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 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., 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

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 (questionnaire)

CHRONIC KIDNEY DISEASE AND HEMODIALYSIS PRESCRIPTION

Chronic kidney disease (CKD) is a devastating disease with clinical, economic and ethical dimensions, and is a recognized major public health problem. CKD is defined as kidney damage or glomerular filtration rate(GFR) less than 60 ml/min/ 1.73m2 for 3 months or more, regardless of cause ***(Levey et al., 2005).***

The major outcomes of CKD, regardless of cause include progression to ESRD, complications of decreased kidney function, and cardiovascular disease (CVD). Increasing evidence indicates that some of these adverse outcomes can be prevented or delayed by early detection, and treatment (***Remuzzi et al., 2002).***

CKD is the preferred term because another widely used one, chronic renal failure or insufficiency, is not as easily identifiable by patients as a disorder that affects the kidney. In addition, chronic renal failure (CRF) suggests that the kidneys have lost all of their function, whereas CKD covers the spectrum of clinical problems beginning with abnormalities detectable only by laboratory testing to a late stage, labeled uremia. When the kidney fails to perform most of its function, the clinical state is labeled end stage renal disease ESRD, and dialysis or transplantation is required to sustain life ***(Mitch, 2007).***

Causes of chronic kidney disease

CKD results from a large number of diseases that either are systemic and damage the kidney or are intrinsic to the kidney (Table 1). CKD has two characteristics. First, there is chronicity because the kidney damage of CKD is rarely repaired and loss of function persists, unlike the course of acute kidney injury (AKI). Second, loss of kidney function generates even more kidney damage so that CKD progressively worsens even if the disorder that caused it becomes inactive ***(Mitch, 2007).***

Table (1): Causes of CKD

Diabetic Glomerulopathy or nephropathy
Hypertensive nephrosclerosis
Glomerular disease: Glomerulonephritis Amyloidosis, light chain disease Systemic lupus erythematosus, Wegener's granulomatosis[*]
Tubulointerstitial disease: Reflux nephropathy (chronic pyelonephritis) Analgesic nephropathy Obstructive nephropathy (stones, benign prostatic hypertrophy) Myeloma kidney [*]
Vascular disease: Scleroderma [*] Vasculitis[*] Renovascular renal failure (ischemic nephropathy) Atheroembolic renal disease [*]
Cystic diseases: Autosomal dominant polycystic kidney disease Medullary cystic kidney disease

[*] Systemic disease involving the kidney. ***(Mitch, 2007).***

Stages of CKD

KDOQI designates 5 stages, with stage 5 being ESRD, when loss of kidney function (a glomerular filtration rate [GFR] < 15 mL per minute per 1.73 m2) precipitates a need for dialysis or kidney transplant. Patients in stages 1 and 2 may have robust, normal, or slightly lowered GFR with evidence of underlying kidney damage, including proteinuria; large or small kidneys on an ultrasound; or other evidence of compromised function. This classification represents a loss of 50% or more of the adult level of normal kidney function ***(NKF-K/DOQI 2007).*** Additionally, all people with kidney damage are classified as having CKD regardless of their GFR ***(NKF-K/DOQI 2007).***

Table (2): Stages of CKD

Stage	Description	GFR (mL per minute per 1.73 m2)
1	Kidney damage* with normal or increased GFR	> 90
2	Kidney damage* with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney failure	< 15 or dialysis

* Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

Approximately 450, 000 Americans are in stage 5 CKD, or ESRD. The majority of patients almost 20 million occupy the lower stages. Almost 6 million patients have stage 1, more than5 million have stage 2, approximately 8 million have stage 3, and 400, 000 have stage 4 disease. Experts in the field now consider CKD epidemic and estimate another 20 million patients are at risk of developing CKD ***(NKF-K/DOQI 2007).***

