Chapter one

Introduction

1.1General introduction:

Dialysis aims to remove waste products that accumulate in the body due to inadequate kidney function. To determine the dialysis efficiency, a method has been developed which is based on measuring the conductivity of the dialysis solution before entering and after passing the dialyzer. Up to now, this feature is implemented in several types of dialysis machines, and is applicable when running in standard dialysis mode or in the so called post dilution hemodiafiltration mode. However, the feature is not adapted for the so called predilections hemodiafiltration mode. A conductivity raise in the inlet dialysis solution ought to be followed by a simple conductivity raise in the outlet dialysis solution. The hypothesis is that, when running in predilution mode, a raise in the inlet solution will cause a “double raise” in the outlet solution, which will complicate the calculation procedure. As this predilution mode is becoming more and more commonly used in the clinics, there is a need to implement the feature for measuring the dialysis efficiency to this treatment mode [3].

Quantification of the dialysis dose is an essential element in the management of chronic hemodialytic treatment because the adequacy of the dose has a profound effect on patient morbidity and mortality [2]. The most useful and widely applied index to prescribe the dialysis dose (as well as to assess the dose which is actually delivered) is the Kt/V formula.1 It is now well recognized that an adequate delivery of hemodialysis (HD) dose (as measured by Kt/V derived from urea reduction) is a crucial determinant in clinical outcome of chronic HD patients. This requires both prescription of an adequate dose of HD and regular assessment that the delivered treatments are also adequate.

1.2 Problem statement:

The human body carries two symmetrically placed kidneys located in the retroperitoneal space. The kidneys provide homeostasis (maintenance of metabolic equilibrium) of body composition. Proper functioning of the body systems depend on this maintenance.

Loss of functional kidney capacity (defined as ability to make corrections to body homeostasis) will result in the manifestation of symptomatic disorders (a disease state). End stage renal disease am be defined as any disorder that causes a reduction of functional capacity in the kidneys resulting in the need for replacement treatment.

The most prevalent renal replacement therapy in use currently is hemdialysis. According to the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines the minimally adequate dose of thrice-weekly HD in patients with residual renal clearance (Kr) less than 2 mL/min/1.73 m2 should be urea single pool KT/V (excluding residual renal function) of 1.2 per dialysis. Dialysis is a life-saving treatment for kidney failure and the patient often has to accept the new life situation and a considerable emotional adaptation to the technology, which maintain their lives. The uraemic symptoms are not complete resolved, despite dialysis treatment, and the patients have to learn to live with their symptoms.

1.3 Objectives

1.3.1 General Objective:

The main objective is to study and optimize the delivered dialysis dose, and to enable physician to create a complete documentation of the dialysis efficiency.

1.3.2 Specific Objectives

The specific objectives are to:

1. Increase the efficiency

2. Analysis dialysis dose.

3. Monitoring for adequacy of dialysis

1.4 research organization

This thesis consists of six chapters. Chapter one is an introduction. In chapter two it has been mentioned the theoretical background. Chapter three contains a review of the literature. Chapter four explains the methodology. Then in the chapter five is the result and discussion. Finally it was the conclusions and recommendations are in chapter six.

Chapter two

Theoretical Background

2.1 Introduction:

The following chapter will provide the reader with background information and theories necessary for understanding this study.

2.2 Kidney structural:

The human body carries two symmetrically placed kidneys located in the retroperitoneal space [2]. The kidneys provide homeostasis (maintenance of metabolic equilibrium) of body composition [2]. The kidneys are important organs with many functions in the body, including producing hormones, absorbing minerals, and filtering blood and producing urine.

The kidney has several important homeostatic, hormonal, and metabolic functions that include:

- The maintenance of water and electrolyte homeostasis
- Regulation of acid-base balance in conjunction with the respiratory system
- Excretion of metabolic waste products, especially the toxic nitrogenous compounds
- Production of renin for blood pressure control and erythropoietin, which stimulates red blood cell production in the bone marrow
- Conversion of vitamin D into active form for the regulation of calcium balance

The kidney is composed of an outer cortex and inner medulla. Portions of the medulla extend into the cortex as the medullary rays, collections of straight renal tubules. The medulla contains multiple cone-shaped lobes, known as medullary pyramids. These urinary lobes are fused in the cortex. The urine drains into the renal pelvis, which is the initial part of the ureter. The hilum of the kidney is the site of entry and exit for renal artery, renal vein, and ureter [15].

2.2.1 Nephron

The nephron is the structural and functional unit of the kidney. There are about two million nephrons in each kidney. Nephrons begin in the cortex; the tubules dip down to the medulla, and then return to the cortex before draining into the collecting duct. The

collecting ducts then descend towards the renal pelvis and empty urine into the ureter [15].

The components of a single nephron include:

- renal corpuscle
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule

Different sections of nephrons are located in different parts of the kidney:

- The cortex contains the renal corpuscle, proximal, and distal convoluted tubules.
- The medulla and medullary rays contain the loops of Henle and collecting ducts.

Throughout the length of the nephron, capillaries called peritubular capillaries lie adjacent to all segments of the tubule. They originate from the efferent arteriole and are important for solute transport throughout the tubule.

2.2.2Renal Corpuscle

The renal corpuscle is responsible for the filtration of the plasma. It contains two structures: the glormerulus and Bowman's capsule. The glomerulus is a cluster of capillary loops enclosed by Bowman's capsule, which is part of the renal tubule.

Bowman's capsule has two layers:

- The visceral layer is in contact with the glormerulus, and is composed of specialized epithelial cells known as podocytes.
- The parietal layer is the outer layer, and is composed of simple squamous epithelial cells. This layer is continuous with the epithelium of the proximal convoluted tubule.

The space between the two layers is named Bowman's space, and this space contains the ultrafiltrate of plasma. The plasma has to pass through a filtration barrier of three layers to enter Bowman's space: the capillary endothelium, the podocyte layer, and their fused

basement membrane. Bowman's space is continuous with the proximal convoluted tubule [15].

Blood enters the renal corpuscle via afferent arterioles and then leaves via efferent arterioles. The part of renal corpuscle where afferent and efferent arterioles are located is known as the vascular pole. On the opposite end of the vascular pole is where the renal tubule begins and is known as the urinary pole.

Mesangial cells can also be found within the glomerulus. These cells secrete a matrix of basement membrane-like material to support the structure of the glomerulus.

2.2.3Promixal Convoluted Tubule

The proximal convoluted tubule is the first segment of renal tubule. It begins at the urinary pole of the glomerulus. This is where the majority (65%) of the glomerular filtrate is reabsorbed. The convoluted portion of the tubule leads into a straight segment that descends into the medulla within a medullary ray and becomes the loop of Henle.

2.2.4Loop of Henle

The loop of Henle forms a hair-pin structure that dips down into the medulla. It contains four segments: the pars recta (the straight descending limb of proximal tubule), the thin descending limb, the thin ascending limb, and the thick ascending limb. The turn of the loop of Henle usually occurs in the thin segment within the medulla, and the tubule then ascends toward the cortex parallel to the descending limb. The end of the loop of Henle becomes the distal convoluted tubule near its original glomerulus. The loops of Henle run in parallel to capillary loops known as the vasa recta. Recall from Physiology that the loop of Henle serves to create high osmotic pressure in the renal medulla via the counter-current multiplier system. Such high osmotic pressure is important for the reabsorption of water in the later segments of the renal tubule [15].

2.2.5Distal Convoluted Tubule

The distal convoluted tubule is shorter and less convoluted than the proximal convoluted tubule. Further reabsorption and secretion of ions occur in this segment. The initial segment of the distal convoluted tubule lies right next to the glomerulus and forms the juxtaglomerular apparatus.

2.2.6Juxtaglomerular Apparatus

The juxtaglomerular apparatus is a specialized structure formed by the distal convoluted tubule and the glomerular afferent arteriole. It is located near the vascular pole of the glomerulus. The main function of the apparatus is the secretion of renin, which regulates systemic blood pressure via the renin-angiotensin-alodosterone system. The juxtaglomerular apparatus is composed of:

- The macula densa, a collection of specialized epithelial cells of the distal convoluted tubule. These cells are enlarged as compared to surrounding tubular cells. The cells of the macula densa sense sodium chloride concentration in the tubule, which in turn reflects the systemic blood pressure.
- The juxtaglomerular cells of the afferent arterioles, which are responsible for secreting renin. These cells are derived from smooth muscles cells of afferent arterioles.
- The extraglomerular mesangial cells, which are flat and elongated cells located near the macula densa. Their function is currently unclear.

2.2.7Collecting Ducts

The terminal portion of the distal tubule empties through collecting tubules into a straight collecting duct in the medullary ray. The collecting duct system is under the control of antidiuretic hormone (ADH). When ADH is present, the collecting duct becomes permeable to water. The high osmotic pressure in the medulla (generated by the counter-current multiplier system/loop of Henle) then draws out water from the renal tubule, back to vasa recta.

2.2.8Renal Pelvis and Ureter

Numerous collecting ducts merge into the renal pelvis, which then becomes the ureter. The ureter is a muscular tube, composed of an inner longitudinal layer and an outer circular layer. The lumen of the ureter is covered by transitional epithelium (also called urothelium). Recall from the Laboratory on Epithelia that the transitional epithelium is unique to the conducting passages of the urinary system. Its ability to stretch allows the dilation of the conducting passages when necessary. The ureter connects the kidney and the urinary bladder.

2.2.9Urinary Bladder

The ureter empties the urine into the bladder. The transitional epithelium continues over the surface of this organ. The thickened muscular layers become interwoven and cannot be clearly identified at this point.

2.2.10Urethra

The urethra carries the urine away from the bladder to the outside of the body. In the male, it is joined by the genital system. The epithelium changes from transitional to stratify or pseudo stratified columnar in the urethra, and to stratify squamous in the distal end of the urethra.

