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 ***(Locatelli et al., 2004)***.

Appropriately then, 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 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) has become a public health concern worldwide as the total number of ESRD patients requiring renal replacement therapy has been growing dramatically ***(Bello et al., 2005).***

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), previously called ESRD or chronic renal failure ***(Afifi, 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 services ***(Ministry of Health and Population, 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.

HEMODIALYSIS PRESCRIPTION

Uremia is a quite complex syndrome encompassing a metabolic disorders and accumulation of various sized uremic toxins ***(Vanholder et al., 2003)***; that it would be impossible for intermittent renal replacement therapy (RRT) to replace the homeostatic role of the kidneys. Hence**,** the importance of providing at least adequate dialysis ***(Eknoyan, 2005)***.

Table (1): Indications for renal replacement therapy include the following:

1. Severe metabolic acidosis
2. Hyperkalemia
3. Pericarditis
4. Encephalopathy
5. Intractable volume overload
6. Failure to thrive and malnutrition
7. Peripheral neuropathy
8. Intractable gastrointestinal symptoms
9. In asymptomatic patients, GFR of 5-9 mL/min-

(Lameire and Van, 2010)

Eradication of uremic symptoms was supposed to predict good long term results of dialysis-low morbidity and mortality. This approach of assessing adequacy is subjective, requires

very careful monitoring of patients, and is time consuming ***(Twardowski, 2003)***.

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)***.

Optimal care of the patient receiving long-term HD requires broad knowledge of the HD technique and appropriate prescription according to patient- and device-dependent variables ***(Ikizler and Schulman, 2005).***

Table (2): Elements of Hemodialysis Prescription

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

(Brenner and Rectors, 2008)

1- Dialyzers

Types of dialyers and its choice

The dialyzers are classified either according to it's synthetic material into: cellulose, modified cellulose or synthetic polymers or according to it's hydrokinetics into High-Flux & Low-Flux Dialyzers. All dialyzers in clinical use are of the hollow-fiber type with membranes of cellulose, modified cellulose or synthetic polymers ***(Ronco and Clark, 2005).***

A biocompatible dialysis membrane is one in which minimal reaction occurs between the humoral and cellular components of blood as they come into contact with the surface of the dialyzer ***(Hakim, 1993)***.

Unsubstituted Cellulosic membranes have the propensity to activate the complement system. This activation of complement is partially responsible for the subsequent activation of neutrophils and other leukocytes, making these membranes bioincompatible ***(Chenoweth, 1984)***, whereas substituted cellulosic or synthetic membranes have more biocompatible characteristics ***(Ambalavanan et al., 1999).***

High-flux membranes have ultrafiltration coefficient (K_{uf})values > 12 mL/h/mm Hg, and as high as 80 mL/h/mm Hg. Low-flux membranes have K_{uf} values < 12 mL/h/mm Hg.The K_{uf} is calculated in milliliters of ultrafiltrate per hour per mm

Hg (mL/h/mm Hg) of transmembrane pressure (TMP) ***(Chelamcharla et al., 2005).***

The efficiency and flux are not related to each other. Thus, high efficiency membranes can be either high flux (large surface area and large pores) or low flux (large surface area but small pores), and low efficiency membranes can also be either low flux or high flux ***(Ambalavanan et al., 1999)***.

Although low-flux HD, making use of membranes with low-hydraulic permeability, is still the most widely used extra-corporeal treatment for end-stage renal disease (ESRD), the availability of high-permeability membranes allowed the introduction of the so-called convective treatments in clinical practice [high-flux HD, hemodiafiltration (HDF) and hemofiltration (HF)]. These are characterized by enhanced removal of middle and large MW solutes compared with "conventional" low-flux HD, because of more effective convection ensured by the use of dialyzers with high permeability for water ***(Pozzoni et al., 2006).***

In making a decision about the choice of dialyzer, the most clinical determinants are its capacity to clear a particular solute and its potential for fluid removal ***(Ikizler and Schulman, 2005)***.

Solute transfer in HD is determined by the diffusive and convective permeability of the membrane – defined by the mass

transfer coefficient (Ko) and the sieving coefficient (S), respectively – the membrane surface area (A), the blood and dialysate flow rates ***(Ronco and Clark, 2005).***

Figure (1): Mechanisms of solutes removal in hemodialysis ***(William, 1999).***

The Ko is a composite parameter that incorporates the resistances to mass transfer associated with the membrane and the fluid boundary layers on the blood and dialysate sides of the membrane ***(Ward and Ronco, 2006).***

The mass transfer area coefficient (KoA), expressed in mL/min, for a given solute is the clearance of the dialyzer at infinitely high blood and dialysate flow rates on a theoretical

basis. Therefore, KoA is a measure of the maximum solute removal capacity of the dialyzer ***(Chelamcharla et al., 2005).***

Small solute removal is primarily obtained by diffusion. Convection represents an additional mechanism that is mostly important for larger molecules ***(Ronco et al., 2002).***

The term efficiency refers to the capacity of the dialyzer to remove low-molecular-weight (LMW) uremic solutes. Urea is by far the most extensively studied marker of these solutes ***(Chelamcharla et al., 2005).***

Current dialyzers are classified into high-efficiency and low-efficiency types based on their urea KoA. A high-efficiency dialyzer has a KoA value > 600 milliliter per minute (mL/min), whereas a low-efficiency dialyzer has a KoA value < 450 mL/min ***(Chelamcharla et al., 2005).***

The most commonly used parameter to evaluate delivered dialysis dose is the Kt/V index, where K is the dialyzer urea clearance, t is the duration of dialysis session and V is the patient's urea distribution volume ***(Locatelli, 2003)***.