Hemodialysis

Dialysis is defined as the diffusion of molecules in solution across a semipermeable membrane along an electrochemical concentration gradient ***(Depner, 1991).***The primary goal of hemodialysis is to restore the intracellular and extracellular fluid environment that is characteristic of normal kidney function. This is accomplished by the transport of solutes such as urea from the blood into the dialysate and by the transport of solutes such as bicarbonate from the dialysate into the blood. Solute concentration and molecular weight are the primary determinants of diffusion rates. Small molecules, such as urea, diffuse quickly, whereas compartmentalized and larger molecules, such as phosphate, β2-microglobulin, albumin, and protein bound solutes, such as p-cresol, diffuse much more slowly. In addition to diffusion, solutes may pass through pores in the membrane by means of a convective process driven by hydrostatic or osmotic pressure gradients a

process called ultrafiltration. During ultrafiltration, there is no change in solute concentrations; its primary purpose is the removal of excess total body water ***(Locatelli et al., 2002).***

For each dialysis session, the patient's physiological status should be assessed so that the dialysis prescription can be aligned with the goals for the session. This is accomplished by integrating the separate but related components of the dialysis prescription to achieve the desired rates and total amount of solute and fluid removal ***(Meyer and Hostetter, 2007).***

Quantifying the dose and adequacy of dialysis

Measuring the clearance of solutes that accumulate in patients with uremia has become the mainstay for calculating the dose of dialysis and determining its adequacy as delivered. Precise standards and goals of dialysis adequacy are based on the clearance of urea, a byproduct of protein catabolism, which can be readily and accurately measured. The volume of distribution of urea, which is neither lipophilic nor highly protein bound, reflects total body water; consequently, urea is an attractive molecule for quantifying dialysis adequacy through mathematical modeling based on changing blood concentrations ***(Depner, 1991).***

The amount of urea to be removed is usually calculated according to the patient's body size with the use of the following

dimensionless construct, which relates the clearance of urea to its volume of distribution in the patient: Kt/Vurea, where K is the urea clearance of the dialyzer, t is the duration of dialysis, and V is the patient's volume of urea distribution ***(Gotch and Sargent, 1985).***

The importance of clearance of middle molecular weight solutes (500 to 30, 000 daltons) with respect to clinical outcomes has long been debated ***(Vanholder et al., 2008).***

Current high flux hemodialysis membranes have larger pores than did earlier generation membranes, and they permit the passage of larger uremic toxins. Since the β2-microglobulin concentration is easy to measure, it is frequently used as a marker solute for middle molecular weight solutes. Several retrospective, observational studies have suggested an association between the use of high flux hemodialysis membranes and reduced mortality ***(Port et al., 2001).***

Hemodialysis prescription

Table (3): Components of the hemodialysis prescription ***(Himmelfarb and Ikizler, 2010)***

Components		Comments
Dialyzer	Configuration	Hollow-fiber dialyzers are preferred owing to improved safety.
	Membrane biomaterials	Synthetic membranes are used more frequently than cellulose membranes owing to fewer blood–membrane interactions.
	Membrane permeability	High-flux membranes are constructed with larger pores, which allow greater removal of higher-molecular weight solutes, with similar removal of lower-molecular-weight solutes as compared with low-flux membranes.
Treatment time		Usual treatment time is about 4 hours. Longer treatment times allow more fluid removal with less risk of intradialytic hypotension, and the removal of compartmentalized solutes such as phosphate is increased; nevertheless, increased dialysis time has limited effects on removal of many solutes because of decreasing plasma concentrations.
Treatment frequency		Usual frequency is 3 times per week. Increasing the frequency of dialysis to >3 times per week improves solute clearance and fluid removal; effects on clinical outcomes and quality of life are being evaluated in randomized trials.
Blood flow rate		Usual prescription is 200 to 400 ml per minute. Achievable blood flow depends on the type and quality of vascular access. Increasing blood flow increases solute removal; however, increased flow resistance will eventually limit the augmented clearance.
Dialysate flow rate		Usual rate is twice the achieved blood flow rate in order to attain near-maximal solute clearance.

