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Technology**

**MTech Dissertation: Quality of life on nocturnal
haemodialysis versus diurnal dialysis**

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AUTHOR'S DECLARATION

This study represents original work by the author. It has not been submitted to any other Tertiary Institution. Where use of the work by others was made, it has been duly acknowledged in the text.

The research described in this dissertation was carried out in the department of Biomedical and Clinical Technology, Faculty of Health Sciences, Durban University of Technology under the supervision of Prof J.K Adam (Head of the Clinical Technology programme) and the Sunninghill Dialysis Unit, Johannesburg, South Africa under the supervision of DR D.M Campbell (Head Nephrologist at the Sunninghill Dialysis Unit).

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DEDICATION

I dedicate this work to:

My mother and my sister for their constant love, support, guidance, prayers and encouragement.

ABSTRACT

INTRODUCTION

End stage renal disease (ESRD) occurs once 90 % of the kidney function is lost. Patients with ESRD must either undergo medical treatments, like haemodialysis, that substitute the function of the kidney, or they must have a kidney transplant. In the 1970s, haemodialysis treatment took 8 to 12 hours, three times per week. As technology advanced, dialyzers were able to handle more dialysate and higher blood flow rates hence treatment times were shortened to between three and five hours per treatment which has remained the norm until present day. One clinic in Tassin, France remained on the longer dialysis program and noticed advantages for patients who were on extended dialysis times.

One of the major problems with dialysis done in the traditional sense is that it tries to provide a lot of therapy in a short period of time, and it is difficult to clear toxins and fluid in that time, Nocturnal dialysis provides a greater amount of toxin removal over a long period of time.

AIMS AND OBJECTIVES

The main aim of this study was to determine if nocturnal dialysis resulted in improved dialysis clearance, better overall patient health and a better quality of life.

The primary objective of this study was to compare the clearance of small molecules (for example, urea, phosphate, creatinine and potassium) and large retention products (for example Parathyroid Hormone (PTH) and β 2-Microglobulin) between the two haemodialysis procedures. The secondary objective was to compare the quality of life and survival of patients on both nocturnal and daytime dialysis.

METHODOLOGY

Thirty patients with End Stage Renal Disease (ESRD) presenting to the Sunninghill Hospital Dialysis Unit for treatment, who met the inclusion criteria, were recruited to participate in this study.

Blood samples were taken for each participant at a baseline, 3 month and 6 month interval. The Kidney Disease Quality of Life Survey Questionnaire (KDQOL: SF-36™) was also given to each participant to complete. This survey consisted of three parts: 1) Physical Component Summary 2) Mental Component Summary and 3) Burden of Kidney Disease. This survey helped to predict the quality of life of the patients in each group.

RESULTS

In this study, non-significant effects of treatment were found for all small solutes individually. This study showed that there was a statistically significant increase in both dialysis adequacy and the clearance of large molecules (Parathyroid Hormone and Beta-2-Microglobulin) in the nocturnal haemodialysis group.

The results of the KDQOL: SF-36 survey showed that the nocturnal dialysis patients scored higher in both the Physical Component Summary and the Mental Component Summary which means that they felt they were in better physical and mental health. The survey also showed that the nocturnal dialysis patients felt the burden of kidney disease less than those patients dialyzing during the day.

CONCLUSION

Firstly, dialysis adequacy as defined by the formula Kt/V , increased in the nocturnal group while it levelled off in the diurnal group.

Secondly, both the Parathyroid Hormone levels and Beta-2-Microglobulin levels decreased more in the nocturnal group therefore resulting in statistically significant effects of treatment.

The third and final conclusion drawn was that nocturnal haemodialysis resulted in better physical health, better mental health and a lower burden of kidney disease was felt by patients undergoing nocturnal haemodialysis.

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Doctor Diane Campbell – for providing me with the opportunity to work on a project in an area of interest to me

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LIST OF ABBREVIATIONS

| Abbreviation | Meaning |
|--------------|--|
| AV | Arteriovenous |
| AVF | Arteriovenous Fistula |
| AVG | Arteriovenous Graft |
| B2M | Beta-2-Microglobulin |
| BUN | Blood Urea Nitrogen |
| CKD | Chronic Kidney Disease |
| cm | Centimeter |
| CV | Cardiovascular |
| eKt/V | Equilibrated Dialysis Adequacy |
| EPO | Erythropoeitin |
| ESRD | End Stage Renal Disease |
| g | Grams |
| g/L | Grams per litre |
| GFR | Glomerular Filtration Rate |
| HD | Haemodialysis |
| HRQOL | Health Related Quality of Life |
| KDOQI | Kidney Disease Outcomes Quality Initiative |
| Kt/V | Dialysis Adequacy |
| L | Litres |

| | |
|-----------------------|--|
| MCS | Mental Component Summary |
| mg | Milligrams |
| ml/dL | Millilitres per decilitre |
| ml/min/m ² | Millilitres per minute per metre square |
| mls | millilitres |
| mls/min | Millilitres per minute |
| mmol/L | Millimols per litre |
| NCDS | National Cooperative Dialysis Study |
| NHD | Nocturnal Haemodialysis |
| NKF | National Kidney Foundation |
| PCS | Physical Component Summary |
| PermCath | Permanent Catheter |
| PTH | Parathyroid Hormone |
| SF-36 | Renal Disease Specific Quality of Life Initiatives |
| SIP | Sickness Impact Profile |
| UFR | Ultrafiltration Rate |
| URR | Urea Reduction Ratio |
| USA | United States of America |
| USRDS | United States Renal Data System |

CHAPTER ONE: INTRODUCTION

End stage renal disease (ESRD) occurs once 90 % of the kidney function is lost (National Kidney Foundation, 2003). Acute renal failure occurs when the kidney fails suddenly, but this may be a temporary problem, and after a short period of treatment the patient may recover (Faratro, D’Gama & Chan, 2004). If acute renal failure persists, it is referred to as chronic kidney disease (CKD), where damage to the kidney function will never recover (Faratro et al., 2004). Patients with ESRD must either undergo medical treatments, like haemodialysis, that substitute the function of the kidney, or they must have a kidney transplant (Faratro et al., 2004).

The National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI) defines CKD as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60ml/min/1.73m² for three or more months. Once the loss of nephrons and the reduction of functional renal mass reach a certain point, the remaining nephrons begin a process of irreversible sclerosis leading to a progressive decline in the glomerular filtration rate (National Kidney Foundation, 2006).

All individuals with kidney damage are classified as having chronic kidney disease, irrespective of the level of GFR. The rationale for this is because patients with kidney damage are at increased risk of the two major outcomes of chronic kidney disease: loss of kidney function and development of cardiovascular disease. Early diagnosis and treatment of the underlying cause is imperative in patients with chronic kidney disease. This may slow or possibly halt the progression of the disease to End Stage Renal Failure (O’Mara, 2008; National Kidney Foundation, 2006).

Lozano (2012) has stated that people with chronic kidney disease suffer from accelerated atherosclerosis and are more likely to develop cardiovascular disease than the general population. The loss of protein in the urine is regarded as an independent marker for worsening of renal function and cardiovascular disease. Chronic kidney disease globally resulted in 735,000 deaths in 2010 up from 400,000 deaths in 1990 (Lozano, 2012). Chronic Kidney Disease is divided into five stages as described by O’Mara (2008) and NKF (2006). Between the five stages kidney function reduced from more than 90% in stage 1 to less than 15% by stage 5. The five stages are represented in Table 1.

Table 1: The different stages of Chronic Kidney Disease (NKF, KDOQI Clinical Practice Guidelines for CKD, 2002)

| The five stages of chronic kidney disease | | | | | |
|--|--|---|--|---|--|
| | STAGE 1 | STAGE 2 | STAGE 3 | STAGE 4 | STAGE 5 |
| Amount of kidney function remaining at each stage | More than 90% | 60 to 89% | 30 to 59% | 15 to 29% | Less than 15% |
| Description of each stage | Early kidney damage with normal or even increased function. | Worse kidney damage with reduced function. | Even worse kidney damage with less function. | Kidney damage is so severe with such poor function that the kidneys are barely able to keep the person alive. | End-stage Renal Disease: kidney function is severely impaired. The kidneys are not working well enough to keep the person alive. |
| Symptoms | No symptoms observed. Urea and creatinine levels are normal. | No symptoms observed. Urea and creatinine levels are normal, or mildly elevated. | Early symptoms occur and may include tiredness, poor appetite, and itching. Creatinine level rises, excess urea is present, and anemia may begin to occur. | Tiredness, poor appetite, and itching may get worse. | Symptoms may include poor sleeping at night, difficulty breathing, itchiness, and frequent vomiting. High levels of creatinine and urea are present. |
| eGFR (estimated Glomerular Filtration Rate) | 90 ml/min or more | 60 – 89 ml/min | 30 – 59 ml/min | 15 – 29 ml/min | 15 ml/min or less |
| Treatment options* | Identify cause and try to reverse it. | Monitor creatinine level, blood pressure, and general health and well-being. Try to stop or slow the worsening kidney function. | Continue to try to stop or slow the worsening kidney function. Patient learns more about the disease and treatment options. | Plan and create access site for dialysis. Receive assessment for possible transplant. | Start renal replacement therapy: dialysis or transplantation. |

The dialysis access is a long-term method of accessing the patient's blood for treatment (Faratro et al., 2004). There are three types of access: Arteriovenous (AV) Fistula, Arteriovenous (AV) Graft, or a Permanent Catheter (Permcath). The AV fistula is considered to be the first choice, because they generally last longer and there are fewer complications with infection and blood clotting since no foreign materials are involved (National Kidney Foundation, 2006). The suitability of the access is dependent on each individual patient.

Haemodialysis (HD) is the most common treatment option for ESRD patients. This treatment involves blood being taken from the body and circulated through a machine with an artificial kidney called a dialyzer, which performs ultrafiltration through a semipermeable membrane (The Kidney Foundation of Canada, 2004). The blood flows on one side of the membrane and the dialysis fluid passes on the other side in a counter flow (The Kidney Foundation of Canada, 2004). The excess water and waste products pass from the blood into the dialysis fluid, which is then discarded, and the cleaned blood is returned to the body (The Kidney Foundation of Canada, 2004). The blood tubing that carries the blood from the patient to the dialyzer is called the "arterial" segment, and the tubing that carries the cleaned blood back is called the "venous" segment (Faratro et al., 2004).

Conventional HD involves patients coming to the hospital three times a week, for three to four hour sessions, where a nurse administers and monitors the patient's treatment (Lamsdale, 2007). After receiving treatment, many patients feel exhausted and not well due to the large fluctuations in blood volume and solute clearance, putting stress on the bodily functions (Lamsdale, 2007).

Nocturnal Haemodialysis (NHD) is a special type of haemodialysis. Nocturnal dialysis is dialysis performed at night with the main difference being that blood is filtered for eight hours instead of the standard three or four hours (The Kidney Foundation of Canada, 2004). The advantage of nocturnal dialysis is that if one adds the hours up, one gets more dialysis delivered.

Weekly, one would get between 10 and 12 hours on regular dialysis, but on nocturnal dialysis one would get about 24 hours. The blood is cleaner, and a lot of the restrictions placed on dialysis patients are lessened. They often use less

medicine and can have a more liberal diet (McFarlane, Bayoumi, Pierratos and Redelmeier, 2003). Lamsdale (2007) noted that patients treated on NHD felt better due to fewer fluctuations in blood volume and solute clearance thus alleviating some of the stress on the other bodily functions.

In the 1970s, haemodialysis treatment took 8 to 12 hours, three times per week. As technology advanced, dialyzers were able to handle more dialysate and higher blood flow rates hence treatment times were shortened to between three and five hours per treatment. One clinic in Tassin, France remained on the longer dialysis program and noticed advantages for patients who were on extended dialysis times (Laurent and Charra, 1998).

While dialysis is a lifesaving treatment for many people with kidney disease, it can be very inconvenient and the process just does not clean the blood as effectively as well-functioning kidneys do. But nocturnal dialysis, a newer option, is starting to change all that. Nocturnal haemodialysis was conceived by the late Robert Uldall (Uldall, Ouwendyk & Francoeur, 1996)

The big benefit to nocturnal dialysis is that the blood is filtered for about eight hours at a time. One of the major problems with dialysis done in the traditional sense is that it tries to provide a lot of therapy in a short period of time, and it is difficult to clear toxins and fluid in that time, Nocturnal dialysis provides a greater amount of toxin removal over a long period of time (McFarlane et al., 2003).

After studying dialysis treatment programs in different countries, it was discovered that the best outcomes were in France, where patients are haemodialyzed for eight hours, three days a week. This supported the idea that “more is better” (McFarlane et al., 2003).

Despite the growing interest in more frequent haemodialysis, to date, there have been no randomized prospective studies done in South Africa comparing outcomes in patients’ dialyzed using conventional thrice-weekly therapy with long slow nocturnal haemodialysis. The relevance of this study is to assess the impact of Nocturnal Haemodialysis versus Diurnal dialysis in the South African population as previous studies were performed in Europe and Asia.

The main aim of this study was to determine if nocturnal dialysis resulted in improved dialysis clearance, better overall patient health and a better quality of life.

The primary objective of this study was to compare the clearance of small molecules (for example, urea, phosphate, creatinine and potassium) and large retention products (for example Parathyroid Hormone (PTH) and β 2-Microglobulin) between the two haemodialysis procedures. The secondary objective was to compare the quality of life and survival of patients on both nocturnal and daytime dialysis.

CHAPTER TWO: BACKGROUND AND LITERATURE REVIEW

This chapter consists of the literature review which analyses the existing literature regarding the topic and explains the reason for this particular research to be done.

2.1 Background

Patients undergoing chronic haemodialysis have many problems, including salt and water retention, phosphate retention, secondary hyperparathyroidism, hypertension, chronic anaemia, hyperlipidaemia and heart disease. Almost half of the patients on dialysis have diabetes, which leads to additional complications. To address all these problems, patients may require fluid restrictions, phosphate binders, calcimimetic drugs, antihypertensive medication, hypoglycaemic agents, erythropoietin iron supplements, and a variety of other medications (Loghman-Adham, 2003; Saran et al., 2003).

Management of these health issues places multiple, complicated and unavoidable demands on a patient's lifestyle (Saran et al., 2003). Non-adherence is a rampant problem among patients undergoing dialysis (Cvengros, Christensen & Lawton, 2004) and can impact multiple aspects of patient care, including medications and treatment regimens as well as dietary and fluid restrictions. Overall it has been estimated that about 50% of patients on HD do not adhere to at least part of their dialysis regime (Kutner, 2001).

2.1.1 Functions of the Kidney

The kidneys are a pair of organs found along the posterior muscular wall of the abdominal cavity. The left kidney is more superior than the right kidney due to the larger size of the liver on the right side of the body. The kidneys are considered to be retroperitoneal organs because they lie behind the peritoneum lining the abdominal wall. A thin layer of fibrous connective tissue forms the renal capsule surrounding each kidney. The renal capsule provides a stiff outer shell to maintain the shape of the soft inner tissues (O'Sullivan, McCarthy, Kumar & Williams, 1998).

The kidneys excrete natural waste products, including urea and creatinine, as well as foreign substances like alcohol and drugs, from the body (Faratro et al., 2004). The kidneys also regulate the water and electrolyte (dissolved salts) balance and the acid-base balance (Faratro et al., 2004). The kidneys produce and secrete important hormones, including renin, erythropoietin (EPO), and vitamin D. Renin is involved in regulating blood pressure, EPO is used to stimulate the bone marrow to produce red blood cells, and vitamin D is needed to absorb the calcium from food in the intestine (Faratro et al., 2004).

The primary function of the kidneys is the excretion of waste products resulting from protein metabolism and muscle contraction. The liver produces a toxic waste product called ammonia, but is able to convert this into uric acid and urea which is less toxic to the body. The muscles in the body use creatine as an energy source and produce creatinine as a waste product. Ammonia, uric acid, urea and creatinine all accumulate in the body over time and need to be removed from circulation to maintain homeostasis. The kidneys filter out these four waste products from the bloodstream allowing the body to excrete them in the form of urine. Kidneys with ESRD perform sub-optimally in removing these products which leads to a build-up of these products making a person very ill (O'Sullivan et al., 1998).

Electrolytes are minerals and salts such as magnesium, sodium and potassium. These electrolytes are found in foods that are consumed and are essential to the body's good health. However, an abundance or lack thereof can lead to sickness. Kidneys affected with ESRD cannot regulate the levels of electrolytes and changes in body functions occur. Sodium can cause tissues to retain water. Excess potassium can cause abnormal heart rhythm, which may lead to cardiac arrest. Too little magnesium can affect the heartbeat and cause changes in mental state whereas too much can lead to weakness (Pierratos, Ouwendyk & Rassi, 1999)

Pierratos et al., (1999) also described that healthy kidneys make certain hormones. The Parathyroid Hormone (PTH) activates Vitamin D into a substance called Calcitrol, which helps the body to absorb calcium. Bones become fragile and may break if not enough calcium is absorbed by the body. Erythropoietin is another hormone synthesized by the kidneys. This hormone stimulates the body to produce red blood cells, which will in turn carry oxygen throughout the body. If the red blood

cell count is low, anaemia may develop, leaving behind feelings of fatigue and weakness.

Renin is an enzyme produced by the kidneys which helps to regulate sodium and potassium levels in the blood as well as regulate blood pressure. When blood pressure drops, renin is released and starts a chemical reaction in the body that produces a substance called Angiotensin. This substance causes the blood vessels to narrow raising blood pressure. Angiotensin also signals the adrenal glands (found on top of the kidney) to release a hormone called Aldosterone (Abboud and Henrich, 2010). Aldosterone tells the kidney to retain sodium and excrete potassium. By retaining sodium, the body keeps more water in the system which raises the blood volume and blood pressure. Kidneys in ESRD sometimes make too much renin which keeps blood pressure levels high, making this high blood pressure difficult to treat (Abboud and Henrich, 2010).

2.1.2 Symptoms of Kidney Failure

The waste products accumulate in kidney disease and lead to different symptoms. When kidneys become diseased or damaged, waste products and fluids build up in the body. Symptoms of nausea and loss of appetite, feeling weak and irritable may also arise. There is water retention in the limbs or generally throughout the body (oedema). The blood pressure can be raised (hypertension) and a decreased production of red blood cells can lead to the lowering of haemoglobin (anaemia) (Kooistra MP, 2003).

Plasma levels of substances such as urea and creatinine start to show measurable increases only after the glomerular filtration rate has decreased to 50% (Lindsay, Alhejaili & Nesrallah, 2003a). On testing blood and urine samples, the following changes may be seen in conjunction with increased levels of urea and creatinine:

Albuminuria or Proteinuria – Albumin, a vital protein component is lost in the urine.