Strategies to increase urea Kt/V include:

A. Increasing urea clearance (K)

K can be increased by increasing dialyzer blood flow, dialysate flow, or the KoA of urea.An increase in blood or dialysate flow rate does not lead to substantial increases in K

unless the KoA of the dialyzer is substantially higher than the blood and dialysate flow rates ***(Chelamcharla et al., 2005).***

Hassell et al. concluded that even in patients with low access flows, increasing the dialyzer blood flow rate (BFR) leads to an increase in delivered Kt/V regardless of the vascular-access flow rate. Low access flow should in general not be a reason to reduce BFR ***(Hassell et al., 2001)***.

Hauk et al. concluded that increasing dialysate flow rate (DFR) from 500 to 800 mL/min is associated with a significant increase in Kt/V ***(Hauk et al., 2000)***.

B. Increasing the treatment time

Effective treatment time must accurately reflect the exact amount of time during which diffusion occurred at the prescribed BFR and DFR ***(NKF K/DOQI clinical practice guidelines, 2001)***.

The trend toward shorter HD session length reversed when quality improvement programs (QIP) and the publication of clinical practice guidelines (CPG) focused attention on achieving urea reduction ratio (URR) (>65% to 70%) and Kt/V_{urea} (>1.2–1.4 per session) goals ***(Kurella and Chertow, 2005).***

After maximizing parameters of K, increases in delivered dose could be achieved only by lengthening time (t). Thus,

increasing the session length has a marginal effect on the net clearance of smaller, easily diffusible MW solutes, such as urea as they are cleared efficiently during HD ***(Kurella and Chertow, 2005)***.

However, increasing the session length will enhance solute clearance significantly for some small solutes (eg, phosphate) as there is a significant rebound in plasma concentration after HD ***(Kurella and Chertow, 2005).***

In contrast, the removal of larger solutes is relatively inefficient during HD, the plasma concentration of larger solutes remains high during dialysis; therefore, their net clearance is proportional to total treatment time. Thus, increasing session length increases the removal of larger MW solutes more so than smaller MW solutes ***(Kurella and Chertow, 2005)***

In addition to solute control, longer sessions may decrease hemodynamic instability during HD, and thus attenuate volume overload and improve BP control ***(Kurella and Chertow, 2005).***

The effect of HD session length on mortality independent of conventional markers of dialysis adequacy is unclear among patients undergoing standard three times per week dialysis therapy ***(Kurella and Chertow, 2005).***

2- Time

The clearance of any of a solute, such as urea, can be increased by lengthening the dialysis treatment. Because the typical dialysis prescription often emphasizes optimal blood and dialysate flows and the selection of dialyzers with large mass transfer coefficient characteristics, the duration of dialysis is often the sole variable that can be used to augment solute clearance during an individual dialysis session ***(Charra et al., 1992).***

The duration of the dialysis procedure may also be important in achieving adequate volume homeostasis. A longer duration of the dialysis procedure allows for a lower net UF rate per hour for a given targeted UF goal over the course of the procedure. This, in turn, may result in fewer intradialytic symptoms such as hypotension and cramping ***(Charra et al., 1992).***

3- Blood and Dialysate flow

Prescriptions of the blood flow and dialysate flow rates are critical elements of the dialysis prescription that can be altered to modify solute clearance. However, as blood and dialysate flow rates increase, resistance and turbulence within the dialyzer also increase. As a result, increases in nonlinear flow within hollow fibers occur, leading to a decline in the clearance per unit flow of blood or dialysate. The resulting

flow-limited mass transfer indicates that solute clearance will approach an asymptotic rate as blood flow or dialysate flow increases. The flow-limited mass transfer and membrane-limited mass transfer (defined by the specific dialyzer and the solute being measured) together determine clearance characteristics. A similar relationship is obtained for solute clearance and dialysate flow rate ***(Sigdell and Tersteegen, 1986).***

