Current Status of the Implication of the Clinical Practice Pattern in Hemodialysis Prescription in Regular Hemodialysis Patients in (Cairo) Sector D-Egypt

Thesis

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INTRODUCTION

Studies examining the link between research evidence and clinical practice have consistently shown gaps between the evidence and current practice. Some studies in the United States suggest that 30%-40% of patients do not receive evidence-based care, while in 20% of patients care may be not needed or potentially harmful. However, relatively little information exists about how to apply evidence in clinical practice, and data on the effect of evidence-based guidelines on knowledge uptake, process of care or patient outcomes is limited ***(Locatelliet al., 2004).***

The care of dialysis patients has been the prime focus of nephrology, particularly after the widespread availability of maintenance dialysis when it became evident that mortality of dialyzed patients was high and their quality of life was far from adequate***(Eknoyan et. al,2002).***

Guidelines practiced on anemia and actual practices are much different with different places and patients according to treatment. Moreover, in individual countries and individual units within countries local circumstances relating to economic conditions; organization of health care delivery or even legal constraints may render the immediate implementation of best practice guidelines

difficult or impossible. Nevertheless, they provide a goal against which progress can be measured ***(Locatelli et al., 2004).***

Compliance with clinical guidelines is an important indicator of quality and efficacy of patient care , at the same time their adaptation in clinical practice may be initiated by numerous factors including; clinical experts, patient performance, constrains of public health policies, community standard, budgetary limitation and methods of feeding back information concerning current practice***(Cameron, 1999).***

End-stage renal disease (ESRD) is one of the main health problems in Egypt. Currently, hemodialysis represents the main mode for treatment of chronic kidney disease stage 5 (CKD5) ***(Afifi&Karim,1999).***

Although hemodialysis is often used for treatment of ESRD, no practice guidelines are available in Egypt. Healthcare facilities are seeking nowadays to develop practice guidelines for the sake of improving healthcare service ***(Afifi&Karim,1999).***

AIM OF THE WORK

To study the pattern of current clinical practice in hemodialysis prescription in regular hemodialysis patients in Egypt and to compare this pattern with standard international guidelines in hemodialysis prescription , stressing on anemia, bone disease management and adequacy of dialysis.

Chapter 1

Hemodialysis Overview

Despite the widespread use of peritoneal dialysis and renal transplantation, hemodialysis (HD) remains the main renal replacement therapy in most countries worldwide. More than 1.7 million patients are currently treated with HD in about 28,500 dialysis units worldwide. Despite significant advances in our understanding of the biology of chronic kidney disease and the risk factors for poor outcome on HD and improved dialysis technology, the annual mortality in HD patients varies from 10% to 25% internationally, depending on demographic and possibly genetic factors **(Peter et al., 2010).**

The aim of the HD system is to deliver blood in a safe manner from the patient to the dialyzer, to enable an efficient removal of uremic toxins and fluid, and to deliver the cleared blood back to the patient. The main components of the dialysis system are the extracorporeal blood circuit, the dialyzer, the dialysis machine, and the water purification system. The dialysis machine delivers dialysis fluid with the intended flow rate, temperature, and chemical composition. The dialysis machine has monitoring and safety systems for air, blood, conductivity, and pressure; blood and dialysate pumps; a heating system; a dialysate mixing and

degassing unit; and an ultrafiltrate balancing system. The role of the water purification system is to produce water for dialysis that complies with set chemical and microbiologic standards.(**Misra M.2005)**

Indications for Starting Chronic Dialysis Therapy

Patients should be considered for initiation of chronic hemodialysis therapy once the estimated glomerular filtration rate (GFR) is less than 15 mL/minute. In most patients, the four variables in the Modification of Diet in Renal Disease (MDRD) equation can be used to estimate the GFR. A 24-hour urine collection for creatinine and urea should be considered in those patients who have reduced muscle mass due to medical conditions such as amputations or limitation on mobility due to congestive heart failure, claudication, chronic lung disease requiring oxygen therapy, etc. There are no randomized trials that suggest an optimal time to initiate chronic dialysis therapy, so clinical judgment is important in making this decision in individual patients **(Michael & Shahriar 2009).**

1. Earlier initiation of dialysis—There are specific indications for starting chronic hemodialysis therapy at a level above a GFR of 15 ml/minute. These conditions include intractable fluid overload not responsive to diuretics, hyperkalemia unresponsive to

medical therapy, metabolic acidosis not fully corrected by medical therapy, malnutrition or weight loss not ascribed to other medical conditions, or decreasing functional status. It may also be desirable to start home dialysis therapies at a higher level of GFR to minimize training difficulties due to neurologic dysfunction at lower levels of GFR.