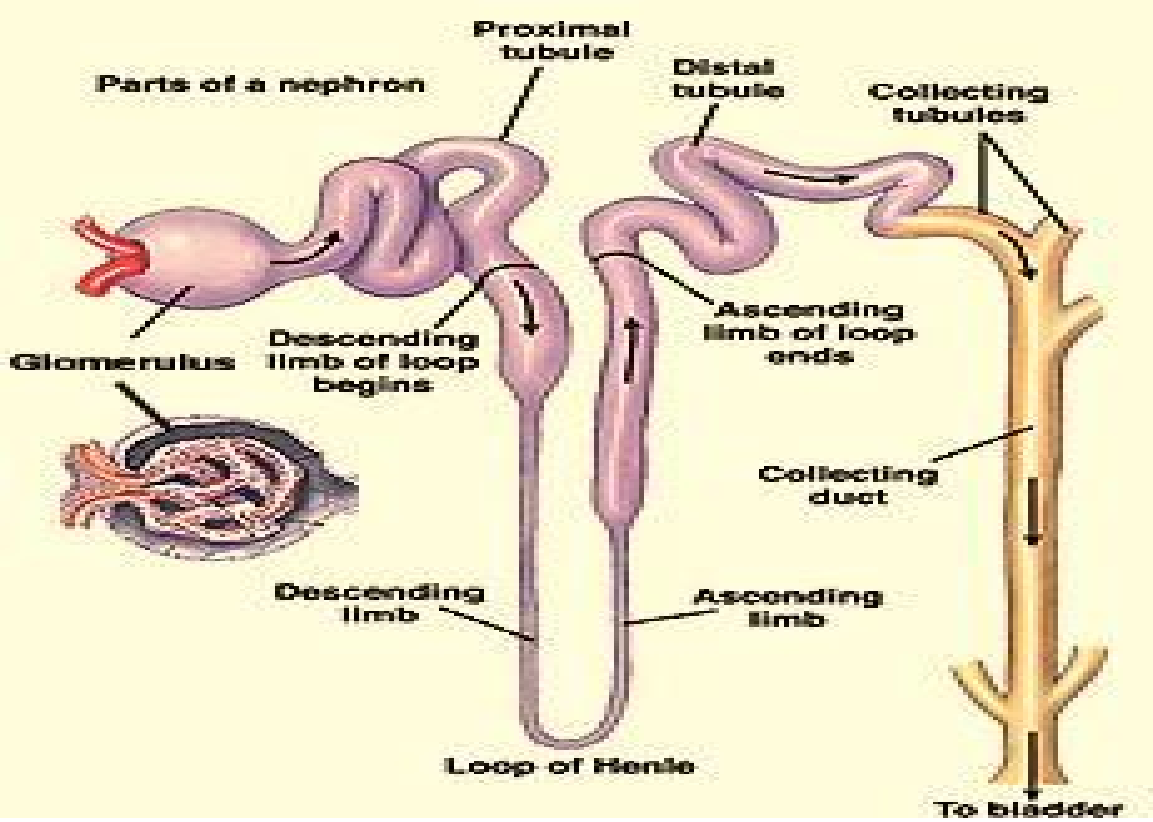

Figure (2.1) Microscopic structure of the kidney and urine

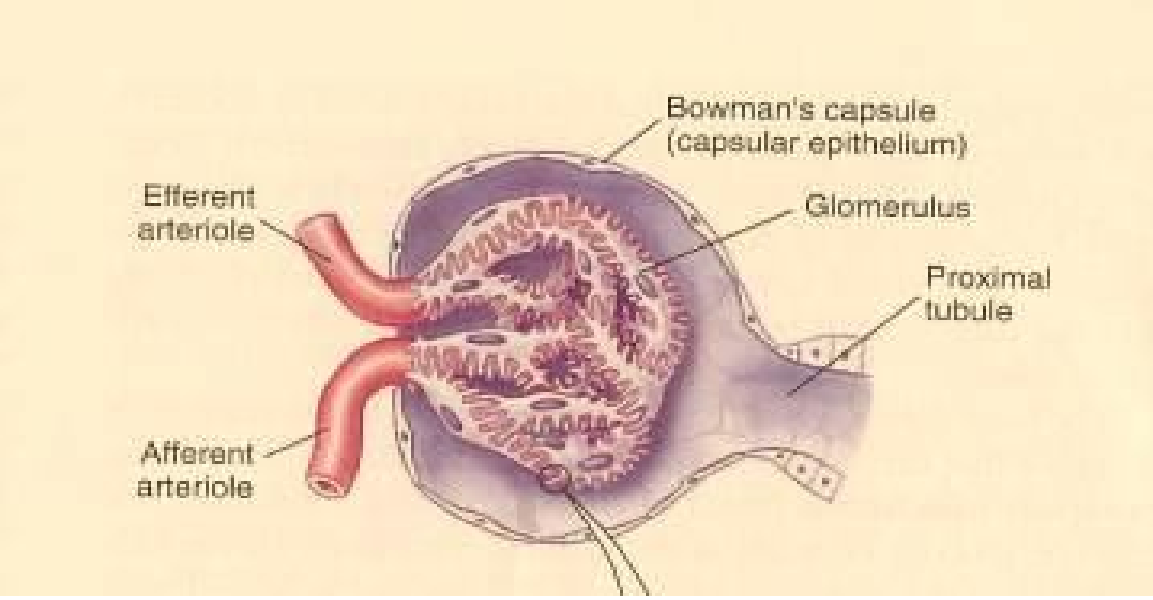

Figure 2.2Renal Corpuscle and Filtration

2.3 End Stage Rend Disease (ESRD):

End Stage rend disease can be defined as any disorder that causes a reduction of functional capacity in the kidneys resulting in the need for replacement treatment. This Functional capacity is typically measured by following the glomerular filtration rate (GFR) [2].

Renal failure is a condition where the kidney function is inadequate. As the renal function deteriorates, disorders will rapidly develop in most of the major body organs and internal systems; a syndrome commonly known as uremia [3].

Renal failure (RF) is characterized by the progressive decline in the capacity of the kidneys to eliminate toxic solutes. RF is divided into acute- (ARF) and chronic renal failure (CRF). ARF is an acute damage of the kidney tissues often reversible or partly reversible, caused by hypoxic, toxins etc. e.g. after serious trauma, surgery, intoxications. CRF usually shows a progressive decrease of GFR and is usually irreversible and related to increased blood levels of azotemic substances. CRF develops in stages during different time periods, up to decades. Only in the last stage, ESRD, is renal replacement therapy e.g. haemodialysis needed. Most people with a decrease in renal function will never reach

ESRD. It is worth mentioning that the renal function is decreased successively as a result of normal ageing. The most common causes of CRF are the primary renal diseases; chronic glomerulonephritis (of infectious or immune origin), polycystic disease, pyelonephritis (ascending infection of the urinary tract) and the secondary renal diseases; diabetes mellitus, renal arteriosclerosis e.g. due to hypertension (leading to nephrosclerosis), systemic vasculitis, amyloidosis, myeloma[1].

2.3.1Uraemia and its symptoms:

Uraemia is intoxication wrote Jonas Bergström 1985.29 Uraemia is derived from two Greek words, which mean urine in the blood. The uraemic syndrome involves almost all organs and organ systems and gives a number of symptoms, functional disturbance of enzymes, organells and cells leads to an overall change for the worse which untreated ends in coma and death. During the 1700-century, observations from Holland by Boerhaave. The uraemic syndrome is a complex “intoxication” of retention of nitrogenous waste products resulting in multifactorial problems where the disturbances in several metabolic functions are reflected in clinical problems [1].

2.3.2Urea:

Urea has been used as a marker of uraemic retention for over 100 years and its role as a marker for dialysis adequacy has been discussed and argued. Urea is an organic compound of carbon, nitrogen, oxygen and hydrogen, (NH2)2CO, and the molar mass is 60.07g/mol. The so called urea cycle is carbon dioxide, water, asparate and ammonia in a metabolic pathway which is necessary because ammonia is a common metabolic waste product mostly from the breakdown of amino acids and must be neutralized due to its toxicity. Urea is the most accepted uraemic marker, but there is a controversy as to its role in the uraemic intoxication37. Urea seems to be a surrogate marker and representative for the removal of other solutes with impact on morbidity and survival [1].

2.4 Dialysis machine:

Dialysis machines are artificial kidneys that perform most, but not all, kidney functions for patients who have permanent or temporary renal failure. The machines use hemodialysis to cleanse the blood and balance its constituents. With this process, the

patient's blood is circulated through the machine where it is filtered and balanced for electrolytes, pH, and fluid concentration before being returned to the patient. One common problem with renal failure is water retention, so it is common for the process to remove several pints of fluid from the patient's blood [18].

There are two basic classes of dialysis machines: clinical units, which are commonly cabinet-size machines operated by trained technicians; and home-use dialysis machines, which are smaller and sometimes portable.

A machine used in dialysis that filters patient blood to remove excess water and waste products when the kidneys are damaged, dysfunction, or missing.

2.4.1Machine has three parts:

1. Hydraulic part

2. Modules part.

3. Screen or monitor part.

Control in hydraulic is volume control

The main function of heamodialysis machine is preparing dialysis solution called (dialysate), it has conductivity and temperature adjusted, and this process in hydraulic part.

Processing of clearance in artificial kidney (dialyzer) exist when the blood pump draw the blood from patient to dialyzer and return to the patient throw air detector (block air to return to patient) and monitoring the pressure of venous (return blood), all those process in modules part.

Control and monitoring of dialysis process exist in screen part.

The equipment also already has contained comprehensive self-test and fault-indication capabilities, which require additional circuitry and the use of components that include self-test features [18].