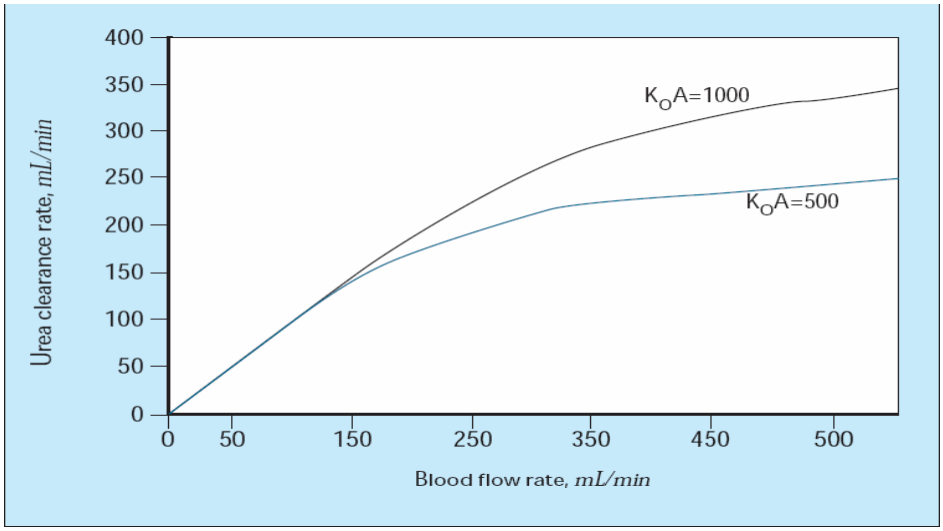

Figure (2): Comparison of urea clearance rates between low- and high-efficiency hemodialyzers (urea KoA =500 and 1000 mL/min, respectively). The urea clearance rate increases with the blood flow rate and gradually reaches a plateau for both types of dialyzers. The plateau value of KoA is higher for the high-efficiency dialyzer. At low blood flow rates (<200 mL/min), however, the capacity of the high-efficiencydialyzer cannot be exploited and the clearance rate is similar to that of the low-flux dialyzer. Ko-mass transfer coefficient; A-surface area ***(William, 1999).***

In clinical practice, the efficacy of angioaccess may affect solute clearance obtained at a given prescribed blood flow rate. Access blood flow is a function of pressure and resistance. When

blood is pumped out of the access into the dialyzer, a lower resistance circuit is created, which generally results in an increase in total access blood flow. The increased blood flow increases pressure in the venous drainage of the access during dialysis. Should venous outflow be restricted, there is an increased likelihood of backflow (termed *recirculation*) from the venous to the arterial side of the access. Backflow, or recirculation, is also facilitated by greater negative pressure at the arterial needle at higher blood pump speeds when there is impaired arterial flow. During recirculation, "dialyzed" blood reenters the dialytic circuit, thereby decreasing the efficiency of solute clearance. Recirculation will also increase when dialysis needles are placed in close approximation within the dialysis access ***(Sherman and Levy, 1991)***.

4- Ultrafiltration rate

The maintenance of the euvolemic state is an important aspect of adequate dialysis. It is important to emphasize that the dialysis membrane and its K_{uf} are almost never the limiting factors for fluid removal. The limiting factors are usually the plasma refilling rate and tolerance of the patient ***(Chelamcharla et al., 2005)***.

The standard HD prescription targets fluid removal to a clinically derived estimate of dry weight. Dry weight is currently defined as the lowest weight a patient can tolerate

without the development of symptoms or hypotension ***(Henderson, 1980).***

Since physiologic dry weight is that weight resulting from normal renal function, vascular permeability, serum protein concentration, and body volume regulation, dry weight in HD should theoretically be lower than physiologic to prophylax interdialytic weight gains. In most instances, dry weight is estimated by trial and error, and the degree of imprecision is reflected in the development of intradialytic symptoms or chronic volume overload with poor control of BP ***(Charra et al., 1996).***

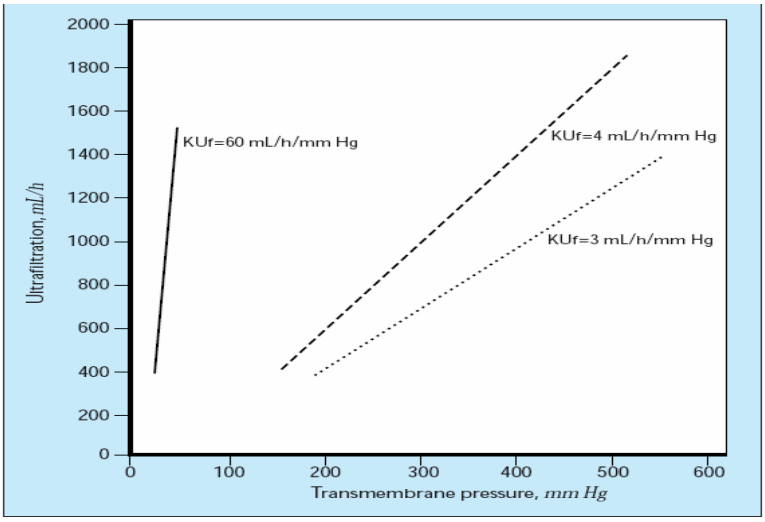

Figure (3): Water permeability of a membrane and control of volumetric ultrafiltration in hemodialysis. The water permeability of a dialysis membrane can vary considerably and is a function of membrane thickness and pore size. The water permeability is indicated by its ultrafiltration coefficient (KUf). The KUf is defined as the number of milliliters of fluid per hour that will be transferred across the membrane per mm Hg pressure gradient across the membrane ***(William, 1999).***