- (i) **Hypoalbuminaemia** – Inadequate amount of protein in the blood
- (ii) **Hyperlipidaemia** – Excess amount of fats in the blood
- (iii) **Anaemia** – Decrease in the number of red blood cells
- (iv) **Hypocalcaemia** – Inadequate amount of calcium in the blood

(v) **Hyperkalaemia** – Increase in the level of potassium in the blood

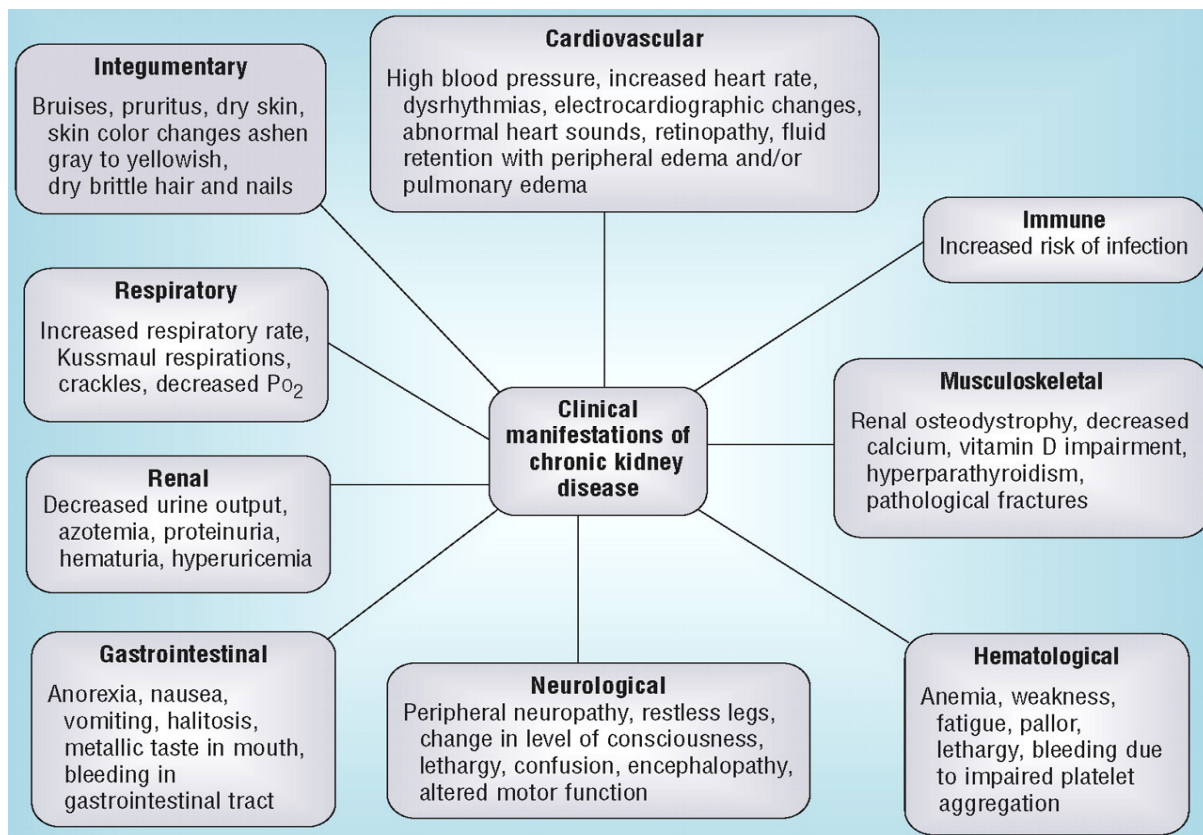


Figure 1: Clinical manifestations of Chronic Kidney Failure (*National Institute of Health, 2005*). Figure 1 illustrates the symptoms that occur in the different parts of the body in chronic kidney failure.

2.1.3 Etiology of Kidney Disease

The two main causes of kidney disease are Diabetes Mellitus (38%) and Hypertension (24%). Glomerulonephritis accounts for 15% of cases while Polycystic Kidney Disease accounts for 5%. All other causes account for 18% (Mitch, 2007). The main causes are discussed below.

2.1.3.1 Diabetes Mellitus

Diabetes can harm the kidneys by causing damage in three different ways; via the blood vessels in the kidney, nerves in the body or damage to the urinary tract. Over time, high sugar levels in the blood cause blood vessels in the kidney to narrow and become clogged. Without enough blood, the kidneys become damaged and albumin ends up in the urine (Figure 2) (Loghman-Adham, 2003).

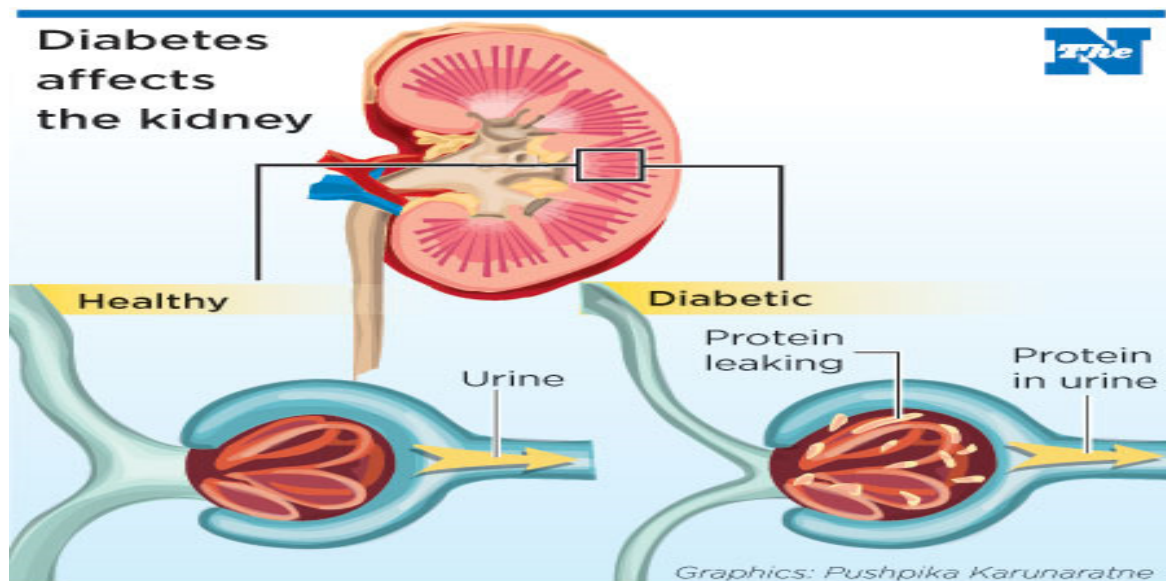


Figure 2. Diabetes and kidney failure as shown by protein leaking into the urine (Pushpika Karunaratne, 2003).

Diabetes causes nerve damage in all parts of the body including the bladder. This damages the ability of a full bladder to relay messages to the brain. The pressure from a full bladder can cause kidney damage. Bacteria may cause urinary tract infections from urine that stays in the bladder for prolonged periods of time. Bacteria grow rapidly in urine that has a high sugar level. Most of these infections affect the bladder but they can sometimes spread to the kidneys (Loghman-Adham, 2003).

2.1.3.2 Hypertension

Blood pressure is the force of blood against the walls of the blood vessels as the heart pumps blood throughout the body. If the pressure against the vessel walls is too high, it is said that an individual has Hypertension. Hypertension can either be a cause of kidney failure or a complication of it (Lacson and Lazarus, 2007)

Over time, hypertension damages blood vessels around the body. This reduces blood supply to important organs like the kidneys. Hypertension damages the filtering units of the kidney and as a result, the kidneys stop removing waste products and extra fluid. The extra fluid in the blood vessels may build up and raise blood pressure even more. The kidneys play a key role in keeping our blood pressure within a healthy range. Diseased kidneys are less able to help regulate blood pressure and as a result blood pressure increases (Lacson and Lazarus, 2007)

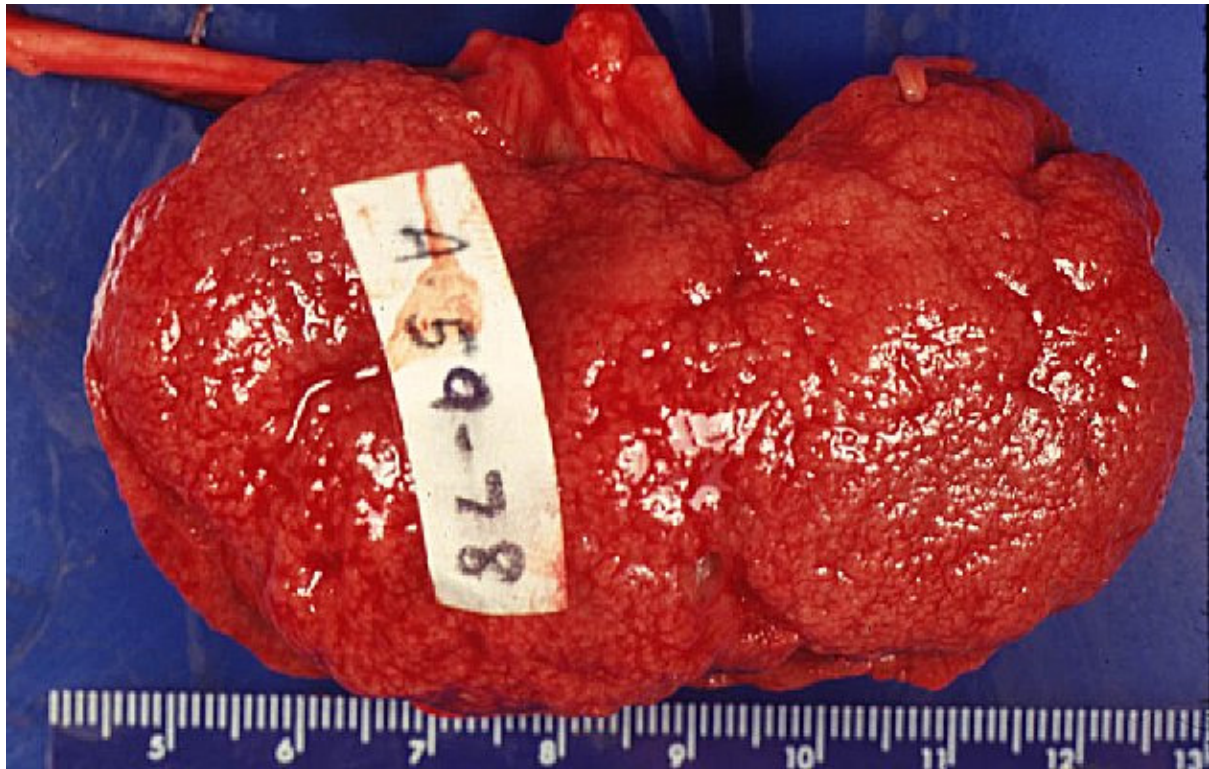


Figure 3. Hypertension and kidney disease (Lacson and Lazarus, 2007). *Figure 3 illustrates what happens to the kidney when a person has hypertension. The kidney bears the **finely granular surface** typical of people who have had high blood pressure for a long time. As individual nephrons are replaced by scar tissue, the contraction of the scar produces the "**sandpaper kidney**" effect.*

2.1.3.3 Nephrotic Syndrome

A syndrome is a combination of signs and symptoms characteristic of a specific condition. A large number of kidney disease patients develop this condition. In this condition, large amounts of protein are lost in the urine (Mitch, 2007).

Normally less than 200mg of protein is lost in the urine whereas in nephrotic syndrome as much as 30g of protein can be lost in the urine every day. As a result, the level of proteins in the blood falls and this produces swelling of the face and body (called oedema) due to retention of water or fluid. Nephrotic syndrome can happen if there is associated inflammation of kidney (Glomerulonephritis). The glomerulus normally has a 'sieve' like structure and when blood passes through the glomerulus the water and minerals escape through this sieve. The sizes of holes in the sieve are very small and through this the larger protein molecules do not escape. In some

types of glomerulonephritis the size of these holes increase leading to loss of protein or albumin in the urine (Kooistra, 2003). Figure 4 compares a healthy kidney with a diseased kidney.

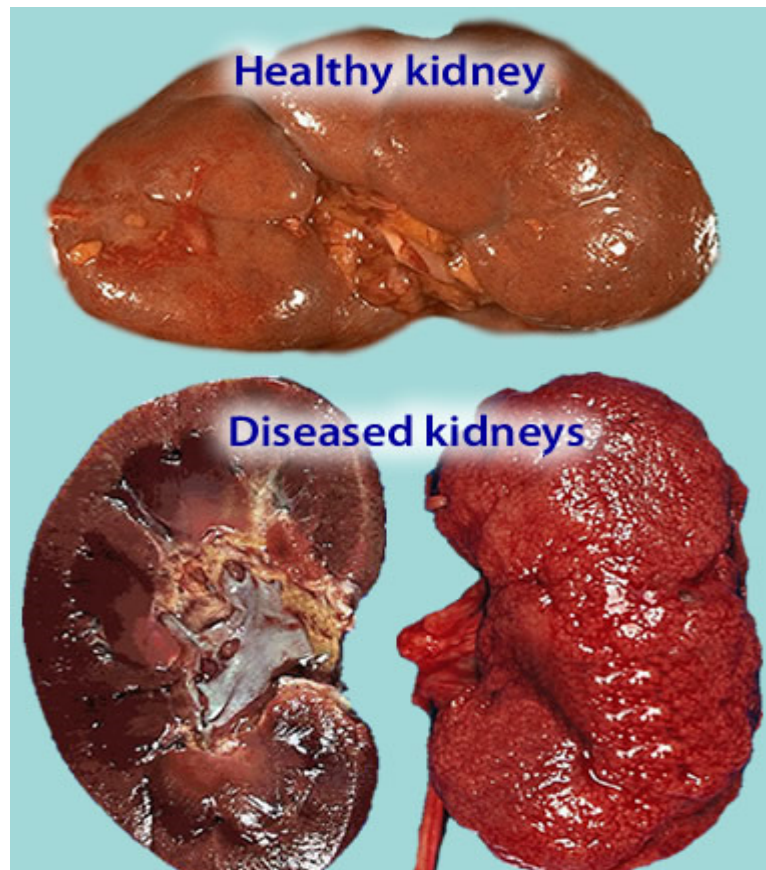


Figure 4. A healthy kidney compared to a diseased kidney (*National Institute of Health, 2005*). The **bumpy surface** of the diseased kidney can be noted along with the **fibrous thickening** at the entrance of the kidney.

2.1.3.4 Polycystic Kidneys

This is an inherited condition. In this condition, many cysts (small bags filled with a watery substance) replace the normal kidney surface (Figure 5). It affects both the kidneys and causes them to increase to twice or thrice its normal size (Figure 6 and Figure 7). Polycystic kidney disease can present in children or in adults. This disease can be silent for many years and can first present after the age of forty years and in the presence of anaemia (Mitch, 2007).

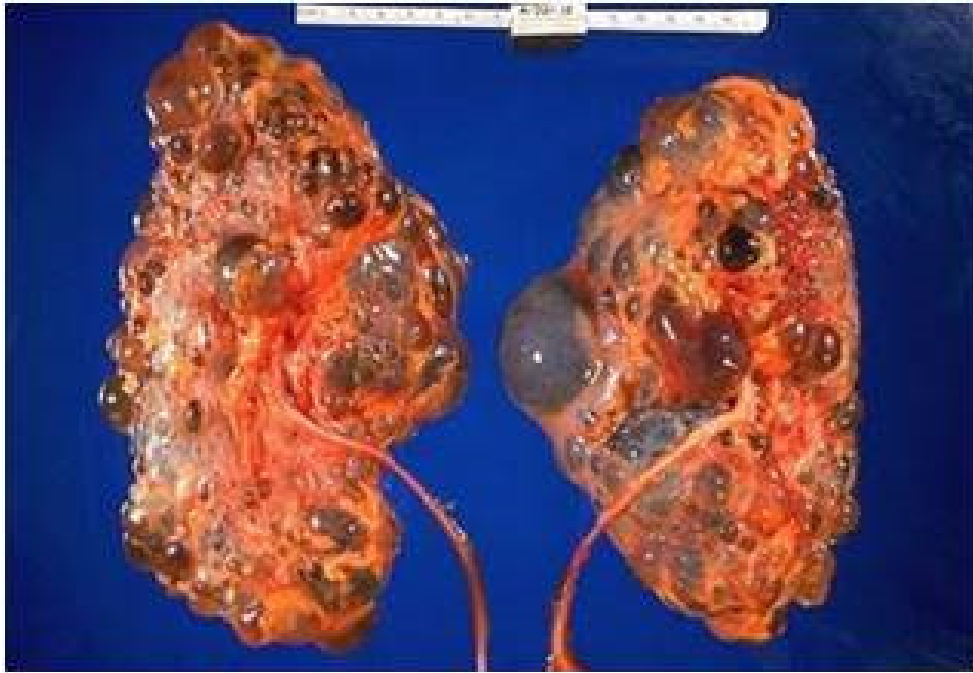


Figure 5: Polycystic Kidney Disease. *The image shows the abundance of cysts, filled with a watery substance, that cover the surface of the kidney (CDC/Dr. Edwin P Ewing Jr, 1972)*

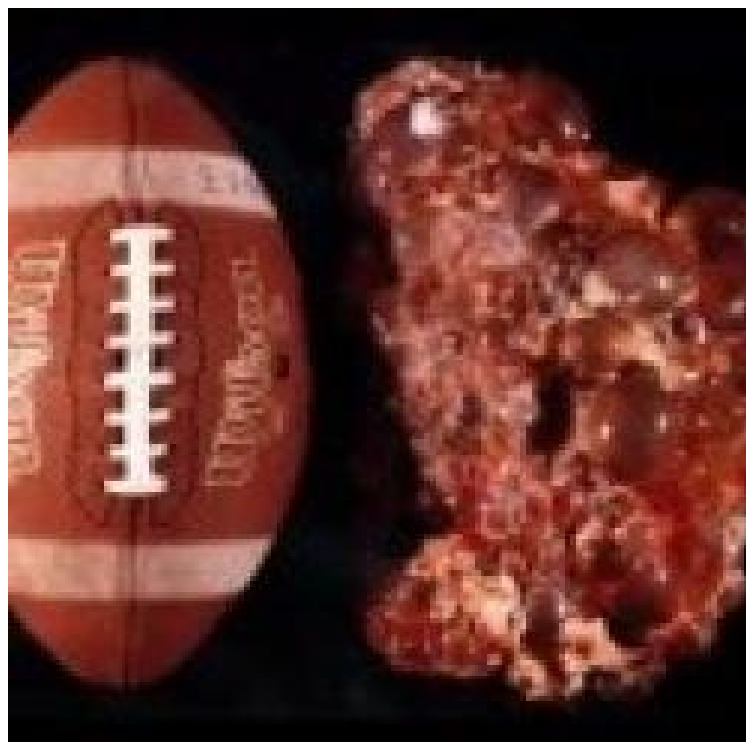


Figure 6. The abnormal growth of polycystic kidneys. *This image shows that polycystic kidneys grow as large as a rugby ball and in some cases, even bigger (National Institute of Health, 2003).*

