Role of on-line haemodiafiltration in improving cardiovascular morbidities in pediatric end stage renal disease patients

Thesis

Submitted for partial fulfillment of MD degree in Pediatrics

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2012

سُبْحَانَكَ لا عِلْمَ لَنَا إلا مَا عَلَّمْتَنَا

إنكَ أنتَ العَلِيمُ الحَكِيمُ

(سورة البقرة - الآية ٣٢)

Acknowledgement

*First of all, thanks to **ALLAH** who gave me the will to start, the power to continue and the goal to reach.*

*It's a pleasure to express my deepest thanks and profound respect to my honored professor, **Prof. Dr. Fatina Fadel, Professor of Pediatrics, Faculty of Medicine , Cairo University,** for her continuous encouragement, valuable supervision and guidance throughout this work. It has been an honor and a privilege to work under her generous supervision.*

*I would like to express my sincere appreciation to **Assist. Prof. Dr. Samuel Makar, Assistant Professor of Pediatrics, Faculty of Medicine, Cairo University** for his continuous guidance, supervision and valuable suggestions. No matter what I say could ever express my deepest thanks to him.*

*Words cannot express my feelings of gratitude and respect to **Dr .Hanan Zekri, Lecturer of Pediatrics, Faculty of Medicine, Cairo University.** She was (from the start) helping, encouraging and supporting. In the true meaning of words I can't thank her enough for her time and her effort.*

*I'm also deeply grateful and would like to express my sincere thanks and gratitude to **Dr. Dina Hesham, Lecturer of Chemical Pathology, Faculty of Medicine, Cairo University** for her continuous instructing guidance and sincere help and valuable support.*

I would also like to thank all the staff members of nephrology department, endocrinology lab unit, echocardiography lab and arrhythmia clinic who made my research easier with their generous help and cooperation.

Last but not the least, I am deeply thankful and always indebted to my parents and my family, who were always supporting and encouraging me.

Contents

Abstract

Background: Cardiovascular disease is an important cause of morbidity and mortality in patients undergoing maintenance dialysis. There is evidence supporting a direct role for the uremic milieu, and an indirect role as well, for enhanced cardiovascular complications. On-line dialysis modalities, such as on-line hemodiafiltration, raise particular concerns because not only small molecules are removed more effectively as compared to low-flux hemodialysis, but in addition, a considerable clearance of so-called middle molecular weight (MMW) substances is obtained including those involved in cardiovascular morbidities.

Objectives: To assess the effect of on-line hemodiafiltration on removal of uremic toxins that cannot be removed during conventional hemodialysis, e.g. homocysteine, and improving the chronic inflammatory state associated with chronic kidney disease and the possible impact of these changes on myocardial function in chronic hemodialysis patients.

Methods: In this study, we compared different clinical, lab and radiological data of 30 chronic hemodialysis pediatric patients on low-flux hemodialysis with the same data after 6 months of initiation of predilution on-line hemodiafiltration to clarify the possible impact of on-line hemodiafiltration on cardiovascular system in those patients.

Key words: On-line hemodiafiltration, homocysteine, cardiovascular morbidities, chronic inflammatory state.

List of abbreviations

AAMI	American Association for the advancement of Medical Instrumentation
ACE	Angiotensin converting enzyme
ADEMEX study	"ADEquacy of peritoneal dialysis in MEXico" study
ADMA	Asymmetric dimethyl arginine
ADP	Adenosine diphosphate
AFB	Acetate free biofiltration
AGEs	Advanced glycosylation end products
ALP	Alkaline phosphatase
ANP	Atrial natruritic peptide
ARBs	Angiotensin receptor blocker
ASE	American society of echocardiography
ATP	Adenosine triphosphate
B_2M	Beta 2 microglobulin
BMI	Body mass index
BP	Blood pressure
BSA	Body surface area
BUN	Blood urea nitrogen
C^{ε}	Carbon end
Ca	Calcium
Ca X P	Calcium phosphorus solubility product
CAPD	Chronic ambulatory peritoneal dialysis
CFU	Colony-forming unit
CIN	Chronic interstitial nephritis
CKD	Chronic kidney disease
Cl	Chloride
CMPF	3-Carboxy 4-methyl 5propyl 2-furanopropionic acid
CONTRAST study	the "Dutch CONvective TRAnsport Study"
CPNT	Centre of Pediatric Nephrology and Transplantation
Crea	Creatinine
CRF	Chronic renal failure
CRP	C- reactive protein
CVD	Cardiovascular disease
Da	Dalton
DBP	Diastolic blood pressure

