ROLE OF ON-LINE HAEMODIAFILTRATION IN BONE DISEASE IN CHILDREN WITH CHRONIC KIDNEY DISEASE

Thesis

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ABSTRACT

Background: on-line hemodiafiltration (HDF) is a technique of renal replacement therapy which combines diffusion with convection and uses ultrapure dialysate as a replacement fluid, this technique allowing removal of middle molecular weight uremic toxins. **Aim:** To compare the

effect of on-line hemodiafiltration versus conventional HD regarding the control of renal osteodystrophy.

Methods: This study included 16 pediatric patients with age range 4-16 with ESRD on maintenance hemodialysis, they were converted to on-line HDF for three months. Clinical, laboratory and radiological manifestations of ROD were compared for both modalities. **Results:** The mean level of serum **P** decreased from 4.9mg/dl to 4.2mg/dl (p=.04), the mean level of **PTH** decreased from 749pg/ml to 404pg/ml (p=0.001), with significant improvement in **bony pains** (p=.029) and no change in the **X-ray** findings.

Conclusion: On-line HDF improves the control of ROD in children with ESRD.

Key words:

Chronic kidney disease, Hemodialysis, On –line hemodiafiltration, PTH, renal osteodystrophy, Ultrapure dialysate

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List of Abbreviations

ABD	Adynamic bone disease
ALP	Alkaline phosphatase
AVF	Arteriovenous fistula
AVG	Arteriovenous graft
BALP	Bone-specific alkaline phosphatase
BMD	Bone mineral density
CaR	Calcium sensing receptor

CKD	Chronic kidney disease
CKD-MBD	Chronic kidney disease- mineral bone disease
CRF	Chronic renal failure
DEXA	Dual-energyX-ray absorptiometry
EPO	Erythropoietin
ESRD	End stage renal disease
FGF-23	Fibroblast growth factor -23
GRF	Glomerular filtration rate
HD	Hemodialysis
HDF	Hemodiafiltration
HF	Hemofiltration
ICTP	Type 1 collagen cross-linked telopeptide
LVH	Left ventricular hypertrophy
NKF/DOQI	National Kidney Foundation Disease Outcome Quality Initiative
PICP	Procollagen type I carboxyl terminal propeptide
PTFE	Polytetrafluoroethylene
PTH	Parathyroid hormone
PUJ	Pelvi-ureteric junction obstruction
PUV	Pelvi-urethral valve
ROD	Renal osteodystrophy
SCD	Sudden cardiac death
TMR	Transmembrane receptor
UKM	Urea kinetic modeling

UTI	Urinary tract obstruction
VDR	Vitamin D receptor
VUR	Vesico-ureteric reflux

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INTRODUCTION

Chronic kidney disease (CKD) is a term used to describe patients with kidney damage or decreased level of renal function for three months or more, irrespective of the underlying condition .It is defined as the presence of kidney damage or GFR below 60ml/min/1.73m2 (***Hogg et al., 2003).***

Disordered regulation of mineral metabolism occurs early in the course of CKD and results in alterations in bone modeling, remodeling and growth ***(Drueke et al., 2006).*** Renal osteodystrophy is a term applied to the changes in mineral metabolism that occur uniformly in CKD ***(Martin et al., 2004)***.

Renal osteodystrophy has been classified, primarily by alterations in bone turnover to:

1- High bone turn-over: excessive levels of circulating PTH result in increased bone turn-over and osteitis fibrosa cystica is the advanced lesion of secondary hyperparathyroidism (***Mucsi et al., 2005).***

2- Low-turn-over bone disease.

In patients with ESRD on HD, solute removal capacity of uremic toxins is enhanced by on-line HDF .In this technique, a certain amount of freshly prepared ultrapure dialysate is taken from the dialysate inlet line and processed with multiple filtration steps before being used as a replacement fluid (***Ronco et al., 2006***).

HDF expands the spectrum of uremic toxin removal from small-sized solutes, as in conventional HD, to middle-sized and large molecular weight solutes by combining convective clearance with diffusion. The use of on-line HDF has been proposed to improve the control of hyperparathyroidism and renal osteodystrophy in patients with ESRD (***Canaud et al., 2007***).

AIM OF THE WORK

The aim of this study is to compare between conventional hemodialysis and on-line hemodiafiltration regarding the control of the clinical, biochemical and radiological manifestations of renal osteodystrophy in children with ESRD.

CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is a serious public health problem, with national surveys showing a considerably higher prevalence than appreciated previously. In the United States there is a rising incidence of kidney failure that is associated in many cases with poor outcomes and high cost ***(Coresh et al., 2001).***

The term chronic kidney disease (CKD) is used to describe patients with kidney damage or decreased level of renal function for three months or more, irrespective of the underlying condition. It is also defined as the presence of kidney damage or GFR below 60ml/min/1.73m2 according to the National Kidney Foundation Disease Outcome Quality Initiative (NKF/DOQI) classification (Table1) ***(Hogg et al., 2003).***

Table 1: Criteria for the Definition of CKD

A patient has CKD if either of the following criteria is present:
1. Kidney damage for >3 months, as defined by structural or functional

abnormalities of the kidney, with or without decreased GFR, manifested by 1 or more of the following features:

• Abnormalities in the composition of the blood or urine

• Abnormalities in imaging tests

• Abnormalities on kidney biopsy

2. GFR <60 ml/min/1.73 m2 for >3 mo, with or without the other signs of kidney damage described above.

(Hogg et al., 2003)

Stages of chronic kidney disease:

NKF/DOQI classified CKD in to 5 stages, based on the level of GFR, as shown in table 2.

Table 2: Classifications of stages of chronic kidney disease.

Stages	GFR (ml/min/1.73m)	Description
1	≥ 90	Kidney damage with normal or increased GFR
2	60-89	Kidney damage with mild reduction of GFR
3	30-59	Moderate reduction of GFR
4	15-29	Severe reduction of GFR
5	<15(dialysis)	Kidney failure

(***NKF/DOQI 2002).***

Risk factors

Although level of GFR, proteinuria, and hypertension are strongly associated risk factors for CKD progression, other reported risk factors associated with CKD progression include low birth weight or prematurity, uric acid, lead or heavy metals, hyperlipidemia, metabolic acidosis, oxidative stress and disorders of bone and mineral metabolism (***Abitbol et al., 2009).***

While there is ongoing research to clarify the role of these risk factors in renal progression, the search for genetic susceptibility to CKD and its progression in humans has offered not only new directions for research, but also potential targets for intervention (***Ravani et al., 2009).***

It is likely that the number of individuals at risk for CKD exceeds the number of patients known to have CKD. Pediatric patients who are at increased risk of developing CKD include those with disorders such as those shown in (Table3).

Table 3: Disorders that increase the risk of CKD.

- Family history of polycystic kidney disease or other genetic kidney disease.
- Children with a history of acute kidney failure resulting from perinatal hypoxemia or other acute insults to the kidneys.
- Renal dysplasia or hypoplasia.
- Urologic disorders-especially obstructive uropathies.
- Vesicoureteral reflux associated with recurrent urinary tract infections and scars in the kidneys.
- Prior history of acute nephritis or nephrotic syndrome.