes detachment of the head of the cross - bridge, and a re - alignment of the cross - bridge to its perpendicular state. It has been proposed that ADP release and ATP binding are blocked by positive strain and phosphate release by negative strain. (Smith and Geeves 1995.)

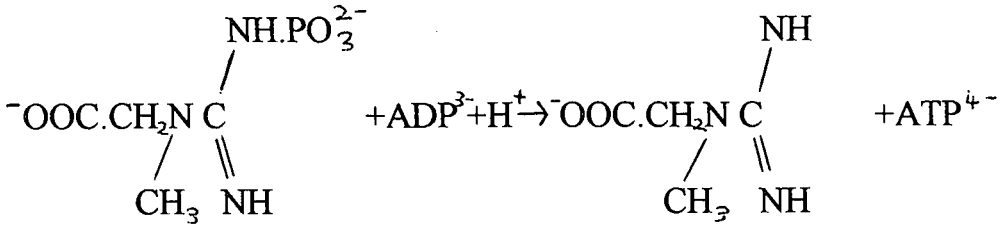
The working stroke produced by a single actin - myosin interaction is approximately 4nm, and the average force generated is approximately 1,7 pN under isometric conditions (Molloy et al. 1995).

Approximately 100 detachment - reattachment cycles take place per second under high load conditions, this decreasing to approximately 20 detachment - reattachment cycles per second under low load conditions (Piazzesi and Lombardi 1995).

2.1.5 *ATP Production during vigorous exercise*

During vigorous exercise, as previously discussed, it is chiefly the anaerobic pathways that are utilized in the production of ATP. These pathways are: 1) glycolysis and 2) the phosphagens. Glycolysis (the biochemical pathway) will be diagrammatically presented separately under section 2.1.8.1 of the literature review.

The phosphagens may be described as "energy-rich" because their phosphate group can be transferred directly to ADP to form ATP. They are phosphorylated guanidine compounds, and are found in most living organisms. In vertebrates the phosphagen is invariably phosphocreatine (also known, less correctly, as creatine phosphate). The transfer of the phosphate group is catalysed by the enzyme creatine kinase. (Clark et al. 1995.)



Phosphocreatine Creatine

Fig 2.1: The Phosphorylation reaction of ADP by Phosphocreatine

ADP phosphorylation by phosphocreatine is especially important in the initial stages of muscular work. It is the major source of ATP for the muscle for the first 4-5 seconds of exercise. During this time a new steady rate of glycolysis has not yet been established. It has been suggested that the ATP required for very short explosive bouts of exercise, such as power lifting movements and shot-putting may be provided almost exclusively by the phosphagens, more specifically by phosphocreatine. The concentration of phosphocreatine in human quadriceps muscle is approximately 18 micromol.g-1. (Clark et al. 1995.)

Phosphocreatine degradation is the most readily available source of ATP in the cells. Phosphocreatine in the cell may be equated with a biochemical capacitor. (Kushmerick 1995.)

2.1.6 *Biochemical Changes Occurring at the Initiation of Exercise*

Under resting conditions, the ATP required in all types of muscle fibres is obtained via aerobic metabolism (oxidation of glucose, fatty acids, etc.). Because the demand for ATP is very low, even a very poor blood supply will provide enough fuel and oxygen to maintain an appropriate level of oxidation. (Toth and Poehlman 1995.)

When exercise is initiated, however, the situation changes dramatically. The change in the demand for ATP is very large - perhaps several hundred times greater. During this period ATP must be generated from endogenous fuels because the blood supply takes some time to adjust to the increased demand for oxygen and fuels. These endogenous fuels are phosphocreatine and glycogen. (Radda 1996.)

Because of the near-equilibrium nature of the phosphagen reactions, the degradation of phosphocreatine is the first source of ATP. Since the store of phosphocreatine is small compared with the rate of ATP utilization, this pathway is only effective for a few seconds, after which the metabolism of other fuels must occur. From the assumption that maximum activity of the glycolytic enzyme, 6-phosphofructokinase, provides a quantitative index of the maximum anaerobic glycolytic flux, it can be calculated that the maximum rate of ATP utilization in human muscle is about 3 micromol.sec-1.g-1. The concentration of phosphocreatine in human muscle is about 18 micromol.g-1, and in severe short-lasting exhaustive exercise about 13 micromol of phosphocreatine is actually broken down. This would provide energy for about four seconds. (Radda et al. 1995.)

The use of phosphocreatine during the initial period would give time for metabolic control to increase the flux through non equilibrium reactions catalysed by the enzymes phosphorylase, 6-phosphofructokinase and pyruvate kinase. In this way glycolysis will take over ATP production smoothly from phosphocreatine. (Radda et al. 1995.)

It is likely that some glycogen in the muscle is completely oxidised to carbon dioxide and water since there will be a small quantity of blood within the blood vessels of the muscle. Also, Type I fibres contain myoglobin, an oxygen binding molecule with a structure similar to that of haemoglobin. (Guyton 1992:646.)

It is unlikely, however, that the contribution of this ATP is significant prior to vasodilation at the beginning of exercise. Therefore the conversion of glycogen to

lactate must provide a considerable proportion of the ATP requirements. (Pittman 1995.)

Evidence exists that anaerobic glycolysis is the major source of ATP during the initial stages of explosive exercise:

First, the blood lactate levels of an exercising man reach a peak within the first 30 seconds of beginning a bout of maximal exertion (Yamamoto and Kanehisa 1995).

Secondly, a number of people possess a congenital deficiency of the enzyme glycogen phosphorylase in their muscles. This is known as McArdle's syndrome. If these patients attempt to perform vigorous exercise, they rapidly become fatigued, and their muscles develop cramps and become painful, causing them to stop the effort. These symptoms and signs are due to the fact that these patients cannot produce ATP via the degradation of glycogen, thus rapidly depleting their supply of intracellular ATP. If these patients, however, begin to exercise at a low intensity, thus allowing the blood supply to the muscle to be increased, supplying the muscle with fatty acids and glucose, with glycogen phosphorylase no longer necessary. In this way, these patients may exercise at a level that would previously have resulted in extreme fatigue, pain and cramps. (Pernow et al. 1967.)

2.1.6.1 Phosphocreatine occurance and supplementation

In humans, more than 95% of the total body creatine is found in the skeletal muscles. Approximately two thirds of this is phosphorylated (phosphocreatine), with the remainder occurring in its free form. (Balsom et al. 1994.)

The breakdown product of creatine is creatinine, which is eliminated. The extent of this breakdown is approximately 2g per day. Part of this is replaced by exogenous sources, especially the ingestion of meat and fish. The remainder is synthesized from arginine, glycine and methionine. (Balsom et al. 1994.)

Increases in the arginine and methionine levels in muscles have been demonstrated with creatine supplementation. These increases have resulted in improved performance of high intensity intermittent exercise. (Birch et al. 1994.)

Neither maximal oxygen uptake, nor endurance exercise performance appears to be enhanced by creatine supplementation (Balsom et al. 1994).

Creatine supplementation has also been shown to increase the rate of

phosphocreatine resynthesis after exercise in some individuals (Greenhaff et al. 1994).

2.1.7 *Control of Rate of Utilization of Phosphocreatine and Glycogen*

2.1.7.1 Phosphocreatine utilization

Initiation of the process of contraction occurs when Ca2+ stimulates the myofibrillar ATPase. This leads to a decrease in the concentration of ATP (ATP is consumed in energising the myofibrillar cross-linkages), with a corresponding increase in those of ADP, phosphate and protons:

$$ATP^{4-} + H2O \Rightarrow ADP^{3-} + Pi^{2-} + H+$$

During the first seconds of strenuous exercise, such changes will favour ATP synthesis from phosphocreatine. The creatine kinase reaction is displaced as follows:

$$H+ + ADP^{2-} + \text{phosphocreatine}^{2-} \Rightarrow ATP^{4-} + \text{creatine}$$

This reaction is very sensitive to small changes in reactant concentration, which permits the rapid regeneration of ATP. The forward and reverse components of this reaction are very large, and this reaction remains very near equilibrium. (Potter et al. 1995.)

2.1.7.2 Glycogen utilization

The control of the rate of glycogen utilization presents a major metabolic problem, in that the rate of glycolysis must increase from a very low rate (resting state) to the very high rate necessary during, for example, a 100m sprint. This is an increase of at least 1000X. If this massive increase in flux through, for example, the 6-phosphofructokinase reaction, was caused solely by known metabolic regulators of this enzyme, the concentration changes would have to be several hundredfold (the regulation of this enzyme is by the relief of the inhibition by ATP (allosteric inhibitor) by AMP, fructose-6-phosphate, fructose bisphosphate and ammonia). (Radda et al. 1995.)

The largest change in the concentration of the known regulators of glycolysis is the fourfold change occurring in the concentration of phosphocreatine. Thus, for these regulators to be involved in the control of flux through this reaction, the regulatory

mechanism must be very sensitive. It is suggested that this is achieved by co - operativity and the operation of a substrate cycle between fructose 6 - phosphate and fructose bisphosphate, catalysed by the simultaneous activities of 6 - phosphofructokinase and fructose bisphosphatase. (Smolen 1995.)

The hypothesis for control suggests the following sequence of events in the athlete's muscle:

Some time before the race, while the sportsperson is resting, the glycolytic flux will be low. The activities of both 6 - phosphofructokinase and fructose bisphosphatase will be very low. Thus, the ratio: cycling rate/flux, is very low. During the period immediately before the race or event, feelings of anticipation and excitement will result in the secretion by the adrenal gland of epinephrine and norepinephrine. These stimulate the activities of both enzymes, elevating the cycling rate and the ratio: cycling rate/flux. When the race begins, the myofibrillar ATPase activity increases, resulting in increases in the concentrations of AMP, phosphate and possibly fructose bisphosphate, and decreases in the concentrations of ATP and phosphocreatine. Because the ratio: cycling rate/flux is high, very large increases in the rate of fructose 6-phosphate phosphorylation may be produced by small changes in these concentrations. When the maximum power output is achieved, inhibition of the activity of fructose bisphosphatase may occur reducing the cycling rate somewhat. (Newsholme and Leech 1983:362.)

2.1.8 Muscle Metabolism when the Demand for ATP Exceeds the Aerobic Capacity

The rate of ATP production by the aerobic pathways in an exercising muscle is limited by the amount of oxygen delivered to the muscle. When the demand for ATP exceeds the supply via oxidation, anaerobic glycolysis is the mechanism by which this demand is met. As the rate of conversion of glycogen is increased, the rate of ATP generation is increased, and the muscle will be able to achieve a greater power output. This will only be possible for a limited period, until the glycogen in the muscle is exhausted, or until the decrease in the pH causes inhibition of 6-phosphofructokinase. It is the accumulation of protons, rather than the level of lactic acid that causes fatigue. (Yamamoto and Kanehisa 1995.)

This will be discussed further under section 2.1.9.

2.1.8.1 Glycolysis

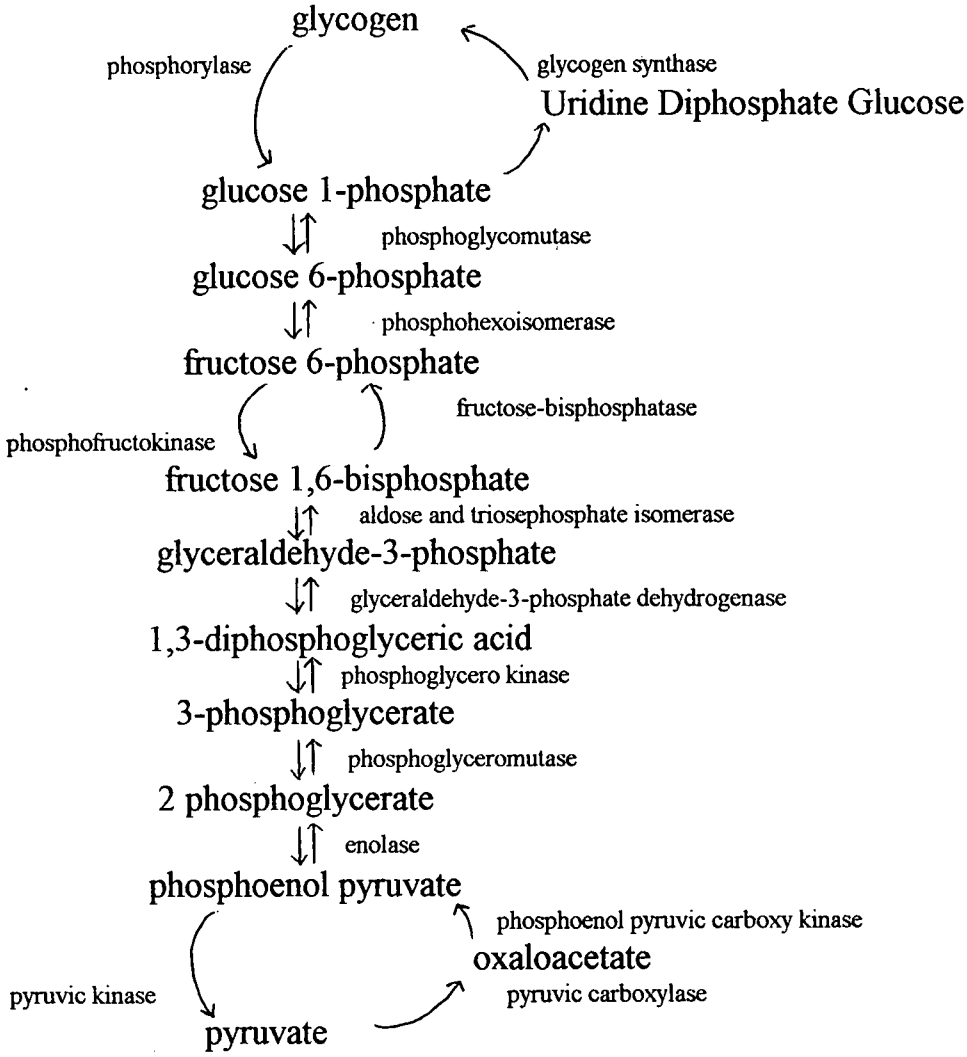


Figure 2.2: Pathway of glycolysis, showing sites at which substrate cycling occurs (Newsholme and Leech 1983:364).

2.1.9 Muscle Fatigue

Muscle fatigue may be defined as the failure to maintain the expected or desired force or power output (Baker et al. 1994).

Along the activation pathway from the central nervous system to within the muscle cell, numerous possible sites of fatigue have been named. The precise mechanism and specifics of the fatigue phenomenon are largely unknown, because the fatigue protocols used in studies and trials vary widely.

Two major phases of fatigue in muscle have been shown.

The initial phase is characterized by an increase in the tetanic calcium levels (which directly activates the contractile process). Thus activation of the muscle fibres was unimpaired, and the fatigue is seen to arise from metabolic inhibition of the contractile process. (Westerblad and Allen 1991.)

This was confirmed by the fact that this phase of fatigue was not relieved by caffeine, which significantly increases the release of calcium from the sarcoplasmic reticulum. (Westerblad et al. 1991).

The second phase of fatigue, however, takes place in an environment of decreased intracellular calcium, and this phase could be reversed by the addition of caffeine. Thus this phase seems to be due to impaired activation of the contractile process. (Baker et al. 1994.)

2.1.9.1 Metabolic Basis of Fatigue During Explosive Exercise

The time taken for fatigue to set in during vigorous exercise may be measured in seconds rather than minutes. This is also true for isometric contractions (because if a tension in the muscle of more than 30% of the maximum is maintained, compression of the blood vessels in the muscles occurs, and blood flow to the muscle is markedly reduced ie. the muscle becomes ischaemic). (Edwards et al 1972.)

During such exercise, glycolysis results in the production of both lactate and protons. In experiments involving laboratory sprinting, the intramuscular pH has been shown to decrease from a resting value of 7.0 to about 6.5 - 6.4 and the blood pH changes from 7.4 to about 6.8 - 6.9. These pH changes occur despite the fact that some of the protons produced will be buffered both intra- and extracellularly by various buffers including intracellular protein and the carbonic acid/hydrogen carbonate system. (Sahlin 1978.)

It has been widely assumed that the lactate ion is responsible for fatigue, but this is not the case; muscle continues to contract with a high power output in the presence of a high concentration of lactate, provided that the pH stays near 7.0 (Hermansen 1979).

It has been shown that a decrease in pH below 7.0 reduces the power output in an isolated skeletal muscle preparation. It is thus the intracellular accumulation of protons that results in fatigue. (Westerblad and Lannergren 1991.)

The exact mechanism of this phenomenon is unclear, but there are a number of suggestions.

First, a decrease in pH has been shown to increase the Ca2+ binding capacity of the sarcoplasmic reticulum. This would result in less Ca2+ being released into the sarcoplasm upon electrical stimulation of the muscle, thus decreasing the stimulation of the contractile process. (Nakamura and Schwartz 1972.)

Alternatively, or in addition, a fall in pH could interfere with the interaction between actin and myosin by reducing myofibrillar ATPase activity. There is some evidence for a direct effect of pH on the contractile apparatus since, with isolated muscle fibres that have had their plasma membrane removed ("skinned fibres") the maximum tension that could be developed upon addition of Ca2+ was lower at pH 6.5 than at pH 7.0. (Donaldson et al.1978.)

Another explanation is based on the properties of the glycolytic enzyme, 6-phosphofructokinase. There is a marked increase in the inhibition of this enzyme by a decrease in pH below 7.0. It is proposed that the fall in pH occurring during strenuous exercise causes inhibition of this enzyme, with a corresponding decrease in the rate of ATP formation. It follows that in this case fatigue would be due to a lack of substrate (ATP) for the myofibrillar ATPase. There is, however, some evidence that does not support this explanation; first, the ATP concentration in fatigued muscle is only decreased to about 3 mmol, which is still sufficient to saturate myofibrillar ATPase. (The Km for myofibrillar ATPase for ATP is about 0.1 mmol). (Erecinska et al. 1995.)

Secondly, other ATP requiring processes in the cell eg. ion transport, continue to function in a fatigued muscle (Newsholme and Leech 1983:366).

2.1.9.2 Non - metabolic components of fatigue

In severe fatigue situations, the fatigue continues to deepen despite a lack of change or even partial recovery of the metabolic components involved in muscle contraction (especially the level of inorganic phosphate). This may be attributed to activation impairment at the level of excitation - contraction coupling. (Baker et al. 1994.)

It was postulated that this force inhibition may be due to some extent to transmission failure at the neuromuscular junction. Recently it has been found that this phase of fatigue also occurs in directly stimulated muscle, lacking functional neuromuscular junctions. Thus it seems that the non - metabolic phase of fatigue in unrelated to

transmission failure at the neuromuscular junctions. (Bigland - Ritchie et al. 1982.)

2.2 Anatomy

2.2.1 *The Human Thigh*

2.2.1.1 Osteology of the Lower Limb

The bones involved in flexion and extension movements at the knee are the femur, patella, tibia and fibula.

The muscles that cause articulation of the knee joint are connected to these bones.

2.2.1.2 Musculature of the Thigh

According to Moore (1985: 412-430), the musculature of the thigh may be divided into three major compartments: the anterior, medial and posterior compartments. Each of these compartments has its own general function:
-the anterior compartment houses the muscles most responsible for extension of the leg
-the medial compartment houses the muscles causing adduction of the thigh
-the posterior compartment houses the muscles causing flexion of the leg

2.2.1.2.1 Muscles of the anterior compartment

Iliopsoas

The iliopsoas muscles act together in flexing the thighs.

-Psoas major
origin: T12 to L5 vertebrae and intervertebral discs
insertion: lesser trochanter of the femur

-Iliacus
origin: iliac crest, iliac fossa, and ala of the sacrum
insertion: tendon of psoas major and femur, inferior and anterior to lesser trochanter

Quadriceps Femoris

The quadriceps femoris muscles act together to bring about extension of the leg. These muscles share a common insertion into the base of the patella and via the patellar ligament into the tibial tuberosity.