DBPI	Diastolic blood pressure index
DNA	Deoxyribonucleic acid
DOPPS	Dialysis Outcomes & Practice Patterns Study
DT	Mitral deceleration time
DTT	Dithiothreitol
E/A ratio	Early diastole/ atrial contraction ratio
ECG	Electrocardiography
EDTA	Ethylene diamine tetraacetic acid
EF	Ejection fraction
ESA	Erythropoiesis stimulating agents
ESRD	End stage renal disease
EU	Endotoxin unit
FS	Fractional shortening
FSGS	Focal segmental glomerulosclerosis
GFR	Glomerular filtration rate
HCT	Hematocrit
Hcy	Homocysteine
HD	Hemodialysis
HEMO study	The “HEMOdialysis” study
HF	Heart failure
HF	Hemofiltration
HGB	Hemoglobin
HMG-CoA	3- Hydroxyl 3- methyl glutaryl CoA
Hs-CRP	High sensitivity C- reactive protein
HTN	Hypertension
HUS	Hemolytic uremic syndrome
IL	Interleukin
iNOS	Inducible nitric oxide synthase
IVSTD	Interventricular septum thickness in diastole
K	Potassium
K/DOQI	Kidney disease outcome quality initiatives
kDa	Kilo Dalton
LDL	Low density lipoprotein
LMW	Low molecular weight
LVH	Left ventricular hypertrophy
LVIDD	Left ventricular internal diameter in diastole
LVMI	Left ventricular mass index
MBP	Mean blood pressure
MBPI	Mean blood pressure index

MCP	Monocyte chemoattractant protein
MHz	Mega Hertz
MIA	Malnutrition- inflammation- atherosclerosis
MICS	Malnutrition- inflammation complex syndrome
mmHg	Millimeter mercury
MMW	Middle molecular weight
MTHFR	Methylene tetrahydrofolate reductase
MW	Molecular weight
Na	Sodium
NADH	Nicotinamide adenine dinucleotide hydrogen
NKF	National kidney foundation
NO	Nitric oxide
OL-HDF	On-line haemodiafiltration
OPB	Oral phosphate binder
P	Phosphorus
PAH	Para amino hippuric acid
PAI-1	Plasminogen activator inhibitor-1
PD	Peritoneal dialysis
PEM	Protein energy malnutrition
PTFE	Poly tetrafluoroethylene
PTH	Parathyroid hormone
PUJO	Pelviureteric junction obstruction
PUV	Posterior urethral valve
PWTD	Posterior wall thickness in diastole
QOL	Quality of life
RISCAVID study	“RISchio CArdiovascolare nei pazienti afferenti all area Vasta In Dialisi”
RO	Reverse osmosis
SAH	S- adenosyl homocysteine
SAL	Sterility assurance level
SAM	S- adenosyl methionine
SBP	Systolic blood pressure
SBPI	Systolic blood pressure index
SDMA	Symmetric dimethyl arginine
T4	Thyroxine
tHcy	Total homocysteine
THF	Tetrahydrofolate
TMP	Trans membrane pressure

TNF	Tumor necrosis factor
UF	Ultrafiltration
USRDS	United States registry data system
UTI	Urinary tract infection
VC	Vascular calcification
VSMC	Vascular smooth muscle cell
VUR	Vesico-ureteric reflux

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Introduction and aim of the work

Introduction:

Reviewing the current picture of uremic toxins reveals its complexity. Focusing on cardiovascular damage as a model of uremic effects resulting in substantial morbidity and mortality, most molecules with potential to affect the function of a variety of cell types within the vascular system are difficult to remove by conventional dialysis. Examples are the larger middle molecular weight molecules and protein-bound molecules. Recent clinical studies suggest that enhancing the removal of these compounds, whether through improving the removal of toxins or the search for pharmacologic strategies blocking responsible pathophysiologic pathways, is beneficial for survival of patients on maintenance hemodialysis ***(Vanholder et al., 2008)***.

Furthermore, repetitive exposure to cytokine-inducing substances (pyrogens) results in chronic inflammation, which may significantly contribute to some of the long-term complications in dialysis patients especially cardiovascular one ***(Canaud et al., 2001)***.

On-line dialysis modalities, such as on-line haemodiafiltration, raise particular concerns because not only small molecules (<5 kDa) are removed more effectively as compared to low-flux hemodialysis, but in addition, a considerable clearance of so-called middle molecular weight substances (5–50 kDa) is obtained ***(Van der Weerd et al., 2008)***.

Aim of the work :

1- To assess the effect of on-line hemodiafiltration on:

- Predialysis serum total Homocysteine level as a reflection of uremic toxins implicated in cardiovascular morbidities, and not commonly removed during conventional HD.

- High-sensitivity C-reactive protein as a marker of chronic inflammatory state.

2- to study the effect of on-line HDF on myocardial function (including left ventricular hypertrophy, systolic, and diastolic dysfunction) in chronic kidney failure patients on maintenance hemodialysis and the possible correlation with other clinical and lab parameters.

REVIEW OF LITERATURE

Uremic milieu in chronic kidney disease