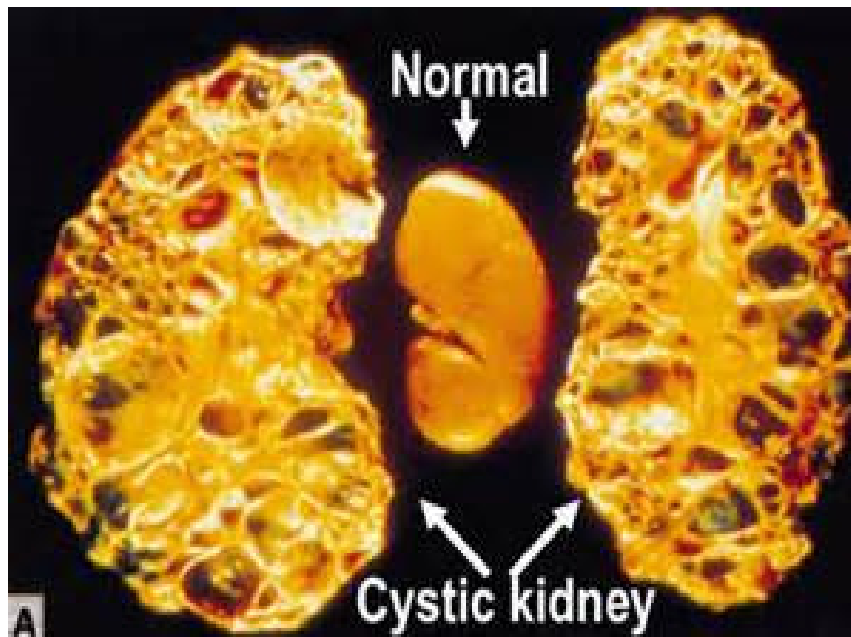


Figure 7. A normal kidney compared to a cystic kidney. *The size of a normal kidney is 12cm in length, 6cm in breadth and a width of 3cm (Mitch, 2007).*

2.1.4 Access for Haemodialysis

Haemodialysis requires access to the patient's bloodstream, a mechanism for the transport of the blood to and from the dialyzer. Access is achieved by dialysis catheters, arteriovenous fistulas or arteriovenous grafts (Figure 8).

a) Arteriovenous Fistulas (AVF)

The AV fistula is a surgical connection between an artery and a vein usually in the arm (Faratro et al., 2004). This means patients who have weak blood vessels would not be good candidates for this type of access. The AV fistula should not be used for at least two months after the surgery in order to allow the venous walls to mature and strengthen (Faratro et al., 2004). For treatment, the AV Fistula involves connecting two needles into the access site, which are connected to the dialysis tubes of the machine.

b) Arteriovenous Grafts (AVG)

The AV graft is similar to the AV fistula, but the artery and vein are indirectly connected with a soft synthetic tube, either straight or looped, and grafted under the skin (Faratro et al., 2004). For treatment, the AV Graft also involves connecting two

needles into the access site, which are connected to the dialysis tubes of the machine.

c) Percutaneous Catheter (PermCath)

The PermCath is implanted surgically into the right or left atrium of the heart through the internal jugular vein or subclavian vein (Faratro et al., 2004). For treatment, the PermCath is connected directly to the dialysis tubes without cannulation.

Problems with these accesses commonly include clotting (due to decreased blood flow) and infection (mainly in catheters but can also occur in arteriovenous grafts).

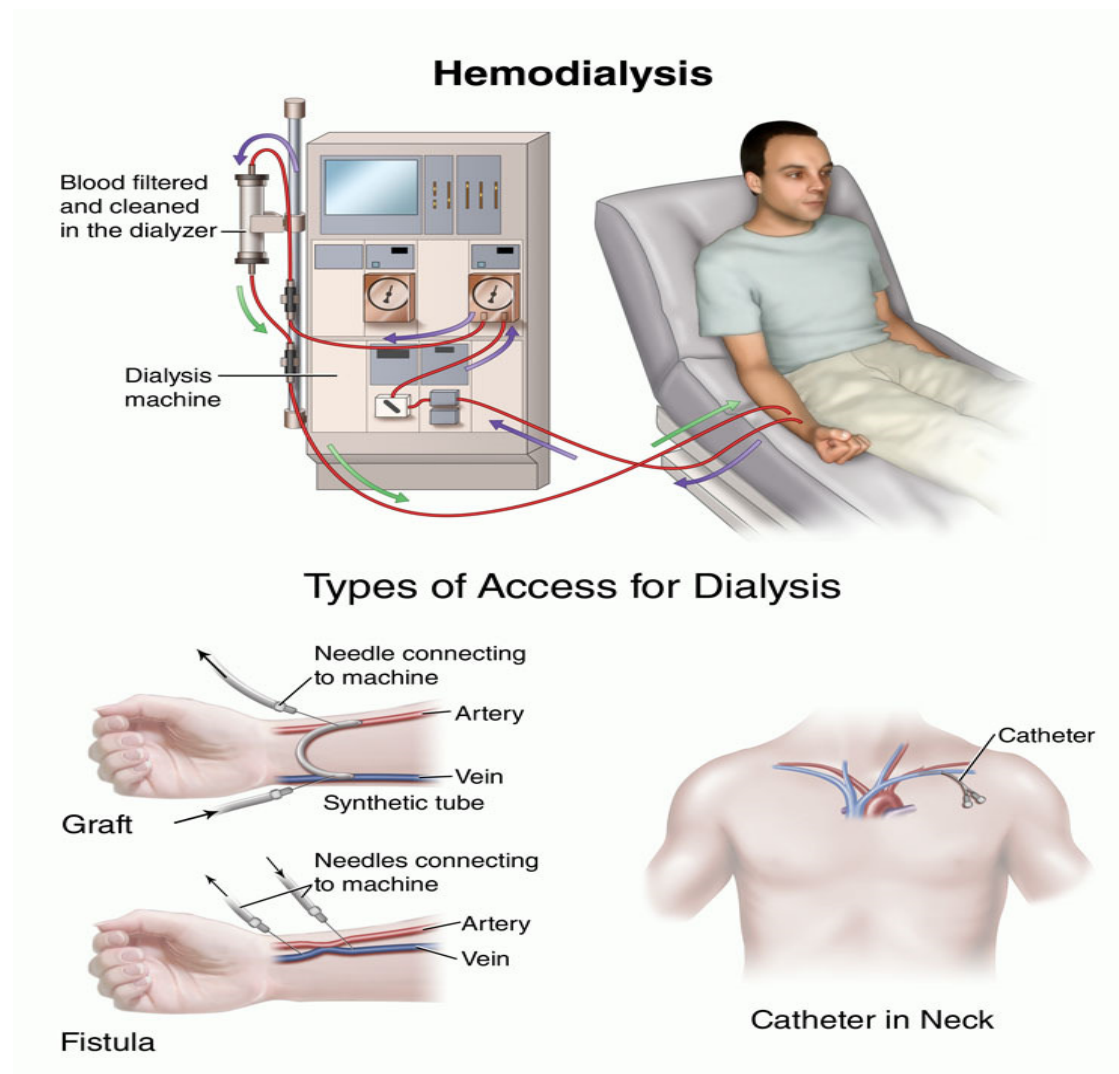


Figure 8. An illustration of haemodialysis and the 3 types of accesses (RelayHealth and/or affiliates, 2007).

2.2 Literature Review

In the early 1960's haemodialysis was a procedure that would last 8 to 10 hours, every alternate day. Treatment was confined to patients who had acute kidney disease (reversible kidney failure) because a patient's veins could only be used for 7-10 treatments. This resulted in dialysis only being available to a limited number of people (Blagg, 2007)

Through the 1970's and 1980's dialysis technology continued to improve rapidly. Dialysis machines were developed with more reliable ultrafiltration control (fluid removal) and more efficient dialyzers were produced (Blagg, 2007).

In 1993, Dr. Robert Uldall and Dr. Andreas Pierratos began nocturnal haemodialysis for patients in Toronto, Canada. The success of these treatments demonstrated that by increasing the time spent on dialysis, negative outcomes from dialysis were reduced and lifestyle outcomes improved (Uldall et al., 1996)

2.2.1 Clinical benefits of Nocturnal Dialysis

By almost every measure, the longer sessions, even with the slower pump speeds, resulted in improved dialysis clearance, better overall patient health and quality of life after Nocturnal Haemodialysis. Because the overnight sessions are longer, there is more time to clear as much waste as possible from the blood. Some benefits included improved dialysis results, alleviation of sleep apnea, improvement in sexual performance, lowering of blood pressure, reduction in the amount of medications and improving cardiac function (Hanly and Pierratos, 2001).

One of the biggest benefits of nocturnal dialysis is that it has been found to decrease the medications that the patients need to take (McGregor, Buttimore & Lynn, 2001). For example, the longer sessions remove more phosphorus than conventional dialysis (O'Sullivan et al., 1998). Consequently, many patients can lower the number of phosphate binders they have to take, and some are able to completely discontinue the medications. Lower phosphorus levels contribute to better long-term bone health (McGregor et al., 2001).

Nocturnal Dialysis improves appetite, eliminates the need of dietary restrictions and increases intake of protein, as measured by normalized protein catabolic rate and dietary intake (Ipema et al., 2012). Total body nitrogen improves in NHD patients even though there is loss of amino acids into the dialysate (Pierratos et al., 1999). It also improves intake of other nutrients such as lipids, phosphorous with preservation of calcium, phosphorous and potassium levels in blood (Shorr, Manns & Culleton, 2011).

Since nocturnal dialysis results in improved dialysis clearance, better overall patient health and a better quality of life, it is expected that nocturnal haemodialysis will take its place among the treatment modalities offered to patients. It has all of the elements necessary - improved outcome, patient and provider satisfaction and lower cost - to have a major impact on the delivery of dialysis (Pierratos, Ouwendyk & Francoeur, 1998b).

2.2.2 Clearance of small and middle molecules

Solutes are classified by their molecular weight. Small solutes have a molecular weight of <500 Daltons, middle molecules range between 500 and 12000 Daltons and larger molecules weigh in excess of 12000 Daltons (Hanly, Chan & Pierratos, 2003). Nocturnal dialysis provides a higher quantity of solute removal and a more physiological modality of solute removal than conventional thrice weekly haemodialysis (Rocco, 2009).

The typical dialysis patient faces both a poor quality of life and a significantly shortened survival, which is often blamed on Uraemia (Lindsay et al., 2003b). Uraemia is a clinical syndrome associated with the effects of fluid retention, the effects of renal disease and related comorbid diseases (Mucsi et al., 1998). Larger molecular weight substances are the most likely contributors to uremia (Table 2) (Lindsay et al., 2003b). Regardless of the causes, this uremic state persists in many of the patients who have reached their dialysis adequacy targets, which raises the possibility that more intensive haemodialysis could improve patient outcomes (Mucsi et al., 1998; Lindsay et al., 2003b)

Table 2. Most currently known uremic solutes and their molecular weights
(*Primer on Kidney Disease, 1998*).

| Compound | MW | Compound | MW |
|--------------------|-----------|--------------------------|-----------|
| Nitric oxide | 30 | Guanidinoacetate | 177 |
| Urea | 60 | Hippurate | 179 |
| Methylguanidine | 73 | <i>myo</i> -Inositol | 180 |
| Phenol | 94 | ADMA/SDMA | 202 |
| Phosphate | 96 | Dimethylarginine | 202 |
| <i>p</i> -Cresol | 108 | Spermine | 202 |
| Creatinine | 113 | CMPF | 240 |
| Hypoxanthine | 136 | Pseudouridine | 244 |
| Spermidine | 145 | Indoxyl sulfate | 251 |
| Xanthine | 152 | Phenylacetylglutamine | 264 |
| Urate | 168 | β -Endorphin | 2465 |
| Guanidinosuccinate | 175 | Parathormone | 9425 |
| Indole-acetate | 175 | β_2 -Microglobulin | 11818 |

CMPF, carboxymethylpropylfuranpropionic acid; ADMA, asymmetric dimethylarginine; SDMA, symmetric dimethylarginine.

2.2.2.1 Urea

Urea is an organic chemical compound and is essentially the waste produced by the body after metabolizing protein. It is produced when the liver breaks down protein or amino acids, and ammonia. The kidneys then transfer the urea from the blood to the urine. The average person excretes about 30g of urea a day but a small amount is also secreted in perspiration (Mosby's Medical Dictionary, 8th edition, 2009).

Most patients are familiar with the blood urea nitrogen (BUN) value, which measures the amount of urea nitrogen in the blood (Pierratos et al., 1999). Ideally, patients and their families are given education about hemodialysis well in advance of them needing it, this includes information regarding a renal diet, discussion and explanation of blood results and information surrounding the different types of treatment modalities (Klang et al., 1998). It is suggested that patient education should be ongoing for patients with end-stage renal failure initiated during the predialysis stage and continued after maintenance dialysis has been established (Klang et al., 1998).

The lower the BUN level, the better. Levels are lowest for approximately half an hour after dialysis, at which point the score increases, a phenomenon called urea rebound (Pierratos et al., 1999).

Studies by Pierratos (1999) show that three times per week nocturnal dialysis patients have much lower urea rebound than patients receiving conventional dialysis. This may be one of the reasons patients feel better after nocturnal haemodialysis. Because the overnight sessions are longer, there is more time to clear as much waste as possible from the blood. The standard measure for dialysis effectiveness is Kt/V (K – dialyzer clearance; T – dialysis time; V – volume) and the benchmark range is 1.2 to 1.4. Before nocturnal dialysis, many patients had Kt/V ratings of less than 1. Now, after switching to nocturnal haemodialysis, most have ratings of 1.2 or 1.4 – and many are even 1.8 or 2.0. Patients on nocturnal haemodialysis have a higher Kt/V (adequacy of dialysis) indicating their blood is cleaner (Brissenden et al., 1998).

Urea was chosen by the National Cooperative Dialysis Study (NCDS) as the clearance marker for the Kt/V since it is a reflection both of dietary protein intake and of the efficiency of removal of small uremic toxins (Lowrie et al., 1981). Measuring the clearance of solutes that accumulate in patients with uraemia has become the mainstay for calculating the dose of dialysis and determining its adequacy as delivered (McFarlane, 2009).

Studies have shown that NHD significantly improves small solute clearance (measured as percentage reduction in urea (PRU) or equilibrated Kt/V (e Kt/V)). A single centre study from Toronto has shown that PRU increased from 74% to 89% when they converted 39 patients from conventional HD to NHD (Bugeja et al., 2009). A multicentre study has compared single session e Kt/V of 655 NHD patients to matched 15,334 conventional HD patients. The single session e Kt/V of conventional HD patients was 1.46 ± 0.32 whereas that of nocturnal HD group was 2.21 ± 0.56 (Lacson and Diaz-buxo, 2001). These studies highlight that nocturnal haemodialysis improves small solute clearance (Daugirdas et al., 2010).

2.2.2.2 Calcium, Phosphates and the Parathyroid Hormone (PTH)

Calcium is a major mineral and is the most abundant mineral in the human body. Most of it is stored in the bones and teeth (about 99%), and the rest is in the blood, muscles and extracellular fluid. Calcium is necessary for strong bones and teeth,

plus it plays an important role in blood clotting, muscle contraction, hormonal secretion and normal nervous function (Heidenheim et al., 2003).

Phosphates are an organic compound necessary for mineralization of bone and other key cellular processes. Phosphates are extremely important in living cells, particularly in the storage and the use of energy and the transmission of genetic information within a cell and from one cell to another (Plante, 2006). Phosphates are widely distributed in the body, the largest amounts being in the bones and teeth. They are continually excreted in the urine and faeces and must be replaced in the diet. Inorganic phosphates function as buffer salts to maintain the acid base balance in the blood, saliva, urine and other bodily fluids (Blacher et al., 2001; Young et al., 2005).

The Parathyroid Hormone (PTH) is produced by the parathyroid glands that regulate the amount of calcium and phosphorus in the body. These are small glands located behind the thyroid gland in the neck. If the blood calcium becomes low, the parathyroid gland will respond by producing more PTH. PTH will absorb calcium from the bones to correct the low blood calcium level (Mosby's Medical Dictionary, 8th edition, 2009). If patients fail to maintain PTH levels in the safe range, they risk the following:

- Bone Disease- bone and joint pain, weak and brittle bones or broken bones
- Loss of independence
- Increased risk of death

Hyperparathyroidism is the most common cause of renal bone disease. Hypocalcaemia is the most powerful stimulus of PTH secretion as it may result in an increase more than twice that induced by hyperphosphataemia (Heidenheim et al., 2003). Therefore, calcium balance and regulation are very important when treating hyperparathyroidism (Kutner N, Brogan & Kutner MH, 1986).

More frequent haemodialysis sessions and longer session lengths may offer improved phosphorus control. Hyperphosphataemia is common in advanced CKD and ESRD and has been associated with bone disease and increased

cardiovascular morbidity and mortality (Pierratos, 2004; McFarlane, 2011). Phosphorus removal by conventional thrice-weekly haemodialysis and peritoneal dialysis is generally inadequate (Heidenham et al., 2003).

Studies have consistently shown improved phosphate control in patients on nocturnal dialysis. A randomized controlled trial has shown the NHD group had a significantly more decreased level of phosphate compared to CHD patients, despite the marked reduction in the use of phosphate binders in NHD group (Walsh et al., 2010).

Coronary calcification is a significant risk factor for Cardiovascular (CV) disease in patients with ESRD. Chan and colleagues (2002a) noted that these patients have about 10 times the burden of coronary calcification and show progression of calcification over as short a period as a year. Preliminary studies done by Chan et al., (2002a) have suggested an association between this accelerated vascular calcification and high phosphate levels. Phosphate usually comes from food and normally is not sufficiently cleared by intermittent haemodialysis. The increased hours spent on nocturnal haemodialysis results in superior calcium-phosphate balance and speculation was made that this balance could possibly prevent the progression of coronary calcification (Chan et al., 2002b).

2.2.2.3 Beta-2-Microglobulin (β 2M)

Middle molecules, consisting mostly of peptides and small proteins with molecular weight the range of 500-60,000 Daltons, accumulate in renal failure and contribute to the uremic toxic state. Beta-2-microglobulin with a molecular weight of 11,000 Daltons is considered representative of these middle molecules (Raj et al., 2000). In patients on long-term dialysis, beta-2-microglobulin accumulation manifests with cysts at the ends of long bones, a disease that is known as Dialysis Related Amyloidosis or β 2-Amyloidosis (Drueke, 2000).