-Rectus Femoris
origin: iliac spine and groove superior to acetabulum
action: also flexion of the thigh

-Vastus Lateralis
origin: greater trochanter and lateral lip of the linea aspera of the femur

-Vastus medialis
origin: intertrochanteric line and medial lip of the linea aspera of the femur

-Vastus intermedius
origin: anterior and lateral surfaces of the body of the femur

Tensor Fascia Latae

The tensor fascia Latae abducts and flexes the thigh, helps to keep the knee extended, and steadies the trunk on the thigh.

origin: anterior superior iliac spine and the external lip of the iliac crest
insertion: iliotibial tract, which inserts into the lateral condyle of the tibia

Sartorius

The sartorius muscle flexes the thigh and leg, and aids in abducting and rotating the thigh.

origin: anterior superior iliac spine
insertion: superior part of the medial surface of the tibia

2.2.1.2.2 Muscles of the medial compartment

These are the adductor group of thigh muscles.

Pectineus

origin: pecten pubis (pectineal line of the pubis)
insertion: pectineal line of the femur
action: adducts and flexes the thigh

Gracilis

origin: body and inferior ramus of the pubis
insertion: superior part of the medial surface of the tibia
action: adducts the thigh and flexes the leg

Adductor Longus

origin: body of the pubis, inferior to the pubic crest
insertion: the middle third of the linea aspera of the femur
action: adducts and flexes the thigh

Adductor Brevis

origin: the body and inferior ramus of the pubis
insertion: the pectineal line and proximal part of the linea aspera of the femur
action: adducts the thigh and to some extent flexes it

Adductor Magnus

origin: the inferior ramus of the pubis, the ramus of the ischium, and the ischial tuberosity
insertion: the gluteal tuberosity, linea aspera, the medial supracondylar line, and adductor tubercle of the femur
action: adducts and extends the thigh

Obturator Externus

origin: the margins of the obturator foramen and the obturator membrane
insertion: the trochanteric fossa of the femur
action: laterally rotates the thigh

2.2.1.2.3 Muscles of the posterior compartment

Three large muscles make up the hamstring muscles. Their action is mainly to bring about extension of the thigh and flexion of the leg.

Semitendinosus

origin: ischial tuberosity
insertion: the medial surface of the superior part of the tibia
action: also with semimembranosus can medially rotate the tibia on the femur, particularly when the knee is semi - flexed

Semimembranosus

origin: ischial tuberosity
insertion: the posterior part of the medial condyle of the tibia
action: also with the semitendinosus can medially rotate the tibia on the femur, particularly when the knee is semi - flexed

Biceps Femoris

origin: the long head originates on the ischial tuberosity by a common tendon with semitendinosus muscle. The short head originates on the lateral lip of the linea aspera and lateral supracondylar line of the femur.
insertion: the head of the fibula
action: also laterally rotates the leg when the leg is flexed

2.3 Homoeopathy

Homoeopathy is a therapeutic method that clinically applies the Law of Similars and that uses substances in weak or infinitesimal doses (Jouanny 1991:11).

2.3.1 Principles of Homoeopathy

Modern homoeopathy had its beginnings at the end of the 18th century. A German physician by the name of Samuel Hahnemann, in approximately 1790, began to discover and record the principles and laws involved in the utilization of attenuated or diluted doses of substances. (Nightingale 1988:10.)

The first law of homoeopathic therapy is the "Law of Similars". This may be stated simply as: the same things which cause the dis - ease, cure it. (Jouanny 1991:12.)

According to Jouanny (1991:13,14), the law may be divided into three parts:
-all pharmacologically active substances cause a set of symptoms characteristic of the substance used when said substance is administered to healthy people
-all sick people display a set of morbid symptoms which are characteristic of their disease. These morbid symptoms may be defined as being changes in the patient's way of feeling or behaving, brought about by his disease.
-the cure, evidenced by the disappearance of all the morbid symptoms, may be obtained by prescribing, in weak or infinitesimal doses, the substance whose experimental symptoms in healthy people are similar to those symptoms displayed by the ill patient

Homoeopathy is a therapy that stimulates innate healing mechanisms of the body. Homoeopathic remedies serve as the specific stimulus to the body to bring about the changes or activity in the body organs and systems that will lead to healing. The stimulation secondary to the administration of a homoeopathic remedy is usually directed towards peak function or optimization. (Jouanny 1991:91.)

It has been established that the dosage of a medicine strongly influences the effects. This phenomenon is described in the Arndt - Schulzt Law: " every drug has a stimulating effect in small doses, while larger doses inhibit, and much larger doses kill."

CHAPTER 3. Materials and Methods

3.1 Study Design and Protocol

The format of this study was of a double-blind clinical trial.

After an initial 30 second test (day 0) of the participants' work capacity, each participant received a bottle of drops to be taken as directed for 7 days. On day 7 the tests were repeated, and the drops no longer taken. The third tests were conducted on day 35.

3.2 Subjects

Forty-one subjects took part in the trial. The subjects were all male Caucasians between the ages of 17 and 23 years, and all in good health on the dates over which the tests were performed.

3.3 Ethics

The performance of tests on human beings invariably raises ethical questions and considerations. As for this study, the key issues would be as follows:
-Utilization of human test subjects
-Utilization of subjects under the age of 18 years
-Administration of substances in a combination never before used (as far as this researcher knows)

3.3.1 Human test subjects

Human subjects were chosen for this trial due to the nature of the substances used and the parameters being tested. Because the effect of a homoeopathic preparation was being tested, and homoeopathic preparations often bring about subjective as well as objective changes in subjects, it was necessary to perform the tests on organisms capable of relating and expressing these changes. Also, to test the anaerobic work capacity of an organism, the organism would have to be motivated to perform explosive work, and this is most easily accomplished with humans.

In accordance with the philosophies of homoeopathy, no harm would be done to those taking part in the trial. The tests were performed on the Akron isokinetic tester, making it virtually impossible to have the subjects injure themselves while performing the tests.

3.3.2 Subjects less than 18 years of age

All subjects accepted less than 18 years of age had to obtain their parents' consent to take part, and a letter explaining the nature of the trial was sent to all the parents concerned.

3.3.3 Administration of substance combinations never before used

Although the substance combination had never been used before, the substances were used in extremely low concentrations (parts per hundred million), and were both dilutions of substances that occur in the human body in some quantity.

3.4 Interventions

3.4.1 Homoeopathic Preparations

Homoeopathic medicines are all prepared utilizing some form of serial dilution method. Most commonly, the dilution factor is 1 part substance diluted with 99 parts solvent, or 1 part substance diluted with 9 parts solvent. These are termed the centesimal and decimal dilution factors respectively, and medicines prepared using these dilution factors would be termed C and D medicines. A number would be written before or after the C or D to denote the number of times that the medicine has been diluted in this manner. For example: D30.

The solvent used in the production of homoeopathic medicines is a mixture of alcohol and pure water.

Medicines prepared in accordance with the original Hahnemanian technique, by which clean, separate bottles are used in each serial dilution, are indicated by an H after the C or D (centesimal or decimal respectively).

Numbered bottles of either (placebo) or (phosphocreatine 4CH and glycogen 4CH in equal quantities) were prepared by a qualified pharmacist, who retained the codes until the completion of the trial. The bottles were 20 ml amber glass dropper bottles, labelled as follows:

-Take 10 drops on the tongue three times daily.

It was explained to the participants that they should not take the drops between 15 minutes before and 30 minutes after meals, and that they should avoid coffee during

the five-week period over which the test was performed.

The bottles were randomized in such a way that in every set of four bottles, two contained the active preparation, and the other two the placebo substance.

Participants were instructed to continue with their lives as usual, and not to change their eating habits or exercise programmes during the test period, as these factors seemed the most likely other variables that may influence their performance.

3.4.2 Placebo Preparation

20 ml of 30 % alcohol in amber 20 ml glass dropper bottles with identical labelling to the active preparation.

3.4.3 Active Preparation/ Test substance

10 ml of phosphocreatine 4CH was added to 10 ml of glycogen 4CH in amber 20 ml glass dropper bottles, which were labelled:
-Take 10 drops on the tongue three times daily.
The phosphocreatine 4CH and glycogen were obtained From Dolisos Laboratories in France via Natura Laboratories in Pretoria. They were prepared in 30 % alcohol so as to taste identical to the placebo substance.

3.5 Measurement and other Observations

An Akron isokinetic tester was used to measure the total work done during flexion and extension over the 30-second test interval. The maximum displacement per second was 195 degrees per second.

Other parameters measured simultaneously included:
-peak flexion torque
-total flexion power
-endurance ratio for flexion
-peak extension torque
-total extension power
-endurance ratio for extension

At the first and second follow - up tests the participants were questioned regarding general health and whether they felt any changes while taking or after taking the preparations.

3.6 Statistical Analysis

3.6.1 Nonparametric Statistics

Statistical evaluation of the results of this study was performed using nonparametric tests.

Intra - group comparisons were carried out using the Wilcoxon signed - ranks test, and inter - group comparisons were carried out using the Mann - Whitney U test. These tests were selected because the sample size in each group was less than 25, the minimum requirement for parametric tests.

3.6.1.1 Wilcoxon signed - ranks test

To use this test, we rank the absolute values of the differences of the measured values from the mean. Then we assign the original signs of the differences to the ranks and calculate two sums: the sum of the ranks with negative signs and the sum of the ranks with positive signs.

Assumptions:
-the sampled population is symmetric
-the sample is a random sample of size n from a population with unknown median M.
-the variable of interest is continuous
-the scale of measurement is at least interval
-the observations are independent

This test was used to test whether the placebo and treatment groups showed statistically significant improvement.

3.6.1.2 Mann - Whitney's U test

Assumptions:
-the data consists of a random sample of observations from population 1 and another random sample of observations from population 2
-the two samples are independent
-the variable observed is a continuous random variable
-the measurement scale employed is at least ordinal
-the distribution functions of the two populations differ only with respect to location, if they differ at all

This test is employed to test whether there was a statistically significant difference in improvement between the two groups. This is done by testing whether indeed the median (parameter) of the treatment group was statistically less (significantly) than that of the placebo group.

3.6.2 Intra - group comparisons

Wilcoxon's Signed Rank Test was used to test whether both, or any one of the placebo and treatment groups showed statistically significant increase in the following parameters:

-peak flexion torque
-work done during flexion
-total flexion power
-endurance ratio for flexion
-peak extension torque
-work done during extension
-total extension power
-endurance ratio for extension

The hypotheses were stated as follows:
-Work done during flexion:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD>0

-Work done during extension:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD>0

-Peak flexion torque:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD>0

-Peak extension torque:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD>0

-Total flexion power:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD>0

-Total extension power:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD>0

-Endurance ratio for flexion:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD<0

-Endurance ratio for extension:
Null hypothesis: H0: nD=0
Alternative hypothesis: H1: nD<0

3.6.3 Inter - group comparisons

Mann-Whitney's U-test was used to test whether there was a statistically significant difference in change in the following parameters between the placebo and treatment groups:

-peak flexion torque
-work done during flexion
-total flexion power
-endurance ratio for flexion
-peak extension torque
-work done during extension
-total extension power
-endurance ratio for extension

3.6.3.1 For the initial test:

The hypotheses were stated as follows:

-Work done during flexion:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Work done during extension:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Peak flexion torque:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Peak extension torque:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Total flexion power:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Total extension power:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Endurance ratio for flexion:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

-Endurance ratio for extension:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt is not = np

3.6.3.2 For the Follow-up tests:

-Work done during flexion:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt > np

-Work done during extension:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt > np

-Peak flexion torque:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt > np

-Peak extension torque:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt > np

-Total flexion power:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt > np

-Total extension power:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt > np

-Endurance ratio for flexion:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt < np

-Endurance ratio for extension:
Null hypothesis: H0: nt=np
Alternative hypothesis: H1: nt < np

CHAPTER 4. Results

4.1 Criteria for the admissibility of the data:

-the subjects had to fulfill the requirements for participation in the study:
  -17 to 23 years of age
  -male
  -Caucasian
  -to be in good health in the opinion of the researcher
-the tests had to be performed on (for the first follow - up), or as close to as possible (for the second follow - up test) the days described in the *study design* (days 7 and 35 respectively)
-the tests had to be performed on the same machine, using identical parameter settings each time
-the machine had to be calibrated on the same day that the tests were performed
-the same leg had to be tested in each test
-the participants had to continue with their normal lifestyle during the test period

4.2 Results of Intra - group tests (Wilcoxon's signed rank test):

These tests were performed to test whether there was a statistically significant increase or decrease in the named parameters between the initial and first follow - up, and the initial and second follow - up assessments.

4.2.1 Treatment Group

4.2.1.1 Initial vs First Follow - up

-Peak flexion torque:

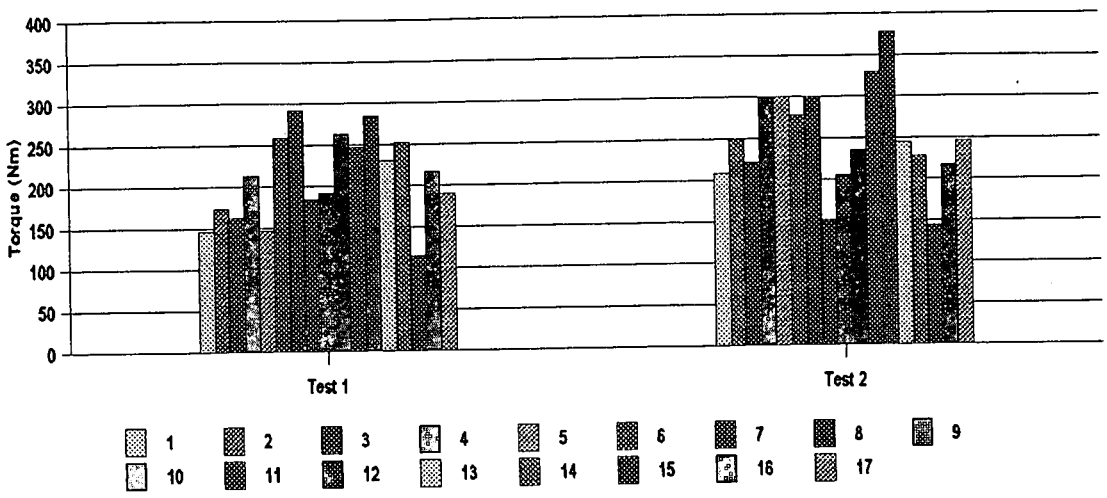


Figure 4.1: Peak flexion torque - initial vs 1st follow - up

$p=0.0052399$ ($p<0.05$)
This implies that the median peak flexion torque increased in the second test.

-Work done during flexion:

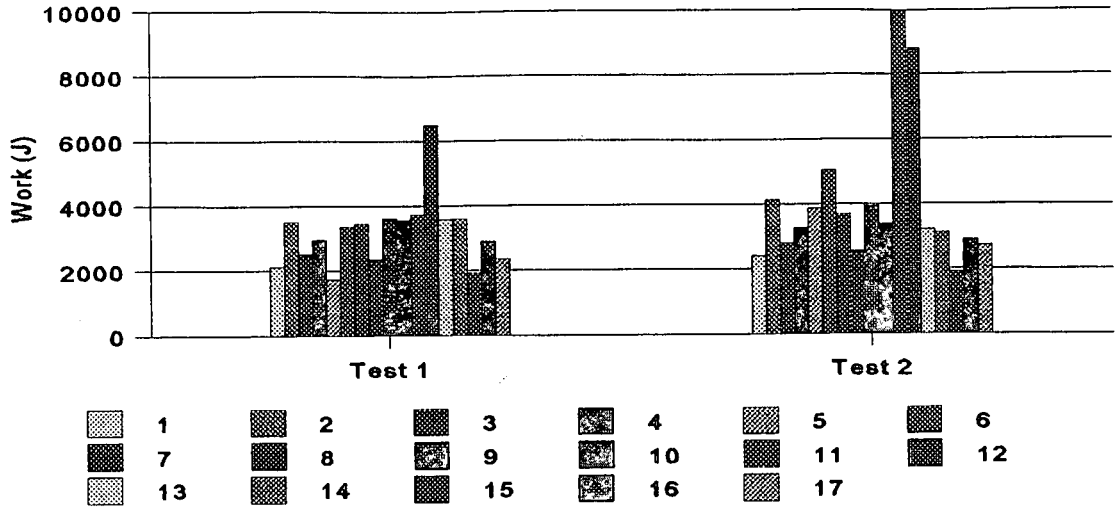


Figure 4.2: Work done during flexion - initial vs 1st follow - up

p=0.0093175 (p<0.05)
This implies that the median work done during flexion increased in the second test.

-Total flexion power:

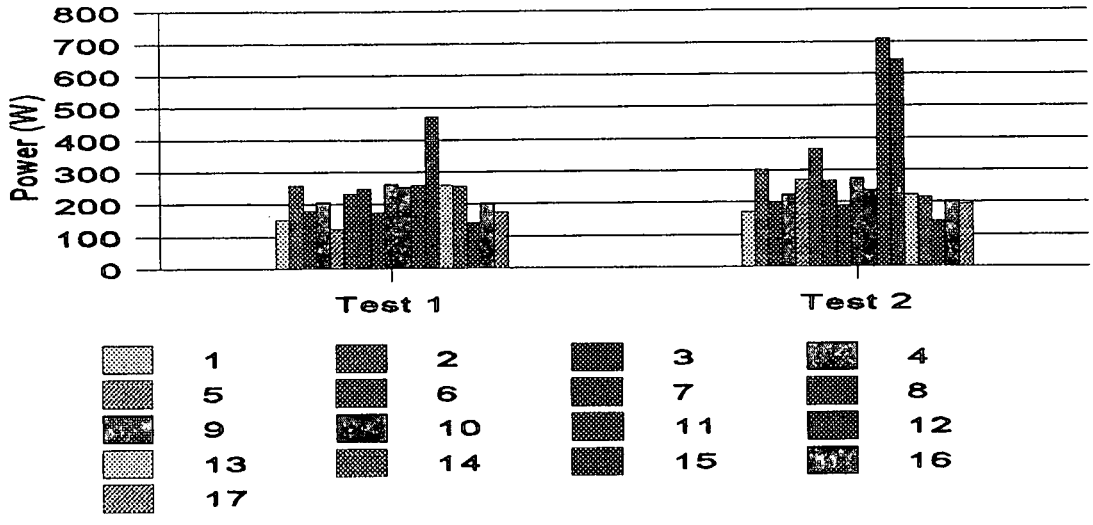


Figure 4.3: Total flexion power - initial vs 1st follow - up

p=0.0122456 (p <0.05)
This implies that the total flexion power increased in the second test.

-Endurance ratio for flexion:

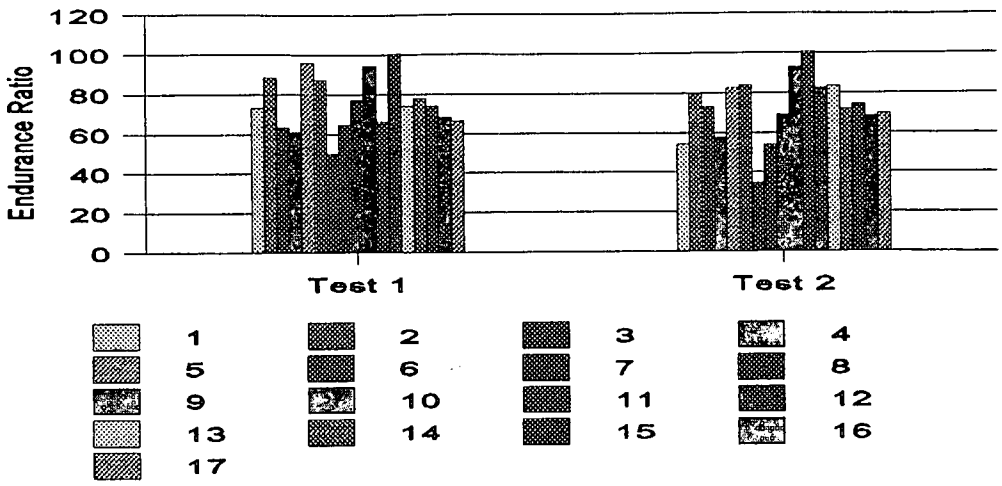


Figure 4.4: Endurance ratio for flexion - initial vs 1st follow - up

p=0.0635785 (p>0.05)
Therefore we accept H0. This implies that there was no change in the median endurance ratio for flexion.