2.4.2Extracorporeal Circuit:

The patient's blood is continuously pumped from an artery, a large vein, or a surgically modified vein to allow high blood flow rates. Its pressure is monitored both upstream and downs-tream from the peristaltic blood pump. Before the blood enters the dialyzer, heparin is added to prevent clotting. A syringe pump is used to deliver the heparin at a precisely controlled rate.

The blood then enters the dialyzer where it passes across a large-surface-area, semipermeable membrane with a dialysate solution on the other side. A pressure gradient is maintained across the membrane to ensure the proper flow of compounds out of and into the blood. After cleansing and balancing within the dialyzer, the blood is passed through an air trap to remove any air bubbles before it is returned to the patient. An air bubble sensor ensures that no air bubbles remain.

Blood-pressure, oxygen-saturation, and sometimes hematocrit levels (blood cell concentration) are monitored for proper operation of the machine and to ensure patient safety. For maximum effectiveness, fresh dialysate is continually pumped through the dialyzer during operation [18].

2.4.3Dialysate Circuit:

In clinical settings, dialysate is usually premixed to the proper concentration for direct use. The main components of the dialysate circuit include

• Deaeration

• Dialysate proportioning and conductivity

• Dialysate formulation

• Monitors, alarms, and conductivity

• Ultrafiltration: Volumetric and flow-sensor control

• Dialysate disinfection and rinsing

• Emergencies

Once pure product water has been generated, bicarbonate and acid solutions are mixed with water to form dialysate solution, mixing or proportioning may be done by the individual machine or centrally in a dialysis unit, Several components of proportioning ensure safe dialysate that is monitored by a series of alarms, pumps, and monitors, Fluid ultrafiltration occurs by volumetric or flow sensor controllers, Disinfection prevents bacterial overgrowth [19].

2.4.4Conductivity

• Conductivity is the amount of electrical current conducted through a dialysate and reflects electrolyte concentration

• A constant voltage is applied across two electrodes 1 cm apart in the dialysate flow. If the concentration of electrolytes changes, the voltage will change

• Conductivity should be between 12–16mS/cm (millisiemens per centimeter).

The greater the number of ions, the greater the conductivity of the dialysate

• Conductivity can be affected by temperature, or concentration of acid to base

• Alarms will stop dialysate flow if conductivity is out of limits [19].

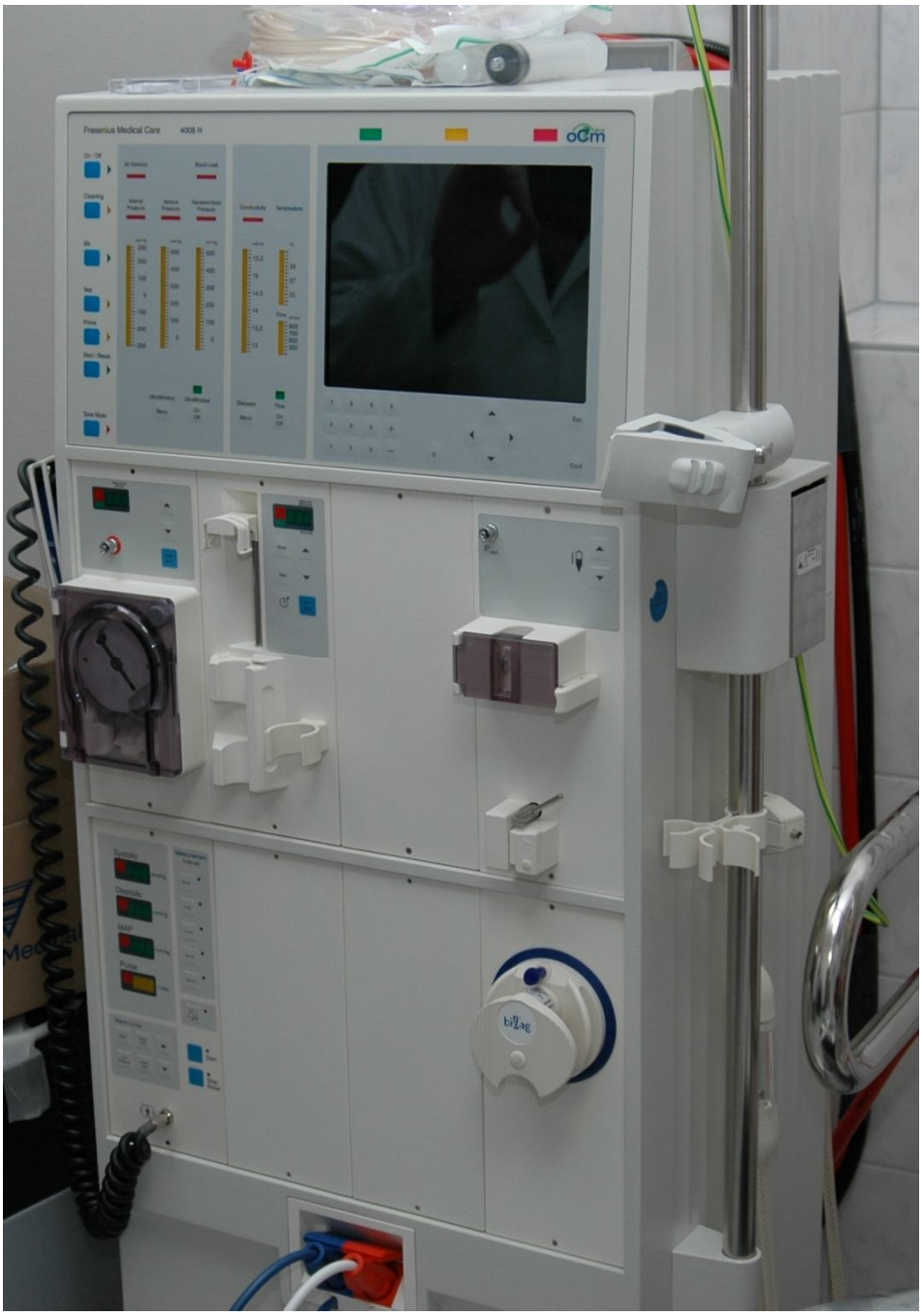

Figure (2.3) heamdialysis machine

2.5 Hemodialysis (HD):

The first successful haemodialysis treatment in human was reported in 1944. Haemodialysis as a routine treatment for RF was initiated in the1960s and has become a main treatment for ESRD.Hemodialysis is the most common extracorporeal treatment method for patients with renal failure [3]. The Hemodialysis prescription is designed to return the patient to homeostasis by removing water, waste metabolites, excess electrolytes and re-establishing the acid\base balance. The Nephrologists approximates the patient's ideal weight and body water volume. The mathematical description of hemodialysis (HD) includes two parts one) explanation of the exchange between patient's blood and dialysate fluid across a semi permeable membrane of the dialyzer, and two) characterization of the solute removal from the patient. The solute transport across the dialyzer membrane depends on the difference in hydrostatic pressure and solute concentration gradients between both sides of the membrane and also on the permeability of the membrane to the solute [16].

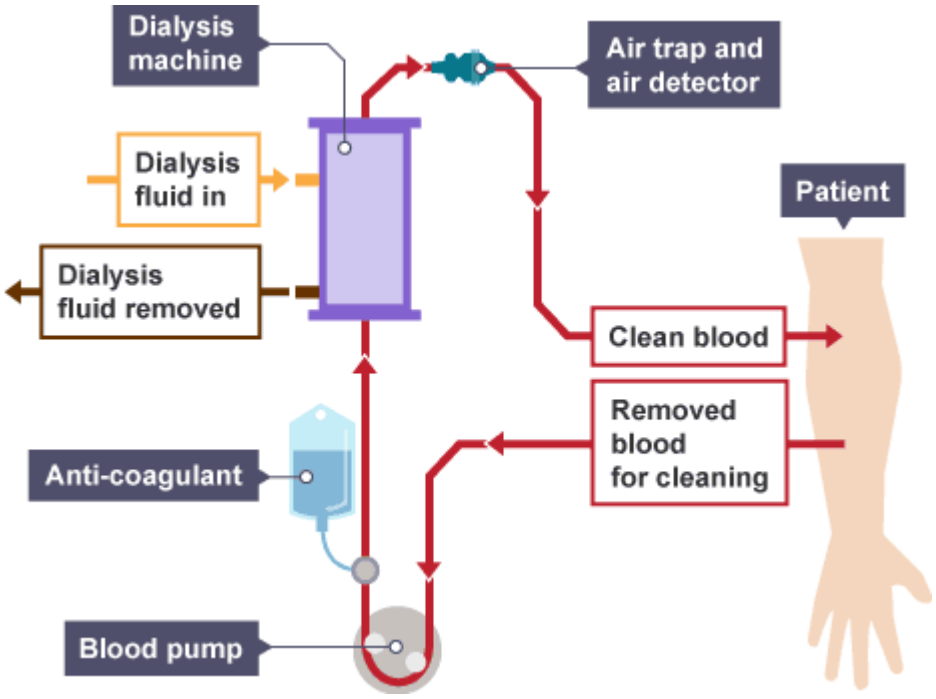

Figure2.4 the simple flow diagram of dialysis process

In a haemodialysis unit it is necessary to have a water treatment system, which produces clean water for the dialysis machines. Drinking water is normally used for the production of dialysis water, called RO-water (RO = reverse osmosis). The drinking water is passing through several steps of filters before it enters into the dialysis machine. The dialysis machine produces the dialysis fluid, called dialysate, by mixing RO-water, with electrolytes and bicarbonate [1].

The fluid that is mixed by the dialysis machine is called dialysate. The dialysate is pumped normally with a flow rate of 500 ml/min (can be adjusted) through the dialyser at the opposite side, to the patients' blood, of the semipermiable membrane. The compositions of the dialysate create a concentration gradient to promote diffusion over the membrane. The pure dialysate not containing waste products from the patient has a composition with the purpose to normalizing the plasma water, electrolytes, pH, and waste solute removal, in the patient. Table (2.1) shows the range of common solute concentration in dialysate and in serum (healthy and uraemic), respectively.