Studies have suggested that the longer duration of NHD results in a greater clearance of β 2M and smaller molecules (Tentori, 2010). In a study comparing conventional three times a week dialysis with NHD, beta-2-microglobulin pre-dialysis levels progressively declined from 27.2 ± 11.7 mg/dL at initiation of nocturnal

haemodialysis to 13.7 ± 4.4 mg/dL by 9 months, and then remained stable thereafter on nocturnal haemodialysis (Pierratos et al., 1999; Nesrallah, 2005).

2.2.3 Quality of Life

Beyond improved dialysis outcomes, nocturnal dialysis has many benefits to patients' overall health and well-being. Sleep apnoea affects almost 50 percent of conventional dialysis patients (Hanley et al., 2001). It causes people to stop breathing for periods of ten seconds or more during the night, disrupting sleep and leaving them feeling fatigued during the day. Nocturnal haemodialysis actually helps correct sleep apnoea and increase restorative sleep in many patients. These benefits can continue even on the dialysis off-nights (Hanly and Pierratos, 2001).

Studies show that nocturnal dialysis patients, on the whole, are healthier and more alert. In addition to the alleviation of sleep apnoea, they report increased energy and stamina, even improvement in their sex lives. Overall, patients in nocturnal units feel more "in control of their lives." Their eating patterns improve, they experience less depression and are better able to function socially (McPhatter et al., 1999).

Sleep apnoea, when untreated, leads to the inability to think and reason clearly, and causes weight gain, hypertension and cardiovascular disease. It is common knowledge that sleep is related to uremic symptoms, patients who are under-dialyzed often complain about insomnia. Poor quality of sleep is highly associated with conventional haemodialysis (CHD). It is an independent risk factor that can be effectively corrected with nocturnal haemodialysis (Argekar et al., 2007). In a study of 14 patients who were converted from 4 hour CHD to 8 hour NHD, it was shown that the frequency of sleep related events decreased. This confirmed its value as a treatment option for dialysis patients with sleep apnoea (Chen et al., 2006).

Many people who choose nocturnal dialysis report having a better quality of life. Psychologically, nocturnal dialysis patients state that they have more control over their life (Hanley and Pierratos, 2001). There is more time to work, attend school, take care of children and enjoy social events during the day because the daytime hours are not spent on dialysis. The nighttime dialysis schedule makes the patient feel "more normal" because nonproductive time, where the patient would be

“sleeping anyway,” is now used for treatment (Hanley and Pierratos, 2001). Some feel that they no longer need to tell people about their treatment, because the nocturnal dialysis schedule does not interfere with one’s working or social life. Staff members who work the nocturnal dialysis shift, comment on how nocturnal patients feel a new zest for life. Patients also have a higher Kt/V (adequacy of dialysis) indicating that the blood is cleaner (Brissenden et al., 1998).

Equally important, the increased feeling of well-being means that more patients can pursue employment. In one group of 19 patients in the nocturnal haemodialysis study, full-time employment increased by 12 percent among those who wanted to work, and two patients who had retired decided to return to work. In another sample, 50 percent of unemployed patients went back to work during their first year of nocturnal dialysis (McPhatter et al., 1999).

When 23 daily nocturnal dialysis patients were compared with 22 conventional (thrice weekly) patients using standard quality assessment tools, those patients on nocturnal dialysis therapy had fewer symptoms such as dizziness and cramps. Fluid and blood pressure were controlled, and fewer headaches were experienced. Patients were able to increase their fluid intake and when given the choice to return to less conventional therapy, all elected to remain on the nocturnal program (Heidenham et al., 2003).

Brissenden et al., (1998) examined the effect of NHD on Sickness Impact Profile (SIP; composed of 12 subscales with lower scores indicating improvement). Only subscale scores for which a statistically significant improvement or trend toward improvement were reported. The SIP showed an improvement in the total score (14 to 9.5; $p = 0.03$), eating (14.2 to 3.7; $p = 0.003$), and household management (25.6 to 15; $p = 0.01$). Trend to improvement was seen in ambulation (17.2 to 11.1; $p = 0.07$), mobility (3.9 to 2.9; $p = 0.08$), and social interaction (16.4 to 11.4; $p = 0.07$).

Heidenheim et al., (2003) published the results of the London group, which used the Renal Disease Specific Quality of Life indicators, also known as the SF-36 (composed of 8 subscales from 0 to 100 with higher scores indicating improvement). The SF-36 showed improvements in social functioning (54.2 to 79.2; $p = 0.006$),

physical functioning (60.6 to 69; $p = 0.008$), and role-physical (39.2 to 36.1; $p = 0.05$).

2.2.4 Survival

Survival on nocturnal haemodialysis is higher than expected, and studies suggest that patients receiving nocturnal haemodialysis have a mortality rate that is about one third of what is seen in similar patients receiving conventional haemodialysis (Myers et al., 2010).

Survival benefit is considered as the most important outcome of dialysis therapy. A number of reports on nocturnal dialysis have addressed this issue. A group from USA analyzed the data from United States Renal Data System (USRDS) in both NHD and CHD patients. Despite, the differential effect in the sample sizes, they found the mortality rate in 94 NHD patients was a third of that in 940 CHD patients (McPhatter et al., 1999).

Dialysis for eight hours overnight, three times weekly reduces the risk of death by nearly 80 percent compared to conventional four hour dialysis (Morris et al., 1989). In a study done in Turkey, 224 CHD patients were switched to nocturnal dialysis. According to the researchers, after an adaptation period of about a month, patients slept well without any complaints. The patients remained on nocturnal dialysis for about one year. Their outcomes were compared with a similar group who continued on CHD three times weekly, the nocturnal hemodialysis group showed an 80% reduction in overall death rates (Chertow et al., 2010).

Nocturnal haemodialysis led to improvements in a wide range of outcomes (Rocco, Eckardt and Berns., 2011). The hospitalization rate during follow up was one-fourth of that observed in the CHD group. Most importantly, the results confirmed that longer dialysis produces significantly better patient outcomes with a 78 percent reduction in mortality rate (Ranganathan and John, 2012).

Patients receiving NHD had better blood pressure control, leading to a two-thirds reduction in blood pressure medication (Laurent and Charra, 1998). They were also at a lower risk for a drop in blood pressure that normally occurs with CHD. Levels of

mineral phosphate decreased towards normal despite a 72 percent reduction in patients taking phosphate binders. All these outcomes either did not change or deteriorated in patients on CHD (Lindsay et al., 2003b).

This chapter focused mainly on the benefits of nocturnal dialysis as a treatment option as shown by the literature review

CHAPTER THREE: MATERIALS AND METHODS

This chapter showcases the materials and methodology used to achieve the aim of the study. The main aim of this study was to determine whether nocturnal dialysis resulted in improved dialysis clearance, better overall patient health and a better quality of life.

3.1 Study Design and Population

This was both a retrospective and prospective, comparative, quantitative study that was conducted at the Sunninghill Dialysis Unit in Gauteng on patients undergoing haemodialysis. Data was collected as far back as 3 months to ensure data collection was completed during the timeframe of the study. Blood samples for data collection were drawn at three time intervals for this study. The biochemical values which were being compared for each group included Urea (pre and post dialysis), Creatinine, Calcium, Phosphate and Potassium. Haematological values included Haemoglobin, PTH and β 2-Microglobulin.

The sampling method that was used was stratified sampling as the population (in this case, patients undergoing dialysis) was divided into sub-populations (nocturnal dialysis and daytime dialysis). A sample size of 30 outpatients only, receiving dialysis at Sunninghill Hospital, was used in this study, 15 patients on nocturnal dialysis and 15 patients on daytime dialysis.

The sample size was determined by taking into consideration that Sunninghill Hospital was hosting the pilot project for the new treatment option; Nocturnal Dialysis. More dialysis centres in different provinces were opened but did not fall within the timeframe of this study. Therefore a sample size of $n > 25$ was considered statistically significant for this study. Further stratification of the study groups into male versus female was not required.

Ethical approval was obtained from the Durban University of Technology Ethics Committee and permission was also obtained from the hospital.

Thirty patients with End Stage Renal Disease (ESRD) presenting to the Sunninghill Hospital Dialysis Unit for treatment, who met the inclusion criteria, were recruited to participate in this study. Information about the study and consent forms was provided in the patient's language of preference. Patients were informed about the purpose and requirements of the study. Patients were informed that participation in the study was entirely voluntary and that they were entitled to withdraw at any point without affecting the medical treatment rendered to them. They were also informed that all information used in the study was confidential and that any data reported in scientific journals or published would not include information identifying them as a patient in the study.

All patients recruited into the study were under the care of a consultant nephrologist, who had diagnosed them with ESRD. As this was a pilot project for nocturnal dialysis as a new treatment option, patients were given the choice as to remain on CHD or switch over to NHD.

3.2 Selection Criteria

In this study, only compliance regarding dietary and fluid intake were considered as factors.

Compliance is defined as the fulfilment by a patient of a caregivers prescribed course of treatment (Mosby's Medical Dictionary, 8th edition, 2009).

Patients on dialysis follow low sodium, low protein diet. Fluid intake per day is calculated using the following formula:

Amount of urine passed in 24hours (if any) + 500mls = Fluid intake per day

3.2.1 Inclusion Criteria

1. Patients on dialysis > 3 months
2. Patients between the ages of 18 and 70 years
3. Patients who are compliant with dialysis fluid and diet restrictions.
4. Patients who don't have constant access problems

3.2.2 Exclusion Criteria

1. Patients on acute dialysis
2. Patients with severe cardiac problems
3. Patients who are non-compliant
4. Patients who have constant access problems.

3.3 Data Collection Plan

There were 2 main objectives in this study:

- 1) To compare the clearance of small molecules (for example, urea, phosphate, creatinine and potassium) and large retention products (for example Parathyroid Hormone (PTH) and β 2-Microglobulin) between the two haemodialysis procedures.
 - 2) To compare the quality of life and survival of patients on nocturnal and daytime haemodialysis (This is both a retrospective and prospective, comparative, quantitative study that will involve performing follow ups every 3 months for a duration of 6 months).
- Data collection occurred after ethical clearance was obtained from DUT-IREC
 - Blood samples, which are routinely done every 3 months in the dialysis unit, were taken and sent to the pathology lab for testing.
 - The biochemical values which were being compared for each group included Urea (pre and post dialysis), Creatinine, Calcium, Phosphate and Potassium.
 - Haematological values included Haemoglobin, PTH and β 2-Microglobulin.
 - An overall dialysis adequacy (Kt/V) was calculated using these values and compared for the two groups (Nocturnal and Daytime) as well.
 - Each patient was given The Quality of Life Survey Questionnaire (KDQOL: SF-36TM) to complete during the third month of the research.
 - All data (Questionnaire and blood results) was sorted and coded by the researcher and analyzed by a biostatistician.

3.4 Initiation and Disconnection of Dialysis

Each patient was required to have an individualized dialysis prescription that needed to be prescribed by a physician or nephrologist. The prescription included the following:

- Session length
- Blood flow rate (300mls/min or higher). This is dependent on cardiac function, co-morbidity or prevention of dialysis disequilibrium.
- Size of the dialyzer
- Dialysis solution and flow rate
- Fluid Removal: Use of a control device according to cardiovascular stability. Never remove more than 4L of fluid without a doctor's prescription.
- Anticoagulation according to clotting times

3.4.1 Rinsing and priming the dialyzer

The rinsing of the dialyzer was important, because it may reduce the incidence or severity of anaphylactic dialyzer reactions by virtue of removal of allergens (eg. ethylene oxide in dialyzers) and the removal of air. The blood compartment of the dialyzer was rinsed with saline. After the dialyzer had been rinsed, it was used within 10 minutes.

The blood lines and the dialyzer was primed with no less than 500mls of 0.9% saline, ensuring that the lines are fully primed and that there was no air in the blood circuit. The machine had to complete all built in function checks before dialysis could commence.

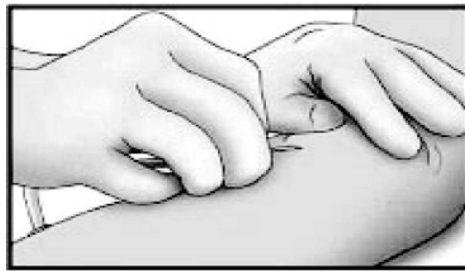
3.4.2 Initiation of dialysis

All patients, when they entered the unit, were required to weigh on the scale provided to determine the pre-dialysis weight and thus determine how much fluid could be removed. When they were made comfortable in their dialysis chairs, a pre blood pressure and temperature was recorded and a blood glucose level for diabetic patients was taken. For AVF/AVG patients, a pillow was placed under the arm that was to be cannulated, for added comfort.

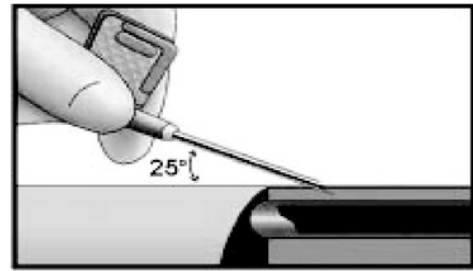
A clean technique was used for all cannulation techniques. Two needles were inserted for each treatment. The access site for fistulas and/or grafts was cleansed using povidine-iodine or hibitane alcohol. A tourniquet was used before the vessel was palpated. To allow easier needle insertion, the skin was pulled taut (this compresses the nerve endings, blocking pain sensation to the brain for \pm 20 seconds). An approximately 25° - 35° angle of insertion was used for fistulas and a 45° angle was used for grafts. Once the AVF vessel or AVG is entered, the blood flashback was visible in the needle tubing. The needle was taped down securely and checked for a good flow (Figure 9). When both needles were in, the patient was ready to be connected to the machine.

Aneurysms occur when the needles are repeatedly placed in the same spots on the access making the tissue underneath soft which leads to an increased bleeding time when the needles are removed (Figure 10).

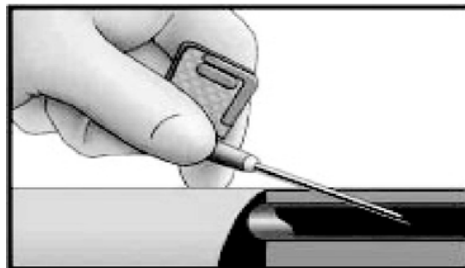
A sterile technique was used for all catheters due to the higher risk of infection. The exit site was examined at each treatment for signs of infection, cleaned with povidine-iodine and dressed. The hub caps of the catheter were removed and soaked in povidine-iodine for use at the end of treatment. 2.5mls of blood was aspirated from each lumen and thrown away; this blood contains the heparin lock used in the previous treatment. The patency of each lumen was tested with a 20ml syringe. Lumens were covered with gauze soaked in alcohol and are now ready for connection to the machine.



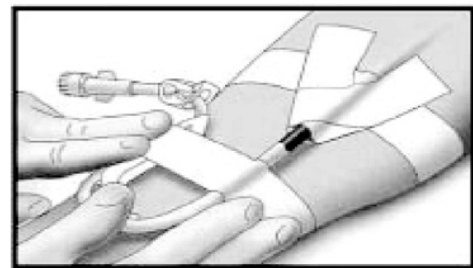
A



B



C



D

Figure 9. Cannulation of AVF and AVG. *This image portrays the steps taken when cannulating an AVF and an AVG. (Medsystems HemoDYNAMIC Devices, 2005).*



Figure 10. Aneurysms from cannulation. *This image shows white scar tissue formation from repeatedly cannulating the same spot on an arteriovenous fistula. (D. Brouwer, 2006).*

3.4.3 Connection to dialysis machine

The arterial line was connected to the arterial needle/lumen of catheter. The saline line was clamped and the blood pump was started, running at a speed of 150mls/min and not more. As the blood reached the dialyzer, it was tapped gently to expel residual air. When the blood reached the end of the venous line, the pump was stopped; the venous line was clamped and attached to the venous needle or lumen.

The venous line was then unclamped, blood pump started again and the dialyzer was turned arterial side up. A heparin loading dose was given once the blood reached the dialyzer and the heparin was connected. The desired amount of fluid to be removed is set on the machine as well as the blood pump speed and arming of the air detector as air emboli can be fatal.

3.4.4 Intra dialysis monitoring

- Hourly blood pressure readings together with machine observations
- Blood transfusions: Blood Pressure was measured at the commencement of each unit, every fifteen minutes for the first hour and every half an hour thereafter for the duration of the transfusion
- Hypotensive/Hypertensive episodes: Blood Pressure was monitored every 15-30 minutes
- Record was made of any unusual events e.g. nausea and vomiting, hot flushes, headaches or cramping.

3.4.5 Disconnection from dialysis machine

The blood in the extracorporeal circuit was returned using saline. The blood pump was stopped and the arterial line and needle/lumen was clamped. The arterial line was disconnected and to it, a 15 gauge hypodermic needle was attached and promptly inserted into the saline bag. The pump was then run until the saline reached the venous needle/ lumen and then the venous line was disconnected.

AVF/AVG: Needles were removed from patient and exit site was held with gauze until it stopped bleeding.

Catheters: Each lumen was flushed with 10 mls of saline. The correct amount of 5000 iu/ml heparin (heparin lock) was inserted into each lumen according to catheter specifications. The ports were then covered with a dressing.

A post-dialysis BP and weight was recorded for each patient.

3.5 Technique for drawing blood samples

The blood for pre-dialysis blood urea nitrogen (BUN) was drawn before dialysis was started to prevent this sample from reflecting any impact of dialysis. Dilution of the pre-dialysis sample with saline or heparin was avoided in order to prevent the pre-dialysis BUN from being artificially low, resulting in a falsely low Kt/V (dialysis adequacy) and/or URR (urea reduction ratio). Blood samples were routinely taken every three months for the duration of the study.

3.5.1 Pre dialysis blood sampling method for AVF and AVG

1. A 20 ml syringe of blood was drawn from the arterial needle prior to connecting the arterial blood tubing or flushing the needle.
2. A sample was not drawn if haemodialysis was already initiated and if saline or heparin was present in the lines.

3.5.2 Pre dialysis blood sampling method for a PermCath

1. The heparin lock was withdrawn from the arterial port of the catheter
2. For adult patients, using the sterile technique, 10 ml of blood was withdrawn from the arterial port of the catheter.
3. A new syringe was then used to withdraw the sample
4. Haemodialysis was then initiated as per unit protocol. All pre dialysis blood samples were taken to the pathology laboratory.