-Peak extension torque:

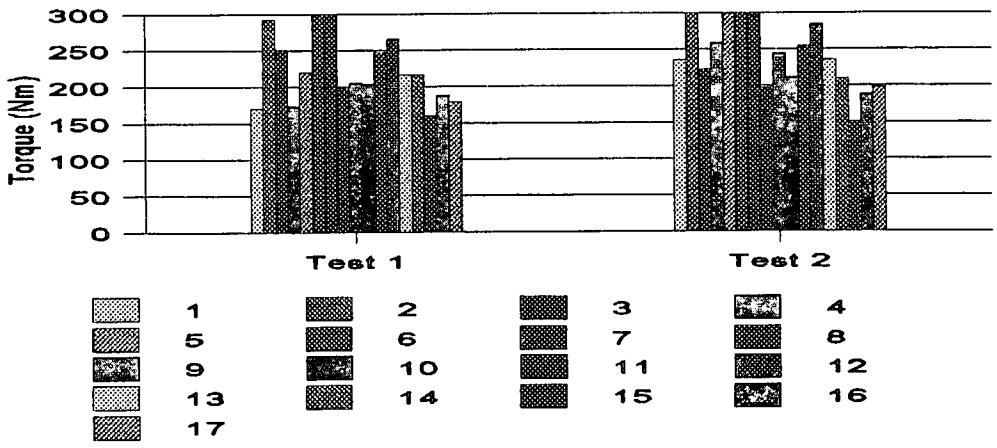


Figure 4.5: Peak extension torque - initial vs 1st follow - up

p=0.0177322 (p<0.05)
This implies that the median peak extension torque increased in the second test.

-Work done during extension:

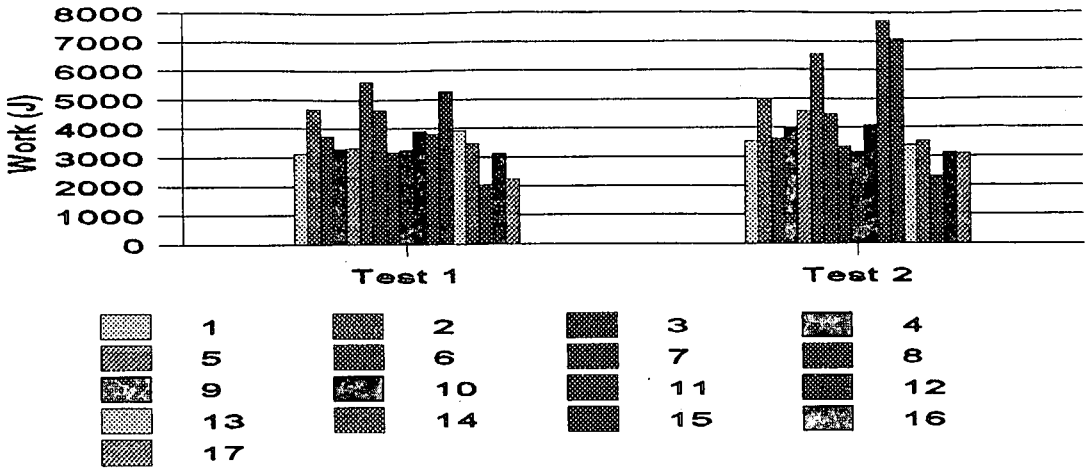


Figure 4.6: Work done during extension - initial vs 1st follow - up

$p=0.0070214$ ($p<0.05$)
This implies that the median work done during extension increased in the second test.

-Total extension power:

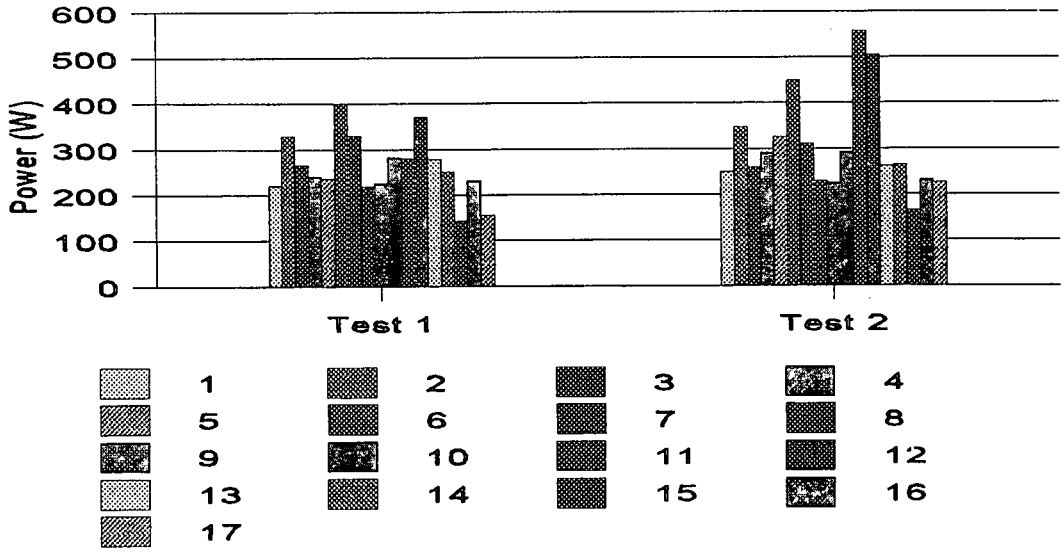


Figure 4.7: Total extension power - initial vs 1st follow - up

$p=0.0038723$ ($p<0.05$)
This implies that the total extension power increased in the second test.

-Endurance ratio for extension:

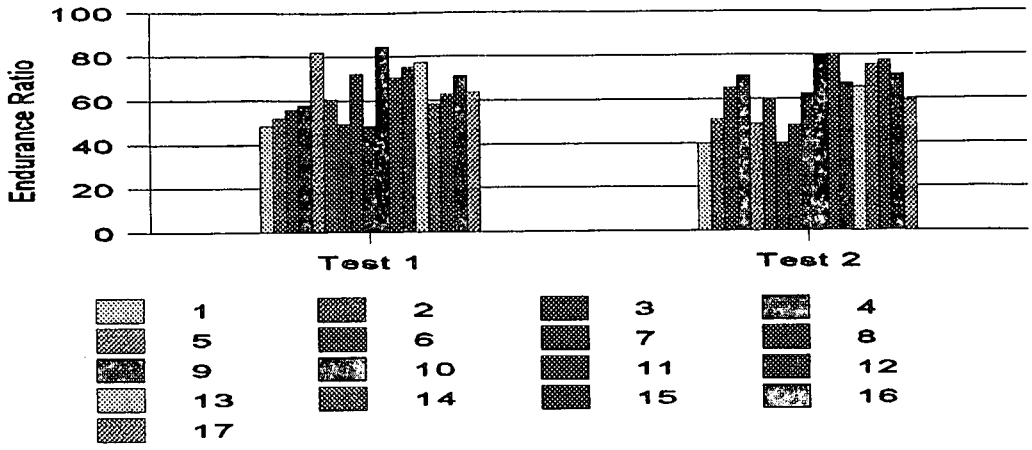


Figure 4.8: Endurance ratio for extension - initial vs 1st follow - up

p=0.4383585 (p>0.05)
Therefore we accept H0. This implies that there was no change in the second test.

4.2.1.2 Initial vs Second Follow - up

-Peak flexion torque:

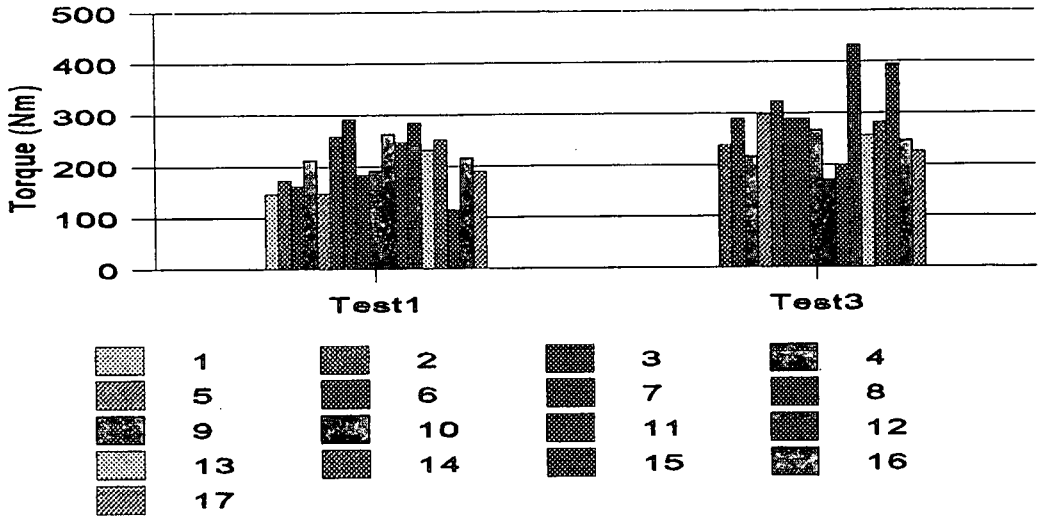


Figure 4.9: Peak flexion torque - initial vs 2nd follow - up

p=0.0052399 (p<0.05)
This implies that the median peak flexion torque increased in the second test.

-Work done during flexion:

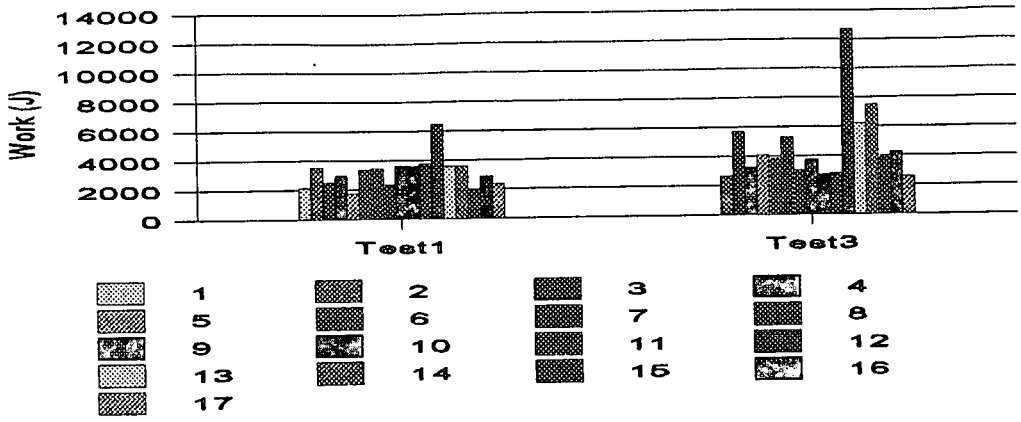


Figure 4.10: Work done during flexion - initial vs 2nd follow - up

p=0.0070214 (p<0.05)
This implies that the median work done during flexion increased in the second test.

-Total flexion power:

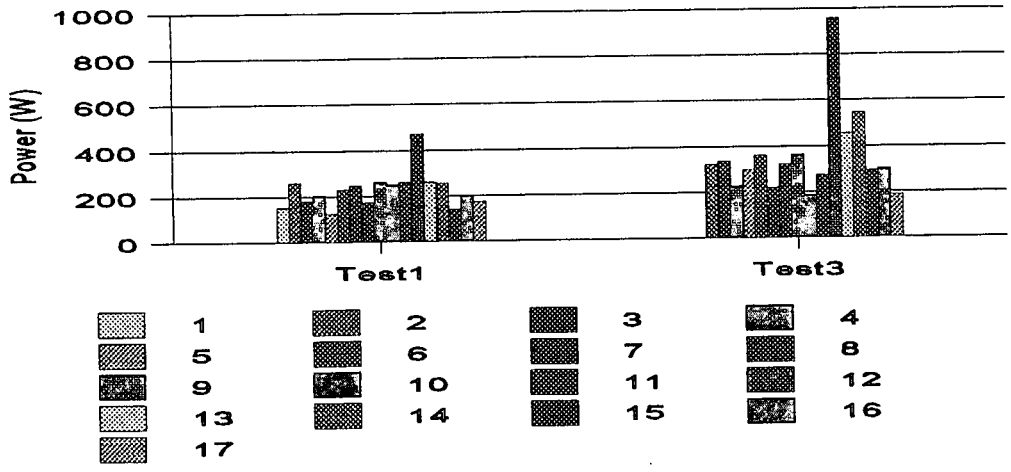


Figure 4.11: Total flexion power - initial vs 2nd follow - up

p=0.0012433 (p <0.05)
This implies that the total flexion power increased in the second test.

-Endurance ratio for flexion:

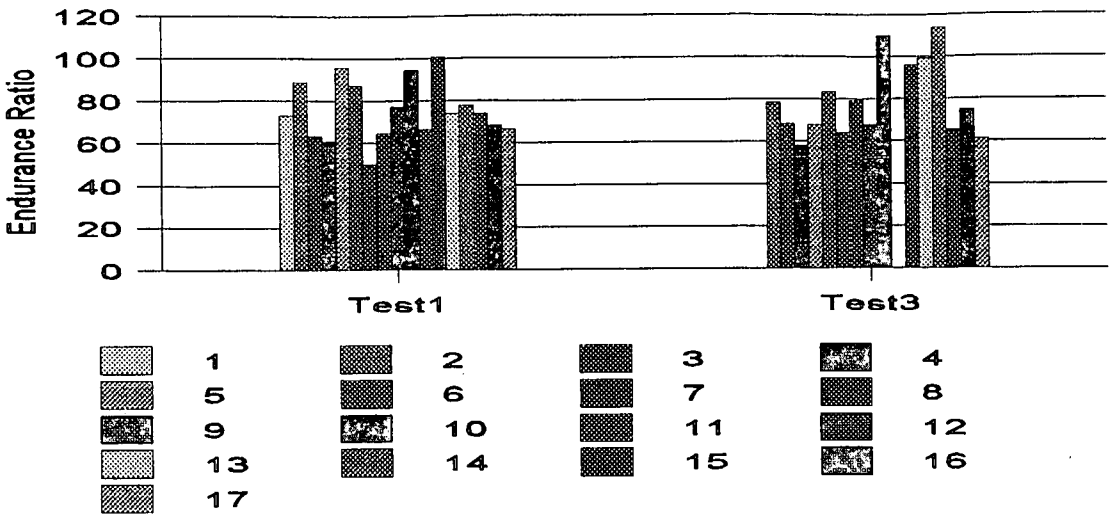


Figure 4.12: Endurance ratio for flexion - initial vs 2nd follow - up

p=0.330139 (p>0.05)
Therefore we accept H0. This implies that there was no change in the median endurance ratio for flexion.

-Peak extension torque:

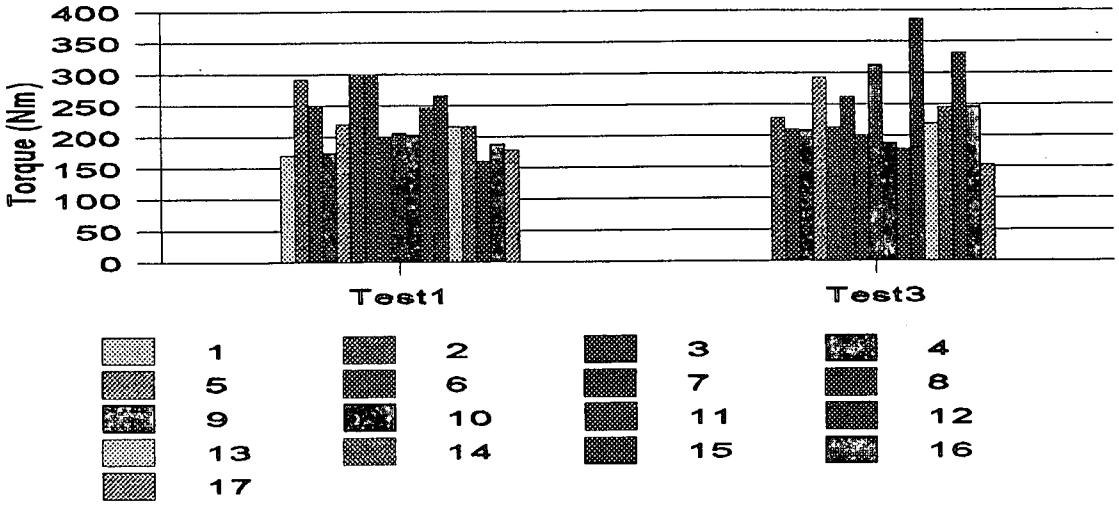


Figure 4.13: Peak extension torque - initial vs 2nd follow - up
p=0.259022 (p>0.05)
Therefore we accept H0. This implies that there was no change in the peak extension torque.

-Work done during extension:

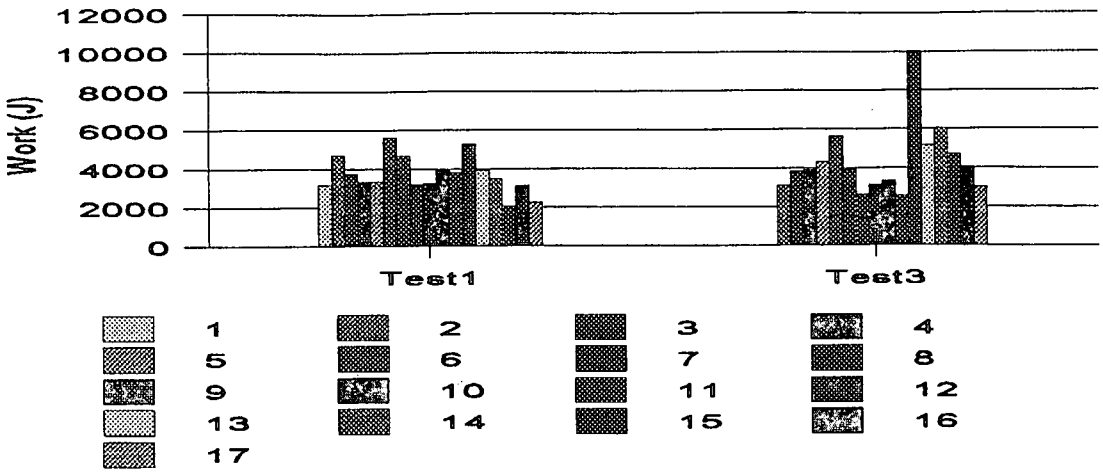


Figure 4.14: Work done during extension - initial vs 2nd follow - up

p=0.112153 (p>0.05)
Therefore we accept H0. This implies that there was no change in the work done during extension

-Total extension power:

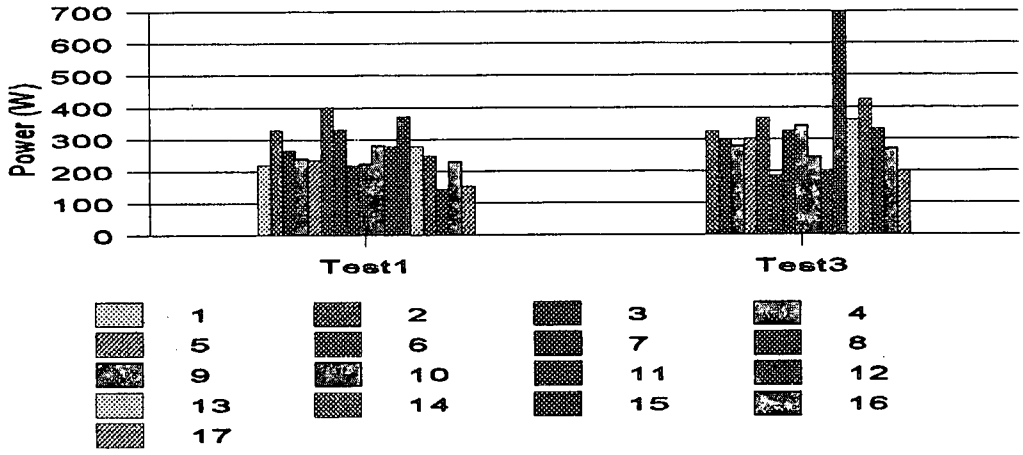


Figure 4.15: Total extension power - initial vs 2nd follow - up

p=0.023252 (p<0.05)
This implies that the total extension power increased in the second test.