Table 2.1 the concentration of solutes in dialysate compared to serum

Solute	Concentration in the dialysate (mmol/L)	Concentration in serum (mmol/L) healthy (uraemic)
Sodium	135-145	136-146
Potassium	0-4	3.5-5.0 (4.5-6.5)
Calcium	1.0-2.0	2.2-2.6
Magnesium	0.25-1.0	0.7-1.1
Clorides	98-112	98-106
Bicarbonate	27-38	22-28
Glucose	0-11	3.3-5.6
Acetate	2.5-10	<0.1
Creatinine	0	0,6- 1,2 (3.5-30)
Urea	0	15-45 (100-500)

2.5.1Transport of substances during haemodialysis:

The primary goal of dialysis is to prevent the accumulation of toxic solutes in the patients' tissues by removing them from the blood. The removal of solutes from the blood compartment decreases the concentration of solutes, and sets up tissue to blood gradients all through the body that refill the blood compartment with solutes. The degree of each gradient is dependent on properties of both the membrane and the solute behaviour, for example transport rates over the membrane of the solute or solute mobilization from tissue in the body. The dialyser removes the solute that is the normal marker, urea, rapidly. The main transport mechanism of waste solutes during HD is diffusion over a semipermiable membrane in the dialyzer, and it is in the nature of the diffusion process, that a higher gradient gives higher diffusion rates, which means that the diffusion is highest at the beginning of the dialysis treatment [1].

Table 2.2 few molecules and their molecular weight

Substance	Molecular weight in Dalton (D)
Albumin	69 000
β2-microglobulin	11 800
Uric acid	168
Creatinine	113
Phosphate	96
Urea	60
Calcium	40
Potassium	39
Sodium	23
Bicarbonate	61
Water	18

2.6 Transport Mechanisms:

There are three different types of physical transport mechanism behind dialysis: diffusion, osmosis and ultra filtration (convection) [3].

2.6.1 Diffusion:

Diffusion is the physical process in which dissolved solutes move from an area of high solute concentration, through a semi-permeable membrane, to another area of lower solute concentration[3] .The driving force of the process is the concentration gradient, and the transport continues until equilibrium is reached and the solute concentration is the same everywhere.

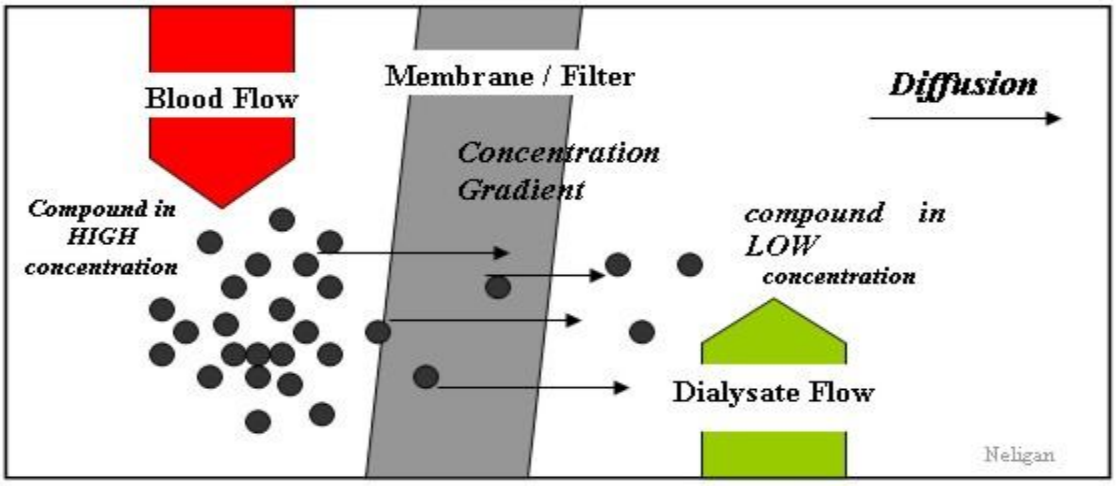

Figure (2.5) Diffusion

2.6.2 Osmosis:

Osmosis is the net movement of water across a selectively permeable membrane driven by a difference in the amounts of solute on the two sides of the membrane. In dialysis, this refers not to water movement across the hemodialyzer membrane, but across cell membranes within the body-either from within the red cells to the blood plasma.

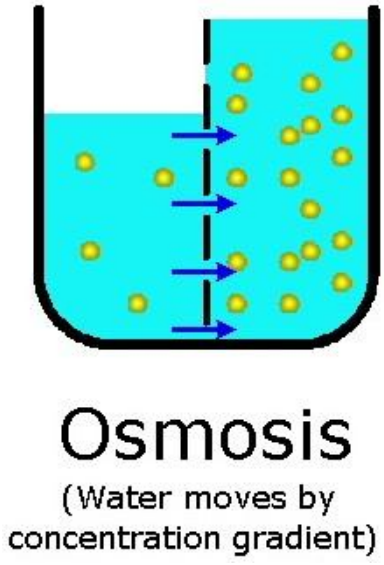

Figure2.6The Osmosis

2.6.3 Ultra filtration:

Ultra filtration (UF) is a type of membrane filtration in which hydrostatic pressure forces a liquid against a semi permeable membrane. A semi permeable membrane is a thin layer of material capable of separating substances when a driving force is applied across the membrane. This process was known as convection.

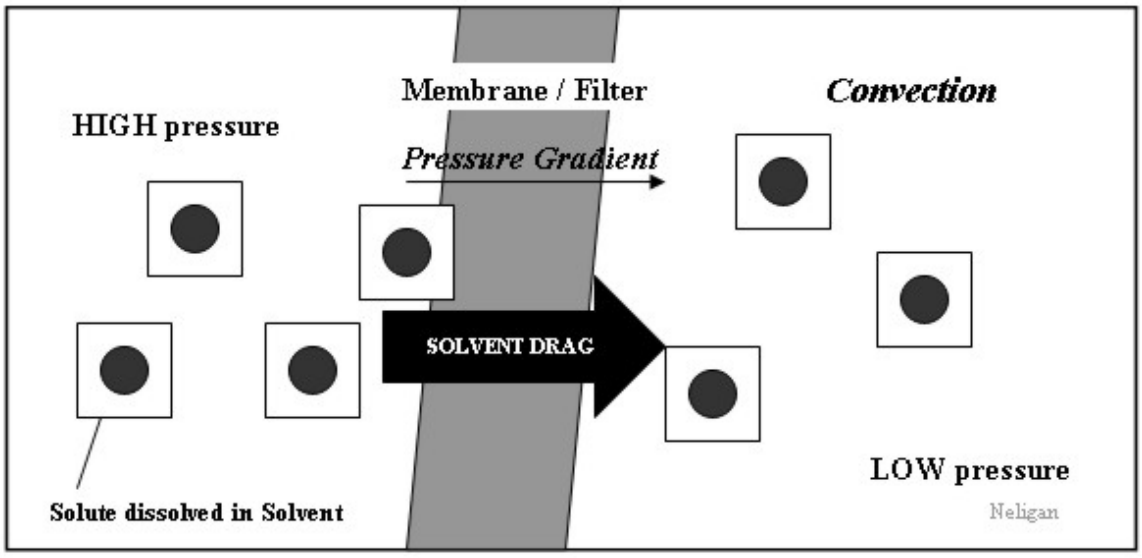

Figure 2.7The ultafiltration

2.7 Hemofiltration:

Hemofiltration is a similar treatment to hemodialysis, but it makes use of a different principle. The blood is pumped through a dialyzer or "hemofilter" as in dialysis, but no dialysate is used. A pressure gradient is applied; as a result, water moves across the very permeable membrane rapidly, "dragging" along with it many dissolved substances, including ones with large molecular weights, which are not cleared as well by hemodialysis. Salts and water lost from the blood during this process are replaced with a "substitution fluid" that is infused into the extracorporeal circuit during the treatment.

2.8 Hemodiafiltration (HDF):

Hemodiafiltration (HDF) is the combining of hemodialysis and hemofiltration in one process.

2.9 Dialysis dose:

The dialysis dose can be defined as the quantity of dialysis treatment delivered for a given period of time. In general the dialysis dose is measured by the comparison between the baseline and final concentration of defined substance in the blood of the patient. The more efficient the dialysis session, the greater the reduction of this given substance is [6].

Quantification of the dialysis dose is an essential element in the management of chronic hemodialytic treatment because the adequacy of the dose has a profound effect on patient morbidity and mortality [4]. The most useful and widely applied index to prescribe the dialysis dose (as well as to assess the dose which is actually delivered) is the Kt/V formula. It is now well recognized that an adequate delivery of hemodialysis (HD) dose (as measured by Kt/V derived from urea reduction) is a crucial determinant in clinical outcome of chronic HD patients. This requires both prescription of an adequate dose of HD and regular assessment that the delivered treatments are also adequate. The most important resource of dialysis efficiency is the delivery of solute by blood flow. The relation between blood flow and clearance reaches a plateau once clearance becomes surface dependent [17].

Mass transfer relationships describe the movement of mass. These relationships are applied to hemodialysis to measure dialysis dose. Dialysis is necessary to remove waste products from the blood. One waste product is urea, but urea itself is not very toxic, but its level is suggested to represents the level of many other waste products that built up in the blood when kidneys fail. Two urea-based parameters are generally used to assess dialysis adequacy clinically today, also recommended by national and international guidelines, namely urea reduction ratio (URR) and Kt/V. Twenty years ago dialysis adequacy was equal to Kt/V65 but today, parameters based on urea clearance are only one component of dialysis adequacy. “Adequate dialysis” should also involve other parameters considered in the care of dialysis patients such as volume status, blood pressure control, nutrition, and anaemia correction [1].