3.5.3 Post dialysis blood sampling method

The recommended method for blood sampling post dialysis is using the slow flow/stop pump sampling technique:

1. At the completion of haemodialysis, the dialysate flow was turned off and the ultrafiltration rate (UFR) decreased to 50 ml/hr.
2. The blood flow was decreased to 50 to 100 ml/min for 15 seconds. This fills the arterial needle tubing and the arterial blood line with non-recirculated blood (in case there is any access recirculation) by clearing the dead space in the arterial needle tubing and the arterial blood line.
3. With the blood pump still running at 50 to 100 ml/min, the blood sample for post-dialysis BUN measurement was drawn from the arterial sampling port closest to the patient. This ensures the post dialysis BUN sample is performed on undialyzed blood.
 - Vascular access recirculation (AR) is defined as the return of dialyzed blood to the arterial segment of the access bypassing the systemic recirculation, thereby resulting in reducing the efficiency of dialysis (National Kidney Foundation, 2006).
 - Immediately upon completion of HD, if AR was present, some of the blood remaining in the access and extracorporeal circuit actually is recirculated blood. If the blood sample is drawn immediately upon completion of dialysis, just-dialyzed blood that has recirculated into the access will dilute the sample (NKF, 2006).
 - Decreasing blood flow to 100 mL/min reduces the entry of cleared blood into the access and stops AR (NKF, 2006).
4. The blood pump was stopped and complete patient disconnection procedure as per dialysis unit protocol was performed.

3.6 Calculation of the dialysis adequacy

To determine whether the dialysis procedure was removing enough urea, the dialysis clinic periodically (every 3 months) tests a patient's blood to measure dialysis adequacy. Blood was sampled at the start of dialysis and at the end. The levels of urea in the two blood samples were then compared. Two methods are generally used to assess dialysis adequacy URR (Urea Reduction Ratio) and Kt/V (Dialysis Adequacy).

3.6.1 Calculation of URR

URR is one measure of how effectively a dialysis treatment removed waste products from the body and is commonly expressed as a percentage. Patients generally live longer and have fewer hospitalizations if the URR is at least 60%.

Example: Pre dialysis urea: 50mg/dL
 Post dialysis urea: 15mg/dL
 Amount of urea removed: $(50\text{mg/dL} - 15\text{mg/dL}) = 35\text{mg/dL}$

The amount of urea removed is expressed as a percentage of the pre dialysis urea (50mg/dl).

→ $35/50 \times 100 = 70\%$

3.6.2 Calculation of Kt/V

Kt/V takes into account two additional factors; urea generated by the body during dialysis and extra urea removed during dialysis along with excess fluid therefore making it a more accurate measurement than URR. KDOQI has adopted a Kt/V of 1.2 as a standard for dialysis adequacy.

In this measurement:

- K: stands for dialyzer clearance (the rate at which blood passes through the dialyzer expressed in millilitres per minute (ml/min)).
- t: stands for time

- Kt: the top part of the fraction; is dialyzer clearance multiplied by time. This represents the volume of fluid completely cleared of urea during a single treatment.
- V: the bottom part of the fraction; is the volume of water a patient's body contains

Example: If a dialyzers clearance is 300ml/min and a dialysis session lasts for 180 minutes (3 hours), Kt: $300 \times 180 = 54000 \text{ mls} = 54 \text{ litres}$

The body is about 60 percent water. If the patient weighs 70 kg: $V = 70 \times 60/100$
 $= 42 \text{ litres}$

The Kt/V for that patient will then be: $54 \text{ litres} / 42 \text{ litres} = 1.3$

3.7 Kidney Disease Quality of Life SF-36 Survey (KDQOL SF-36)

The survey that was used is the Kidney Disease Quality of Life survey which was developed in 1994 by the Kidney Disease Quality of Life Working Group as a kidney disease-specific measure of Health Related Quality of Life (HRQOL). Health-related quality of life is the impact of a chronic disease and its treatment on patients' perceptions of their own physical and mental function (Schatell et al., 2003).

Validity of the KDQOL-SFTM was confirmed by the hypothesized positive correlations between the comorbidities and dialysis dose. Moreover, dialysis targeted dimensions were more sensitive in detecting relevant differences pertaining to kidney diseases than generic dimensions. The KDQOL-SFTM was able to detect clinical changes over time. The psychometric properties of the KDQOL-SFTM were good and the different dialysis-targeted dimensions were informative with a high reliability and validity. These results support the application of the KDQOL in studies evaluating dialysis therapy (Korevaar et al., 2002).

Each patient was given The Quality of Life Survey Questionnaire (KDQOL: SF-36) by the researcher to complete during the third month of data collection as this gave the nocturnal dialysis patients adequate time to adjust to the new modality and the questions could be answered accurately. The survey could be completed while the

patient was still on the machine or they could take it home to complete and bring it back. The survey took an estimated 15 minutes to complete.

Data for this survey was analysed using the online KDQOL-Complete Programme.

The survey consisted of three parts:

1. **Physical Component Summary-** The lower the score, the higher the risk of hospitalization or death. A higher score means better physical health.
2. **Mental Component Summary-** This included items about general health, activity limits, ability to accomplish desired tasks, depression and anxiety, energy levels and social activities. A higher score means better mental health.
3. **Burden of Kidney Disease-** Included questions on how much kidney disease interferes with daily life, causes frustration and makes the patient feel like a burden. A higher score means a less burden.

3.8 Statistical Methodology

IBM®SPSS®Statistics version 20 was used for data analysis. A p value <0.05 was considered as statistically significant. Quantitative outcome data were tested for normality using Kolmogorov-Smirnov tests. Most variables were found to be acceptably normally distributed, therefore parametric tests were used. Repeated measures ANOVA testing was used to compare the change in time over the three time points between the two treatment groups. A significant time x group interaction effect indicated a significant treatment effect. Profile plots were generated in order to assess the direction and trend of the effect. Variables which were not normally distributed were tested non parametrically using Mann Whitney tests on the change between baseline and 6 months.

CHAPTER FOUR: RESULTS

This chapter will reveal and explain the results obtained in the study conducted. Tables, graphs and profile plots are used to illustrate the results from both the quantitative and qualitative data.

4.1 Population Demographics and Characteristics

Thirty participants were enrolled in this study. The baseline demographics and characteristics are summarized in Figures 11 – 14.

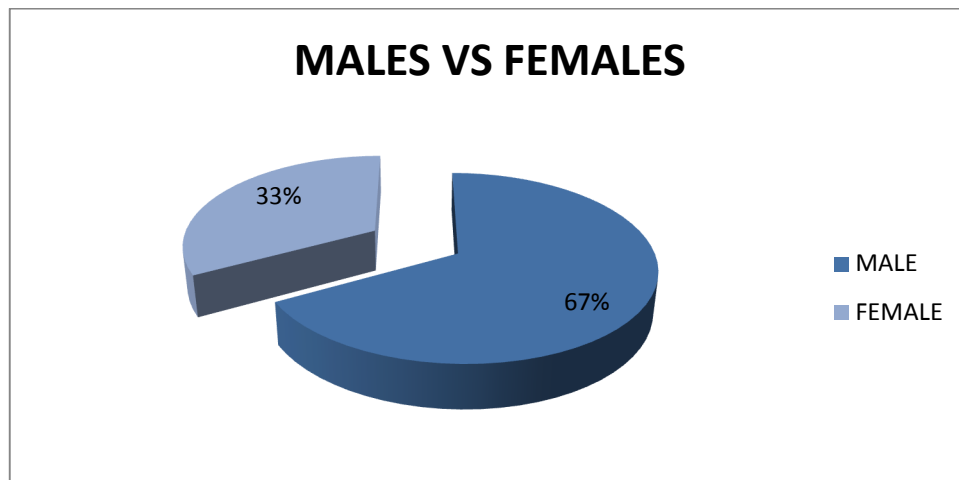


Figure 11. Male versus Female Patients. More than half of the sample population (67%) were male patients

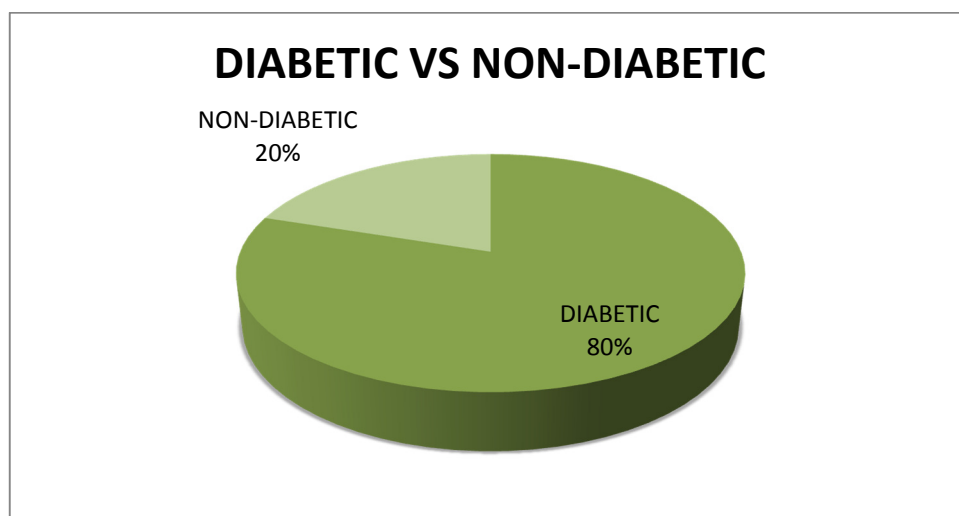


Figure 12. Diabetic versus Non-Diabetic patients. The majority of the population (80%) were diabetic.

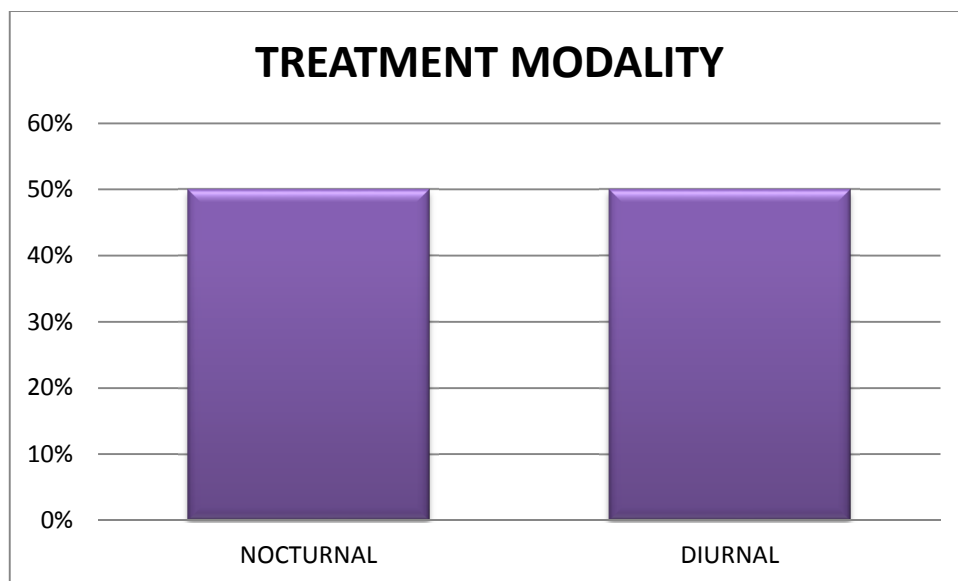


Figure 13. Graph showing the different treatment modalities used. Equal numbers of patients (50%) were used from each modality.

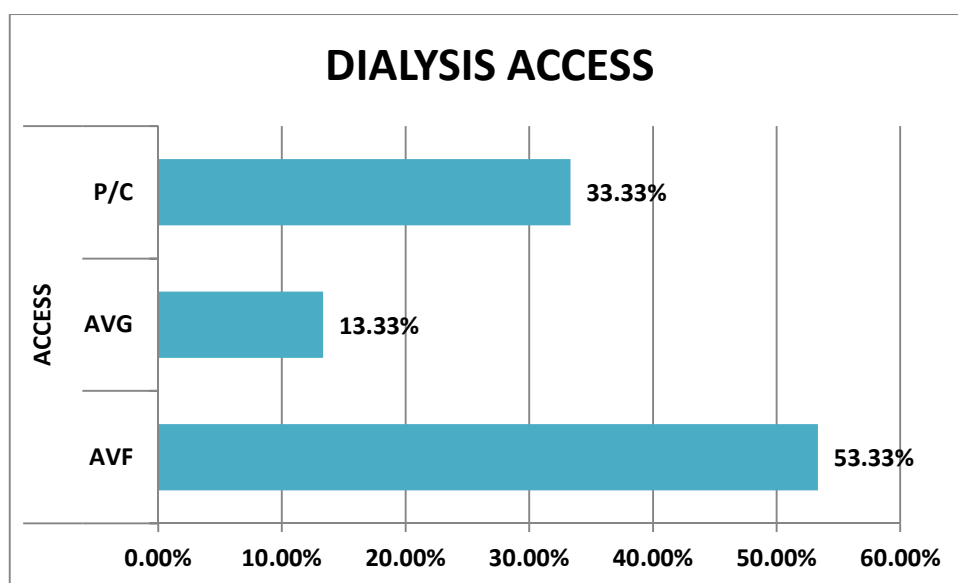


Figure 14. A graph depicting the types of dialysis access used. The trend favoured the Arteriovenous Fistula (54%).

Table 3: Sample characteristics for the entire study group (n=30) except where otherwise noted.

| Characteristic | <i>n</i> (%) or mean value |
|--|-----------------------------------|
| HIV +ve | 3 (10) |
| Dry Weight: Diurnal | 68.8 kg |
| Dry Weight: Nocturnal | 72.6 kg |
| Age: Diurnal | |
| Male: | 43 years |
| Female: | 47 years |
| Age: Nocturnal | |
| Male: | 47 years |
| Female: | 40 years |
| Primary cause of kidney failure: | |
| Hypertension | 10 (33.3) |
| Diabetes | 9 (30) |
| Lupus | 2 (6.6) |
| Glomerulonephritis | 5 (16.6) |
| Polycystic Kidney Disease | 2 (6.6) |
| Nephrotic Syndrome | 2 (6.6) |
| Longest duration of a patient on haemodialysis in this study | 30 years |
| Shortest duration of a patient on haemodialysis in this study | 7 months |
| | |

4.2 Urea Level

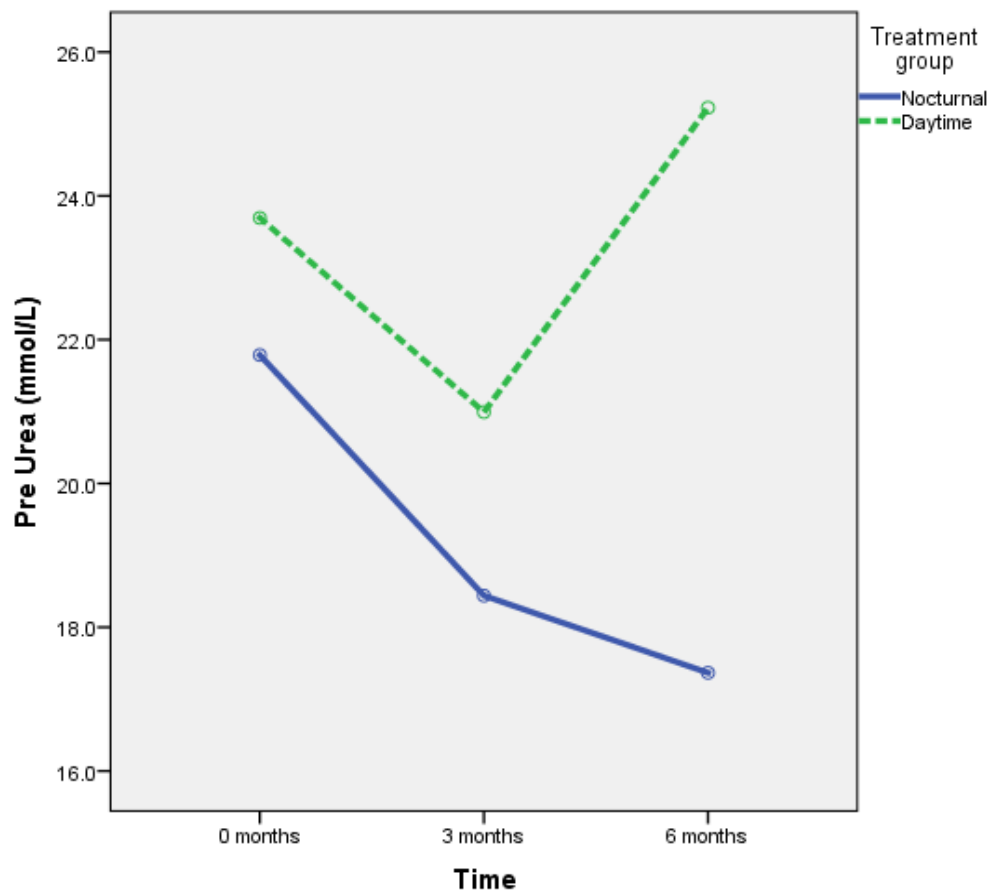


Figure 15: Profile plot of mean pre urea levels by treatment group over time. Repeated measures ANOVA testing was done for mean pre urea levels. Blood samples were drawn and sent to the pathology lab for all participants in the study ($n=30$) at each of the three time intervals (0 months, 3 months and 6 months). A non-statistically significant effect of treatment was found between the two groups ($p=0.053$) although the profile plot of figure 15 shows that between 0 and 3 months, the mean level of pre urea was similar between the two groups and between 3 and 6 months, pre urea levels decreased in the nocturnal group while it increased in the daytime group.

Although there were baseline differences between the two groups, regarding age, sex, duration of kidney disease, choice of dialysis treatment and cause of renal disease, the mean level of pre urea decreased in the nocturnal group while it increased overall in the daytime group (Figure 15).