-Endurance ratio for extension:

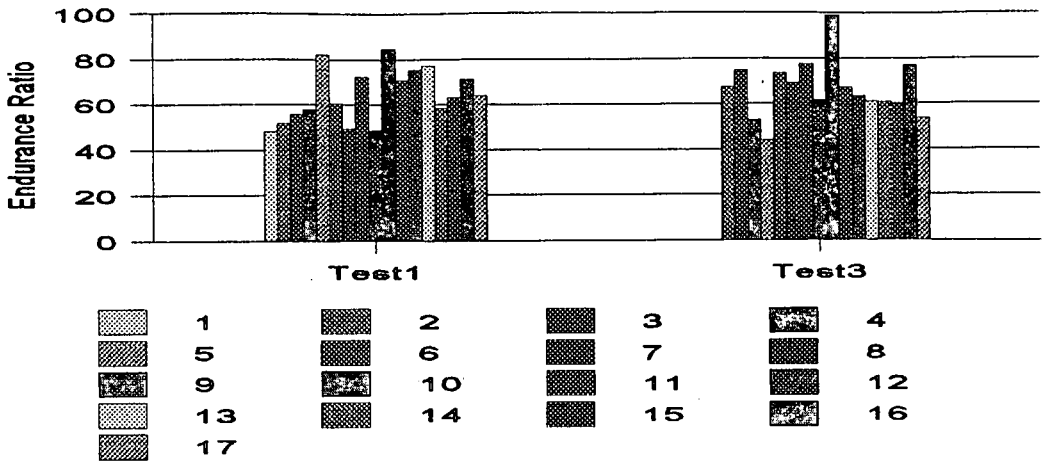


Figure 4.16: Endurance ratio for extension - initial vs 2nd follow - up

p=0.211422 (p>0.05)
Therefore we accept H0. This implies that there was no change in the second test.

4.2.2 Placebo Group

4.2.2.1 Initial vs First Follow - up

-Peak flexion torque

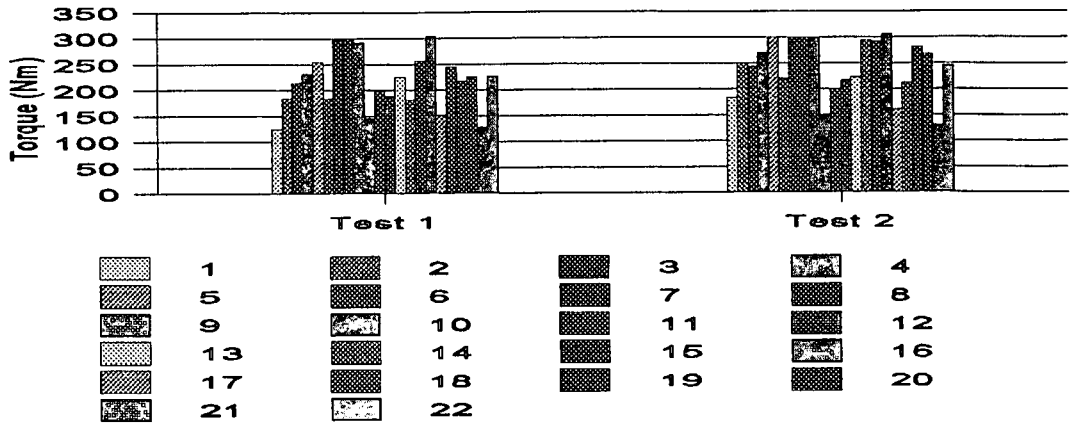


Figure 4.17: Peak flexion torque - initial vs 1st follow - up

$p=0.000340356$ ($p<0.05$)
This implies that the median peak flexion torque increased in the second test.

-Work done during flexion:

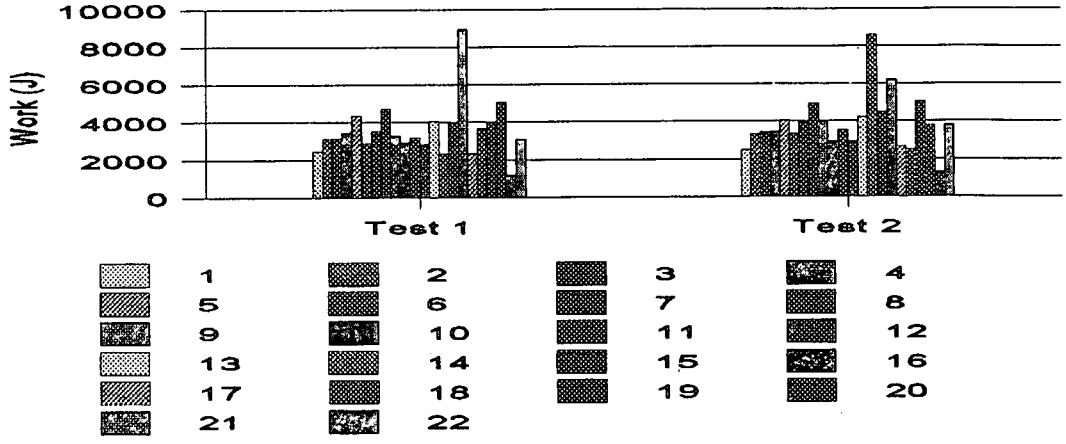


Figure 4.18: Work done during flexion - initial vs 1st follow - up

$p=0.0345260$ ($p<0.05$)
This implies that the median work done during flexion increased in the second test.

-Total flexion power:

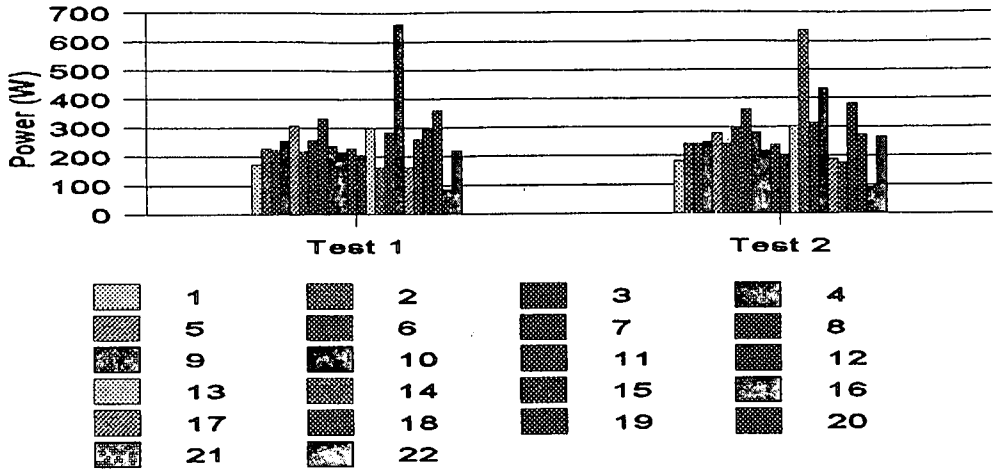


Figure 4.19: Total flexion power - initial vs 1st follow - up

p=0.059575 (p >0.05)
Therefore we accept H0. This implies that there was no change in the total flexion power.

-Endurance ratio for flexion:

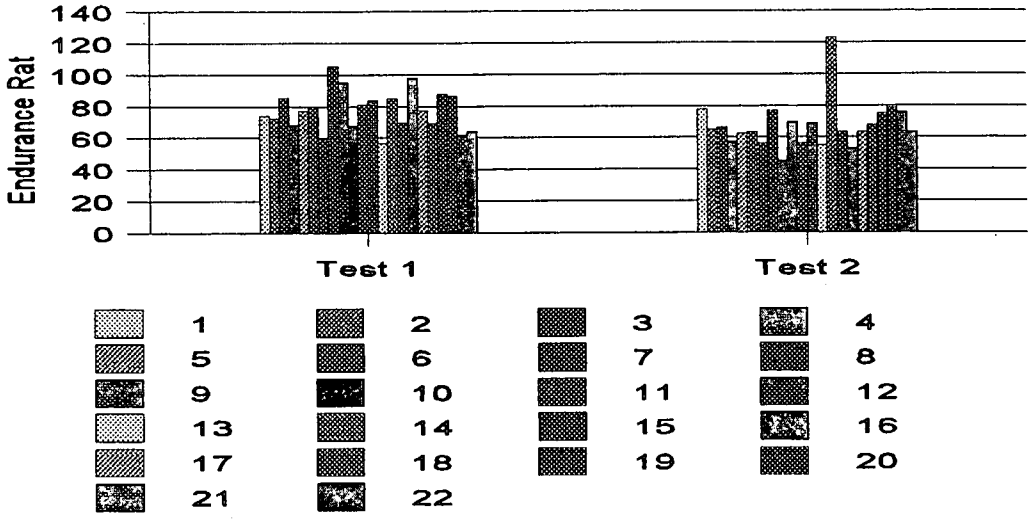


Figure 4. 20: Endurance ratio for flexion - initial vs 1st follow - up

p=0.00319458 (p<0.05)
This implies that the median endurance ratio for flexion increased in the second test.

-Peak extension torque:

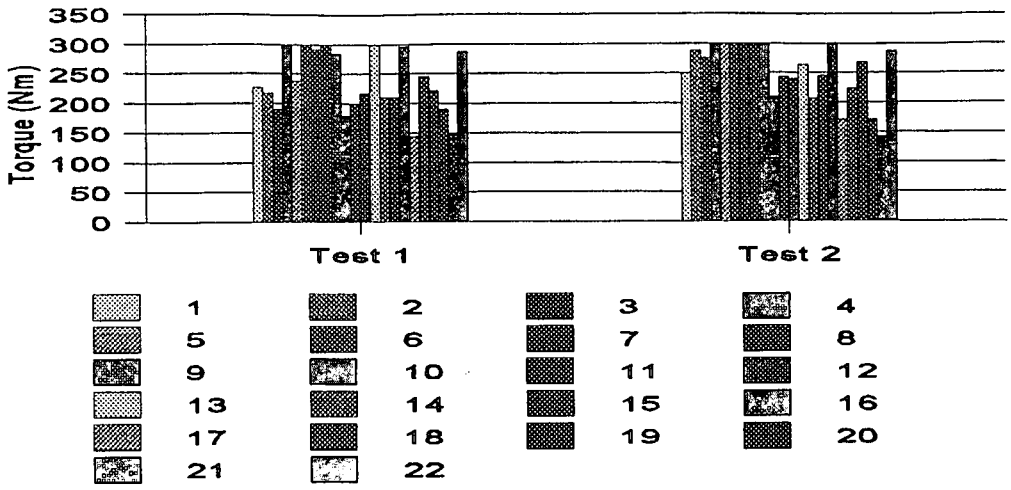


Figure 4.21: Peak extension torque - initial vs 1st follow - up

p=0.00736765 (p<0.05)
This implies that the median peak extension torque increased in the second test.

-Work done during extension:

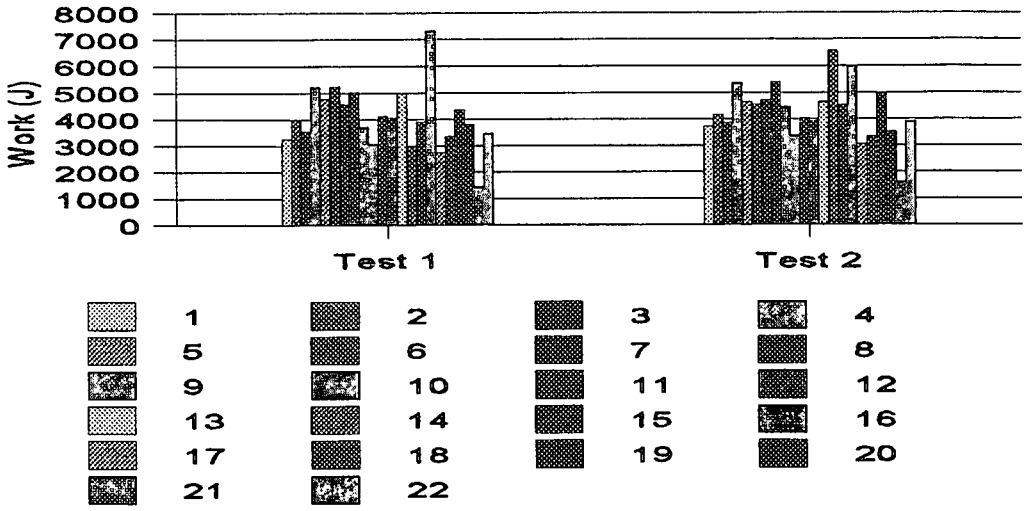


Figure 4.22: Work done during extension - initial vs 1st follow - up

p=0.0426543 (p<0.05)
This implies that the median work done during extension increased in the second test.

-Total extension power:

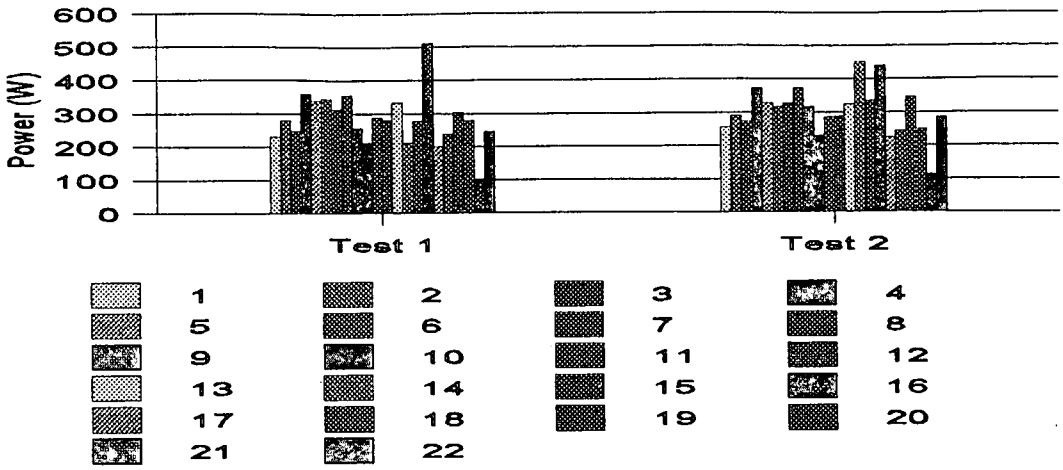


Figure 4.23: Total extension power - initial vs 1st follow - up

p=0.01742755 (p<0.05)
This implies that the total extension power increased in the second test.

-Endurance ratio for extension:

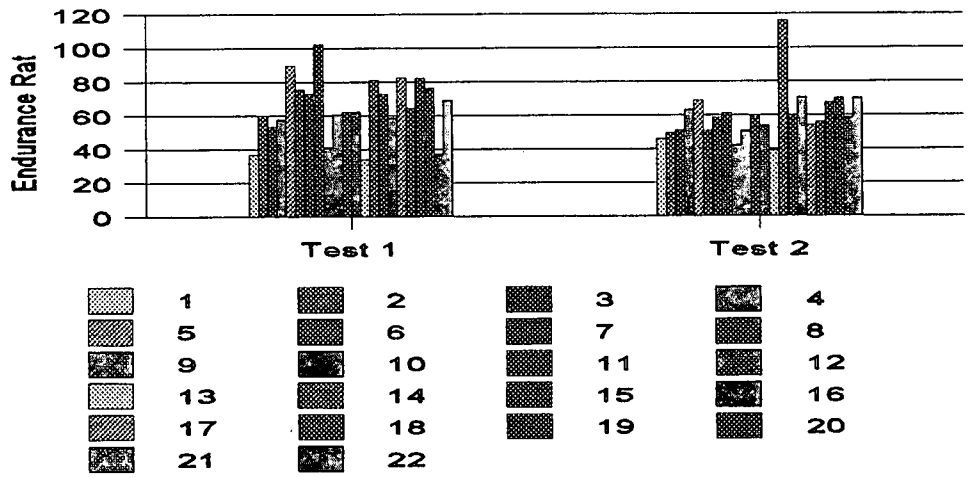


Figure 4.24: Endurance ratio for extension

p=0.0456849 (p<0.05)
This implies that the endurance ratio for extension increased in the second test.

4.2.2.2 Initial vs Second Follow - up

-Peak flexion torque:

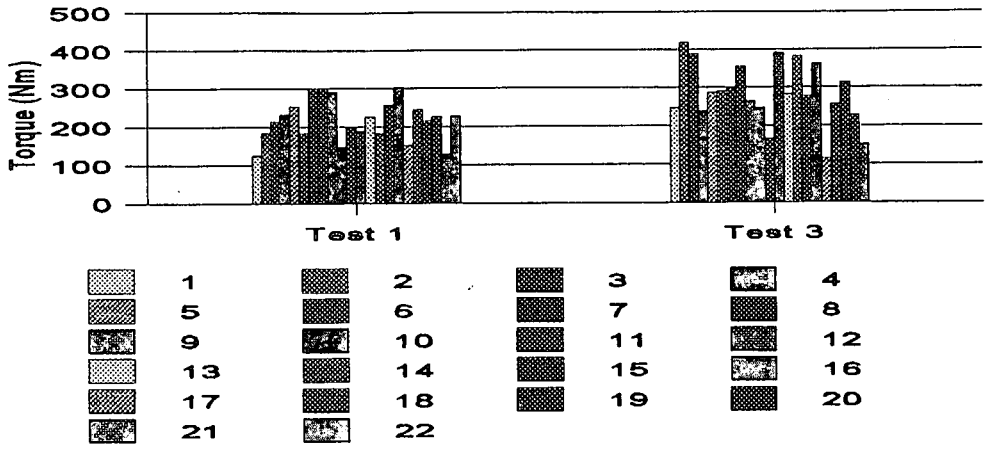


Figure 4.25: Peak flexion torque - initial vs 2nd follow - up

$p=0.00098965$ ($p<0.05$)
This implies that the median peak flexion torque increased in the second test.

-Work done during flexion:

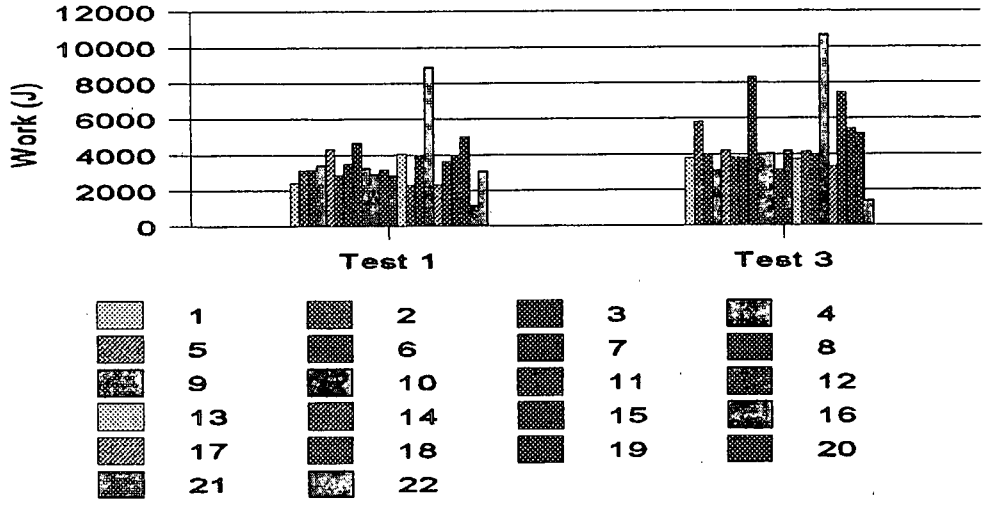


Figure 4. 26: Work done during flexion - initial vs 2nd follow - up

$p=0.000373864$ ($p<0.05$)
This implies that the median work done during flexion increased in the second test.

