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 ***(Irving et al.., 2006).***

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., 2004a).***

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

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

1. 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 (K/DIGO 2010), stressing on anemia, bone disease management and adequacy of dialysis.

2. Statement of the current status of dialysis patient in Egypt

HEMODIALYSIS PRESCRIPTION

Hemodialysis (HD) is the routine renal replacement therapy for more than 300,000 patients in the United States who have reached end-stage renal disease. The goals of HD are straightforward and include restoring the body's intracellular and extracellular fluid environment and accomplishing solute balance by either removal from the blood into the dialysate or from the dialysate into the blood. Optimal care of the patient receiving long-term HD requires appropriate prescription according to patient- and device dependent variables ***(Ikizler and Schulman, 2005).***

Elements of Hemodialysis Prescription:

1-Time and Frequancy of sessions:

Due to high mortality and morbidity rates and inter and intradialytic symptoms associated with conventional intermittent HD three times a week, different modalities of HD treatment based on variations in dialysis time and frequency have been developed in the last years:

1. Intermittent conventional hemodialysis (HD): a) A HD session of 3–5 h three times a week b) Long intermittent HD: A HD session of more than 5.5 h three times a week, c) Conventional hemodiafiltration (HDF): A HDF session of 3–5 h three times a week.

2. Extended HD > 3 times/week.

3. Daily (Quotidian) dialysis (at least 6 times/week): a) Short daily HD 2– 3 h/6–7 times a week, b) Long nocturnal daily HD 6–10 h/6–7 nights a week, c) Daily hemodiafiltration: 2–2.5 h/6 times a week ***(Tattersal et al., 2007).***

Are there specific indications for increasing the duration of HD?

The ideal length of dialysis is still controversial. The length of the dialysis should be individualized according to the requirements of each patient. Some recommendations may be made: A dialysis session of 8 h three times a week increases both the dialysis dose and time ***(Charra et al., 2004).***

Uncontrolled study suggests that it results in better blood pressure control with a significant reduction in antihypertensive drugs, fewer intradialytic complications, improvement of nutritional status and an increased survival. Increased treatment time reduces the ultrafiltration rate and may benefit patients with hemodynamic or cardiovascular instability ***(Kurella and Chertow, 2005).***

Increasing treatment time makes it easier to meet the body weight target in unstable hemodialysis patients with high comorbidity **(*Charra et al., 2004*).**

An increase in the treatment time improves solute removal. This is particularly true for the clearance of middle molecules such as beta 2- microglobulin (β2m) in comparison with less time and similar Kt/V ***(Leypoldt, 2005*)**.

Treatment time should be increased in patients with poor phosphate control. Increasing dialysis time and/or frequency are practical and effective options for increasing phosphate removal by HD ***(Leypoldt, 2005).***

Impact on mortality:

The effect of length of the dialysis sessions on patient mortality is controversial (***Kurella and Chertow, 2005***). Some indirect evidence suggests that a longer dialysis improves the survival of dialysis patients. Long slow HD 3 × 8 h a week has been associated with a high survival rate and a reduced cardiovascular mortality, mainly attributed to the adequate control of blood pressure ***(Charra et al., 2004*)**.

Are there specific indications for increasing frequency?

An increase in frequency of dialysis results in lower interdialytic weight gains and should benefit patients with hemodynamic instability or large fluid weight gains. An increased frequency has been shown to facilitate the achievement of body weight target in unstable hemodialysis patients with high comorbidity. Improved tolerance to dialysis

(fewer muscle cramps, headaches and dizziness) and hemodynamic stability with a marked reduction in the number and severity of intra-dialysis hypotensive episodes has been reported ***(Okada et al., 2005).***

High blood pressure is common and difficult to control in HD patients. Daily HD decreases both systolic and diastolic blood pressure with a reduction in the dose and number of anti-hypertensive drugs. This effect is probably due to better fluid volume control ***(Ayus et al., 2005).***

The prevalence of left ventricular hypertrophy is greater in HD patients than in the general population and is considered a powerful predictor of poor outcome in maintenance HD. Daily HD has been associated with improved cardiac performance and a reduction in left ventricular hypertrophy ***(Nesrallah et al., 2003).***