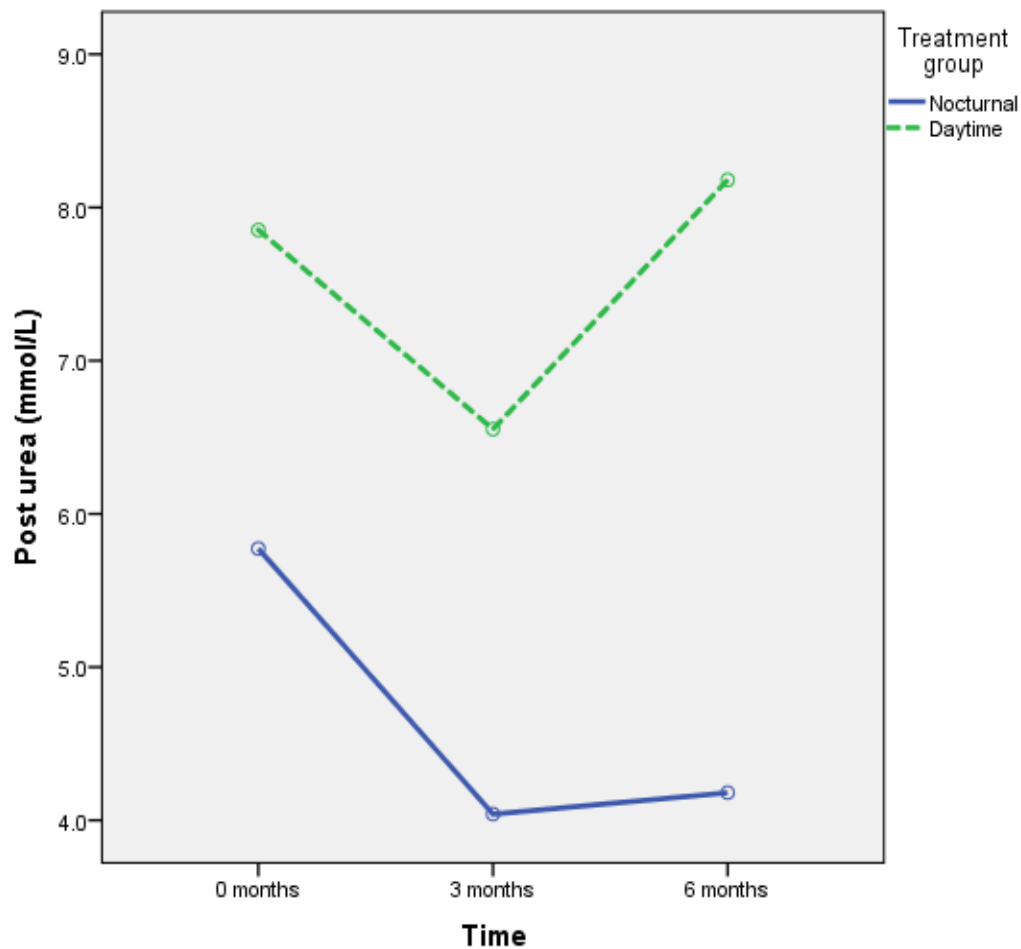


Figure 16: Profile plot of mean post urea levels by treatment group over time. *Multivariate testing for post urea levels was performed for all participants (n=30) across the three times intervals. This yielded a non-statistically significant treatment effect between the two groups ($p=0.185$). Graphically, as seen in figure 16 above, the rate of change of post urea over time was similar between the groups. However between 3 and 6 months, post urea levels in the nocturnal group levelled out whilst an increase in post urea levels was seen in the daytime group.*

The rate of change of urea over time in the two groups was relatively similar between baseline and 3 months, although this levelled out in nocturnal group compared with an increase in the daytime group between 3 and 6 months. However, this trend was not confirmed statistically (Figure 16).

4.3 Creatinine level

Table 4: Showing the Hypotheses Test Summary for Creatinine

| Hypothesis Test Summary | | | | |
|-------------------------|--|---|-------------------|-----------------------------|
| | Null Hypothesis | Test | Sig. | Decision |
| 1 | The distribution of ch_creat is the same across categories of Treatment group. | Independent-Samples Mann-Whitney U Test | .233 ¹ | Retain the null hypothesis. |

Asymptotic significances are displayed. The significance level is .05.

¹ Exact significance is displayed for this test.

The creatinine values were not normally distributed, therefore the change in creatinine value between baseline and 6 months was calculated and compared between the two groups using non parametric independent samples Mann Whitney test. The median change was higher in the nocturnal group (a larger decrease was noted) than the daytime group as shown in Table 4. However, this difference was not statistically significant ($p=0.233$).

4.4 Potassium Measurement

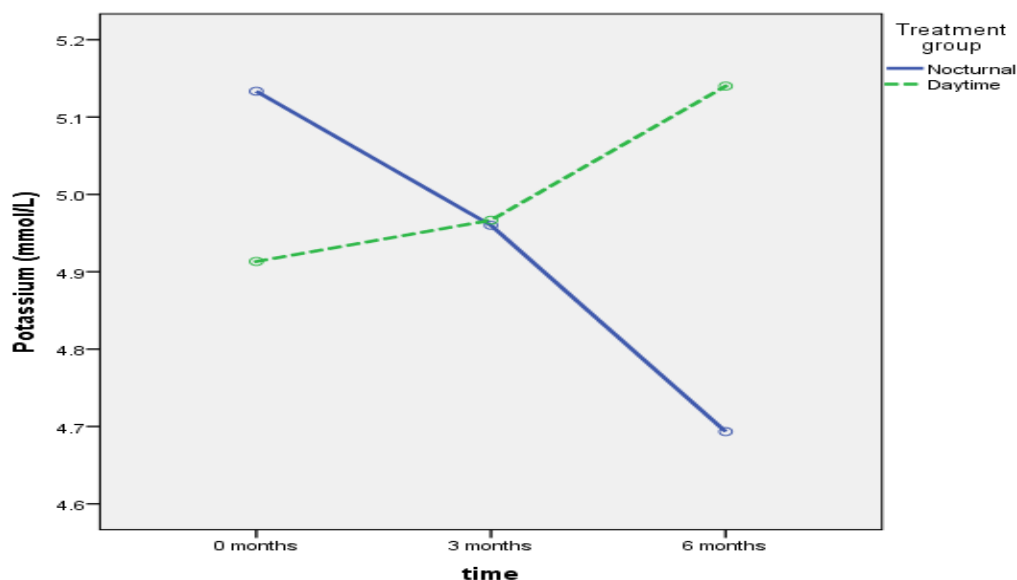


Figure 17: Profile plot of mean potassium levels by treatment group over time. Multivariate testing was done for potassium levels for the nocturnal group ($n=15$) and the diurnal (daytime) group ($n=15$) for each of the three time intervals. This testing did not reveal statistical evidence of a treatment effect ($p=0.344$). The mean value of potassium increased in the daytime group between both the 0 and 3 month time

interval (4.9 mmol/L to 4.95 mmol/L) and between the 3 and 6 month time interval (4.95 mmol/L to 5.15 mmol/L). On the other hand, the mean value of potassium decreased in the nocturnal group from 5.15 mmol/L to 4.95 mmol/L between the 0 and 3 month time interval and further decreased between the 3 and 6 month interval from 4.95 mmol/L to 4.7 mmol/L.

There was no statistical evidence of a treatment effect for potassium ($p=0.344$). However Figure 17 shows that the mean value decreased in the nocturnal group while it increased in the daytime group. However the scale of the changes was small which probably resulted in the non-significant p value ($p= 0.233$).

4.5 Albumin Measurement

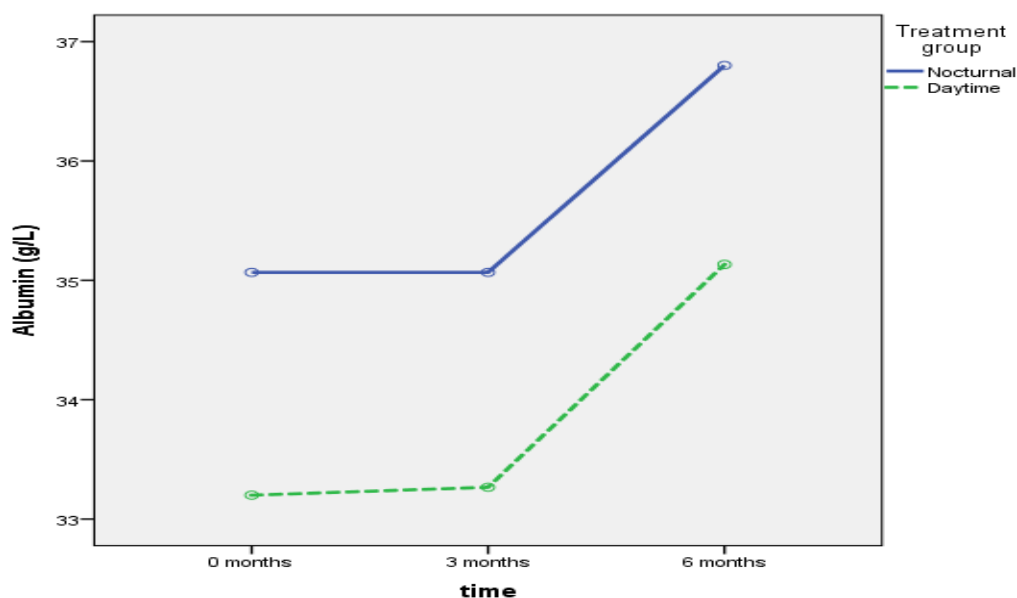


Figure 18: Profile plot of mean albumin levels by treatment group over time. *Blood samples for Albumin levels were taken at each of the 3 time intervals (0, 3 and 6 months) for the entire sample size ($n=30$). Multivariate testing using Wilks Lambda distribution shows that the mean levels of albumin in both groups increased at the same level (lines for both groups are roughly parallel). For both groups, the mean albumin levels levelled off between months 0 and 3 and increased between months 3 and 6. A p -value of 0.979 was found showing no statistical evidence of a treatment effect for albumin.*

There was no statistical evidence of a treatment effect for albumin ($p=0.979$). Figure 18 shows that the mean values increased at the same level in both groups and the lines are roughly parallel. This implies that albumin level will not be affected by the type of dialysis.

4.6 Calcium Measurement

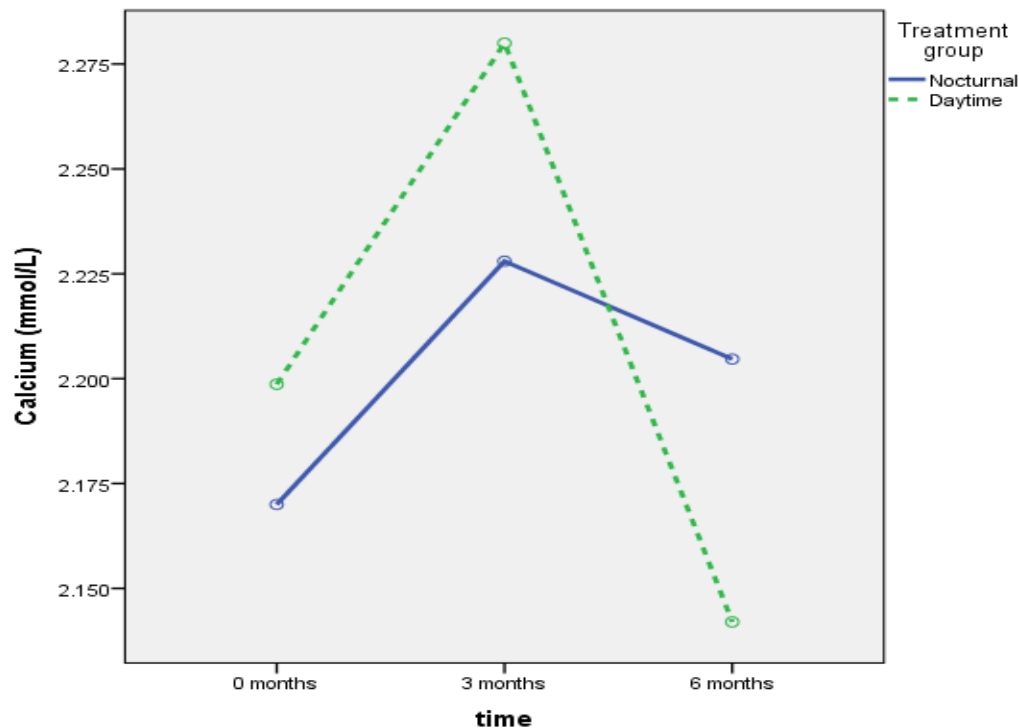


Figure 19: Profile plot of mean calcium levels by treatment group over time. Calcium levels were tested for the entire sample size ($n=30$) at each time interval. The profile plot of the mean values of calcium (mmol/L) over time shows that between 0 and 3 months, mean levels increased in both groups, however between month 3 and 6, the mean values of calcium in the daytime group decreased more than those levels in the nocturnal group. Using Wilks' Lambda distribution in multivariate testing, a p -value of 0.328 was found. This resulted in a non-significant treatment effect probably due to the small scale of changes between mean calcium levels in each group.

Figure 19 shows that the mean value of calcium decreased more in the daytime group overall than the nocturnal group. However the scale of the changes was small which probably resulted in the non-significant p value ($p=0.328$).

4.7 Phosphate Measurement

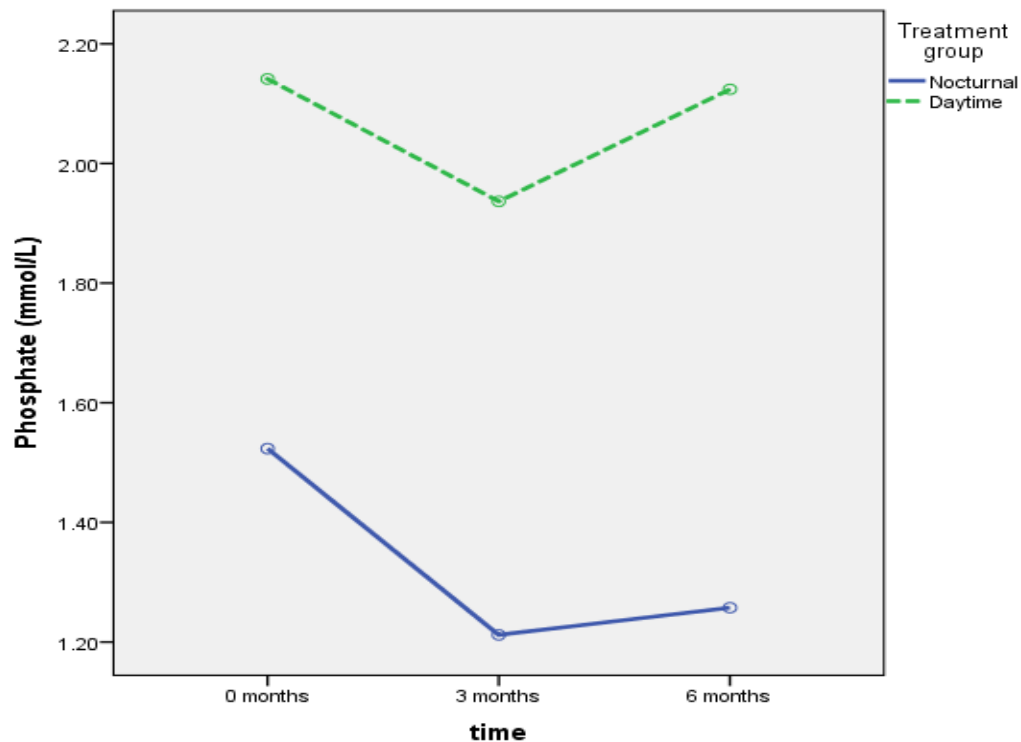


Figure 20: Profile plot of mean phosphate levels by treatment group over time. *Multivariate testing revealed a p -value= 0.691 showing a non-significant effect of treatment for the rate of change of mean phosphate levels over time. Blood samples for phosphate levels (mmol/L) were drawn at all 3 time intervals for the whole sample size ($n=30$). Although the two groups had baseline differences, the mean values of phosphate decreased for both groups between 0 and 3 months. Between 3 and 6 months, mean phosphate levels in the daytime group increased while levels for the nocturnal group levelled off.*

There was no significant effect of the treatment on phosphate levels ($p=0.691$) in Figure 20 although the two groups had significant baseline differences.

4.8 Haemoglobin Measurement

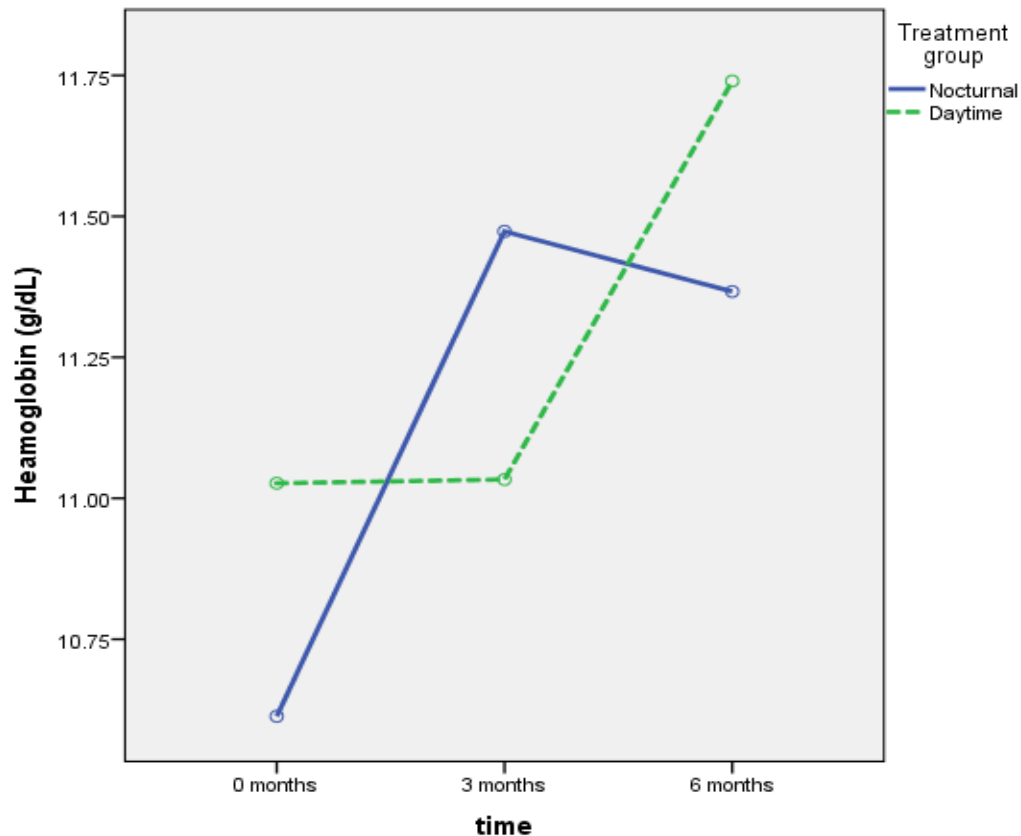


Figure 21: Profile plot of mean haemoglobin levels by treatment group over time. Multivariate testing using Wilks' Lambda distribution showed a non-significant effect of treatment ($p=0.409$) for haemoglobin levels across the three time intervals for both groups ($n=30$). Between months 0 and 3, mean haemoglobin levels increased in the nocturnal group while it levelled off in the daytime group. An increase in haemoglobin levels was then seen in the daytime group between months 3 and 6, while it levelled off in the nocturnal group.

Figure 21 shows that the mean Haemoglobin value increased at different rates in both groups. However the scale of the changes was small which probably resulted in the non-significant p value ($p=0.409$).