-Total flexion power:

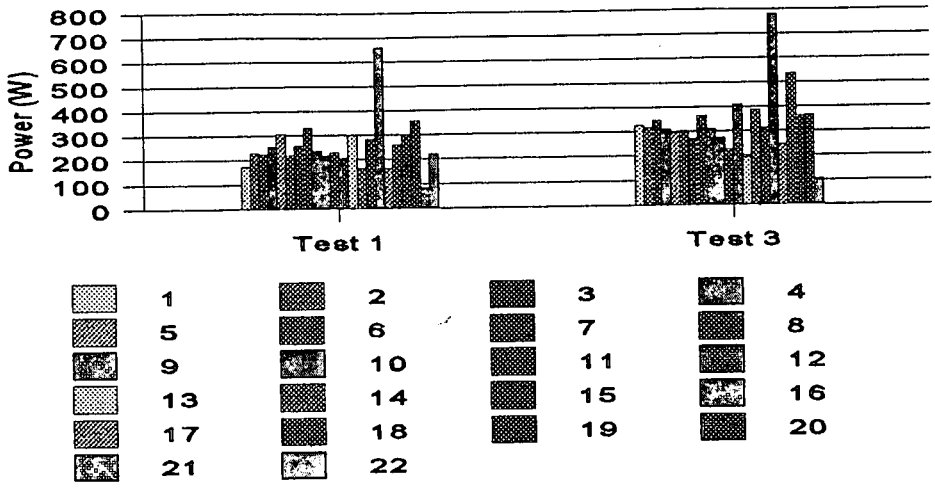


Figure 4.27: Total flexion power - initial vs 2nd follow - up

p=0.000373864 (p <0.05)
This implies that the total flexion power increased in the second test.

-Endurance ratio for flexion:

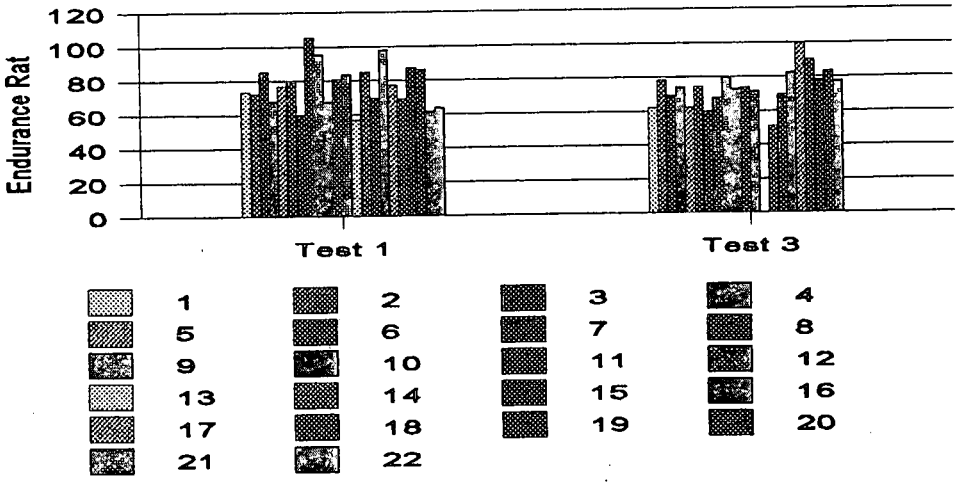


Figure 4.28: Endurance ratio for flexion - initial vs 2nd follow - up

p=0.0630905 (p>0.05)
Therefore we accept H0. This implies that there was no change in the endurance ratio for flexion.

-Peak extension torque:

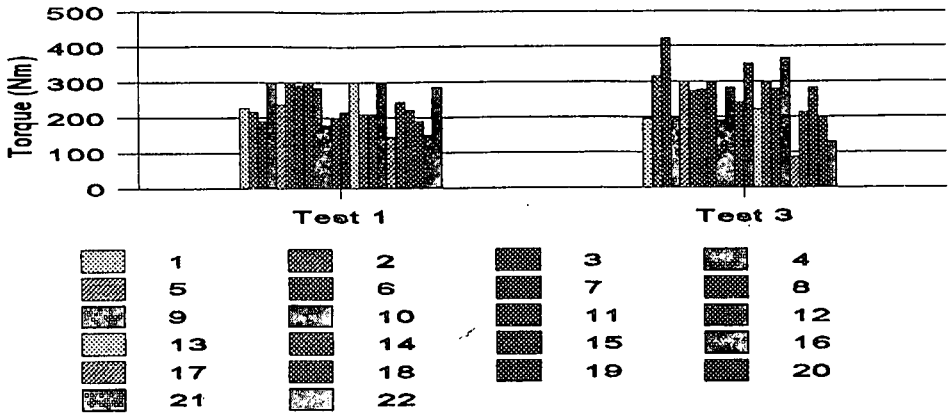


Figure 4.29: Peak extension torque - initial vs 2nd follow - up

p=0.12569 (p>0.05)
Therefore we accept H0. This implies that there was no change in the peak extension torque.

-Work done during extension:

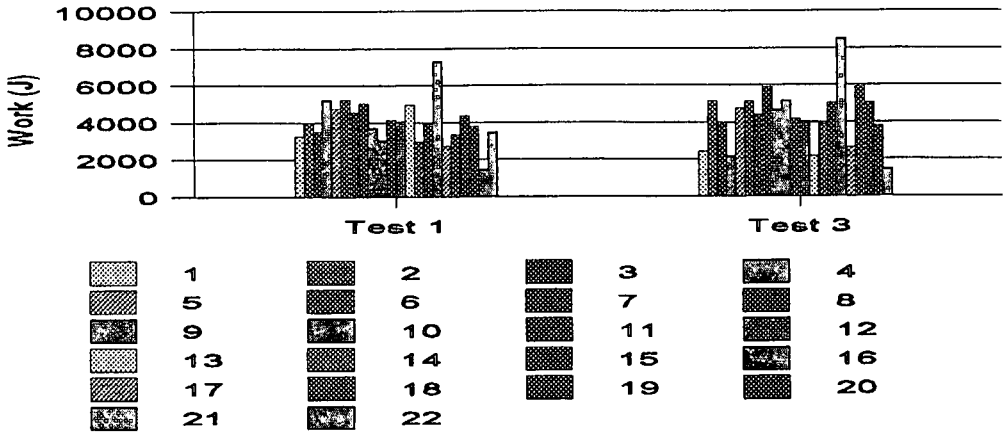


Figure 4.30: Work done during extension - initial vs 2nd follow - up

p=0.087621 (p>0.05)
Therefore we accept H0. This implies that there was no change in the work done during extension.

-Total extension power:

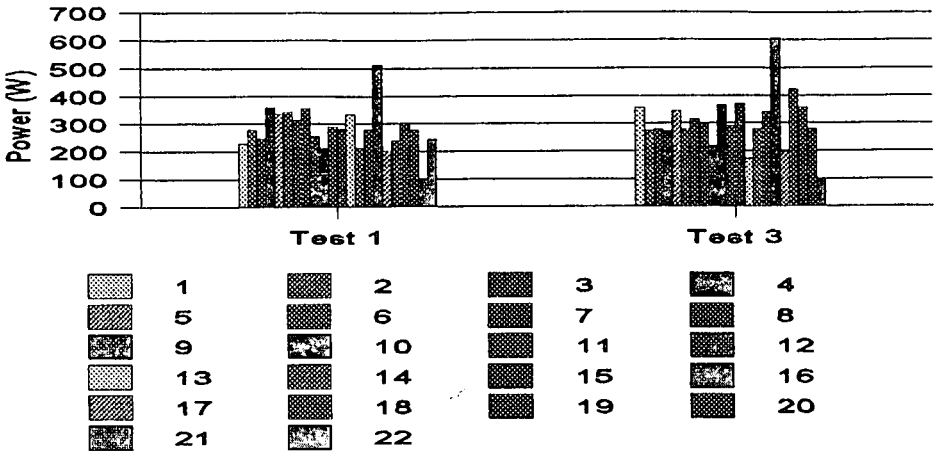


Figure 4.31: Total extension power - initial vs 2nd follow - up

p=0.11865 (p>0.05)
Therefore we accept H0. This implies that there was no change in the total extension power.

-Endurance ratio for extension:

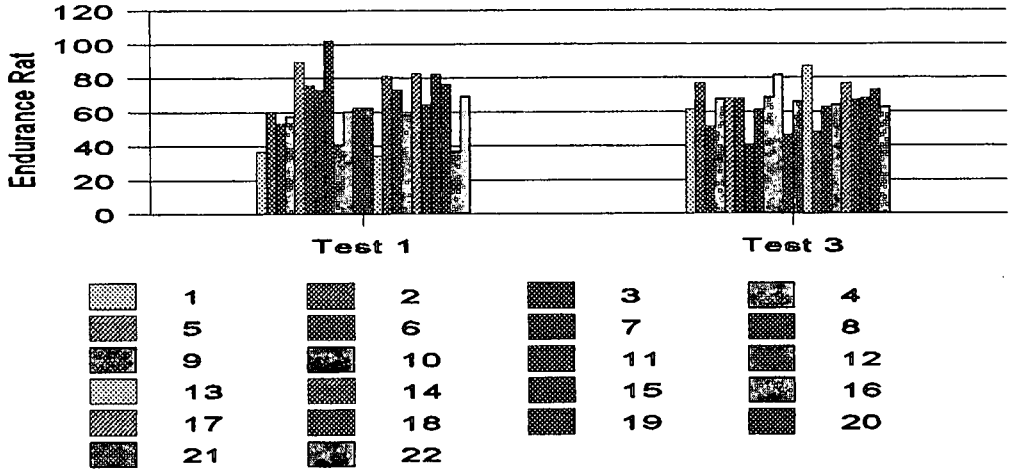


Figure 4.32: Endurance ratio for extension - initial vs 2nd follow - up

p=0.4722855 (p>0.05)
Therefore we accept H0. This implies that there was no change in the endurance ratio for extension.

4.2.3 Summary of results

	Initial vs. 1st Follow - up	Initial vs. 2nd Follow - up
Peak flexion torque	increased	increased
Work done - flexion	increased	increased
Total flexion power	increased	increased
Endurance ratio - flexion	no change	no change
Peak extension torque	increased	no change
Work done - extension	increased	no change
Total extension power	increased	increased
Endurance ratio - extension	no change	no change

Table 4.1: *Intra - group comparison: treatment group*

	Initial vs. 1st Follow - up	Initial vs. 2nd Follow - up
Peak flexion torque	increased	increased
Work done - flexion	increased	increased
Total flexion power	no change	increased
Endurance ratio - flexion	decreased	no change
Peak extension torque	increased	no change
Work done - extension	increased	no change
Total extension power	increased	no change
Endurance ratio - extension	decreased	no change

Table 4.2: *Intra - group comparison: placebo group*

4.3 Results of Inter - Group Tests (Mann - Whitney U Test)

4.3.1 Initial Test

For the initial test, the two - tailed probability of exceedance of the large sample test statistic (Z) was calculated.

-Peak flexion torque

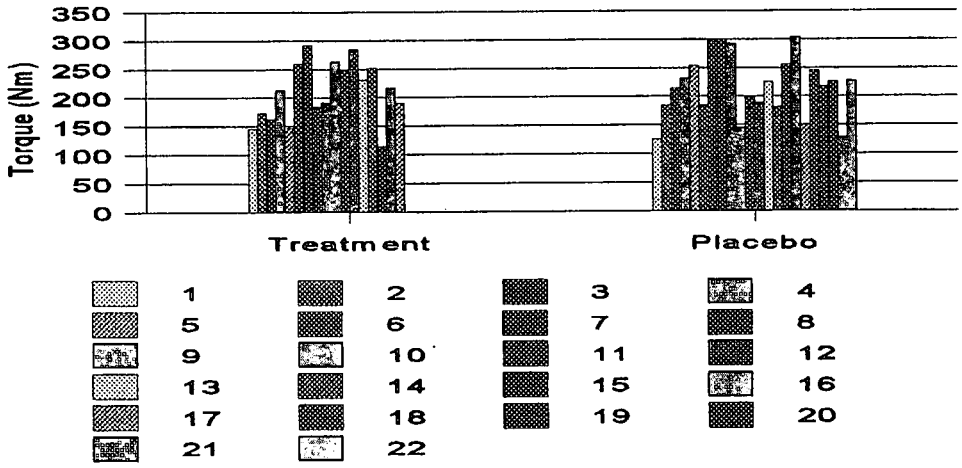


Figure 4.33: Peak flexion torque - initial test

p=0.712605 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Work done during flexion

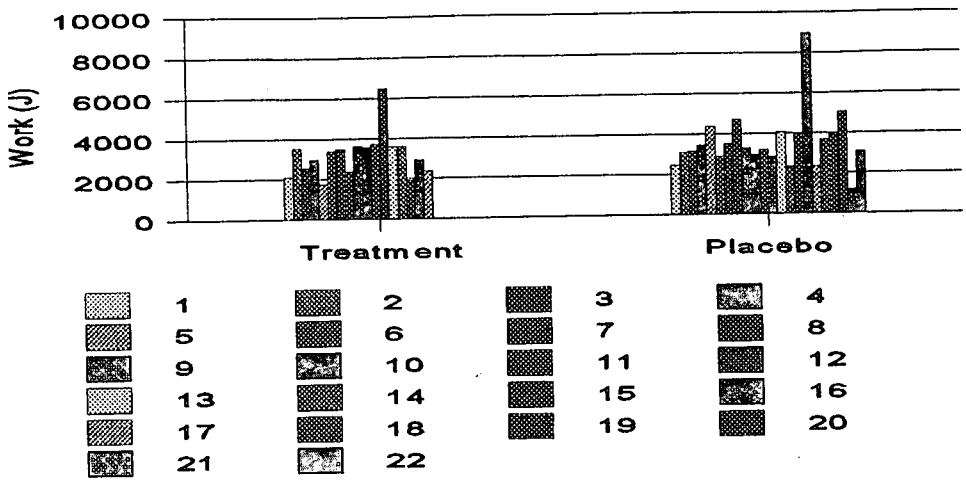


Figure 4.34: Work done during flexion

p=0.403434 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Total flexion power

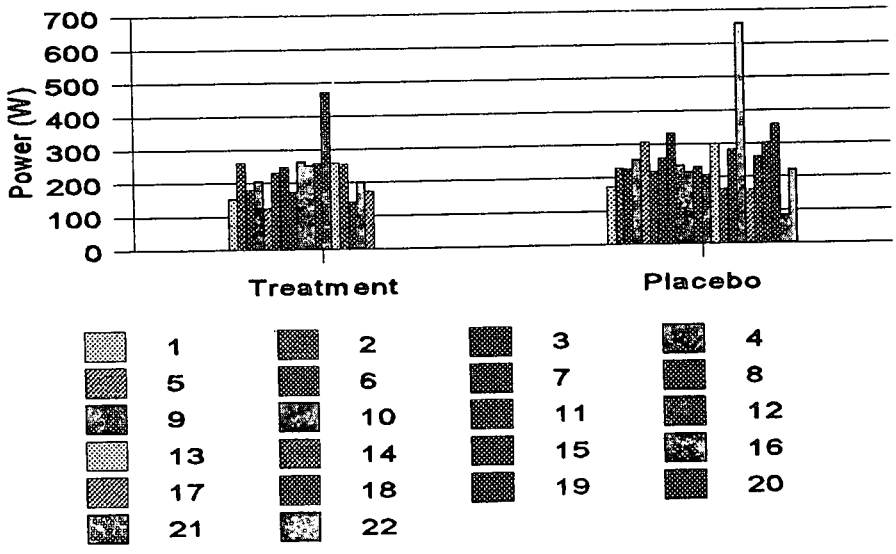


Figure 4.35: Total flexion power - initial test

p=0.275536 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Endurance ratio for flexion

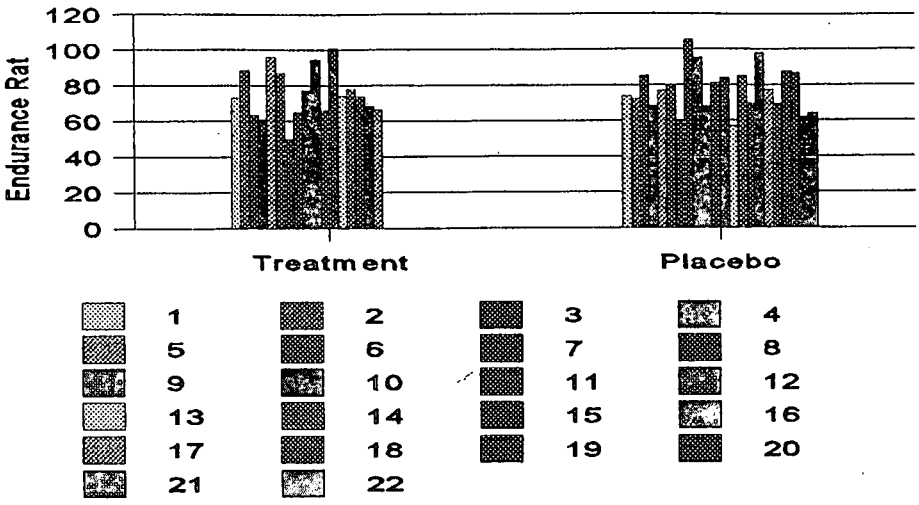


Figure 4.36: Endurance ratio for flexion - initial test

p=0.681311 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Peak extension torque

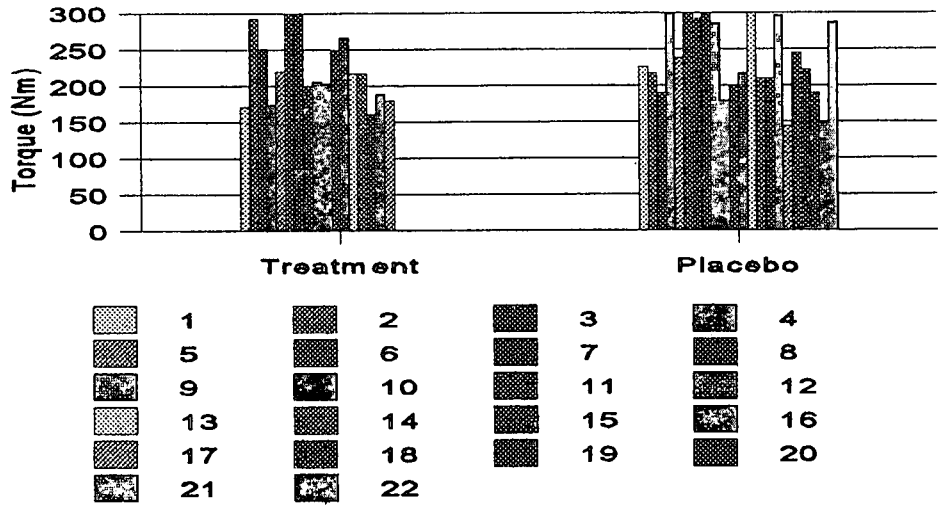


Figure 4.37: Peak extension torque - initial test

p=0.378742 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Work done during extension

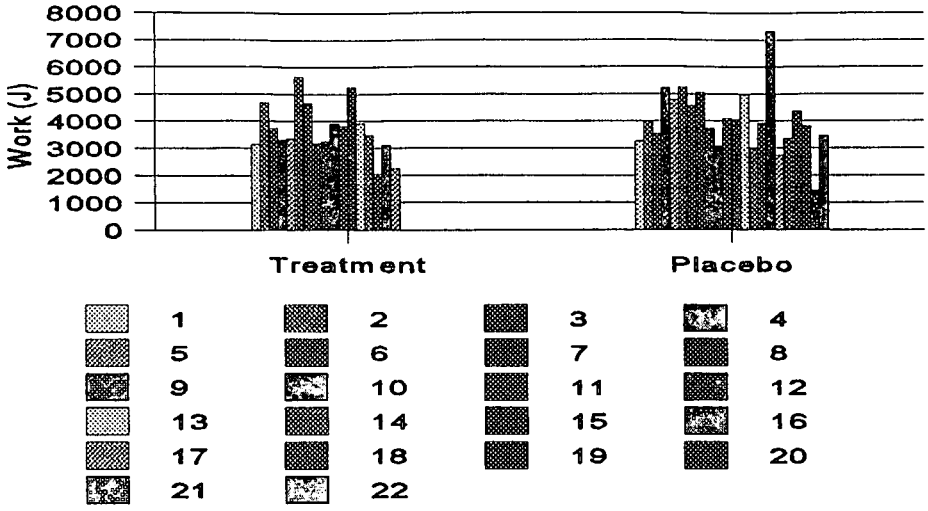


Figure 4.38: Work done during extension - initial test

p=0.301249 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Total extension power

