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Current Status of the Implication of the Clinical Practice Pattern in Hemodialysis Prescription in Regular Hemodialysis Patients in Egypt (Giza) Sector B

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.In recent years, specific clinical guidelines have been developed to optimize the quality of anemia management secondary to chronic kidney diseases(CKD).

As a result, the National Kidney Foundation Kidney Disease Outcome Quality Initiative (K\DOQ I) guidelines and the Renal-European Dialysis and Transplantation Association best practice guidelines have been published in USA & Europe. Therefore; clinical practice guidance help individual physician and physicians as group to improve their clinical performance and thus raise standard of patient care towards optimum levels, They may also help to insure that all institution provide an equally good base line standard of care ***(Cameron,1999).***

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).***

Dialysis Outcomes and Practice Patterns Study (DOPPS) has observed a large variation in anemia management among different countries. The main hemoglobin concentration in hemodialysis patients varied widely across the studied countries ranging between 8g/dl to 11g/dl. The percentage of prevalent hemodialysis patients receiving erythropoietin stimulating agent ’ESA’ has increased from 75% to 83%. The percentage of HD patients receiving iron varies greatly among DOPPS countries range from 38% to 89%, ***(Locatelli et al., 2004).***

There are challenges in implanting clinical guidelines in medical practice. Overall DOPPS data which show that, despite the availability of practice guidelines for treatment of renal anemia, wider variation in anemia management exists as gap between what is recommended by the guidelines and is accomplished in every day clinical practice. Compliance with

clinical guidelines is an importance 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).***

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 PRESCRIPTION

Medical progress has altered the course and thus the definition of uremia, which once encompassed all the signs and symptoms of advanced kidney failure. Hypertension due to volume overload, hypocalcemic tetany, and anemia due to erythropoietin deficiency were once considered signs of uremia but were removed from this category as their causes were discovered. Today the term “uremia” is used loosely to describe the illness accompanying kidney failure that cannot be explained by derangements in extracellular volume, inorganic ion concentrations, or lack of known renal synthetic products. We now assume that uremic illness is due largely to the accumulation of organic waste products, not all identified as yet, that are normally cleared by the kidneys**.(Young-Ki and Jieun ,2014)**

No specific time point demarcates the onset of uremia in patients with progressive loss of kidney function. The features of uremia identified in patients with end-stage kidney failure may be present to a lesser degree in people with a glomerular filtration rate that is barely below 50% of the normal rate, which at 30 years of age ranges between 100 and 120 ml per minute per 1.73 m^2 of body-surface area. Thus, in the United States alone, uremic

symptoms may be present to some degree in an estimated 8 million people who have a glomerular filtration rate below 60 ml per minute per 1.73 m^2 of body-surface area. **(Coresh et al., 2005)**

However, early symptoms of uremia, such as fatigue, are nonspecific, making the condition difficult to identify. At present, moreover, we can slow progression to kidney failure but can treat uremia only by replacing kidney function. Thus, the question of whether a patient has uremia comes down to whether dialysis or a transplant would be beneficial.**(Twardowski, 2003)**

Treatment of uremia is now dominated by dialysis, in large part because donor kidneys are in short supply. In the United States in 2004, approximately 100,000 people began receiving kidney-replacement therapy for end-stage renal disease, and 335,000 people were receiving ongoing treatment with dialysis,in some cases, patients are treated with dialysis for decades, but overall outcomes are disappointing. The 5-year survival rates between 1995 and 1999 were under 35% for both hemodialysis and peritoneal dialysis. Patients treated with dialysis are hospitalized on average twice a year, and their quality of life is often low**.(USRDS, 2006)**

Not all of the illness of a patient undergoing dialysis can be ascribed to uremia. Indeed, the evolution of dialysis has made the effects of uremia more difficult to distinguish, since the severity of classic uremic symptoms is attenuated. Instead, patients undergoing dialysis now have a new illness, which Depner aptly named the "residual syndrome." This illness comprises partially treated uremia; ill effects of dialysis, such as fluctuation in the extracellular fluid volume and exposure to bioincompatible materials; and residual inorganic ion disturbances, including acidemia and hyperphosphatemia. In many patients, the residual syndrome is complicated by the effects of advancing age and systemic diseases that were responsible for the loss of kidney function**. (Depner , 2001)**

Although patients undergoing dialysis have a complex illness, there are compelling reasons to believe that inadequate removal of organic wastes is an important contributor. Dialysis is initiated when uremic symptoms, among which anorexia and lethargy are usually the most prominent, advance to the point at which treatment is expected to effect an improvement. The glomerular filtration rate at this point averages about 7% of the normal value. As compared with such a low glomerular filtration rate, conventional dialysis provides only slightly better removal of

many solutes and inferior removal of some**.(NKF-KDIGO clinical practice guideline, 2013)**

Renal replacement therapy does keep patients alive, but because of these limitations, it does not completely relieve uremic symptoms. The fact that transplantation reverses this residual syndrome constitutes strong evidence for the ill effects of toxic solute accumulation despite dialysis. Successful transplantation, which can restore the glomerular filtration rate to more than half the normal value, markedly improves the overall quality of life and enhances specific functions, including sleep, sexual function, cognition, exercise capacity, and, in children, growth**. (Valderrabano et al., 2001)**

Hemodialysis (HD) therapy has been one of the true success stories in the annals of medical science. Before the availability of this treatment, the diagnosis of kidney failure was a death sentence. **(Butman and Nissenson, 2005)**