4.9 URR Level

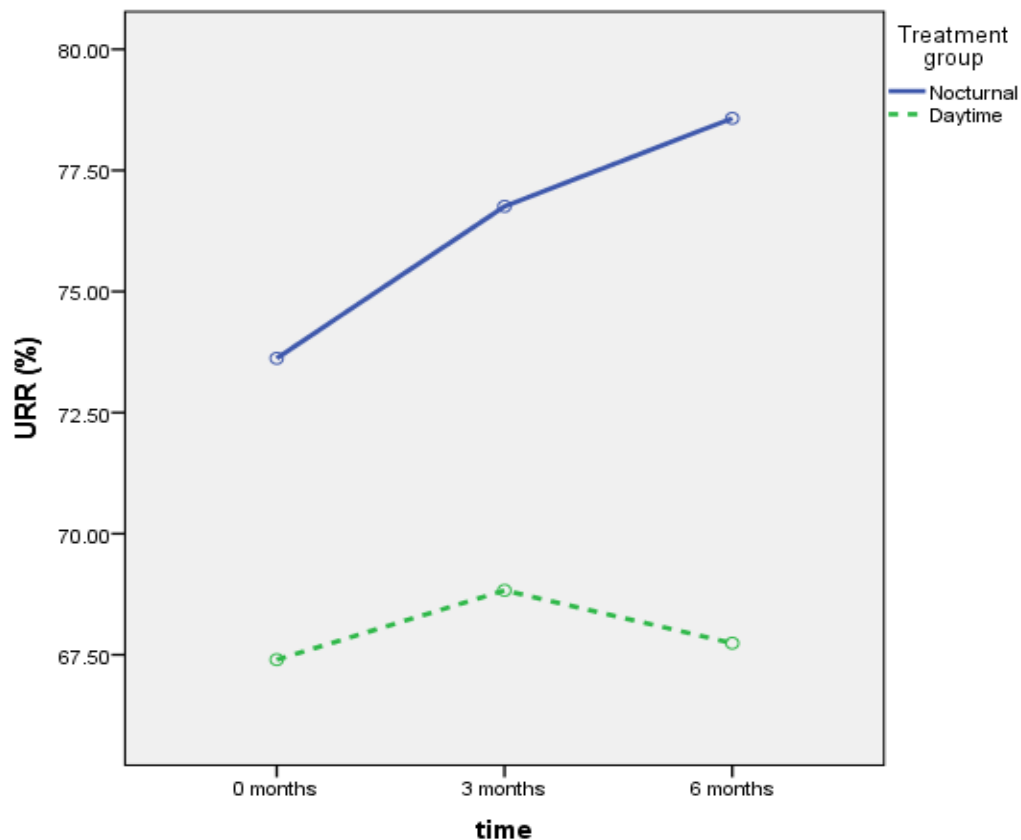


Figure 22: Profile plot of mean URR levels by treatment group over time. *Multivariate testing was done for URR for all participants of the study (n=30) across the three different time intervals. A non-significant p-value of 0.188 was found through testing via Wilks' Lambda distribution. The mean URR levels remained level between 0 and 3 months and between 3 and 6 months for the daytime group. For the nocturnal group, an increase in URR levels was seen between 0 and 3 months and again between 3 and 6 months.*

There was no significant effect of the treatment on URR levels ($p=0.188$) although the two groups had significant baseline differences and the mean value for the nocturnal group increased while that of the daytime group levelled off (Figure 22).

5.0 Kt/V Levels

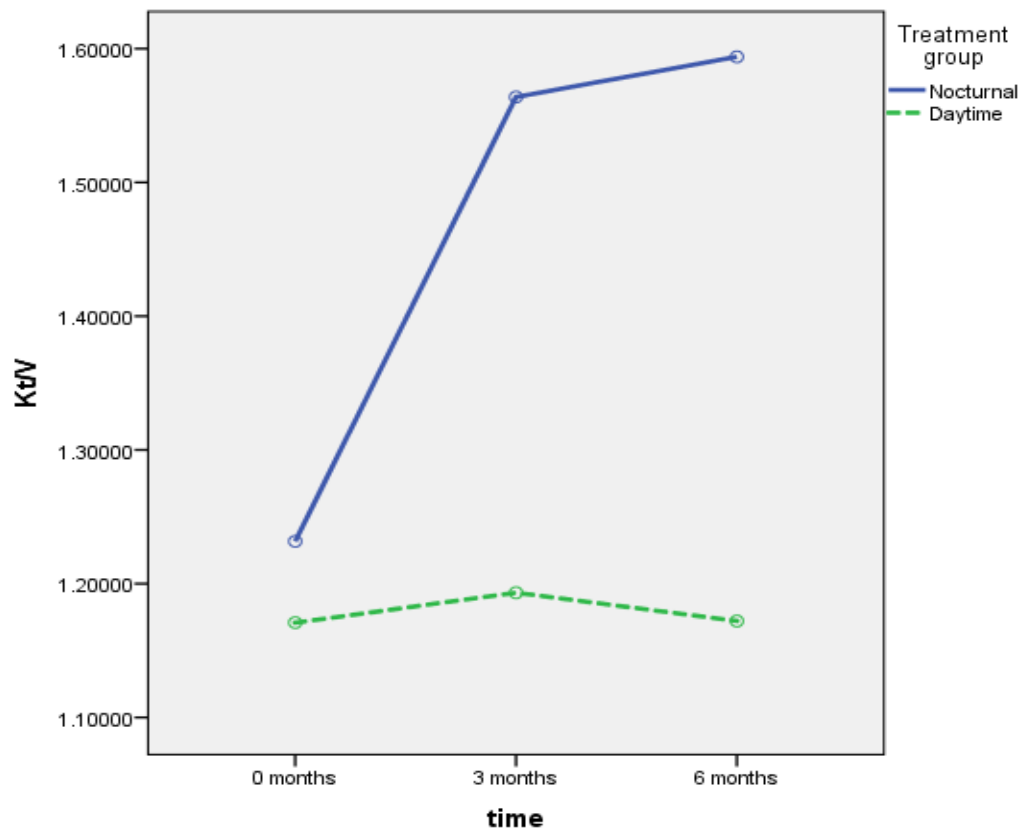


Figure 23: Profile plot of mean Kt/V levels by treatment group over time. Dialysis adequacy as defined by Kt/V was calculated and analysed using multivariate testing at each time interval (0 months, 3 months and 6 months). Kt/V was calculated for each participant in the study (n=30) and the mean levels were plotted in Figure 23. In the daytime group, dialysis adequacy remained level between 0 and 3 months and again between 3 and 6 months. In the nocturnal group however, an increase in dialysis adequacy (Kt/V) was seen between months 0 and 3 and Kt/V levelled off between months 3 and 6. Using multivariate testing, a significant effect of treatment was found for the rate of change of Kt/V levels over time ($p=0.015$).

Figure 23 shows there was a significant effect of the treatment on Kt/V levels ($p=0.015$). The nocturnal group experienced an increase in Kt/V levels while the daytime group was level over time.

5.1 Parathyroid Hormone Measurement

Table 5. Measured Parathyroid Hormone levels and corresponding p-values, mean and variance values.

| Parathyroid Hormone (PTH) | Mean | Variance | p-value |
|---|--|--|----------|
| PTH at baseline interval between both the diurnal and nocturnal groups | Diurnal (n=15): 483.3867 <hr/> Nocturnal (n=15): 724.7467 | Diurnal (n=15): 103512.1 <hr/> Nocturnal (n=15): 243913.4 | 0.123989 |
| PTH at 6 month interval between both the diurnal and nocturnal groups | Diurnal (n=15): 724.747 <hr/> Nocturnal (n=15): 296.36 | Diurnal (n=15): 243913.4 <hr/> Nocturnal (n=15): 42560.57 | 0.004382 |

Parathyroid Hormone levels were measured only twice in this study, at baseline and again at the 6 month interval for both groups. Table 5 illustrates that the p-value at the baseline interval ($p=0.123$) was found to be non-statistically significant. At the interval of 6 months, however, the analysed data gave a $p\text{-value}= 0.004$ and therefore resulted in a statistically significant effect of treatment. Parathyroid Hormone levels were found to be reduced at the 6 month interval for the nocturnal group, compared to an increase in PTH levels observed in the diurnal group.

5.2 Beta-2-Microglobulin Levels

Table 6. Measured Beta-2-Microglobulin levels in the nocturnal group

| Beta-2-Microglobulin | Mean \pm SD |
|------------------------|------------------|
| B2M levels at Baseline | 46.9 \pm 13.22 |
| B2M levels at 6 months | 24.7 \pm 8.63 |

A paired t-test was done for the Beta-2-Microglobulin levels. These levels were measured only for the nocturnal group at baseline and again at 6 months. Table 6 illustrates that patients in the nocturnal group showed a significant decrease in beta-2-microglobulin levels. Across the timeline of the study, the levels decreased from 46.9 (13.22) at the baseline interval to 24.7 (8.63) at 6 months. $p < 0.001$ was found and therefore showed a significant difference between the two time intervals.

5.3 Quality of Life Survey

The Quality of Life Survey Questionnaire (KDQOL: SF-36) was administered to all the participants in both groups in the third month of data collection. Data for this survey was analysed using the online KDQOL-Complete Programme.

Table 7. Findings of the Quality of Life Survey Questionnaire (KDQOL: SF-36)

| Component of Survey | p-value |
|--------------------------|---------|
| PCS | 0.00545 |
| MCS | 0.00373 |
| Burden of Kidney Disease | 0.00437 |

PCS: Physical Component Summary; MCS: Mental Component Summary

In the Physical Component Summary and Mental Component Summary, a p-value = 0.005 and $p = 0.003$ was found respectively, making these components of the survey statistically significant. In the PCS, the questions included related to physical function, role-physical, bodily pain and general health. For the MCS, questions were focussed on vitality, social functioning, role-emotional and mental health. This meant that the nocturnal patients felt they were in better physical and mental health than the diurnal patients.

As seen in Table 7, the burden of kidney failure also showed a statistically significant effect of treatment with $p = 0.004$, showing that the nocturnal patients felt that the burden of kidney disease was less for them.

CHAPTER FIVE: DISCUSSION OF RESULTS

To date, there have been no randomized prospective studies done in South Africa that compares conventional thrice weekly therapy with long slow nocturnal dialysis. The studies that have been done in other countries by the likes of Pierratos et al., (1998) focussed mainly on blood pressure control and cardiac functioning of those patients on nocturnal haemodialysis.

The results of this study are important because they provide more accurate information on the removal of small and middle molecules and compare the quality of life of both nocturnal dialysis and diurnal dialysis. The results suggest that nocturnal dialysis on a whole provides a better dialysis adequacy than diurnal dialysis and also shows an improvement in the quality of life of nocturnal haemodialysis patients. Furthermore, there were no significant changes in small solute clearance to set nocturnal dialysis apart from diurnal dialysis.

Nocturnal haemodialysis is an important new form of treatment for kidney failure and needs to be investigated further to increase knowledge about this modality of treatment. This is important because the mortality rate and low quality of life associated with patients undergoing conventional thrice weekly treatment is unacceptably high (Pierratos et al., 2004). The institution of more intensive dialysis regimes appears to improve morbidity and possibly mortality. Compared to conventional thrice weekly regimens, dialysis associated with longer duration correlates with enhanced outcomes (Rocco, 2009).

There is a paucity of literature about the comparison of thrice weekly diurnal dialysis versus nocturnal dialysis, which involves patients staying overnight in a dialysis unit and undergoing haemodialysis for 8 hours as opposed to the conventional 4 hour treatment. Part of the problem is that nocturnal dialysis has just been introduced into our country as an alternative treatment modality, and the pilot project was used as a basis for this study. Patients are still sceptical about swapping over to nocturnal haemodialysis as the information regarding this modality is scarce.

Laurent and Charra (1998), McFarlane et al., (2003) and Lamsdale (2007) have all indicated that there were distinct advantages for patients who were on extended dialysis times as there were fewer fluctuations in blood volume and solute clearance thus alleviating some of the stress on other bodily functions.

It is the author's belief, after a thorough review on the literature on nocturnal dialysis that prior to this present study, the beneficial effects of nocturnal dialysis on solute clearance had not been investigated fully. Studies from both the United States and Europe have mainly focussed on the cardiovascular effects of night-time dialysis (Moe et al., 2002; McGregor et al., 2001; Ly and Chan, 2006).

In this cohort (n=30), the clearance of all small solutes individually were statistically non- significant. Figure 15 shows that the mean level of urea decreased in the nocturnal group while it increased in the diurnal group. This trend is consistent with the findings in the study done by Daugirdas et al., (2010) where the urea generation in nocturnal haemodialysis was lower than that of the daytime group. The study also showed that urea generation falls by as much as 75% in the first two hours of nocturnal haemodialysis and then slowly throughout the rest of the treatment (Daugirdas et al., 2010).

In an article by Thompson et al., (2013), nocturnal dialysis was associated with a decrease in potassium levels ($p = 0.0187$). Dialysis duration also predicted a decrease in potassium levels better than dialysis frequency ($p = 0.023$ vs $p = 0.0102$). This information was a significant breakthrough as sudden cardiac death due to unstable potassium levels remains the leading cause of death in haemodialysis (Thompson et al., 2013). Figure 17 shows that the mean value of potassium decreased in the nocturnal group while it increased in the diurnal group, however due to our small sample size, the scale of changes was so small that it resulted in a statistically non-significant p value ($p = 0.344$).

The creatinine levels were compared using the Mann-Whitney tests. It resulted in a non-significant p value of 0.233 but did show a larger decrease in creatinine levels in the nocturnal group compared to the diurnal group. This is consistent with results from the study done by Troidle et al., (2009) where serum creatinine levels decreased from 9.2 ± 1.9 mg/dL to 3.0 ± 1.0 mg/dL in an 8 hour nocturnal haemodialysis session with a statistically significant value of $p < 0.0001$.

Calcium and phosphates were both shown to be non-statistically significant with p-values of 0.328 and 0.691 respectively. Calcium showed a larger decrease in the diurnal group than the nocturnal group. Calcium balance and regulation are very important when treating hyperparathyroidism (Kutner et al., 1986).

Results from a prospective study by Grabe et al., (2006) of 14 ESRD patients converted from conventional haemodialysis to nocturnal haemodialysis showed that after 1 year of nocturnal haemodialysis, serum calcium levels remained unchanged (2.45 ± 0.06 mmol at baseline to 2.51 ± 0.03 at 1 year) but plasma phosphate levels decreased (1.38 ± 0.08 mmol at baseline to 1.07 ± 0.08 at 1 year) (Grabe et al., 2006).

Studies done by Mucsi et al., (1998); Block et al., (2003); Young et al., (2005); Pierratos et al., (1998) and McFarlane, (2003) have consistently shown improved phosphate control in nocturnal haemodialysis. Serum phosphate levels in the Troidle et al., (2009) study showed that phosphate levels decreased from 5.7 ± 1.9 mg/dL to 2.5 ± 0.7 mg/dL in the 8 hour period.

There was a significant effect of treatment on Kt/V levels ($p = 0.015$) in this study in NHD. The nocturnal group experienced an increase in Kt/V levels whereas the diurnal group was level over time. The benchmark range for Kt/V is between 1.2 and 1.4. Before nocturnal dialysis, many patients had KT/V ratings of less than 1. With nocturnal dialysis most have ratings of 1.2 or 1.4 – and many are even 1.8 or 2.0. Patients have a higher Kt/V (adequacy of dialysis) indicating that the blood is cleaner (Brissenden., et al 1998).

Parathyroid Hormone levels were measured only twice in this study, at baseline and again at the 6 month interval for both groups. Table 4 illustrates that the p-value at the baseline interval ($p=0.123$) was found to be non-statistically significant. At the interval of 6 months, however, the analysed data gave a $p\text{-value} = 0.004$ and therefore resulted in a statistically significant effect of treatment. Parathyroid Hormone levels were found to be reduced at the 6 month interval for the nocturnal group, compared to an increase in PTH levels observed in the diurnal group.

These results are consistent with those found by Grabe et al (2006) where the PTH levels of 14 ESRD patients decreased after one year when converted to nocturnal haemodialysis. Parathyroid Hormone levels decreased from 46.5 ± 17.4 at baseline to 13.4 ± 6.3 at the one year measurement (Grabe et al., 2006).

A paired t-test was carried out for the Beta-2-Microglobulin levels. These levels were measured only for the nocturnal group at baseline and again at 6 months. Table 5 illustrates that patients in the nocturnal group showed a significant decrease in beta-2-microglobulin levels. Across the timeline of the study, the levels decreased from 46.9 (13.22) at the baseline interval to 24.7 (8.63) at 6 months. $P < 0.001$ and therefore showed a significant difference between the two time intervals.

Studies have suggested that the longer duration of NHD results in a greater clearance of β 2M and smaller molecules (Tentori et al., 2012). The results of the present study are consistent with the one study comparing conventional three times a week dialysis with NHD, beta-2-microglobulin pre-dialysis levels progressively declined from 27.2 ± 11.7 mg/dL at initiation of nocturnal haemodialysis to 13.7 ± 4.4 mg/dL by 9 months, and then remained stable thereafter on nocturnal haemodialysis (Pierratos et al., 1999; Nesrallah, 2005).

Findings of the Quality of Life Survey Questionnaire (KDQOL-SF36) were as follows:

In the PCS and MCS, a p-value = 0.005 and $p = 0.003$ was respectively found, making these components of the survey statistically significant. In the Physical Component Summary, the questions included related to physical function, role-physical, bodily pain and general health. For the Mental Component Summary, questions were focussed on vitality, social functioning, role-emotional and mental health. This meant that the nocturnal patients felt they were in better physical and mental health than the diurnal patients.

As seen in Table 6, the burden of kidney failure also showed a statistically significant effect of treatment with $p = 0.004$, showing that the nocturnal patients felt that the burden of kidney disease was less for them.

Quality of life surveys conducted by both Brissenden et al., (1998) and Heidenheim et al., (2003) are both consistent with the findings in this study. Brissenden et al.,

(1998) showed trends to improvement in ambulation (17.2 to 11.1; $p = 0.07$), mobility (3.9 to 2.9; $p = 0.08$), and social interaction (16.4 to 11.4; $p = 0.07$) while Heidenheim et al., (2003) showed improvements in social functioning (54.2 to 79.2; $p = 0.006$), physical functioning (60.6 to 69; $p = 0.008$), and role-physical (39.2 to 36.1; $p = 0.05$).

The survival rate was the same for both conventional haemodialysis and nocturnal haemodialysis as no deaths occurred during the timeframe of the study. Some studies suggest that patients receiving nocturnal haemodialysis have a mortality rate that is about one third of what is seen in similar patients receiving conventional haemodialysis (Myers et al., 2010). A group from USA found the mortality rate in 94 NHD patients was a third of that in 940 CHD patients ($P = 0.0001$) (Lindsay et al., 2003).

Study Limitations

As this study was the pilot project for this new treatment modality in haemodialysis, a randomized study could not be performed as patients themselves chose to be on nocturnal haemodialysis because of the lifestyle benefits that were identified (most patients chose nocturnal haemodialysis because of the free time they would have during the day thereby improving their lifestyle and allowing them to continue working without disruptions). The sample size was small and limited the power to detect small changes between the variables leading to non-statistically significant effects of treatment. A major limitation of the study was the paucity of literature on this specific area of nocturnal haemodialysis. Due to time constraints and that data could only be collected from one medical practice the sample size was small and did not allow for sufficient power to detect differences in patient survival.