Daily HD seems to improve nutritional status. After switching to daily HD, appetite and nutritional biochemical parameters improve, such as albumin and pre-albumin. An increase of dry body weight and lean body mass has also been observed in the majority of patients treated with daily dialysis ***(Spanner et al., 2003).***

Daily HD has been considered more physiological than conventional three times a week, with lower peak values of uremic toxins. Mean predialysis BUN levels are significantly

lower in daily HD as compared with conventional HD ***(Heidenheim et al., 2003).***

Improved phosphate control has been reported with nocturnal daily hemodialysis with a reduction in the administration of phosphate-binders. Phosphate removal is closely related to the length of the HD session in daily HD ***(Achinger and Ayus, 2005).***

Daily HD has also been shown to be associated with a decrease in homocysteine levels, C-reactive protein and oxidative stress. On the otherhand a better control of circulating advanced glycation end products (AGE) protein-bound molecules has been observed on short daily dialysis treatment ***(Fragedaki et al., 2005).***

An increase in the hemoglobin concentration and a decrease in the mean erythropoietin dosage have been reported with quotidian HD ***(Rao et al., 2003).***

An evident improved well-being of the patients is reported with daily HD. Once treated by daily HD, patients chose to return to conventional HD three times a week only rarely ***(Halpern et al., 2004).***

Improvement in hospitalization rate has been reported with daily HD compared with conventional HD. More data are needed to corroborate these results ***(Lindsay and Blagg 2003).***

There is a high patient survival rate after switching to daily HD, which has been attributed to patient selection. Technique survival in daily HD is higher for patients who dialyzed at home and lower in patients dialyzed in a dialysis unit. Fewer machine alarms and nursing interventions have been reported in daily HD ***(Okada et al., 2005).***

Potential disadvantages

Potential disadvantages of more frequent HD are related to organization, cost and repeated vascular access punctures. Another problem is that most patients did not accept this kind of treatment regardless of the documented benefits. A daily HD programme requires an appropriate infrastructure and very important logistic changes. Daily HD has an increased cost of disposable materials, treatment preparation time and patient transportation. However, the cost analysis should include potential cost reductions, such as less consumption of medications (erythropoietin, antihypertensive drugs, phosphate binders, etc.) and a reduction in the hospitalization rate. An important drawback for the in-centre hemodialysis patient is the time spent in more frequent trips to the dialysis unit ***(McFarlane et al., 2002).***

Particular advantages of daily long nocturnal HD:

In addition to benefits of daily HD, nocturnal HD reduces peripheral vascular resistance, increases baroreflex sensitivity,

and reduces triglyceride levels with an increase of high-density lipoprotein ***(Bugeja and Chan 2004)***.

In patients with sleep apnoea syndrome, oxygen saturation has been reported to improve with long nocturnal daily dialysis in comparison with conventional three times a week HD ***(Chan et al., 2004).***

Particular limitations of daily long nocturnal HD:

Calcium and phosphate depletion has been reported in long nocturnal HD, due to a high removal. In long nocturnal HD patients all phosphate binders were discontinued and elevated dialysate calcium concentration was required ***(Walsh et al., 2005).***

Daily hemodiafiltration:

Daily hemodiafiltration (2–2.5 h with an exchange volume of 13– 14 liters) six times a week compared with on-line hemodiafiltration (4–5 h) three times a week results in a significant decrease of plasma levels of urea, creatinine, uric acid, β2m and homocysteine. A reduction in the dose of phosphate binders, better blood pressure control without anti-hypertensive medications, disappearance of post-dialysis fatigue, improvement of nutritional status and a marked decrease of left ventricular mass were also reported ***(Maduell et al., 2003).***

2. Dialyzer Type

The criteria of Dialyzer:

-Capacity for solute clearance:

Refers to small solute transfer across membrane (expressed as mass transfer coefficient [KoA]); high-efficiency dialyzers have KoA urea > 450 mL/min. Determined by diffusive and convective clearance. Size, charge, protein binding, and volume of distribution of solute determine clearance rate.Ideal dialyzer should have high clearance of small- and middle-molecula weight uremic toxins and negligible loss of vital solutes Clearance of larger solutes primarily depends on convection ***(Simmons et al., 2004).***

- Biocompatibility:

Dialysis membranes can be made from cellulosic semisynthetic or synthetic material. Cellulosic membranes can cause complement and leucocyte activation while synthetic membranes have the greatest biocompatibility ***(Simmons et al., 2004***).