Unfortunately, despite major advances in the technology of HD and in the management of its complications, the morbidity and mortality of patients on dialysis remain high, at a time that the incidence and prevalence of kidney failure persistently are increasing. Hence, the early and continued concern with the adequacy of dialysis **. (Eknoyan, 2005)**

The principle of hemodialysis involves diffusion of solutes across a semipermeable membrane. Hemodialysis utilizes counter current flow, where the dialysate is flowing in the opposite direction to blood flow in the extracorporeal circuit. Counter-current flow maintains the concentration gradient across the membrane at a maximum and increases the efficiency of the dialysis.Fluid removal (ultrafiltration) is achieved by altering the hydrostatic pressure of the dialysate compartment, causing free water and some dissolved solutes to move across the membrane along a created pressure gradient**. (Abel et al.,1913)**

The dialysis solution that is used may be a sterilized solution of mineral ions or comply with British Pharmacopoeia. Urea and other waste products, potassium, and phosphate diffuse into the dialysis solution. However, concentrations of sodium and chloride are similar to those of normal plasma to prevent loss. Sodium bicarbonate is added in a higher concentration than plasma to correct blood acidity. A small amount of glucose is also commonly used**. (Ikizler and Schulman, 2005)**

A prescription for dialysis by a nephrologist (a medical kidney specialist) will specify various parameters for a dialysis treatment. These include frequency (how many treatments per week), length of each treatment, and the blood and dialysis solution flow rates, as well as the size of the dialyzer. The

composition of the dialysis solution is also sometimes adjusted in terms of its sodium and potassium and bicarbonate levels. In general, the larger the body size of an individual, the more dialysis he/she will need. In North America and the UK, 3-4 hour treatments (sometimes up to 5 hours for larger patients) given 3 times a week are typical. Twice-a-week sessions are limited to patients who have a substantial residual kidney function. Four sessions per week are often prescribed for larger patients, as well as patients who have trouble with fluid overload. Finally, there is growing interest in short daily home hemodialysis, which is 1.5 - 4 hr sessions given 5-7 times per week, usually at home. There also is interest in nocturnal dialysis, which involves dialyzing a patient, usually at home, for 8–10 hours per night, 3-6 nights per week. Nocturnal in-center dialysis, 3-4 times per week, is also offered at a handful of dialysis units in the United States**. (Ikizler and Schulman, 2005)**

Table (1): Elements of Hemodialysis Prescription

Dialyzer
Time & frequency
Blood flow rate
Dialysate flow rate
Ultrafiltration rate
Dialysate composition
Anticoagulation

(Jane Y et al., 2011)

Types of dialyzers:

Exchanges through dialyser membranes aim to: (i) removal of uraemic solutes that are retained because of renal failure (e.g. urea) and (ii)restoration of depleted compounds (e.g. bicarbonate). The originally used cellulosic membranes were derived from cotton and therefore named ‘natural’. The activated complement and leukocytes, inducing an inflammatory reaction as one of the indices of ‘bioincompatibility’ Hemodialysis leukopenia. Pulmonary vascular leukostasis resulting from complement activation by dialyzer cellophane membranes**. (Craddock et al., 1977)**.

Later on, chemically developed ‘synthetic’ polymers appeared to mitigate this activation , furthermore, masking hydroxyl groups, which are responsible for the complement activation with cellulosic membranes, also resulted in more biocompatibility ,therefore, cuprophan and its analogues were called ‘unmodified cellulosic’ *vs* the more biocompatible, later developed ‘modified/regenerated cellulosic’ membranes. **(Hoenich et al., 1995)**

Many synthetic membranes have large pore sizes allowing higher rates of water flux and permitting a higher ultrafiltration capacity as well as a better removal of high molecular weight

'uraemic solutes' than membranes with smaller pore size. Therefore, although a high ultrafiltration rate and the capacity to remove large molecules do not strictly run in parallel, large pore membranes are mostly referred to as 'high-flux', in contrast to 'low-flux' membranes with smaller pores. Five general types of membranes are available at present **(Eknoyan et al., 2002)**

Which dialyser membrane to choose?Types of membranes with some examples:

Unmodified cellulose (low-flux)

Cuprophan
Cellulose diacetate
Cuprammonium rayon

Modified/regenerated cellulose (low-flux)

Hemophan

Synthetic (low-flux)

Polysulfone
Polycarbonate

Modified/regenerated cellulose (high-flux)

Cellulose triacetate

Synthetic (high-flux)

Polysulfone
Polyamide
Polyethersulfone
Polyacrylonitrile
Polymethylmethacrylate

(Port et al., 2001)

Relevant membrane characteristics

Biocompatibility towards leukocytes and the complement system:

Biocompatibility describes materials, which cause only minor biochemical and biological effects. Baseline activation of leukocytes results in inflammation, which is related to vascular disease, the first cause of death in dialysis patients **.** C-reactive protein, a marker of inflammation that is related to mortality **(*Yeun et al.*,2000*)*** is lower when synthetic, biocompatible, high-flux polysulfone is used, compared with unmodified cellulose **(Schouten et al.,2000)**

Subsequently, functional impairment of leukocytes develops as well, e.g. the impaired function of stimulated granulocytes and monocytes, of phagocytosis, of chemotaxis and of surface molecule expression. All these functional defects predispose to infection, the second most frequent cause of death in dialysis patients .**(Vanholder et al. ,1991)**

The bioincompatibility concerning complement and leukocytes, is not so strong when synthetic and modified cellulosic membranes are used **(Combe et al., 1994).**