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List of Abbreviations

AIC	Arterial intimal calcification
AMC	Arterial medial calcification
AVF	Arteriovenous fistula
BFU-E	Burst forming unit- erythroid
CAPD	Continuous ambulatory peritoneal dialysis
CERA	Continuous erythropoietin receptor activator
CKD	Chronic kidney disease stage
CLD	Chronic liver disease
COPD	Chronic obstructive pulmonary disease
CPG	Clinical practice guidelines
CRP	C- reactive protein
CV	Cardiovascular
CVS	Cerebrovascular stroke
DA	Darboepoetin-alfa
DFR	Dialysate flow rate
DM	Diabetes mellitus
DMT1	Divalent metal transporter 1
DOPPS	Dialysis Outcomes and Practice Patterns Study
ERBP	European best practice
EPO	Erythropoietin
ESA	Erythropoiesis stimulating agents
ESRD	End stage renal disease
EUTox	European uremic toxin

List of Abbreviations (cont.)

GN	Glomerulonephritis
HAMP	Hepcidin antimicrobial peptide
HB	Hemoglobin
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HD	Hemodialysis
HDF	Hemodiafiltration
HIV	Human immunodefiiency virus
HMWH	High molecular weight heparin
HTN	Hypertension
IHD	Ishemic heart disease
INF	Interferon
KDOQI	Kidney Disease Outcome Quality Initiative
KDIGO	Kidney disease improving global outcomes
KoA	The mass transfer area coefficient
KUF	Ultrafiltration coefficient
MOH	Ministry of health
MPG-EPO	Methoxy polyethylene glycol-epoetin beta
MPO	Membrane permeability outcome
PTH	Parathormone
PTX	Parathyroidectomy
PVD	Peripheral vascular disease
QB	Dialyzer blood flow

List of Abbreviations (cont.)

QIP	Quality improvement programs
QOL	Quality of life
rHuEPO	Recombinant human erythropoietin
ARIC	Atherosclerosis risk in community
RKF	Residual kidney function
SLE	Systemic lupus erythematosis
spKt/V	Single poolKt/V
SRI	Solute removal index
TNF	Tumor necrosis factor
UF	Ultrafiltration
URR	Urea reduction ratio
USRDS	United States Renal Data System
VDRA	Vitamin D receptor activators
β2M	Beta 2-microglobulin
IPD	Intermittent peritoneal dialysis

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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 ***(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) 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 and 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 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 (Cairo governorate: sector C) and to compare this pattern with standard international guidelines in hemodialysis prescription, stressing on anemia, bone disease management and adequacy of dialysis.

Hemodialysis Prescription

Introduction

Fifty years ago, Belding Scribner and his colleagues at the University of Washington developed a blood-access device using Teflon-coated plastic tubes, which facilitated the use of repeated hemodialysis (HD) as a life-sustaining treatment for patients with uremia ***(Coresh J et al ., 2005).***

The introduction of the Scribner shunt, as it became known, soon led to the development of a variety of surgical techniques for the creation of arteriovenous fistulas and grafts. Consequently, hemodialysis has made survival possible for more than a million people throughout the world who have end-stage renal disease (ESRD) with limited or no kidney function ***(Jonathan and Ikizler, 2010).***

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).***

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).***

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 dialysis prescription

The variables in the HD prescription that may be manipulated by the physician on the basis of clinical assessment are listed in Table 1.

Table 1: Components of the Dialysis Prescription

Dialyzer (membrane, configuration, surface area)
Time
Blood flow rate
Dialysate flow rate
Ultrafiltration rate
Dialysate composition
Dialysate temperature
Anticoagulation
Intradialytic medications
Dialysis frequency

From Himmelfarb J, Chuang P, Schulman G (2008): Hemodialysis. In: Brenner BM. Brenner and Rector's the Kidney, 8th ed, Philadelphia:Saunder, pp. 1957-2006.

1) Dialyzers

The dialyzers are calssified 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).***

The use of cellulose and its derivatives, cuprophane and cellulose acetate, is in decline. The side groups of the cellulosic membranes activate the complement system via the alternate pathway, resulting in the repeated generation of the anaphylatoxins C3a and C5a ***(Kaplow and Goffinet, 1986).***

Synthetic membranes differ from cellulose-based dialyzers in several ways. All cellulose membranes have hydroxyl radicals at the surface that increase their hydrophilicity (membrane wetability). Techniques that mask hydroxyl radicals enhance hydrophobicity and increase protein adsorption ***(Mujais and Schmidt, 1995).***

The creation of larger pore size semipermeable membranes in compact cartridges (high-flux dialyzers), with variable sizes of these pores, enhanced their ability to remove small solutes and middle molecules ***(Vanholder et al., 2010).***

High-flux dialyzers allow the passage and removal of retained solutes of higher molecular weight than do low-flux membranes. Dialyzers are considered as high-flux type if their ultrafiltration coefficient (KUF) exceeds 15 ml/h/mmHg and their ability to clear β2-M exceeds 20 ml/min (low-flux dialyzer clears KUF <15 ml/h/mmHg and β2-M < 10 ml/min) ***(Alp Ikizler and Schulman, 2005).*** However, the fluids (dialysate and water) used

with these high-flux dialyzers should be sterile non-pyrogenic and endotoxin free in order to avoid reverse filtration of endotoxins and blood contamination ***(Henderson , 1993).***

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).***

Conventional and high efficiency HD techniques, using low-flux dialyzers, are incapable of removing larger sized uremic toxins and/or protein-bound toxic molecules of > 500 Dalton . This would result in their accumulation in circulation where they can exert concentration- dependent toxicity, particularly on endothelium and cardiovascular system. Examples of these molecules include uridine adenosine tetraphosphate and endothelin, which exert vasoconstrictive effect, indoxyl sulfate and p-cresylsulfate – p-cresol, which has pro-inflammatory effect and cause endothelial dysfunction together with the pro-inflammatory cytokines, and has been associated with increased cardiovascular mortality ***(Vanholder et al., 2003).***

Other retained molecules which are known to cause harmful effects include β2-M, immunoglobulin light chains, parathyroid hormone, advanced glycation end products and advanced oxidation products ***(Calo ey al., 2007).***

Beta 2-microglobulin, which is considered a surrogate marker of middle molecules, is strongly associated with carpal tunnel syndrome and dialysis-related amyloidosis. Different studies have documented the efficiency of high-flux dialyzers in removing β2-M from the circulation of patients on dialysis, which has been associated with clinical and radiological improvement of carpal tunnel syndrome and dialysis-related amyloidosis ***(Wizemann et al., 2001).***

Observational studies have documented the improvement of survival rates of patients on high-flux-dialyzers when compared with those on low-flux dialyzers. These findings have been confirmed by two large randomized clinical trials: the HEMO study and the MPO study ***(Hornberger et al., 1992).***

In the entire cohort in the HEMO Study, the high-flux arm had no significant effect on the all-cause mortality rate or any of the four arm secondary outcomes. However, the high-flux HD provided significantly less cardiac and cerebrovascular mortality rates after 3.7 years HD than low-flux HD ***(Delmez et al., 2006).***

The Membrane Permeability Outcome (MPO) study, which was conducted in Europe, showed higher survival rate in high-flux HD patients with low serum albumin (≤ 4 g/dl) and diabetic patients ***(Locatelli et al., 2009).***

Following these two major studies, the European Best Practice Guidelines have recommended the use of high-flux