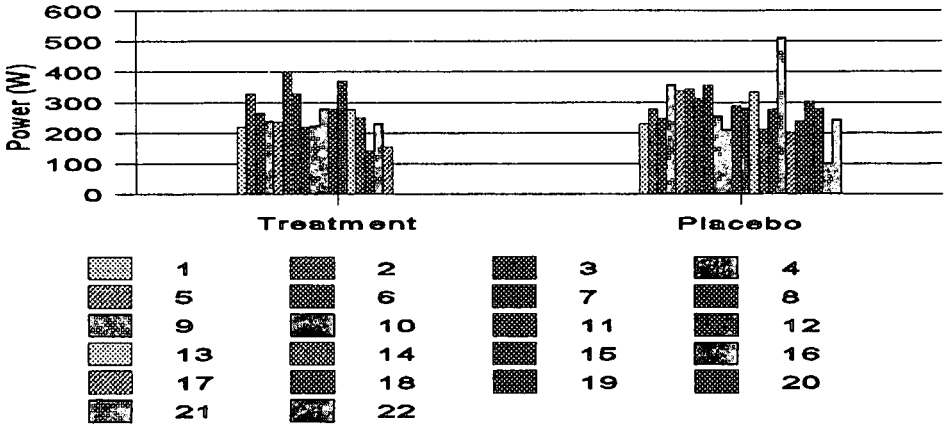


Figure 4.39: Total extension power - initial test

p=0.372314 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Endurance ratio for extension

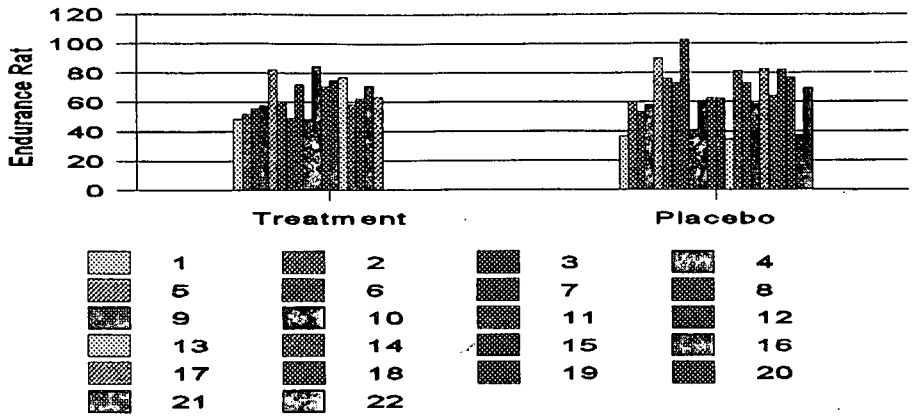


Figure 4.40: Endurance ratio for extension - initial test

p=0.660664 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

4.3.2 First Follow - up

For the follow - up visits, the one - tailed probability of exceeding the large sample test statistic was calculated.

-Peak flexion torque

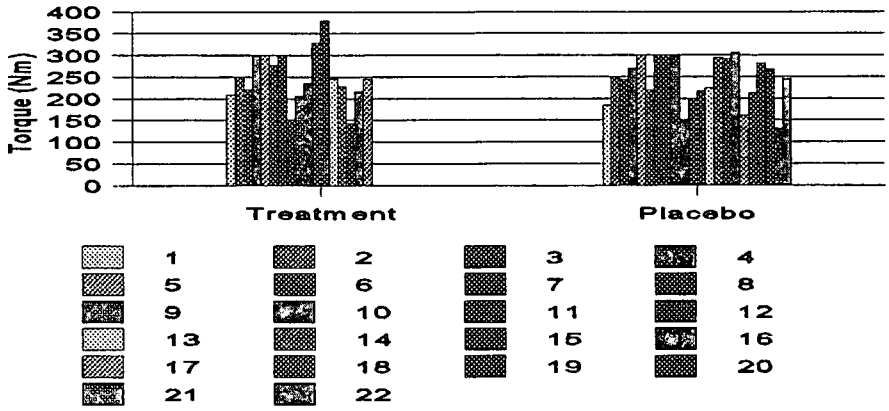


Figure 4.41: Peak flexion torque - 1st follow - up

p=0.4485285 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Work done during flexion

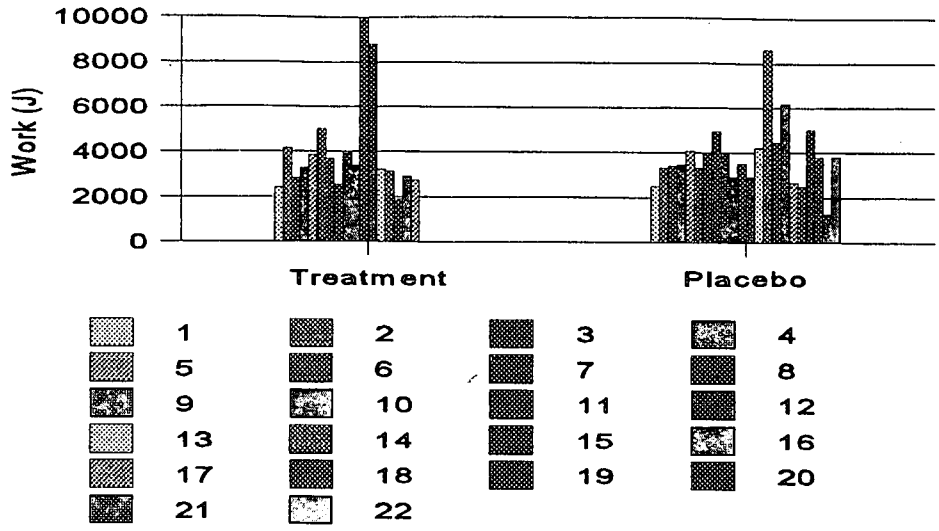


Figure 4.42: Work done during flexion - 1st follow - up

p=0.2264655 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Total flexion power

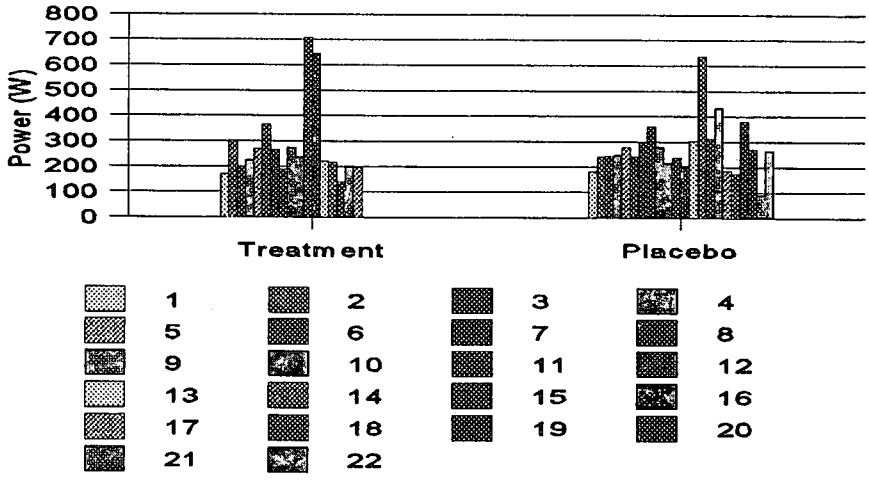


Figure 4.43: Total flexion power - 1st follow - up

p=0.2097805 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Endurance ratio for flexion

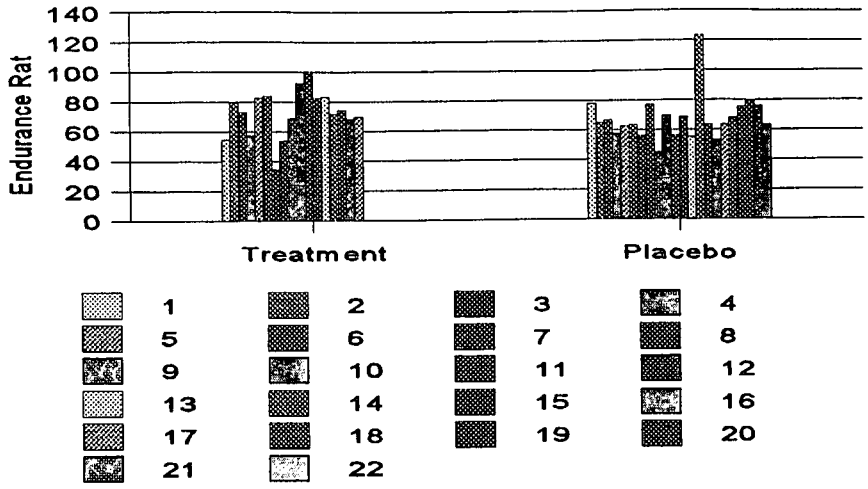


Figure 4.44: Endurance ratio for flexion - 1st follow - up

p=0.04076325 (p<0.05)
Z= -1.74189. This implies that the left sided hypothesis is acceptable. Thus the endurance ratio for flexion is smaller for the placebo group than for the treatment group.

-Peak extension torque

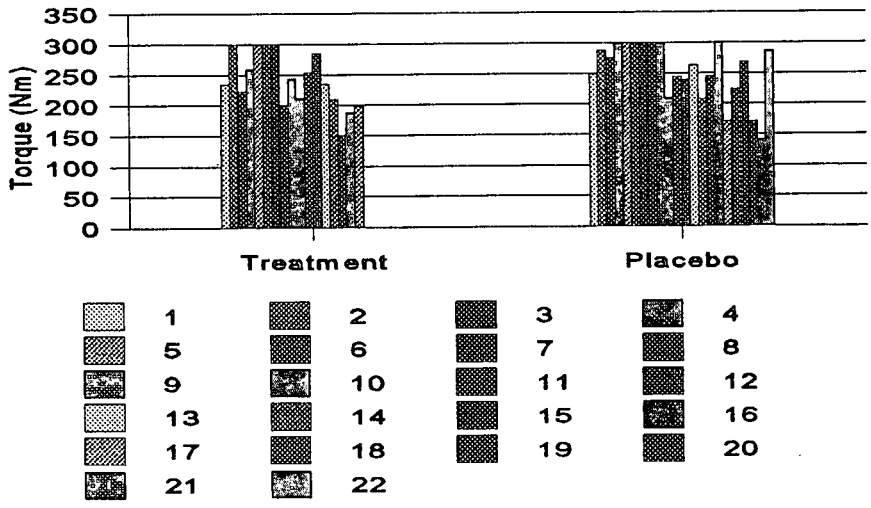


Figure 4.45: Peak extension torque - 1st follow - up

p=0.124274 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Work done during extension

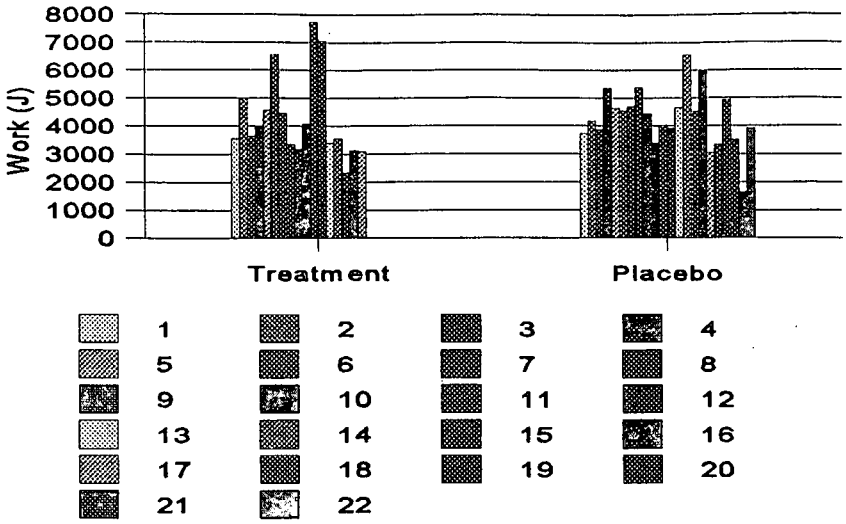


Figure 4.46: Work done during extension - 1st follow - up

p=0.2097805 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Total extension power

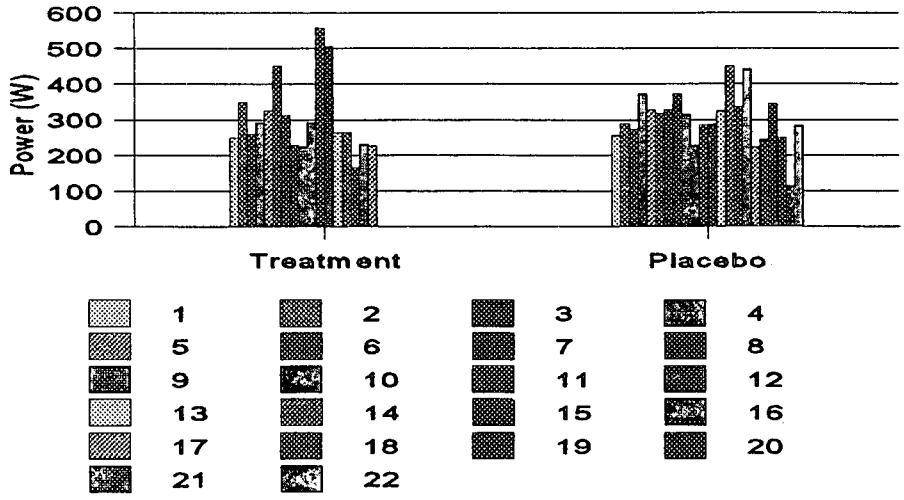


Figure 4.47: Total extension power - 1st follow - up

p=0.243874 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Endurance ratio for extension

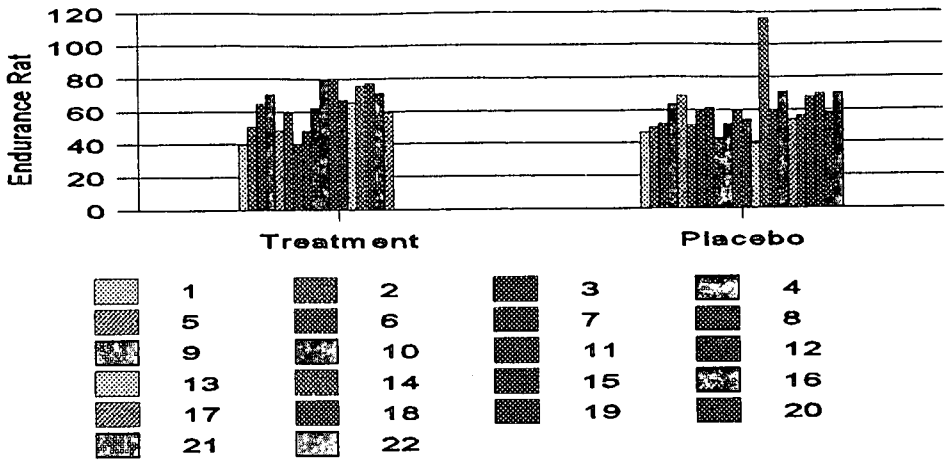


Figure 4.48: Endurance ratio for extension - 1st follow - up

p=0.137768 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

4.3.3 Second Follow - up

-Peak flexion torque

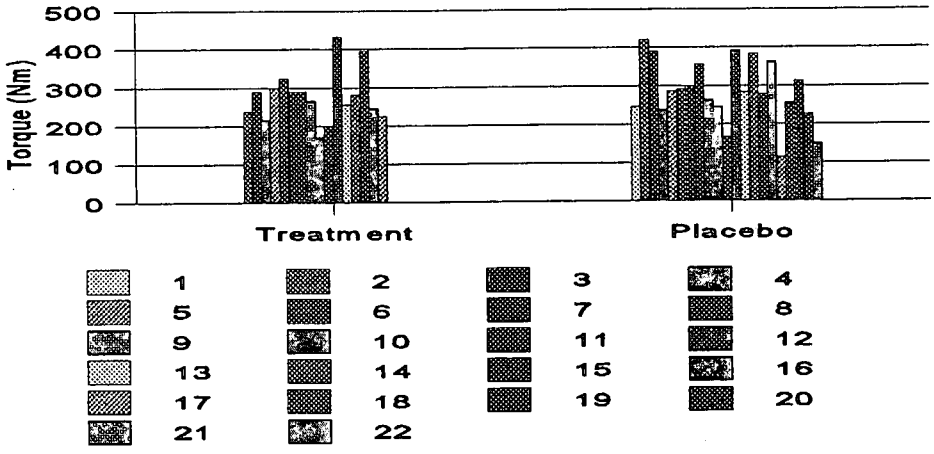


Figure 4.49: Peak flexion torque - 2nd follow - up

p=0.350754 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Work done during flexion

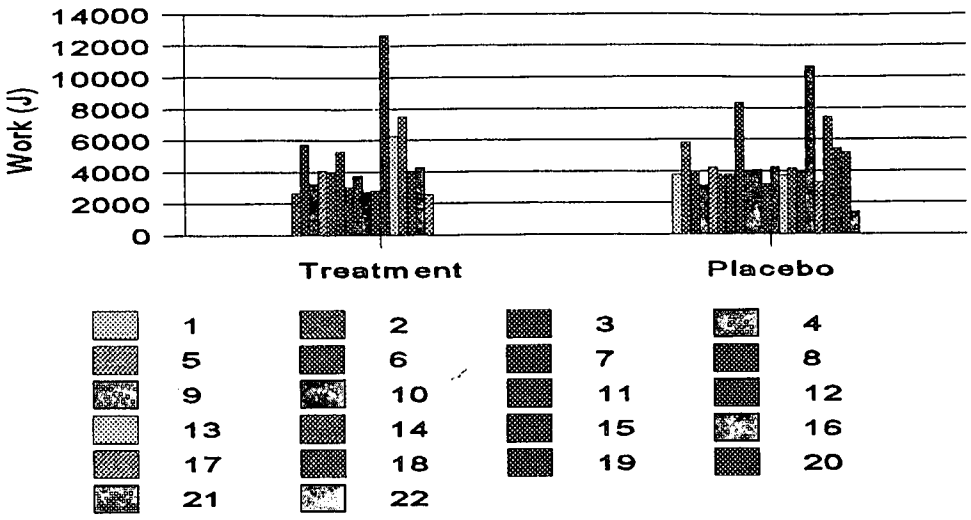


Figure 4.50: Work done during flexion - 2nd follow - up

p=0.2853085 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Total flexion power

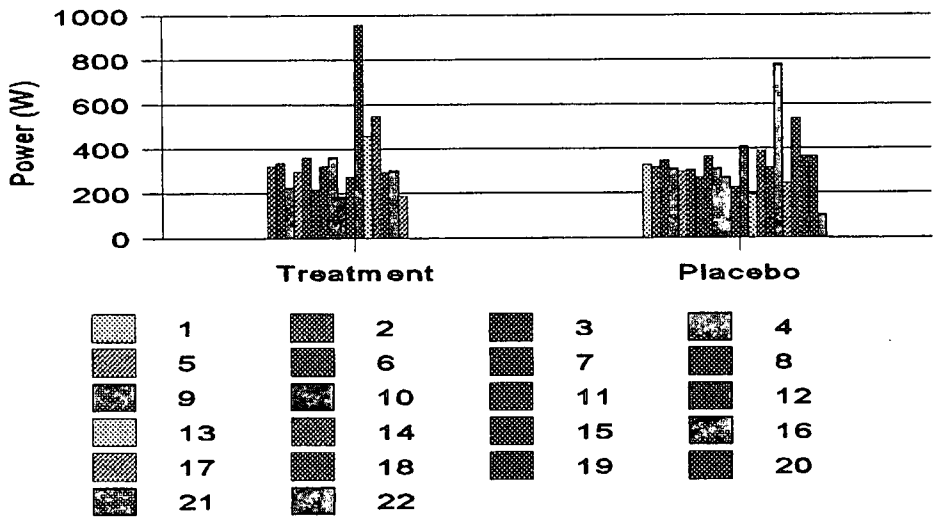


Figure 4.51: Total flexion power - 2nd follow - up

p=0.403116 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Endurance ratio for flexion