2.9.1 Standard methods of determination of the dialysis dose:

2.9.1.1\ Urea Reduction Ratio (URR):

A simple and commonly-used method of determining the dose of dialysis is the calculation of the Urea Reduction Ratio (URR). This involves a direct comparison of pre- and postdialytic urea concentrations and shows the percentage reduction of the urea concentration during dialysis treatment.

$$\boldsymbol{URR = (1 - \frac{Cpost}{Cpre})} \qquad \textbf{(2-1)}$$

Cpost: postdialytic urea concentration/Cpre: predialytic urea concentration

In view of the simplicity of the method, URR is frequently used to determine the dose of dialysis, despite the fact that the method has an in-built analytical weakness which may cause inaccurate results. In contrast to other methods, the URR method does not take into account that urea is also removed from the blood by ultrafiltration [6].

2.9.1.1.1 Relation to URR

The URR or Urea reduction ratio is simply the fractional reduction of urea during dialysis. So by definition, URR = 1 -C/C_0. So 1-URR = C/C_0. So by algebra14, substituting into equation (2-8) above, since ln C/C_0 = - ln C_0/C, we get:

$$\boldsymbol{\frac{K.t}{V} = -\ln(1 - URR)} \qquad \textbf{(2-2)}$$

Sample calculation:

Patient has a mass of 70 kg (154 lb) and gets a hemodialysis treatment that lasts 4 hours where the urea clearance is 215 ml/min.

K = 215 mL/min

t = 4.0 hours = 240 min

V = 70 kg × 0.6 L of water/kg of body mass = 42 L = 42,000 mL

Therefore:

$Kt/V = 1.23$

This means that if you dialysis a patient to a Kt/V of 1.23, and measure the post dialysis and predialysis urea nitrogen levels in the blood, then calculate the URR, then -ln (1-URR) should be about 1.23.

2.9.1.2\Determination of Kt/V:

The formula Kt/V, which is the most commonly used index of the adequacy of the dialysis treatment, is a mathematical representation involving the blood volume which has been completely cleared of urea during a specified dialysis and the urea distribution volume of the patient requiring detoxification. Single-pool KT/V overestimates the removed amount of urea because of the postdialysis urea rebound, i.e., a fast postdialysis increase in urea concentration in plasma, which is a compartmental effect; therefore, the equilibrated KT/V (eqKT/V), estimated by the Daugirdas formula, was introduced to clinical practice [16].

As well as being used as a diagnostic parameter in renal function tests, the term "clearance" is also used in renal replacement therapy. The primary parameter used to determine the volume of blood which has been purified during treatment is the effective in-vivo clearance Keff (mL/min) 42. Clearance is defined as the (hypothetical) volume of blood which has been totally "cleared" of a given substance each minute;

Effective dialysis time t is the actual duration of diffusive blood detoxification (time of dialysis fluid flow in the dialyser with the blood pump operating). Interruptions to the dialysis treatment for therapeutic or technical reasons are considered in the effective dialysis time. The urea distribution volume V is equivalent to the total body fluid, consisting of the proportion of water in blood (7 %) as well as the interstitial (31 %) and intracellular volume compartments (60 %). Upon commencement of dialysis, urea is homogeneously distributed throughout the body; hence, more than 90 % of the urea which accumulates in the human body is not present in blood, but in the interstitial and intracellular volume compartments. Thus, only with continuous diffusion of urea from these compartments into the blood and further transport into the extracorporeal

circulation is the largest proportion of urea present in the body made available for dialysis [6].

2.9.1.3 Rationale for *Kt*/*V* as a marker of dialysis adequacy:

The human body has a large number of physical compartments. The mathematical description of body is usually simplified by considering it as single pool (one compartment) or as a few interconnected pools. In a multicompartment model, the solute and fluid transport between body spaces should be described. The one compartment model assumes that the body acts as a single, well mixed space and is characterized by: 1) high permeability of cells to the solute being modeled, 2) rapidly flowing blood that transports the solute throughout a totally perfused body. The assumptions of one compartment model for urea or creatinine during dialysis are valid as long as the flux of solute into and out of cells is faster than the flux of solute from the extracellular space accessible to dialysis. When the intercompartment flow between body compartments is too slow and constrained in comparison with the solute removal rate from the perfused compartment, then the solute behavior increasingly deviates from that of one compartment kinetics [16].

The relationship between Kt/V and the concentration of urea C at the end of dialysis can be derived from the first-order differential equation that describes exponential decay and models the clearance of any substance from the body where the concentration of that substance decreases in an exponential fashion [14]:

$$\boldsymbol{V\frac{dC}{dt}} = \mathbf{-K.C} \qquad \textbf{(2-3)}$$

Where

.C is the concentration [mol/m^3]

.t is the time [s]

.K is the clearance [m^3/s]

.V is the volume of distribution [m^3]

From the above definitions it follows that $\frac{dy}{dx}$is the first derivative of concentration with respect to time, i.e. the change in concentration with time.

This equation is separable and can be integrated as follows:

$$\int \frac{dC}{C} = \int - \frac{K}{V} dt \qquad \textbf{(2-4)}$$

After integration,

$$\ln(C) = -\frac{K.t}{V} + const \qquad \textbf{(2-5)}$$

Where

Const is the constant of integration

If one takes the antilog of *Equation (2-5)* the result is:

$$C = e - \frac{K.t}{V} + const. \qquad \textbf{(2-6)}$$

Where

e is the base of the natural logarithm

By integer exponentiation this can be written as:

$$C = Co\ e - \frac{K.t}{V}. \qquad \textbf{(2-7)}$$

Where

C_0 is the concentration at the beginning of dialysis [mmol/L] or [mol/m^3].

The above equation can also be written as

$$\frac{K.t}{V} = ln\frac{Co}{C} \quad \textbf{(2-8)}$$

2.9.1.4\ Quantification based on Conductivity Kinetics:

An Instantaneous measurement of metabolic waste transfer during dialysis would allow for improved quality assurance and enable automated control system to be integrated with the dialysis machine. Conductivity Technology is currently use to control the conductivity levels of the dialysate solution before entering the dialyzer. The Conductivity of the dialysate solution is usually held constant for the dialysis session. There is some clinical experience with varied conductivity during the dialysate session from a high value (1 5.0 µS/cm) at the start to a low value (1 3 .5- 14 µS/cm) at the end of the session. This section details the development of a mode1 to capitalize on this technology and directly calculate an instantaneous Kt/V.

The development of this model is the work of Dr. L.J. Garred [13].

2.10 The Online Clearance Monitoring (OCM): Overview of existing method:

Despite the fact that removal of larger molecular weight uremic toxins are very important for the long-term outcome in chronic dialysis, the most widely used dose parameter in dialysis is based on small solute removal. The dose parameter, is a measure of how effective a dialysis treatment is, and among the small solutes, urea clearance (K) is the most common efficiency parameter4. Multiplying K with the treatment time (t) and normalizing it to body size with the urea distribution volume (V), gives the normalized dialysis dose Kt/V [6]. Although the validity of Kt/V is not without controversy, it is today recognized as an important quality control parameter in chronic dialysis.

Today, some dialysis machines have a built-in function it is possible to easily monitor these essential parameters without additional costs during regular ONLINE

Haemodiafiltration in either pre- or post-dilution mode, and during haemodialysis treatments.

That is commercially available and is, in 4008S classic Fresenius Medical Care It provides automatic intradialytic measurement of the delivered dialysis dose Kt/V, the effective in-vivo urea clearance, the accumulated cleared plasma volume Kt and the plasma sodium concentration of the patient [6]. To achieve the objective of developing a low cost method of monitoring clearance, it was necessary to move away from the cost-intensive concept of enzymatic urea analysis. In searching for an alternative, a substance was considered which is present in large quantities in the dialysis concentrations can be measured by the sensors .By means of indirect determination of ion concentrations in the haemodialysis solution (measurement of conductivity at the inflow and outflow of the dialyzer) it is technically possible to determine the diffusion profile of sodium ions across the dialysis membrane and thus calculate the dialysance or ionic clearance (D). On the basis of the dialysance of sodium ions, the “diffusibility” of urea through the membrane (permeability) and thus urea clearance can be determined [6].

Chapter three

Literature review

Car1 D. Goodwin [2] in the subject of this thesis is the kinetic modeling of spent dialysate conductivity. Measurement of hemodialysis treatment adequacy is essential to monitor quality assurance for today's growing dialysis population. The universally accepted measure of hemodialysis dose is kt/v. kt/v above 1.2 has been shown to reduce patient morbidity and mortality. Currently, kt/v is calculated from urea kinetic modeling using predialysis and postdialysis blood samples. A Clinical study to test this model was conducted with 14 patients treated by maintenance dialysis in the renal unit at Thunder Bay Regional Hospital, McKellar site.

Dialysate conductivity data were collected from 85 dialysis sessions on an Integra hemodialysis machine (Hospal- Gambro Canada) equipped with conductivity sensors in both the inlet and outlet dialysate streams [2].

In their study, a simple model of dialysate conductivity kinetics was developed and expressed as equation (3-1). It was proposed that this model might allow direct assessment of dialysis dose, Kt/V, from the outlet dialysate conductivity - time profile during a period of constant inlet dialysate conductivity [2].

$$\boldsymbol{ln|Cdi - Cdo| = ln|Codi - Codo| - \frac{D}{V}t} \qquad \textbf{(3-1)}$$

JOHNNY LIEN [3] with of this study is conductivity measurements of dialysis efficiency in Predilution HDF treatments. During dialysis treatments, there is an interest of measuring the dialysis efficiency for each treatment3. An easy method has been developed and is based on measuring the conductivity of the dialysis fluid. Today this method exists in the dialysis machines for standard hemodialysis (HD) treatments, and for the so called postdilution hemodiafiltration (HDF) treatments at Gambro Lundia AB [3].