- Flux and convection

Synthetic high-flux membranes should be used to delay long-term complications of hemodialysis therapy in patients at high risk (serum albumin<40 g/l). In view of underlying practical considerations, and the observation of a reduction of

an intermediate marker beta-2 -microglobulin, synthetic high-flux membranes should be recommended even in low-risk patients. In order to exploit the high permeability of high-flux membranes, on-line hemodiafiltration or hemofiltration should be considered.The exchange volumes should be as high as possible, with consideration of safety ***(Tattersall et al., 2007).***

Solute removal in hemofiltration/hemodiafiltration:

Middle molecular weight solute removal obtained with highly permeable and biocompatible membranes employed in convective and mixed diffusion/convection strategies is definitely higher than that attainable by 'internal filtration' in high-flux HD ***(Kriete et al., 2005).***

The maximum safe filtration rate is determined by the infusion mode, the blood flow rate, hydraulic permeability, surface area of the dialyser membrane and the patient's characteristics (hematocrit and total protein concentration, coagulability status). These factors, to a different extent, contribute to the establishment of the pressure regimen necessary for the planned filtration. Ultrapure dialysate is mandatory for on-line production of the infusion fluid. The infusion fluid must be sampled periodically to ensure that it is free of endotoxin and meets the standards of microbial purity ***(Pedrini and De Cristofaro, 2003).***

Clinical results of increasing flux:

The above middle-molecular compounds have a pathogenic role or are markers of the most frequent long-term complications and causes of death in HD patients such as dialysis-related amyloidosis, cardio-vascular disease, secondary hyperparathyroidism, inflammation and malnutrition. Reduction of the accumulation and lower long-term levels of these compounds may prevent or delay the appearance of such complications. Significant reductions in the incidence of carpal tunnel syndrome and signs of dialysis related amyloidosis have been reported in two large retrospective studies as a result of high-flux membranes and of convective and mixed dialysis strategies inducing lower chronic β2-m levels. The increased ability of highflux membranes to remove phosphate and control of hyper-phosphatemia associated with improved patient survival. High-flux membranes are more effective than low-flux in controlling renal anemia and reducing the need of erythropoietin therapy ***(Ayli et al., 2005).***

Outcome in high-flux HD and HDF/HF:

The Hemodialysis (HEMO) Study a randomized prospective study, performed to assess the effect of high-flux membranes on mortality in hemodialysis patients. It suggested that among the 1846 patients enrolled in the study, high-flux membranes did not significantly affect the outcome of the all-cause mortality rate ***(Cheung et al., 2006).***

Subgroup analysis of the HEMO study were not in line with its general conclusions, showing that the high-flux intervention was associated with reduced risks of specific cardiac-related events, such as the decreased cardiac mortality and the composite outcome of first cardiac hospitalization or death from cardiac causes***(Cheung et al.,2004)***.

3. Determination of HD Dose/Adequacy

Frequency of adequacy testing:

Numerous studies have shown that low dialysis dose is associated with poor outcome.Inadequate dialysis may be difficult to detect clinically or by routine biochemical tests. Faults in the system for delivering dialysis (which includes the fistula, dialysis machine, prescription, schedule and dialyser) may be unpredictable and results in inadequate dialysis. To prevent adverse effects on the patient due to inadequate dialysis, adequacy measurements are customarily taken monthly along with routine biochemical tests ***(Hecking et al., 2004).***

Method of adequacy testing:

Various methods have been proposed and are in use for calculating dialysis dose. Dose calculated using many of these methods have been shown to relate to outcome. All methods are based on indirect measurement of mass of urea (or a urea surrogate) removed from the patient over a dialysis session.