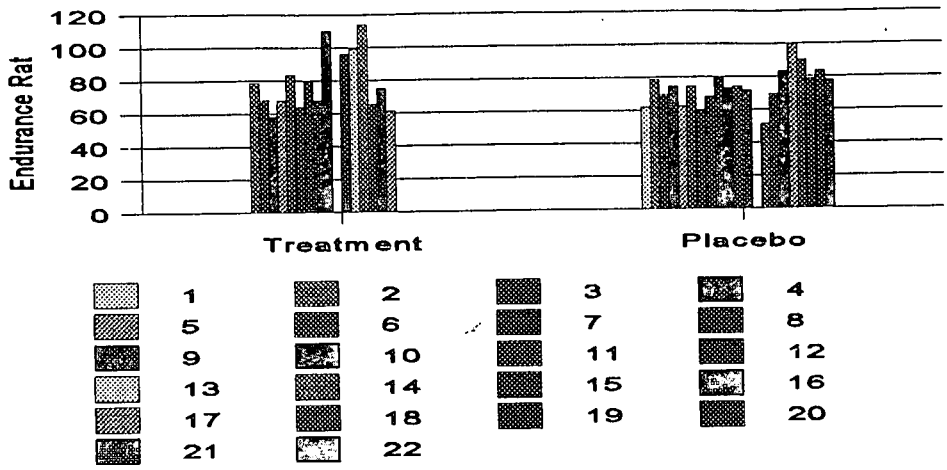


Figure 4.52: Endurance ratio for flexion - 2nd follow - up

p=0.356454 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Peak extension torque

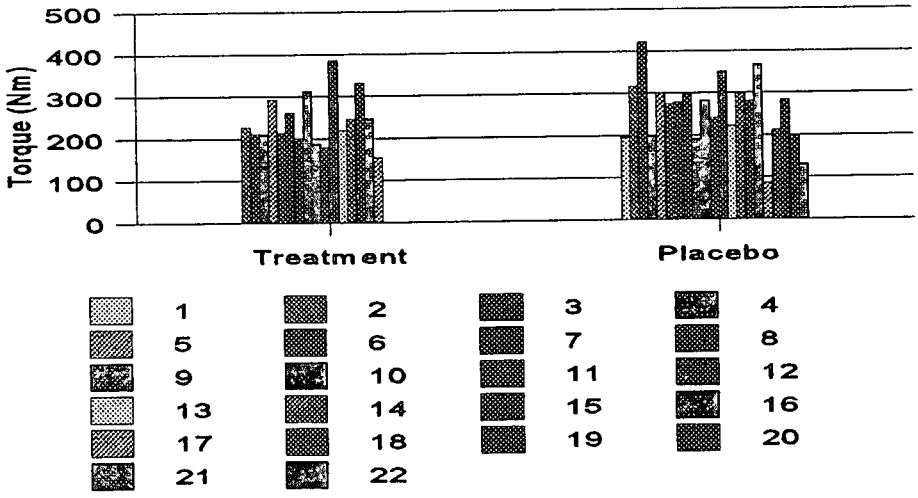


Figure 4.53: Peak extension torque - 2nd follow - up

p=0.217179 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Work done during extension

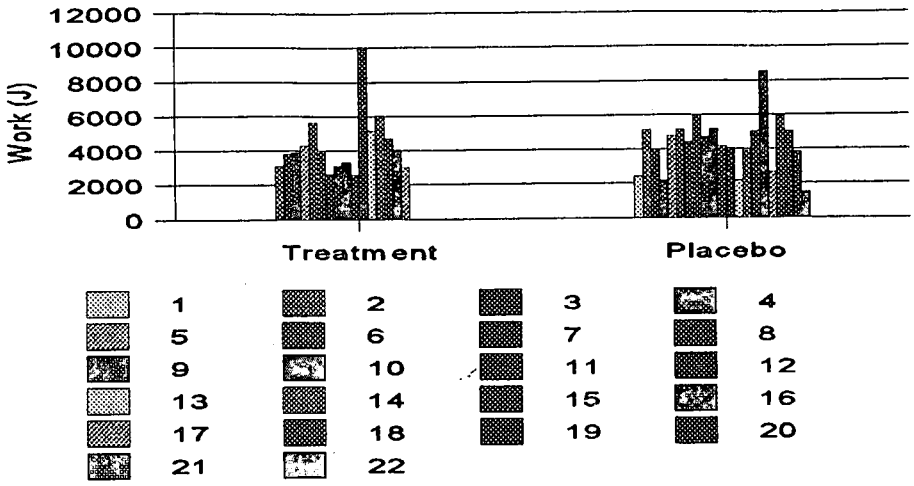


Figure 4.54: Work done during extension - 2nd follow - up

p=0.3894835 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Total extension power

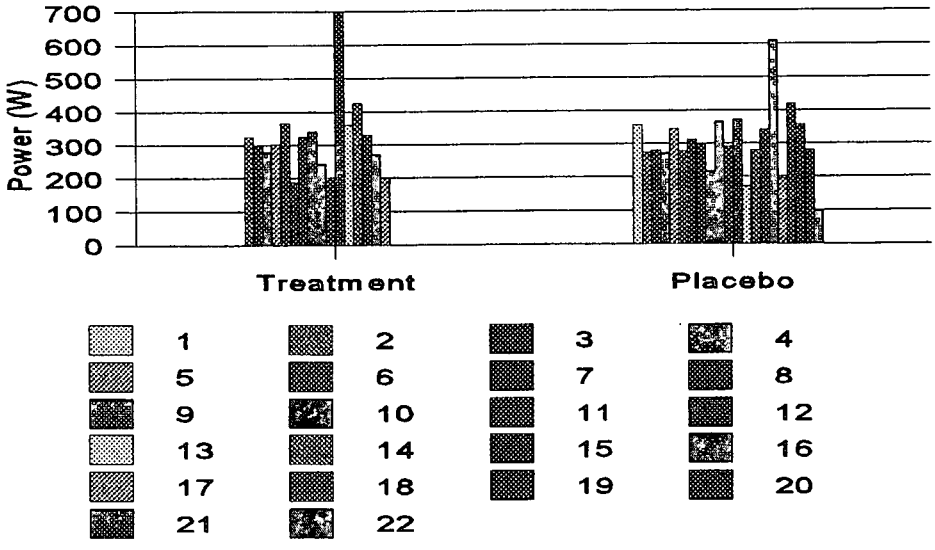


Figure4.55: Total extension power - 2nd follow - up

p=0.385392 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

-Endurance ratio for extension

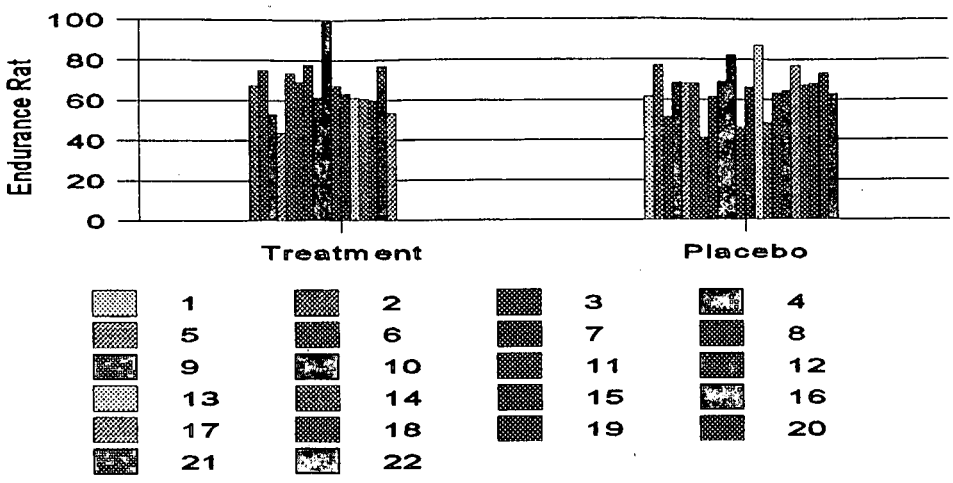


Figure 4.56: Endurance ratio for extension - 2nd follow - up

p=0.4511955 (p>0.05)
Therefore we accept H0. This implies that the two groups are similar.

	Initial Test	1st Follow - up	2nd Follow - up
Peak flexion torque	similar	similar	similar
Work done - flexion	similar	similar	similar
Total flexion power	similar	similar	similar
Endurance ratio - flexion	similar	placebo<tr.	similar
Peak extension torque	similar	similar	similar
Work done - extension	similar	similar	similar
Total extension power	similar	similar	similar
Endurance ratio - extension	similar	similar	similar

Table 4.3: *Inter - group comparison*

CHAPTER 5. Discussion

The results of the trial present an interesting phenomenon in that statistically significant changes in various parameters were seen in both the placebo and treatment groups. The intra - group tests showed similar increases for the placebo and treatment groups. The inter - group comparison showed the two groups to be similar for all parameters for the initial test, similar for all but endurance ratio for flexion (treatment < placebo) for the first follow - up, and similar for all parameters for the final test.

The study did not support the hypothesis that the anaerobic work capacity of human thigh muscle would be increased by the simultaneous administration of phosphocreatine and glycogen in low homoeopathic potency. From the results we deduce that the test preparation was not the cause of the changes in the various parameters. Other, insufficiently controlled variables were responsible for the changes that occurred.

Efforts were made in this study to control all variables, by requesting all participants to continue in their usual lifestyles, and not to change their eating habits or exercise programmes for the duration of the study. We also attempted to provide the same intensity of motivation to all the participants through all the tests.

From our results, these measures were apparently insufficient. The protocol employed in this study has shown itself to be unsuitable for determining homoeopathic preparation efficacy.

In the researcher's opinion, human factors caused the anomalous result, specifically the use of human test subjects.

The existence of sports psychologists and the fact that a large amount of time is spent motivating players during training, and "psyching - up" players before events, is testament to the importance of psychological factors in determining physical performance. Despite the fact that external motivation was the same on all occasions, intrinsic motivation and expectations of the participants may have varied for whatever reason.

Suggestions that athletic performance may be affected by psychological factors are plentiful in the literature.

Athletic performance is affected as a function of intrapersonal (for example, intrinsic motivation) and interpersonal (for example, social support) factors. Iso - Ahola (1995) theorizes that the layer immediately surrounding an athlete's inner core of psychological functioning consists of four intrapersonal factors. These are self - motivation, cognitive capacity and coping skills, affective orientation and mental training skills. Interpersonal factors such as social support and athlete - coach relationship form the layer surrounding these factors. Thus intrinsic factors are seen to be relatively more important in determining athletic performance than extrinsic factors, which we attempted to control in this trial through equal external motivation and no changes in lifestyle.

The effects of psychological factors in athletic performance are demonstrated by the efficacy of behaviour change strategies which form the core of virtually all athletic performance enhancement interventions. These interventions have been shown to be reliably effective in studies, despite variations in treatment conditions, control conditions, and accross different types of dependant measures. (Meyers et al. 1996.)

Given hindsight, this study could be improved in several ways.

First, the tests for anaerobic work capacity could be performed on denervated, electrically stimulated frog or rodent gastrocnenius muscles, bathed first in ringers solution (control), and then in homoeopathic dilutions of phosphocreatine and/or glycogen in ringers solution (experimental). This protocol would exclude factors such as motivational differences and human factors.

Second, using human test subjects, the subjects could be tested pre- and post-administration of the test preparations for changes in phosphocreatine and glycogen, and changes in the rate of phosphocreatine resynthesis after explosive exercise, using 31P-NMR spectroscopy, compared to a placebo group taking an inactive preparation.

CHAPTER 6. Conclusions and Recommendations

Changes in the measured parameters occurred in both the treatment and placebo groups. These changes occurred to a similar extent in both groups. It may be concluded that these changes were not brought about by the administration of phosphocreatine and glycogen in homoeopathic potency.

Recommendations to researchers interested in pursuing this topic would be to test with either a similar product with the measurements being taken at different times (if possible, with very short intervals and with numerous tests), or a different preparation including intracellular buffers in potency, theoretically to prevent a decrease in intracellular pH, the suggested cause of the onset of fatigue.

To perform the tests on electrically stimulated frog gastrocnemius muscle immersed first in ringers solution and then in homoeopathic dilutions of phosphocreatine and/or glycogen may yield good results as motivational differences and human factors are removed from the trial.

References

Baker, A. J., Carson, P. J., Miller, R. G. and Weiner, M. W. 1994. Metabolic and Nonmetabolic components of Fatigue monitored with 31P-NMR. Muscle and Nerve, 17: 1002-1009.

Balsom, P. D., Sonderlund, K. and Ekblom, B. 1994. Creatine in humans with special reference to creatine supplementation. Sports Medicine, 18(4): 268-280.

Bigland - Ritchie, B., Kukulka, C. G., Lippold, O. C. J. and Woods, J. J. 1982. The absence of neuromuscular transmission failure in sustained maximal voluntary contractions. J. Physiol, 330: 265-278.

Birch, R., Noble, D. and Greenhaff, P. L. 1994. The influence of dietary creatine supplementation on performance during repeated bouts of maximal isokinetic cycling in man. European Journal of Applied Physiology, 69(3): 268-276.

Clark, J. F., Kemp, G. J. and Radda, G. K. 1995. The creatine kinase equilibrium, free [ADP] and myosin ATPase in vascular smooth muscle cross - bridges. Journal of Theoretical Biology, 173(2): 207-211.

Daniel, W., 1978. Applied Nonparametric Statistics. Boston, Georgia: Houghton Mifflin Company. ISBN 0-395-29795-6.

Donaldson, S. K. B., Kerrick, W. and Hermansen, L. 1978. Differential, direct effects of H and Ca activated form of skinned fibres from soleus, cardiac and adductor magnus muscles of rabbits. Pflugers Arch., 376: 55-65.

Edwards, R. H. T.,Harris, R. C., Hultman, E., et al. 1972. Effect of temperature on muscle energy metabolism and endurance during successive isometric contractions sustained to fatigue on the quadriceps muscle in man. J. Physiol., 220: 335-352.

Erecinska, M., Deas, J. And Silver, I. A. 1995. The effect of pH on glycolysis and phosphofructokinase activity in cultured cells and synaptosomes. J. Neurochem., 65(6): 2765-2772.

Evans, W. J. 1995. Effects of exercise on body composition and functional capacity of the elderly. J. Gerontol. A. Biol. Sci. Med. Sci., 50:147-150.

Fryer, M. W., Owen, V. J., Lamb, G. D. And Stephenson, D. G. 1995. Effects of creatine phosphate and P(I) on Ca2+ movements and tension development in rat skinned skeletal muscle fibres. J. Physiol. Lond., 482(Pt. 1): 123-140.

Greenhaff, P. L., Bodin, K., Sonderlund, K. and Hultman, E. 1994. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. American Journal of Physiology, 266(5.1):E725-E730.

Guyton, A. C. 1992. Human Physiology and Mechanisms of Disease. Fifth edition. Pennsylvania, USA: W. B. Saunders Company. 690. ISBN 0-7216-4593-3.

Hamalainen, N. And Pette, D. 1995. Patterns of myosin isoforms in mammalian skeletal muscle fibres. Microsc. Res. Tech., 30(5): 381-389.

Hermansen, L. 1979. Effect of acidosis on skeletal muscle performance during maximal exercise in man. Bulletin European de Physiopathologie Respiratoire, 15: 229-238.

Iso - Ahola, S. E. 1995. Intrapersonal and interpersonal factors in athletic performance. Scand. J. Med. Sci. Sports, 5(4): 191-199.

Jontes, J. D. 1995. Theories of muscle contraction. Journal of Structural Biology, 115(2): 119-143.

Jouanny, J. 1991. The essentials of Homoeopathic therapeutics. France: Boiron. 417 p. ISBN 2-86742-014-5.

Kemp, G. J., Hands, L. J., Ramaswami, G., Taylor, D. J., Nicolaides, A., Amato, A. And Radda, G. K. 1995. Calf muscle mitochondrial and glycogenolytic ATP synthesis in patients with claudication due to peripheral vascular disease analysed using 31P magnetic resonance spectroscopy. Clin. Sci. Colch., 89(6): 581 - 590.

Koenig, K. 1927. Ueber die Wirkung extremverduennter (homeopathisieter) Metallsalzoesungen auf Entwikklung and Wachstum von Kaulquappen. Zietschrift fuer die Gesammte Experimentelle Medizin, 56: 581 - 593.

Kushmerick, M. J. 1995. Bioenergetics and muscle cell types. Adv. Exp. Med. Biol., 384: 175-184.

Meyers, A. W., Whelan, J. P. And Murphy, S. M. 1996. Cognitive behavioural strategies in athletic performance enhancement. Prog. Behav. Modif., 30: 137-164.

Milligan, R. A. 1996. Protein - protein interactions in the rigour actomyosin complex. Proc. Natl. Acad., Sci. USA, 93(1): 21-26.

Molloy, J. E., Burns, J. E., Centrex - Jones, J., Tregear, R. T. And White, D. C. 1995. Movement and force produced by a single myosin head. Nature, 378(6553): 209-212.

Moore, K. L. 1985. Clinically Oriented Anatomy. Second edition. Baltimore, USA: Williams and Wilkins. 1101 p. ISBN 0-683-06132-1.

Nakamura, Y., and Schwartz, A. 1972. The influence of hydrogen ion concentrations on calcium binding and release by skeletal muscle sarcoplasmic reticulum. J. Gen. Physiol, 59: 22-32.

Nandi, M., and Raha, D. 1990. Dose dependant effect of Baryta carbonicum and Baryta muriaticum in homoeopathic trituration on experimentally induced high serum lipid concentration in chickens. British Homoeopathic Journal, 79(4): 224-227.

Newsholme, E. A. and Leech, A. R. 1983. Biochemistry for the Medical Sciences. Great Britain: John Wiley and Sons Ltd. 952 p. ISBN 0-471-90058-3.

Nightingale, M. 1988. Holistic First Aid: A handbook for the home. First Edition. London, England: Macdonald and Co. Ltd. 192 p. ISBN 0-356-15198-0.

Pelikan, W. and Unger, G. 1971. The activity of potentized substances: Experiments on plant growth and Statistical Evaluation. British Homoeopathic Journal, 60: 24-27.

Pernow, B. B., Hevel, R. J. and Jennings, D. B. 1967. The second wind phenomenon in McArdle's Syndrome. Acta Med. Scand., Suppl 472: 294-307.

Piazzesi, G. And Lombardi, V. 1995. A cross - bridge model that is able to explain mechanical and energetic properties of shortening muscle. Biophys. J., 68(5): 1966-1979.

Pittman, R. N. 1995. Influence of microvascular architecture on oxygen exchange in skeletal muscle. Microcirculation, 2(1): 1-18.

Potter, J. D., Sheng, Z., Pan, B. S. And Zhao, J. 1995. A direct regulatory role for troponin T and a dual role for troponin C in the Ca2+ regulation of muscle contraction. J. Biol. Chem., 270(6): 2557-2562.

Radda, G. K. 1996. Control of energy metabolism during muscle contraction. Diabetes, 45 Suppl. 1: S88-S92.

Radda, G. K., Odoom, J., Kemp, G. Taylor, D. J., Thompson, C. And Styles, P. 1995. Assessment of mitochondrial function and control in normal and diseased states. Biochim. Biophys. Acta, 1271(1): 15-19.

Reynolds, A. J., Fuhrer, L., Dunlap, H. L., Finke, M. and Kallfelz, F. A. 1995. Effect of diet and training on muscle glycogen storage and utilization in sled dogs. Journal of Applied Physiology, 79(5): 1601-1607.