Components		Comments
Ultrafiltration rate		Should be less than 10 ml per kilogram of body weight per hour to reduce the risk of intradialytic hypotension.
Dialysate composition	Sodium	Between 130 and 145 mmol per liter. Higher sodium concentrations decrease the risk of intradialytic hypotension but increase thirst and interdialytic weight gain
	Potassium	Generally 2 to 3 mmol per liter. Lower levels of dialysate potassium are associated with sudden cardiac death; intradialytic potassium removal is highly variable, and plasma potassium levels rebound about 30% after dialysis.
	Calcium	Generally 1.25 to 1.75 mmol per liter. Only non–protein-bound calcium is removed; higher levels of dialysate calcium increase intradialytic blood pressure.
	Magnesium	Generally 0.5 mmol per liter. The optimal level of magnesium is unresolved, and magnesium flux is difficult to predict.
	Alkaline buffers	Commonly 30 to 40 mmol per liter. Predominantly bicarbonate with a small amount of acetate; bicarbonate concentration can be adjusted to correct metabolic acidosis.
	Chloride	Defined by prescribed cations and alkaline buffers in dialysate.
	Glucose	Commonly 100 to 200 mg per deciliter. Higher levels of glucose promote hypertriglyceridemia.
Intradialytic medications		Erythropoietin, iron, vitamin D analogues, antibiotics.
Anticoagulation		Heparin or other agents.

Treatment time

An important component of the dialysis prescription is treatment time, which can influence the ability to safely remove solutes and accumulated excess fluid. In the 1980s, shortening the treatment time to cut costs while maintaining an adequate level of urea clearance became common practice in the United States. However, subsequent studies revealed that outcomes were adversely affected by shorter treatment times ***(Held et al., 1991).***Advocates for longer treatment times pointed to the better outcomes in Europe and Asia, where treatment times are prolonged ***(Marshall et al., 2006).*** Patients who gain more weight with dialysis are at increased risk for death ***(Kalantar-Zadeh et al., 2009)***, and a longer treatment time is often required for such patients to help maintain fluid balance. Extended treatment times clearly improve blood pressure control and phosphate removal while having a modest effect on overall solute clearance ***(Powell et al., 2009).***

Frequency of dialysis

For more than four decades, the standard schedule for hemodialysis has continued to be three sessions a week ***(Kliger, 2007).*** A majority of studies have shown reductions in blood pressure levels and in the need for antihypertensive medications, with variable effects on regression of left ventricular hypertrophy, a frequent occurrence among patients receiving long term

hemodialysis. Health related quality of life measures appear to improve with more frequent dialysis treatments, whereas mixed results are reported for measures of anemia control and calcium phosphate metabolism ***(Suri et al., 2006).*** A recent randomized, controlled pilot trial compared daily nocturnal hemodialysis with conventional thrice weekly hemodialysis. In the primary analysis, there was a significant reduction in left ventricular mass in the group treated with daily dialysis, as compared with the conventionally treated group ***(Culleton et al., 2007).***

Dialyzer

Types of membranes

Unsubstituted cellulosic membranes

Unsubstituted cellulosic membranes have hydroxyl groups on their glucosan rings, which appears to be responsible for their propensity to activate the complement system via the alternative pathway when these proteins come into contact with blood. This activation of complement is partially responsible for the subsequent activation of neutrophils and other leukocytes, making these membranes bioincompatible ***(Chenoweth, 1984).***

Substituted cellulosic membranes

The replacement of surface hydroxyl groups with acetate groups in cellulose acetate membranes decreases complement activation, thereby increasing biocompatibility, at least by the

criteria of complement and neutrophil activation. The first of this type of membrane was cellulose monoacetate, in which many of the free hydroxyl groups were replaced by acetate residues. These were followed by the development of cellulose diacetate and triacetate membranes with more than three-fourths substitution of the hydroxyl groups, leading to further decreases in complement activation ***(Grooteman et al., 1995).***

Hemophan is another cellulose-based membrane in which free hydroxyl groups are replaced by diethylaminoethyl moieties ***(Schaefer et al., 1987).*** More recently, cellulosic membranes with other substitutions, such as the benzyl groups, have become available (synthetically modified cellulose) ***(Clark and Shinaberger, 2000).***

Synthetic membranes

Several synthetic membranes with high water permeability were developed in the 1960s, primarily for the purpose of hemofiltration ***(Streicher and Schneider, 1985).*** Compared with the thin and symmetric cellulosic membranes, these membranes are thick ($\geq$ 20μm) and may be either symmetric (eg, AN69; Hospa) or asymmetric (eg, polysulfone). The asymmetric composition of the latter membranes refers to the 2-layered structure of the hollow-fiber wall when viewed in cross-section, with an inner thin layer that comes into contact with the blood and plays a major role in regulating solute removal and a thick supporting stroma. The