Measurements were performed on the dialysis machine during simulated treatments, and modification of the existing method was based on the data from these measurements. The results indicate that the method also works for predilution HDF, without requiring any modifications of the existing algorithms [3].

Judging from the results, the existing Diascan feature also works for predilution HDF mode, without requiring any modifications of the algorithms.

Results from comparison between the postdilution and the predilution clearance-values, also confirms the accuracy of the theoretical formula given by equation (3-2).

$$\boldsymbol{K = \frac{Qb.Qd - \int.(Qb - Quf).(Qd + Quf)}{Qd - \int.(Qb - Quf)}} \qquad \textbf{(3-2)}$$

Chapter Four

Methodology

4.1 Equipment and materials:

In this thesis the machine is **4008S** classic from Fresenius Medical Care Company and made at Germany, also the materials from the Fresenius Medical Care it is:

- -Heamdialysis machine 4008S.
- -Acetate concentrates (SK.F).
- -Bicarbonate powders.
- -Blood line sets.
- -Dialyzer size F4, F5 and F6.

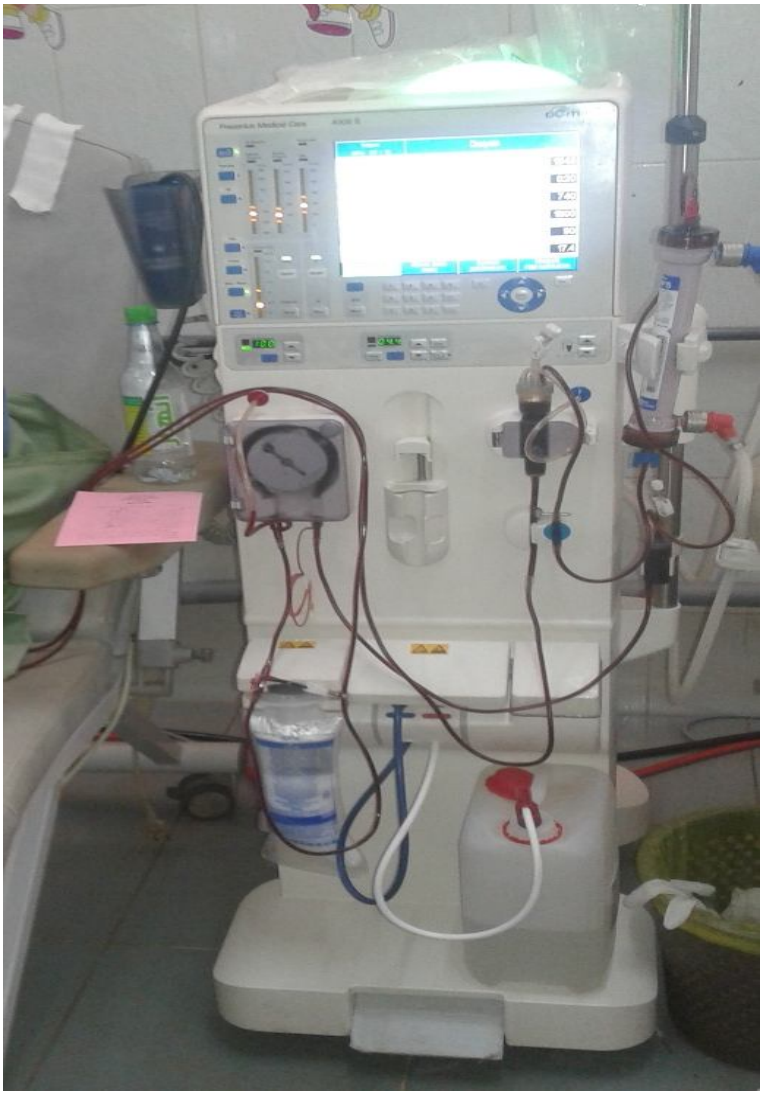

Figure (4. 1) Machine 4008S classic

4.2 Online Clearance Monitoring

Implementation the application of online clearance monitoring (OCM) it is a standard feature integrated in the Fresenius Medical Care. It provides automatic intradialytic measurement of the delivered dialysis dose Kt/V, the effective in-vivo urea clearance, the accumulated cleared plasma volume Kt and the plasma sodium concentration of the patient. The dialysis dose determined by the Online Clearance Monitoring (OCM) is equivalent to a single-pool Kt/V (spKt/V).

Those parameters work on online clearance monitoring (OCM).

1. Dialysis time (t).
2. The gender.
3. The age.
4. The height.
5. The weight.
6. The urea distribution volume (v).

In figure (4.2) is show online clearance monitoring (OCM)

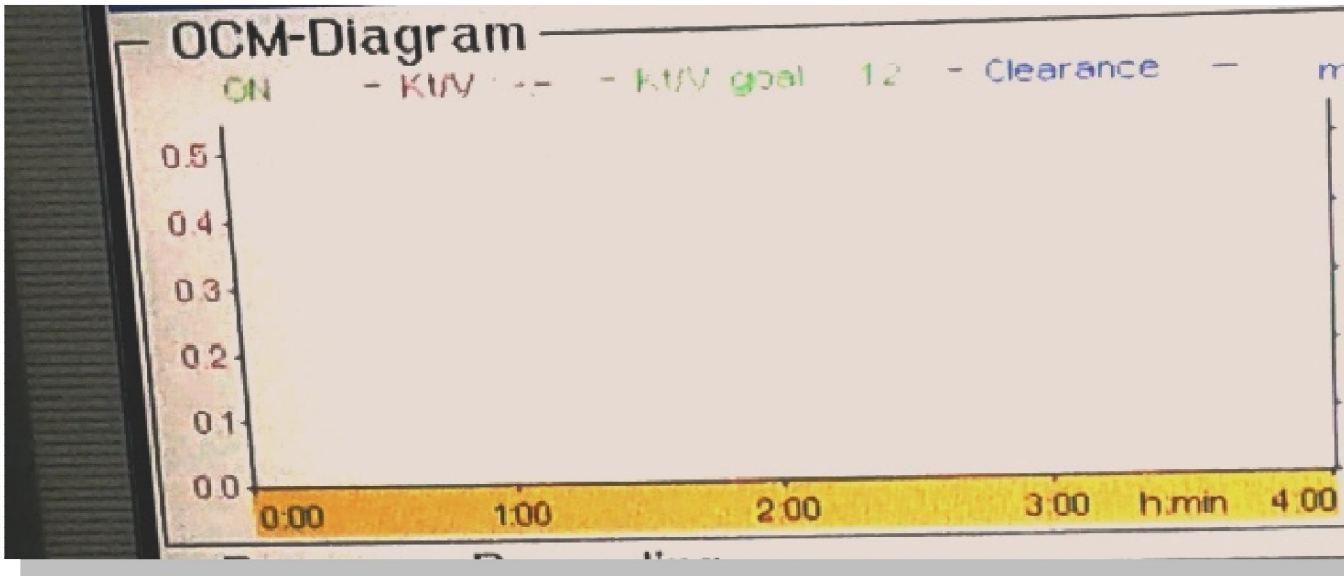

Figure (4. 2) the OCM

4.3 The study of patient:

In this study ten patients were used as samples for study, six of them were male and four were female. The patients were receiving medical treatment at Soba University Hospital. The Online Clearance Monitoring (OCM) was used for five week the total of sessions was (86) sessions.

A comparison between the Online Clearance Monitoring (OCM) and the conventional way of urea clearance, which were used the method of pre urea investigation and post urea investigation. The efficiency of dialysis was achieved by using the following formula.

$$SP^{\frac{KT}{V}} = -\ln\left(\frac{Cpost}{Cpre} - 0.008t\right) \qquad (4-1)$$

It was:

In: log

C post : post urea concentration

C pre: pre urea concentration

t: time of dialysis session

Chapter Five

Result and discussion

5.1 Results:

In the first experiment for patient (A) who has seven sessions in five weeks,

In the monitoring the first patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) was reached in 3 hours and it is better for efficient dialysis.

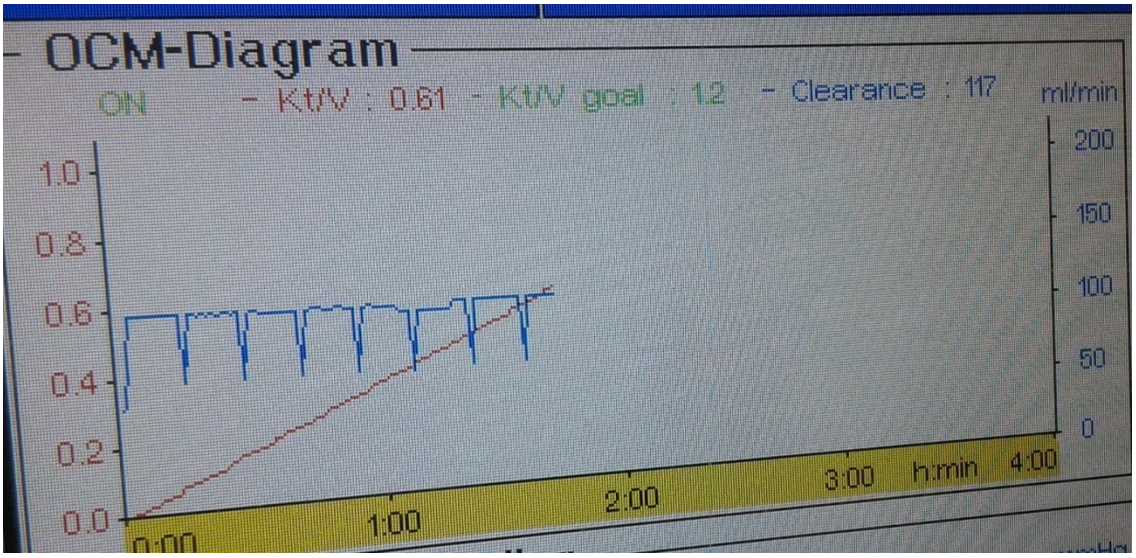

Figure (5-1) the OCM in the mid time

In the anther session it has decrease the time to 3 hours and the result was best

In the second experiment for patient (B) also who has seven sessions in the five week

In the monitoring the second patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) was reached in end of dialysis.