2. Later initiation of dialysis—Patients can be considered for a later initiation of dialysis if they are asymptomatic from a uremic standpoint, have adequate nutritional status, and do not have a decline in either dry weight or serum albumin levels. If renal replacement therapy is delayed, then the patient should be reassessed on a regular basis for a change in these parameters **(Michael & Shahriar 2009).**

DIALYZER DESIGNS

The dialyzer provides controllable transfer of solutes and water across the semipermeable membrane. The flows of dialysate and blood are separated and countercurrent. The semipermeable dialysis membrane separates the blood compartment and the dialysate compartment. The transport processes across the membrane are diffusion (dialysis) and convection (ultrafiltration). The removal of small solutes occurs primarily by diffusion; larger

components, such as β2-microglobulin, aremore effectively removed by convection.(**Peter et.,al 2010)**

Membranes vary with respect to chemical structure, biophysical properties such as transport characteristics, and biocompatibility The original widely used membrane material was cellulose, which is made up of repetitive polysaccharide units containing hydroxyl groups More recent membranes are not cellulose based but instead are built of entirely synthetic materials, such as polyacrylonitrile, polysulfone, polycarbonate, polyamide, and polymethylmethacrylate. These synthetic membranes provide superior biocompatibility and are widely used. (**Peter et.,al 2010)**

Transport of molecules across the dialysis membrane is due to (1) the concentration gradient (diffusive transport) and (2) the hydrostatic pressure gradient across the membrane (convective transport) and is dependent on membrane pore size. Dialyzer efficiency in terms of urea removal depends on the surface area (usually 0.8 to 2.1 m2). High-efficiency dialyzers have a high surface area irrespective of pore size and possess a superior clearance for small molecules but may have small pores and thus a low ability to remove large molecules such as β2-microglobulin. In the recent prospective, randomized Membrane Permeability Outcome (MPO) study, a survival benefit of high-flux membranes

was seen among patients with serum albumin levels of4 g/dl or lower**.(Locatelli ,et .,al 2009)** This finding contrasts with the HEMO study, which did not show any effect in patients with hypoalbuminemia but did show survival benefit in patients on dialysis for more than 3.7 years before the trial. These differences may be related in part to population characteristics (race, recruitment of incident or prevalent patients) and fluxes achieved**(Eknoyan ,et al.2002).**

DIALYSATE FLUID

A. Water Treatment

A standard 4-hour HD session exposes the patient to 120 to 160 liters of water. Therefore, water quality is of paramount importance to the patient's well-being. Standards for chemical quality of water are widely accepted ,but there is less consensus as to acceptable levels of bacterial and endotoxin contamination. Municipal water supplies may contain a variety of contaminants that are toxic to HD patients. Substances added to the water, such as aluminum and chloramines, cause significant morbidity. Aluminum accumulation may result in a severe neurologic disorder (speech abnormalities, muscle spasms, seizures, and dementia), bone disease, and erythropoietin-resistant anemia. Plasma aluminum concentration should be monitored regularly;

levels should be less than 1 μmol/l, and levels above 2 μmol/l should prompt the search for excessive exposure (aluminum-based phosphate binders may be an important source). Chloramines have been associated with hemolysis and methemoglobinemia **(Nystrand ,2008).**

Gram-negative bacteria produce endotoxins (pyrogenic lipopolysaccharides from the outer bacterial cell wall), and fragments of these endotoxins may be responsible for some dialysis-related symptoms. Exposure to bacteria and endotoxin is associated with rigors, hypotension, and fever; even low levels of microbiologic contaminants may contribute to chronic inflammation in HD patients. Use of a polysulfone or polyamide filter in the dialysate line may be adequate to remove endotoxins. Ultrapure water is defined as bacterial count below 0.1 colony forming unit/ml and endotoxin below 0.03 endotoxin unit/ml and is recommended by both European and American guidelines for use with high-flux dialyzers. Ultrapure water represents a basic prerequisite for dialysis modalities using online production ofsubstitution fluid (online hemofiltration or hemodiafiltration) **(Nystrand ,2008).**

B.DIALYSIS SOLUTION

Dialysis fluid can be considered a drug to be adjusted to the individual patient's needs. In modern machines, dialysate is made by mixing two concentrate components, which may be provided as liquid or dry (powder) concentrates. The bicarbonate component contains sodium bicarbonate and sodium chloride; the acid component contains chloride salts of sodium, potassium (if needed), calcium, magnesium, acetate (or citrate), and glucose (optional). These two components are mixed simultaneously with purified water to make the dialysate. Dialysate proportioning pumps ensure proper mixing. The relative amounts of water, bicarbonate, and acid components define the final dialysate composition. Bicarbonate has replaced acetate as the dialysate buffer in most countries. Modern machines allow an alteration of the bicarbonate concentration by changing the mixing ratio of water to bicarbonate. A variable sodium option allows the adaptation of the dialysate sodium concentration to the patient's needs. Glucose is usually added to prevent intradialytic hypoglycemia, but glucose concentrations of 200 mg/dl (11 mmol/l) may result in hyperglycemia and hyperinsulinemia.(**Peter , et.,al 2010)**