The results revealed in this study serve to further strengthen the existing evidence found on Nocturnal Haemodialysis and to compare the impact of NHD with that of CHD here in South Africa.

CHAPTER SIX: CONCLUSION

To the best of the researcher's knowledge, this study represents the first attempt in South Africa to compare 8 hour nocturnal haemodialysis with conventional 4 hour diurnal haemodialysis comparing both the clearance of small molecules, larger retention products and quality of life and survival between the two modalities in a retrospective and prospective cohort of patients already on haemodialysis.

Several important conclusions can be drawn from this study. While dialysis is a lifesaving treatment for many patients with End Stage Renal Disease, it can be very inconvenient and the process does not clean blood as efficiently as normal functioning kidneys do. Nocturnal haemodialysis, the newer option, is starting to change all that due to the longer duration that the blood is filtered for.

Firstly, although non-significant effects of treatment were found for all small solutes individually, dialysis adequacy as defined by Kt/V , increased in the nocturnal group while it levelled off in the diurnal group.

Secondly, previous studies have shown that nocturnal haemodialysis results in greater clearance of larger molecules such as Beta-2-Microglobulin and Parathyroid Hormone. This was proved true in the present study as both the Parathyroid Hormone levels and Beta-2-Microglobulin levels decreased more in the nocturnal group therefore resulting in statistically significant effects of treatment.

The third and final conclusion drawn was that nocturnal haemodialysis resulted in better physical health, better mental health and a lower burden of kidney disease was felt by patients undergoing nocturnal haemodialysis.

Although there was not a large population to compare for this study as it is still a fairly new modality of treatment in South Africa, nocturnal haemodialysis is a potential alternative to conventional diurnal haemodialysis and the beneficial evidence that the present study showed should serve as a stepping stone for a larger randomized controlled study.

Since nocturnal dialysis results in improved dialysis clearance, better overall patient health and a better quality of life, it is expected that nocturnal haemodialysis will take its place among the treatment modalities offered to patients. It has all of the elements necessary to have a major impact on the delivery of dialysis

CHAPTER SEVEN: REFERENCES

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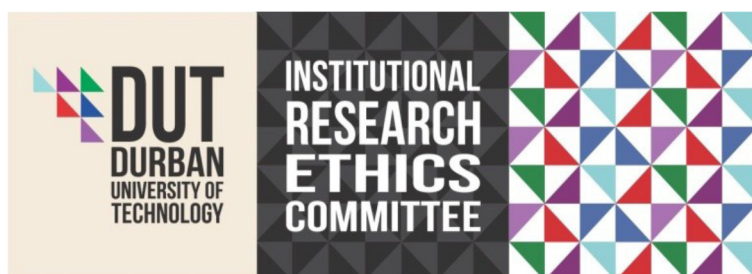
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LETTER OF INFORMATION

Title of the Research Study: Quality of life on Nocturnal Haemodialysis versus Quality of life on Diurnal Haemodialysis

Principal Investigator/s/researcher: Kashka Singh

Co-Investigator/s/supervisor/s: Supervisor: Prof J.K Adam

Co-Supervisor: Dr D. Campbell

Brief Introduction and Purpose of the Study: Hi my name is Kashka Singh and I am studying for a Masters degree at the Durban University of Technology. I would greatly appreciate it if you to take part in my research by completing a questionnaire for my study. In addition, I will also be looking at the bloods that are taken routinely every three months. I am comparing night-time haemodialysis with day-time haemodialysis to see which is better with regards to cleaning of the blood and improving your health.

Outline of the Procedures: Fifteen patients from the night-time haemodialysis and 15 patients from the day-time haemodialysis will be selected for the study. There will be no additional changes to your dialysis procedure and treatment. The only extra information I need from you is for you to complete the questionnaire, which will take approximately 10 minutes of your time. The blood tests that are routinely done i.e. Urea, Creatinine, Potassium, Calcium, Magnesium, Phosphate, Haemoglobin and β_2 - Microglobulin will all be analysed and looked at for my study.

Risks or Discomforts to the Participant: There will be no additional risks or discomfort to you as there will be no change to your normal dialyzing time.

Benefits: The results of this study are expected to benefit the patients directly, as it will show us which form of treatment between the two will have a better quality of life for patients on dialysis.

Reason/s why the Participant May Be Withdrawn from the Study: Your participation in this research is completely voluntary. You may withdraw at any time and this will not affect your routine dialysis treatment.

Remuneration: There will be no form of remuneration. Participation is voluntary.

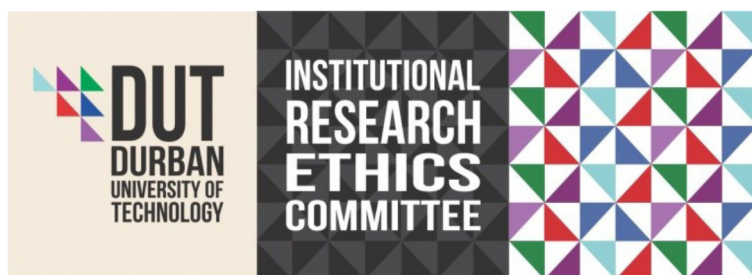
Costs of the Study: You will not be asked to cover any cost relating to the study.

Confidentiality: All the information collected will be kept confidential. You will be allocated a number and all your details will be recorded under that number. This means that anyone who looks at my records will not be able to trace it to you. This is done to protect your privacy. In addition, a statement of confidentiality will be signed by both my supervisors and me.

Research-related Injury: There will be no research-related injury as there will be no alterations made to your dialysis treatment.

Persons to Contact in the Event of Any Problems or Queries:

Please contact the researcher (011 806 1941), my supervisor (031 373 5291) or the Institutional Research Ethics administrator on 031 373 2900. Complaints can be reported to the DVC: TIP, Prof F. Otieno on 031 373 2382 or dvctip@dut.ac.za.



CONSENT

Statement of Agreement to Participate in the Research Study:

- I hereby confirm that I have been informed by the researcher, _____ (name of researcher), about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number: _____,
- I have also received, read and understood the above written information (Participant Letter of Information) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

Full Name of Participant **Date** **Time** **Signature / Right Thumbprint**
 I, _____ (name of researcher) herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

Full Name of Researcher **Date** **Signature**

Full Name of Witness (If applicable) **Date** **Signature**

Full Name of Legal Guardian (If applicable) **Date** **Signature**



BRIEF VAN INLIGTING

Title van die navorsingstudie: Kwaliteit van lewe op Nagtelike Haemodialysis versus Daglike Haemodialysis

Beginsel Ondersoeker / s / navorser: Kashka Singh

Mede-Ondersoeker/s/Toesighouer: Toesighouer: Prof J.K Adam

Mede-Toesighouer: Dr D. Campbell

Kort Inleiding en doel van die studie: Hi my naam is Kashka Singh en ek het vir 'n Meestersgraad by die Durbanse Universiteit van Tegnologie studeer. Ek sou dit baie waardeer as jy deel in my navorsing te neem deur die voltooiing van 'n vraelys vir my studie. Daarbenewens, sal ek dit ook op soek is na aan die bloed wat gereeld elke drie maande geneem. Ek het nagtelike hemodialise vergelyk met daglike hemodialise te sien wat beter is met betrekking tot die skoonmaak van die bloed en die verbetering van jou gesondheid.

Omtrek van die procedures:

Vyftien pasiënte van die nagtelike hemodialise en 15 pasiënte van die daglike hemodialise sal gekies word vir die studie. Daar sal geen addisionele veranderinge aan jou dialise prosedures en behandeling. Die enigste ekstra inligting wat ek nodig het van jou is vir jou om die vraelys te voltooi, wat sal ongeveer 10 minute van jou tyd neem. Die bloed toetse wat gereeld gedoen is d.w.s Ureum, kreatinien, kalium, kalsium, magnesium, fosfaat, Heamoglobien en β 2-Microglobulin sal ontleed word en gekyk vir my studie.

Risiko's of ongemak aan die onderwerp:

Daar sal geen addisionele risiko's of ongemak aan jou as daar sal geen verandering aan jou normale dialise tyd.

Voordele: Die resultate van hierdie studie word verwag om die pasiënte direk baat vind, want dit sal ons jou wys watter vorm van behandeling tussen die twee sal 'n beter kwaliteit van lewe vir pasiënte op dialise.

Rede / s waarom die onderwerp uit die studie ontrek kan word: Jou deelname aan hierdie navorsing is heeltemal vrywillig. Jy kan op eniger tyd onttrek en dit sal geen invloed op jou roetine dialise behandeling.

Vergoeding: Daar sal geen vorm van vergoeding. Deelname is vrywillig.

Koste van die studie: Jy sal nie gevra word om enige koste te dek met betrekking tot die studie.

Vertroulikheid: Al die inligting wat ingesamel word, sal vertroulik gehou word. Jy sal 'n nommer toegeken word en sal al jou besonderhede aangeteken word onder daardie nommer. Dit beteken dat iemand wat kyk na my rekords nie in staat sal wees om dit aan jou op te spoor. Dit word gedoen om jou privaatheid te beskerm. Daarbenewens sal 'n verklaring van vertroulikheid onderteken word deur beide my toesighouers en myself.

Navorsing-verwante besering: Daar sal geen navorsing-verwante beserings wees as daar geen veranderings gemaak aan jou dialise behandeling.

Persone te kontak in die geval van enige probleme of vrae:

Kontak asseblief die navorser (011 806 1941), my toesighouer (031 373 5291) of die Institusionele Navorsingsetiek administrateur op 031 373 2900. Klagtes kan aangemeld word by die DVC: TIP, Prof F. Otieno op 031 373 2382 of dvctip@dut.ac.za



TOESTEMMING

Verklaring van Ooreenkoms om deel te neem in die navorsingstudie:

- Ek bevestig hiermee dat ek in kennis gestel is deur die navorser, _____ (naam van navorser), oor die aard, optrede, voordele en risiko's van hierdie studie – Navorsingsetiek uitklaring nommer: _____
- Ek het ook ontvang, gelees en verstaan die bogenoemde skriftelike inligting (Deelnemer Brief van Inligting) met betrekking tot die studie.
- Ek is bewus daarvan dat die resultate van die studie, insluitend persoonlike besonderhede ten opsigte van my geslag, ouderdom, datum van geboorte, voorletters en diagnose sal anoniem verwerk word in 'n studie verslag.
- In die lig van die vereistes van navorsing, Ek stem saam dat die data wat ingesamel is tydens hierdie studie verwerk kan word in 'n gerekenariseerde stelsel deur die navorser.
- Ek kan op enige stadium, sonder vooroordeel, my toestemming en deelname aan die studie onttrek.
- Ek het voldoende geleentheid om vrae te vra en (van my eie vrye wil) Ek verklaar myself bereid is om deel te neem in die studie.
- Ek verstaan dat beduidende nuwe bevindings ontwikkel gedurende die loop van hierdie navorsing wat verband hou met my deelname sal beskikbaar gestel word vir my.

| | | | |
|---------------------------------|--------------|------------|-----------------------|
| _____ | _____ | _____ | _____ |
| Volle naam van Deelnemer | Datum | Tyd | Handtekening / |
| | | | Reg duimafdruk |

Ek, _____ (naam van navorser) bevestig hiermee dat die bogenoemde deelnemer is ten volle ingelig oor die aard, gedrag en risiko's van die bogenoemde studie.

Volle Naam van Navorser

Datum

Handtekening

**Volle Naam van getuie
(indien toepaslik)**

Datum

Handtekening

**Volle Naam van Voog
(indien toepaslik)**

Datum

Handtekening

Quality of life survey

Patient name: _____

I.D Number: _____

Please circle the answer that best suits your situation

1. How would you best describe your health?

Excellent¹ Very good² Good³ Fair⁴ Poor⁵

2. Compared to a year ago how is your health now?

A lot better¹ Slightly better² The same³ Slightly worse⁴ A lot worse⁵

3. Does your health limit you in any way in performing the activities listed below?

| | Yes a lot ¹ | Yes a little ² | Not at all ³ |
|--|---------------------------|------------------------------|----------------------------|
| a. Strenuous activities, such as running or sports? | | | |
| b. Moderate activities, such as cleaning or playing golf? | | | |
| c. Mild activities, such as walking? | | | |
| d. Climbing several flights of stairs? | | | |
| e. Daily well-being activities such as bathing, dressing yourself? | | | |

- 4. During the last month, have you experienced any of the problems listed below with your work or daily routine because of your health?**

| | Yes ¹ | No ² |
|--|------------------|-----------------|
| a. Decreased amount of time spent on work or activity because of your physical health? | | |
| b. Were restricted in the kind of work because of your physical health? | | |
| c. Accomplished less than you would have liked because of physical limitations? | | |
| d. Did not complete activity as carefully as usual? | | |
| e. Does your health prevent you from working at a job you like? | | |
| f. Found tasks difficult | | |

- 5. In the last month to what degree did your health interfere with your social activities (like visiting with friends or family)?**

Not at all¹ Slightly² Moderately³ Quite a bit⁴ Extremely⁵

- 6. How much of pain have you experienced in the last month?**

None¹ Very little² Mild³ Moderate⁴ Severe⁵ Very severe⁶

- 7. In the last month how much did pain, if any, interfere with your normal routine (including both work and home)?**

Not at all¹ A little bit² Moderately³ Quite a bit⁴ Extremely⁵

8. How satisfied are you?

| | Very dissatisfied ¹ | Little dissatisfied ² | Little satisfied ³ | Satisfied ⁴ |
|--|-----------------------------------|-------------------------------------|----------------------------------|------------------------|
| a. With the amount of time you have to spend with family and friends | | | | |
| b. With the ability to take care of your financial needs? | | | | |
| c. With your home, or place where you live? | | | | |
| d. Your achievement of your personal goals? | | | | |
| e. Your chances for a happy future? | | | | |
| f. Your life in general | | | | |

9. How much time in the last month did you:

| | All ¹ | Most ² | Quite a bit ³ | Some ⁴ | Little ⁵ | None ⁶ |
|------------------------------|------------------|-------------------|-----------------------------|-------------------|---------------------|-------------------|
| a. Feel depressed | | | | | | |
| b. Feel anxious | | | | | | |
| c. Feel calm and peaceful | | | | | | |
| d. Feel full of energy | | | | | | |
| e. Feel downhearted and blue | | | | | | |
| f. Feel happy | | | | | | |
| g. Feel irritable | | | | | | |
| h. Lack concentration | | | | | | |

| | | | | | | |
|--|--|--|--|--|--|--|
| i. Did you get along with everyone around you? | | | | | | |
| j. Did you get confused | | | | | | |

10. Please mark an area that is applicable to you:

| | Completely true ¹ | Mostly true ² | Don't know ³ | Mostly false ⁴ | Definitely false ⁵ |
|--|---------------------------------|-----------------------------|----------------------------|------------------------------|----------------------------------|
| a. I get ill easier than other people | | | | | |
| b. I am as healthy as everyone else | | | | | |
| c. I predict my health is getting worse | | | | | |
| d. My kidney failure interferes too much with my life | | | | | |
| e. Too much of my time is spent dealing with my kidney disease | | | | | |
| f. I am frustrated dealing with my kidney disease | | | | | |
| g. I feel like a burden on my family | | | | | |
| h. I am in control of my life | | | | | |

11. In the last month, how much did the following affect you?

| | No effect ¹ | Some ² | Moderate ³ | Very much ⁴ | Extremely ⁵ |
|---|---------------------------|-------------------|-----------------------|---------------------------|------------------------|
| a. Muscle pain | | | | | |
| b. Chest pain | | | | | |
| c. Cramps | | | | | |
| d. Itchy skin | | | | | |
| e. Dry skin | | | | | |
| f. Shortness of breath | | | | | |
| g. Dizziness | | | | | |
| h. Lack of appetite | | | | | |
| i. Washed out or drained | | | | | |
| j. Numbness in hands or feet | | | | | |
| k. Nausea or upset stomach | | | | | |
| l. Problems with your access (fistula, graft or catheter) | | | | | |

12. How much does kidney disease bother you in each of the areas?

| | No effect ¹ | Some ² | Moderate ³ | Very much ⁴ | Extremely ⁵ |
|--|---------------------------|-------------------|-----------------------|---------------------------|------------------------|
| a. Fluid restriction | | | | | |
| b. Diet restriction | | | | | |
| c. Your ability to work around your house | | | | | |

| | | | | | |
|---|--|--|--|--|--|
| d. Your ability to travel | | | | | |
| e. Being dependent on doctors and medical staff | | | | | |
| f. Stress or worries caused by kidney disease | | | | | |
| g. Time spent on dialysis | | | | | |
| h. Your sex life | | | | | |
| i. Your appearance | | | | | |

13. On a scale of 1-10. 10 being excellent and 1 being terrible, how would you best describe your average sleeping pattern? _____

14. On average how many times do you wake up at night? _____

15. Are you sleepy during the day? Yes / No

16. With respect to your dialysis:

| | Completely true ¹ | Mostly true ² | Don't know ³ | Mostly false ⁴ | Definitely false ⁵ |
|--|------------------------------|--------------------------|-------------------------|---------------------------|-------------------------------|
| a. I am satisfied with my care | | | | | |
| b. The staff support me | | | | | |
| c. The staff understand my needs | | | | | |
| d. It is just as much my responsibility to take care of myself | | | | | |

Thank you for completing the above questionnaire.

STATEMENT OF CONFIDENTIALITY

I, the Clinical Technology student researcher, am bound by the rules of confidentiality in the Sunninghill Dialysis Unit and the guidelines of the South African Medical Research Council (2001).

The following statements of the SAMRC guidelines are binding on me as the principle researcher in the study titled:

Quality of life on Nocturnal Dialysis VS Quality of life on daytime dialysis

- To seek consent in writing from the Sunninghill Dialysis Unit to access medical records within the unit.
- Limit access to those to whom it is essential for the provision of health care (the researcher, the supervisor, the co-supervisor and the Unit Manager).
- To code file names on data collection sheets to ensure patient anonymity
- To destroy the spreadsheet containing the file names and respective codes after the completion of the study.
- To store information derived from medical records for research purposes securely within the archives and, as far as possible, ensure subjects involved are unidentifiable to third parties.

These guidelines will be followed by the Clinical Technology student researcher at all times.

| | | |
|----------------------------------|---------------|-----------------|
| _____ | _____ | _____ |
| Ms K. Singh | Prof J K Adam | Dr D Campbell |
| (Clinical Technology researcher) | (Supervisor) | (Co-Supervisor) |
| _____ | _____ | _____ |
| Date | Date | Date |