In the anther session it had changed some parameters to increase the efficient so increase the blood flow and the result the target of goal (kt/v) (1.2) was reached before the end of dialysis half hour.

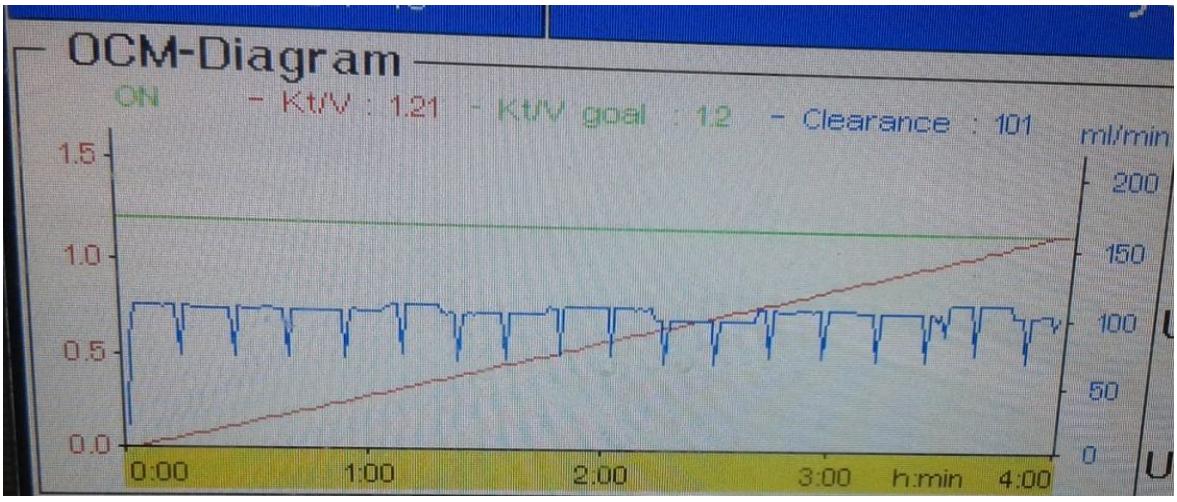

Figure (5-2) OCM in the end of dialysis

In the third experiment for patient (C) who has ten sessions the five weeks.

In the monitoring the third patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) did not reach the end of dialysis it is (1.12).

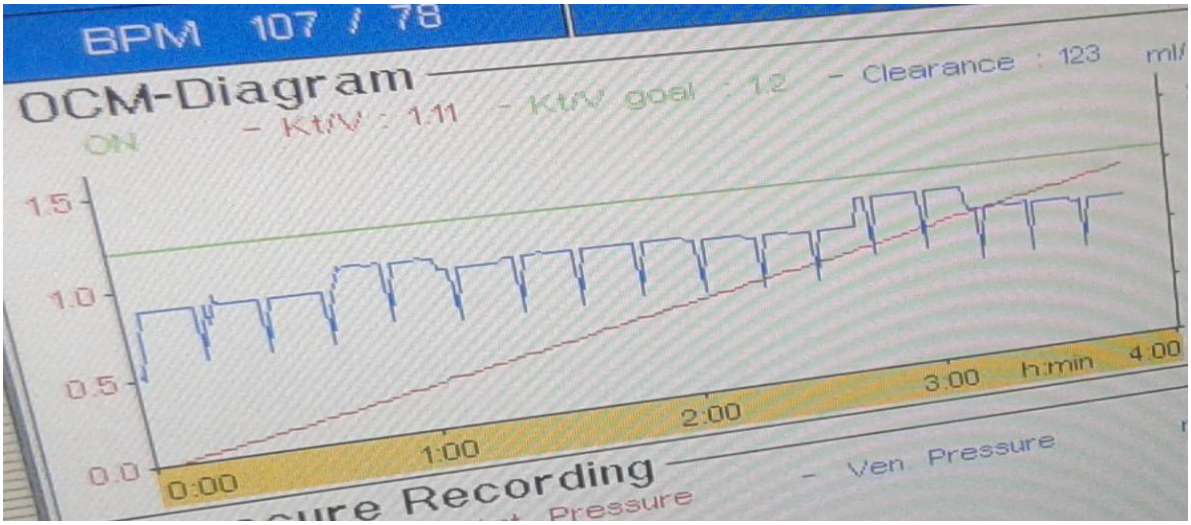

Figure (5-3) the OCM before end the dialysis

Some parameters had been changed to increase the efficient but it was not reached because the patient with catheter not fistula to control the blood flow for that it lost time by stop and start.

In the 4th experiment for patient (D) who has thirteen sessions the five weeks

In the monitoring the 4th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) reached in end of dialysis.

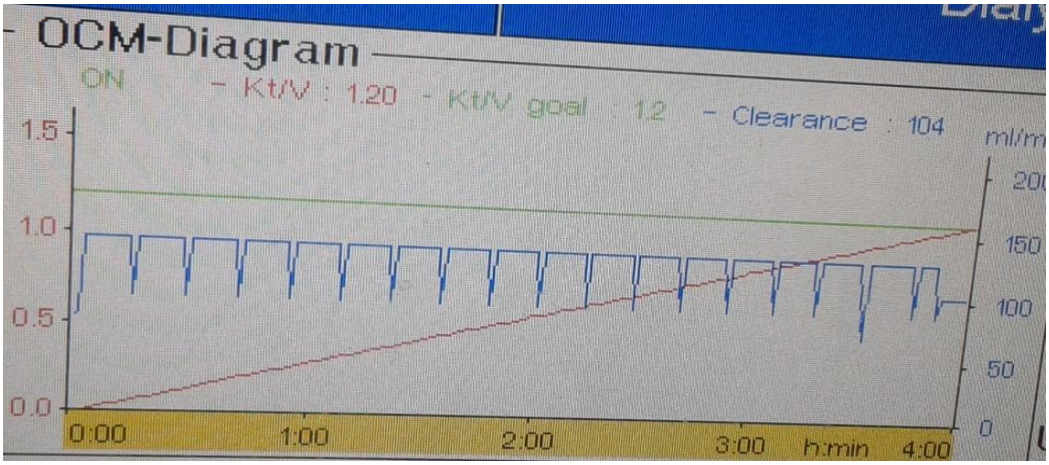

Figure (5-4) OCM in end of dialysis

In the 5th experiment for patient (E) who has eleven sessions the five weeks.

In the monitoring the 5th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) reached in time 3hours and 20 minute it is better for efficient dialysis.

In another session adjust the time in 3hours and half the target of goal (kt/v) (1.2) reached in end of dialysis.

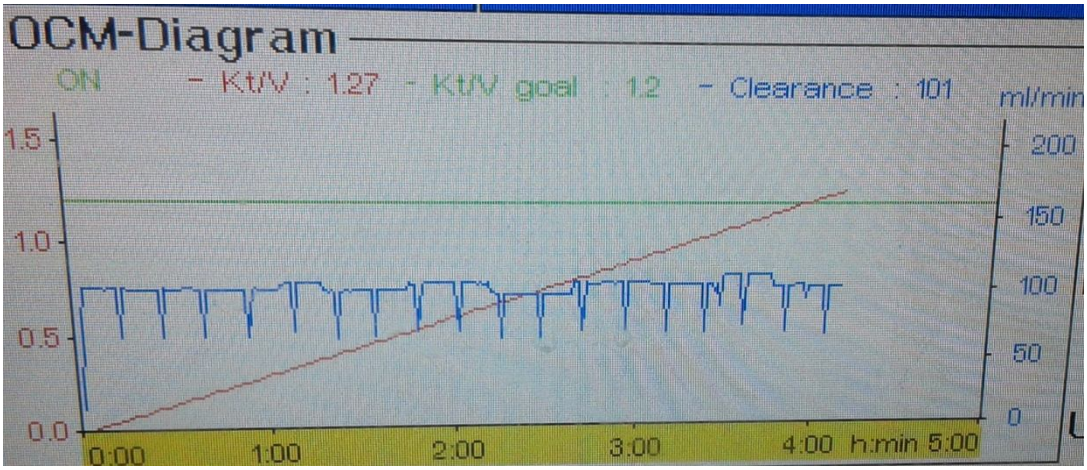

Figure (5-5) OCM before end of dialysis

In the 6th experiment for patient (F) who has eight sessions the five weeks.

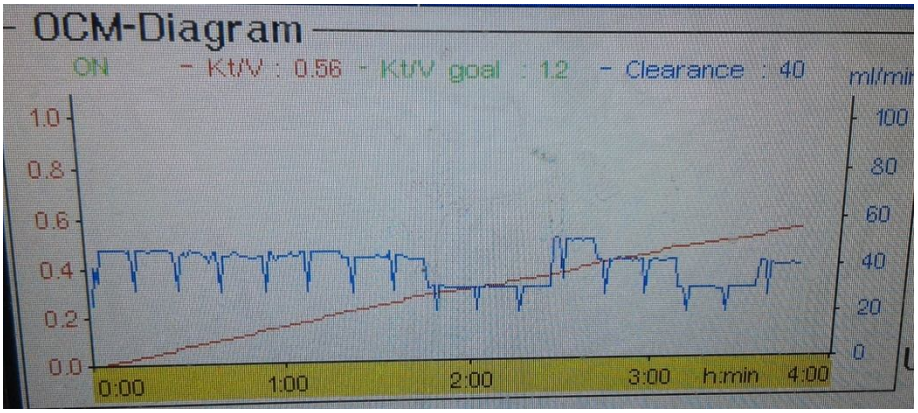

Figure (5-6) OCM before end of dialysis

In the monitoring the 6th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) did not reach in end of dialysis it is reach (1.12).after look for the patient they have many problem for that not stable .