Sahlin, K. 1978. Intracellular pH and energy metabolism in skeletal muscle of man, with special reference to exercise. Acta Physiol. Scand., Suppl. 455: 1-56.

Saltin, B., Henriksson, J., Nygaard, E., et al. 1977. Fibre types and metabolic potentials of Skeletal Muscles in sedentary man and endurance runners. Annal. N.Y. Acad. Sci, 301: 3-29

Sieck, G. C., Zahn, W. Z., Prakash, Y. S., Daood, M. J. And Watchko, J. F. 1995. SDH and actomyosin ATPase activities of different fiber types in rat diaphragm muscle. Journal of Applied Physiology, 79(5): 1629-1639.

Smith, D. A. And Geeves, M. A. 1995. Strain - dependant cross - bridge cycle for muscle. Biophysiology Journal, 69(2): 524-537.

Smolen, P. 1995. A model for glycolytic oscillations based on skeletal muscle phosphofructokinase kinetics. Journal of Theoretical Biology, 174(2):137-148.

Toth, M. J. and Poehlman, E. T. 1995. Resting metabolic rate and cardiovascular disease risk in resistance- and anaerobic- trained middle - aged women. International Journal of Obesity and Related Metabolic Disorders, 19(10): 691-698.

Travnik, L., Pernus, F. And Erzen, I. 1995. Histochemical and morphometric characteristics of the normal human vastus medialis longus and vastus medialis obliquus muscles. Journal of Anatomy, 187(Pt. 2): 403-411.

Tseng, B. S., Marsh, D. R., Hamilton, M. T. And Booth, F. W. 1995. Strength and aerobic training attenuate muscle wasting and improve resistance to the development of disability with aging. J. Gerontol. A. Biol. Sci. Med. Sci., 50: 113 - 119.

Wank, V., Bauer, R., Punkt, K. And Ziegan, J. 1994. Enzyme activity patterns of myosin ATPase, alpha - glycerophosphate dehydrogenase and succinate dehydrogenase within different muscle fibre types. Acta. Histochem., 96(2): 213-218.

Westerblad, H. and Allen, D. G. 1991. Changes in Myoplasmic Calcium concentration during fatigue in single mouse muscle fibres. Journal of General Physiology, 98: 615-635.

Westerblad, H. Lee, J. A., Lannergren, J. and Allen, D. G. 1991. Cellular mechanisms of fatigue in skeletal muscle. American Journal of Physiology, 261:C195-C209.

Yamamotu, M. and Kanehisa, H. 1995. Dynamics of anaerobic and aerobic energy supplies during sustained high intensity exercise on cycle ergometer. European Journal of Applied Physiology, 71(4): 320-325.

Appendix 1

Raw Data from Tests

Subject No. 1: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	124.71	183.35	246.56
Work done during flexion (J)	2433.26	2495.73	3789.88
Total flexion power (W)	173.38	182.31	326.83
Endurance ratio for flexion (%)	73.72	77.96	62.01
Peak extension torque (Nm)	225.88	249.41	194.67
Work done during extension (J)	3249.96	3727.48	2399.14
Total extension power (W)	229.32	255.55	356.45
Endurance ratio for extension (%)	31.61	46.06	61.47

Subject No. 2: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	172.94	249.41	238.11
Work done during flexion (J)	3526.56	4139.83	2651.19
Total flexion power (W)	260.23	302.41	321.96
Endurance ratio for flexion (%)	88.47	79.28	78.47
Peak extension torque (Nm)	291.76	300.00	227.89
Work done during extension (J)	4678.60	5003.60	3096.21
Total extension power (W)	329.32	347.97	324.51
Endurance ratio for extension (%)	51.83	50.82	67.29

Subject No. 3: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	162.35	221.18	289.28
Work done during flexion (J)	2529.80	2818.27	5711.43
Total flexion power (W)	179.37	198.86	336.34
Endurance ratio for flexion (%)	63.33	73.07	68.27
Peak extension torque (Nm)	250.59	222.35	210.61
Work done during extension (J)	3731.38	3626.95	3830.47
Total extension power (W)	265.87	259.07	297.10
Endurance ratio for extension (%)	55.60	64.95	74.82

Subject No. 4: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	183.53	249.41	419.11
Work done during flexion (J)	3100.83	3327.55	5812.43
Total flexion power (W)	228.81	241.85	316.38
Endurance ratio for flexion (%)	72.37	64.96	78.24
Peak extension torque (Nm)	216.47	288.24	316.28
Work done during extension (J)	3984.60	4159.30	5126.91
Total extension power (W)	277.77	289.26	273.17
Endurance ratio for extension (%)	60.12	49.44	76.78

Subject No. 5: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	214.12	243.53	389.16
Work done during flexion (J)	3153.09	3403.63	3978.16
Total flexion power (W)	224.67	242.52	346.34
Endurance ratio for flexion (%)	85.19	66.48	69.27
Peak extension torque (Nm)	189.41	275.29	421.16
Work done during extension (J)	3534.11	3861.65	3982.87
Total extension power (W)	246.96	272.48	279.01
Endurance ratio for extension (%)	53.26	51.36	51.27

Subject No. 6: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	231.76	269.41	238.57
Work done during flexion (J)	3434.82	3448.59	3083.07
Total flexion power (W)	254.11	248.78	310.41
Endurance ratio for flexion (%)	68.08	57.53	74.25
Peak extension torque (Nm)	300.00	300.00	198.29
Work done during extension (J)	5221.41	5360.54	2165.04
Total extension power (W)	357.97	372.80	271.37
Endurance ratio for extension (%)	57.87	63.30	68.11

Subject No. 7: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	212.94	300.00	216.47
Work done during flexion (J)	2972.96	3274.05	3236.37
Total flexion power (W)	206.26	224.99	227.25
Endurance ratio for flexion (%)	60.80	57.48	58.08
Peak extension torque (Nm)	174.12	258.82	209.41
Work done during extension (J)	3303.75	3976.31	3903.10
Total extension power (W)	240.73	291.93	280.17
Endurance ratio for extension (%)	57.74	70.41	52.84

Subject No. 8: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	147.06	300.00	297.65
Work done during flexion (J)	1744.54	3857.11	4071.58
Total flexion power (W)	123.39	271.50	296.67
Endurance ratio for flexion (%)	95.96	82.53	67.81
Peak extension torque (Nm)	220.00	298.82	292.94
Work done during extension (J)	3335.74	4562.45	4302.08
Total extension power (W)	235.37	325.89	302.08
Endurance ratio for extension (%)	82.17	48.67	43.89

Subject No. 9: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	254.12	300.00	287.06
Work done during flexion (J)	4350.64	4056.21	4714.19
Total flexion power (W)	306.23	278.74	295.91
Endurance ratio for flexion (%)	76.94	62.46	62.10
Peak extension torque (Nm)	237.65	300.00	300.00
Work done during extension (J)	4773.00	4626.85	4775.76
Total extension power (W)	337.60	326.47	344.52
Endurance ratio for extension (%)	89.89	68.50	68.02

Subject No. 10: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	258.82	277.65	324.61
Work done during flexion (J)	3374.11	5025.64	3892.78
Total flexion power (W)	231.32	367.11	361.83
Endurance ratio for flexion (%)	87.04	83.74	83.31
Peak extension torque (Nm)	300.00	300.00	212.78
Work done during extension (J)	5627.93	6554.50	5621.19
Total extension power (W)	401.01	450.43	365.45
Endurance ratio for extension (%)	60.64	59.22	73.22

Subject No. 11: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	183.53	220.00	291.71
Work done during flexion (J)	2865.91	3311.48	3803.79
Total flexion power (W)	218.14	241.29	304.11
Endurance ratio for flexion (%)	78.85	63.33	74.28
Peak extension torque (Nm)	300.00	300.00	273.89
Work done during extension (J)	5242.51	4532.71	5129.04
Total extension power (W)	343.97	315.98	277.31
Endurance ratio for extension (%)	75.64	50.72	67.87

Subject No. 12: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	291.76	300.00	289.14
Work done during flexion (J)	3453.35	3689.33	5281.34
Total flexion power (W)	247.28	266.81	218.52
Endurance ratio for flexion (%)	49.69	34.42	63.92
Peak extension torque (Nm)	300.00	300.00	261.89
Work done during extension (J)	4668.43	4459.88	3987.89
Total extension power (W)	330.21	310.91	187.52
Endurance ratio for extension (%)	49.28	39.61	69.09

Subject No. 13: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	300.00	300.00	297.65
Work done during flexion (J)	3502.49	4020.05	3789.75
Total flexion power (W)	256.50	298.16	270.03
Endurance ratio for flexion (%)	59.25	56.21	59.30
Peak extension torque (Nm)	291.76	300.00	277.65
Work done during extension (J)	4570.30	4703.48	4396.49
Total extension power (W)	313.33	327.89	314.03
Endurance ratio for extension (%)	73.02	58.82	40.94

Subject No. 14: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	300.00	300.00	356.98
Work done during flexion (J)	4704.15	4949.64	8329.87
Total flexion power (W)	331.92	361.56	364.33
Endurance ratio for flexion (%)	105.39	77.10	67.78
Peak extension torque (Nm)	300.00	300.00	296.19
Work done during extension (J)	5037.69	5386.39	5912.98
Total extension power (W)	356.32	371.92	297.10
Endurance ratio for extension (%)	102.36	61.05	61.23

Subject No. 15: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	183.53	151.76	298.78
Work done during flexion (J)	2348.14	2555.63	3040.28
Total flexion power (W)	172.83	189.55	321.96
Endurance ratio for flexion (%)	64.45	53.89	79.32
Peak extension torque (Nm)	198.82	197.65	201.62
Work done during extension (J)	3178.75	3343.08	2615.00
Total extension power (W)	218.96	227.58	324.51
Endurance ratio for extension (%)	72.21	48.14	77.61

Subject No. 16: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	291.76	300.00	264.71
Work done during flexion (J)	3268.11	3950.14	4015.00
Total flexion power (W)	236.94	280.08	310.14
Endurance ratio for flexion (%)	95.37	45.11	79.32
Peak extension torque (Nm)	284.71	300.00	191.83
Work done during extension (J)	3711.57	4463.51	4672.43
Total extension power (W)	256.89	315.34	217.73
Endurance ratio for extension (%)	41.21	42.43	68.71

Subject No. 17: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	145.88	147.06	246.56
Work done during flexion (J)	2926.77	2916.24	4051.43
Total flexion power (W)	215.97	217.97	271.73
Endurance ratio for flexion (%)	67.75	69.41	73.29
Peak extension torque (Nm)	178.82	209.41	283.32
Work done during extension (J)	3062.69	3358.81	5170.28
Total extension power (W)	210.97	228.12	365.45
Endurance ratio for extension (%)	60.82	50.98	82.10

Subject No. 18 Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	197.65	198.82	165.88
Work done during flexion (J)	3176.93	3321.02	3127.57
Total flexion power (W)	229.89	238.39	226.18
Endurance ratio for flexion (%)	81.02	56.21	73.99
Peak extension torque (Nm)	198.82	243.53	241.18
Work done during extension (J)	4110.59	4024.17	4155.61
Total extension power (W)	288.64	285.33	290.39
Endurance ratio for extension (%)	62.53	59.21	46.27

Subject No. 19: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	191.76	205.88	267.43
Work done during flexion (J)	3614.67	3944.88	3124.68
Total flexion power (W)	264.04	275.00	363.43
Endurance ratio for flexion (%)	77.11	68.89	67.78
Peak extension torque (Nm)	205.88	243.53	313.28
Work done during extension (J)	3263.34	3159.09	3106.72
Total extension power (W)	225.86	223.99	342.15
Endurance ratio for extension (%)	48.37	62.18	61.23

Subject No. 20: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	263.53	235.29	170.59
Work done during flexion (J)	3568.73	3381.59	2712.82
Total flexion power (W)	252.42	238.02	187.31
Endurance ratio for flexion (%)	94.42	92.72	109.94
Peak extension torque (Nm)	203.53	211.76	188.24
Work done during extension (J)	3910.40	4072.42	3328.60
Total extension power (W)	281.39	292.33	244.38
Endurance ratio for extension (%)	84.71	79.83	98.98

Subject No. 21: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	188.24	216.47	392.76
Work done during flexion (J)	2826.08	2901.78	4211.62
Total flexion power (W)	206.44	202.70	409.72
Endurance ratio for flexion (%)	83.71	68.66	71.67
Peak extension torque (Nm)	216.47	240.00	351.09
Work done during extension (J)	4055.58	3929.69	4019.27
Total extension power (W)	280.70	286.33	371.00
Endurance ratio for extension (%)	62.50	53.71	68.11

Subject No. 22: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	225.88	223.53	283.75
Work done during flexion (J)	4051.30	4211.87	3721.62
Total flexion power (W)	300.48	302.34	192.43
Endurance ratio for flexion (%)	56.77	55.14	48.12
Peak extension torque (Nm)	300.00	263.53	221.72
Work done during extension (J)	4936.77	4644.39	2163.45
Total extension power (W)	333.72	323.77	171.31
Endurance ratio for extension (%)	34.26	38.93	87.16

Subject No. 23: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	247.06	329.41	198.13
Work done during flexion (J)	3724.82	9957.42	2794.58
Total flexion power (W)	259.04	709.5	273.09
Endurance ratio for flexion (%)	66.13	100.55	55.08
Peak extension torque (Nm)	247.06	254.12	178.41
Work done during extension (J)	3806.09	7731.09	2548.59
Total extension power (W)	278.73	557.72	202.71
Endurance ratio for extension (%)	70.59	80.26	67.13

Subject No. 24: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	181.18	294.12	381.67
Work done during flexion (J)	2320.65	8599.32	4121.26
Total flexion power (W)	162.56	637.8	388.15
Endurance ratio for flexion (%)	84.75	123.21	61.22
Peak extension torque (Nm)	202.41	207.06	297.48
Work done during extension (J)	2946.71	6554.10	3888.11
Total extension power (W)	211.00	451.47	279.31
Endurance ratio for extension (%)	81.32	116.19	48.17

Subject No. 25: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	256.47	291.76	278.72
Work done during flexion (J)	3935.23	4463.88	3987.88
Total flexion power (W)	283.18	312.69	312.69
Endurance ratio for flexion (%)	69.57	63.32	69.32
Peak extension torque (Nm)	209.41	244.71	278.71
Work done during extension (J)	3911.80	4518.76	5018.76
Total extension power (W)	277.36	335.15	342.15
Endurance ratio for extension (%)	73.00	59.93	62.78

Subject No. 26: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	303.53	305.88	362.35
Work done during flexion (J)	8953.28	6201.40	10689.41
Total flexion power (W)	660.67	434.40	778.88
Endurance ratio for flexion (%)	97.96	52.97	82.78
Peak extension torque (Nm)	296.47	301.18	367.06
Work done during extension (J)	7336.67	5956.65	8539.90
Total extension power (W)	512.68	441.80	608.49
Endurance ratio for extension (%)	58.98	70.82	64.49

Subject No. 27: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	284.71	378.82	432.94
Work done during flexion (J)	6490.82	8808.25	12727.69
Total flexion power (W)	471.76	645.05	958.71
Endurance ratio for flexion (%)	108.66	82.54	95.96
Peak extension torque (Nm)	265.88	284.71	385.88
Work done during extension (J)	5283.26	7069.86	10039.82
Total extension power (W)	370.98	506.24	696.54
Endurance ratio for extension (%)	75.19	66.95	63.28

Subject No. 28: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	150.59	160.00	114.12
Work done during flexion (J)	2330.49	2665.79	3278.67
Total flexion power (W)	161.68	188.10	244.43
Endurance ratio for flexion (%)	77.30	63.27	99.58
Peak extension torque (Nm)	143.53	170.59	85.88
Work done during extension (J)	2722.94	3027.75	2615.91
Total extension power (W)	200.42	222.29	196.53
Endurance ratio for extension (%)	82.69	54.00	76.96

Subject No. 29: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	244.71	211.76	256.47
Work done during flexion (J)	3645.15	2494.55	7442.85
Total flexion power (W)	259.73	174.74	534.26
Endurance ratio for flexion (%)	69.06	67.76	90.03
Peak extension torque (Nm)	244.71	223.53	211.76
Work done during extension (J)	3345.33	3322.76	5905.17
Total extension power (W)	238.36	243.33	420.76
Endurance ratio for extension (%)	64.5	56.20	66.93

Subject No. 30: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	230.59	244.71	256.47
Work done during flexion (J)	3582.32	3208.27	6221.88
Total flexion power (W)	259.07	222.05	455.64
Endurance ratio for flexion (%)	74.04	83.33	99.26
Peak extension torque (Nm)	216.47	235.29	218.82
Work done during extension (J)	3929.29	3396.02	5124.23
Total extension power (W)	277.25	261.93	359.81
Endurance ratio for extension (%)	77.13	65.48	60.89

Subject No. 31: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	251.76	228.24	282.35
Work done during flexion (J)	3598.11	3117.10	7506.56
Total flexion power (W)	255.12	215.23	546.96
Endurance ratio for flexion (%)	77.82	71.60	113.82
Peak extension torque (Nm)	216.47	209.41	244.71
Work done during extension (J)	3479.12	3541.11	6038.55
Total extension power (W)	249.74	264.67	425.04
Endurance ratio for extension (%)	58.37	75.65	60.40

Subject No. 32: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	141.18	143.53	395.29
Work done during flexion (J)	1929.86	1919.10	4009.72
Total flexion power (W)	140.97	139.83	292.90
Endurance ratio for flexion (%)	73.81	74.14	65.45
Peak extension torque (Nm)	160.00	150.59	331.76
Work done during extension (J)	2041.83	2325.87	4683.89
Total extension power (W)	142.68	163.71	330.49
Endurance ratio for extension (%)	62.90	77.48	59.30

Subject No. 33: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	216.47	281.18	313.28
Work done during flexion (J)	3983.62	5033.16	5413.31
Total flexion power (W)	300.85	381.10	362.38
Endurance ratio for flexion (%)	87.63	75.29	78.42
Peak extension torque (Nm)	221.18	268.24	283.11
Work done during extension (J)	4358.51	4934.33	5017.82
Total extension power (W)	303.11	345.64	356.54
Endurance ratio for extension (%)	82.39	67.71	68.01

Subject No. 34: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	225.82	267.66	227.04
Work done during flexion (J)	5026.30	3784.58	5171.34
Total flexion power (W)	358.14	271.67	363.43
Endurance ratio for flexion (%)	86.43	78.81	83.31
Peak extension torque (Nm)	189.41	170.59	196.47
Work done during extension (J)	3803.26	3502.16	3803.74
Total extension power (W)	277.82	248.93	279.01
Endurance ratio for extension (%)	76.52	69.93	73.23

Subject No. 35: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	216.47	216.47	246.72
Work done during flexion (J)	2907.97	2907.97	4267.34
Total flexion power (W)	201.75	201.75	301.41
Endurance ratio for flexion (%)	68.28	68.28	74.87
Peak extension torque (Nm)	188.24	188.24	246.56
Work done during extension (J)	3127.28	3127.28	4051
Total extension power (W)	231.36	231.36	271.37
Endurance ratio for extension (%)	71.10	71.10	76.92

Subject No. 36: Placebo Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	128.24	130.59	150.59
Work done during flexion (J)	1177.05	1284.73	1394.19
Total flexion power (W)	84.70	92.91	104.47
Endurance ratio for flexion (%)	61.74	75.92	77.68
Peak extension torque (Nm)	149.41	141.18	129.41
Work done during extension (J)	1449.15	1628.08	1459.21
Total extension power (W)	101.27	113.50	100.04
Endurance ratio for extension (%)	37.25	58.43	62.74

Subject No. 37: Treatment Group	Test 1	Test 2	Test 3
Peak flexion torque (Nm)	189.41	245.88	224.76
Work done during flexion (J)	2355.71	2730	2561
Total flexion power (W)	172.51	195.97	187.52
Endurance ratio for flexion (%)	66.45	69.52	61.02
Peak extension torque (Nm)	178.82	197.65	153.68
Work done during extension (J)	2238.72	3080.68	3004.82
Total extension power (W)	154.21	225.61	199.02
Endurance ratio for extension (%)	63.74	59.03	53.44