Hemofiltration(HF)

Hemofiltration differs markedly from HD in the mechanisms by which the composition of the blood is modified. In the simplest

form of HF, blood under pressure passes down one side of a highly permeable membrane, allowing both water and substances up to about 20 kd to pass across the membrane by convective flow, depending on the membrane and its permeability. During HF, the filtrate is discarded and the patient receives a substitution fluid either before (predilution) or after (postdilution) the dialyzer. The substitution fluid contains the major crystalloid components of the plasma at physiologic levels. Both bicarbonate and lactate are used as buffers. The rate of fluid removal and substitution fluid infusion can be adapted to the patient's need. HF is particularly useful as a continuous renal replacement therapy in an intensive care setting **(Forni &Hilton ,1997).**

Hemodiafiltration(HDF)

Hemodiafiltration combines the benefits of HD (high transport rate of low-molecular-weight solutes by diffusion) and HF (high convective transport of substances). HDF is used as both a continuous and an intermittent renal replacement therapy. HDF offers potential benefits regarding anemia correction, inflammation, oxidative stress, lipid profiles, and calcium-phosphate product. Higher costs and, in some countries, the decisions of regulatory boards concerning fluid infusion prevent the widespread use of HDF **(Vaslaki et.,al 2006).**

Vascular Access for Hemodialysis

The appropriate access for a particular patient should be determined prior to placement, taking into consideration patient factors such as life expectancy, co-morbidities, and status of the venous and arterial vascular system. Other factors are determined by the type of access itself, as AVF, AVG, and TC differ in their effect on the circulatory system, the duration of their functionality, and the risk for infection and thrombosis.

A mature AVF is the preferred type of vascular access; it has the lowest long-term complication rates for thrombosis In fact, the primary patency rate of AVFs 5 years after creation is >50%, while <10% of AVGs are still patent **(Beathard ,2000).**

There are 3 types of AVFs:

1.Simple direct fistulas, where artery and vein are connected in their natural position, either with a side-to-side or a side-artery-to-vein-end anastomosis.

2.Transposed vein fistulas, where a vein is moved to connect to an artery in end-to-side fashion to either bridge a larger anatomical distance, or to bring the vein to the surface where it is accessible for cannulation. This procedure requires a tunnel to position the vein in its new location.

3.Translocated vein fistulas, where a vein is removed from its anatomical location and, similar to the placement of a graft, is connected to an artery and vein in end-to-end fashion and requires the formation of a tunnel.

The most common surgical technique today is the side-to-end anastomosis ; it allows a greater distance between artery and vein and the surgical suturing technique is straight forward. However, it is often difficult to determine the appropriate angle between artery and vein and difficult to prevent torsion of the vein along its axis **(Konner ,2003)**

Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) indicate that AVFs should mature at least 14 days before use. Early access of AVFs may need to be combined with lower initial blood flow rates in the range of 200–300 mL/min and smaller dialysis needles. Flow can then be increased over the course of 8–12 weeks, and needles advanced to regular size as fistula maturation is monitored by physical examination **(Rayner , et al 2003).**

Complications of AVFs can be divided into early and late causes. **Early causes** include inflow problems such as small or atherosclerotic arteries, or juxta-anastomotic stenosis. The etiology of this acquired lesion is not entirely clear, but may be related to

manipulating the free end of the vein, torsion, poor angulation, or loss of the vasa vasorum during anatomic dissection. This lesion often can be adequately treated with angioplasty or by surgical revision **(Beathard , et al 2003).**

Late causes for failure of AVFs include venous stenosis, thrombosis, and acquired arterial lesions such as aneurysms or stenosis. Venous stenosis may become apparent as flow decreases over time, worsening weekly Kt/V ([dialyzer clearance_ time]/body volume) or increasing recirculation **(Beathard , et al 2003).**

Arteriovenous graft (AVG)

Until very recently, AVGs were the most commonly used type of dialysis access in the US; however, they do not last as long as AVFs and have higher rates of infection and thrombosis. Grafts can be placed in the forearm, the upper arm, and the thigh, and can have a straight, curved, or loop configuration. Due to their long subcutaneous course, they offer a large surface area for cannulation and can be used about 2 weeks after placement**.(Beathard G.2000)**