In the 7th experiment for patient (G) who has six sessions the five weeks.

In the monitoring the 7th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) reached in end of dialysis.

In the 8th experiment for patient (H) who has twelve sessions the five weeks.

In the monitoring the 8th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) reached in 3.10 hours and it was very good for efficient dialysis.

In the 9th experiment for patient (J) who has nine sessions the five weeks.

In the monitoring the 9th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours it has shown the target of goal (kt/v) (1.2) reached in time 3.50hours it was best for efficient dialysis.

In the 10th experiment for patient (K) who has five sessions the five weeks.

In the monitoring the 10th patient when the Online Clearance Monitoring (OCM) on work and the time of session is 4hours I saw the target of goal (kt/v) (1.2) is reach in end of dialysis .

In the figure (5.3) the window of online clearance monitoring (OCM) the vertical line the OCM and the horizontal line is the time of dialysis.

They are many lines with difference colors the red line is the OCM, the green line is the target of goal (1.2) and the blue line is for clearance.

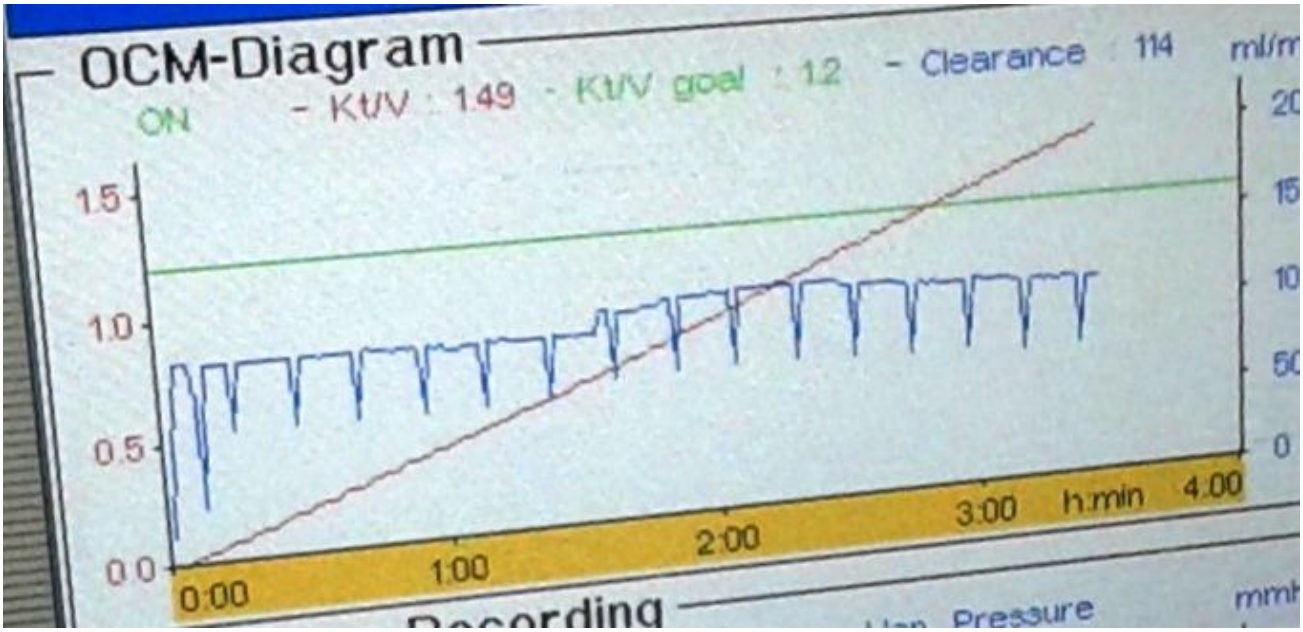

Figure (5. 7) the (OCM)befor end of dialysis

Table (5.1) shown efficiency by conventional

Patient name	sex	Pre urea concentration	post urea concentration	Ratio (kt/v)
(A)	male	115	35	1.3
(B)	female	148	47	1.25
(C)	male	116	35	1.31
(D)	male	135	43	1.25
(E)	female	107	30	1.39
(F)	male	153	56	1.09
(G)	female	111	36	1.23
(H)	male	108	33	1.29
(J)	female	130	38	1.35
(K)	male	140	45	1.24
mean				1.27

Table (5-2) patient's statistics and efficiency by online clearance monitoring

Patient name	sex	Dry weight KG	Height cm	Study of session	Time of dialysis hours	Online clearance monitoring(OCM) Ratio (kt/v)
(A)	male	55	163	7	4.00	1.30
(B)	female	50	155	6	3.54	1.25
(C)	male	62	170	10	3.40	1.24
(D)	male	48	151	13	3.45	1.22
(E)	female	44	155	11	3.35	1.21
(F)	male	35	140	8	3.30	1.12
(G)	female	45	150	6	3.20	1.20
(H)	male	70	172	12	3.50	1.36
(J)	female	52	149	9	3.26	1.23
(K)	male	60	165	5	3.00	1.23
mean				8.7±2.3	3.4±.18	1.24±.04

5.2 Discussion:

In the study there is comparison between the online clearance monitoring (OCM) and without the option of (OCM).

Table6.1blew show the comparator between the online clearance monitoring (OCM) and without

Table5.2 the comparison between (OCM) and without

without (OCM)		With (OCM)
blood sample (expensive) ⇦	Kt/v≥ 1.2	⇨ Dialysate,k,t (no additional cost)
once month/quarterly ⇦	Frequency	⇨ In every session
retrospective ⇦	Control	⇨
staff, syringe, lap time, cost and energy ⇦	Effort	Continuous, online ⇨
inconvenient ⇦	Handling	⇨ None ⇨
unpractical and uncommon ⇦	Quality assurance	Automatic ⇨ Standard

Chapter six

. Conclusion and Recommendation

6. 1Conclusion:

Judging from the result the online clearance monitoring (OCM) application of 4008S is better for monitoring of dialysis dose (kt/v) and also for the plasma sodium concentration.

The online clearance monitoring (OCM) can solve many problems such as documentation, decrease the cost of investigation, monitoring the adequacy of dialysis in every session and assisting the patient's treatment management.

6.2 Recommendation

My recommendations for future works are:

1. More study to compare between the online clearance monitoring (OCM) application and anther application of dialysis dose (kt/v) existing in the machine example Diascan for Gambro company.
2. More test with different types of dialyzer and different dialysis solutions

Reference

[1]. FREDRIKUHLIN DEPARTMENT OF MEDICINE AND CARE
DIVISION OF NURSING SCIENCE & DEPARTMENT OF BIOMEDICAL ENGINEERING LINKÖPING 2006

[2]. Car1 D. Goodwin National Library 1*1 of Canada Acquisitions and Bibliographic Services 395 Wellington Street Ottawa ON K1AON4 Canada

[3]. JOHNNY LIEN Master of Science Thesis Stockholm, Sweden 2009

[4]. Online Clearance Monitoring

[5]. E. Torregrosa de Juan, J. Hernández-Jaras, H. García-Pérez, R. Pons-Prades, C. Calvo-Gordo, A. Ríus-Peris, J. J. Sánchez-Canel and M. Pin-Godos
Nephrology Department. General Hospital of Castellon NEFROLOGÍA. Volumen 26. Número 2. 2006

[6]. Tom Depner 2011October1 4 15 2 01 1 Paris France

[7]. Khalid Al Saran1 .Alaa Sabry2. Mamdouh Abdulghafour1
Ahmed Yehia1.1Prince Salman center for Kidney
Disease, Riyadh, Kingdom of Saudi Arabia; 2Mansoura Urology and
Nephrology center, Mansoura University, Mansoura, Egypt

[9]. www.bbraun-dialysis.com

[10]. J Chowdhury NS 1, Islam FMM 2, Zafreen F3, Begum BA4, Sultana N5, Perveen S6, Mahal M7AFMC Bangladesh. Vol 7, No 2 (December) 2011

[11]. Ehab J Ghali1 MBChB CABM, Arif S Malik2 MBChB FICMS 1 Dept. of Medicine, Al-Kadhimiya Teaching Hospital, 2Dept. of Medicine, College of Medicine, Al-Nahrain University, Baghdad, Iraq.

[12]. Ahmad Taher Azar1 1 Assistant Lecturer, Systems and Biomedical Engineering Department, Misr University for Science and Technology, 6th of October City, Egyp

[13]. Dr. L.J. Garred, Chemical Engineering Department, Lake head University, 1 998.

[14]. P/N 102476-01 Rev A 08/2014

[15]. ps://cnx.org/contents/XJvfBd1g@4/Microscopic-Anatomy-of-the-Kid

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1Institute of Biocybernetics and Biomedical Engineering,

Polish Academy of Sciences, Warsaw, 2Divisions of Baxter Novum and Renal Medicine, Karolinska Institutet, Stockholm, Sweden.

[17] Kidney International, Vol. 42 (1992), pp. 540-558 .1992 by the International Society of Nephrology.

[18]. TUTORIAL 4698 Introduction to Dialysis Machines May 10, 2010.

[19]. Bessie A. Young, MD, MPH, FACP •Associate Professor, University of Washington •Director Home Dialysis, VA Puget Sound Health Care Center.