

Differences between High Flux Dialysis versus High Efficiency Online Hemodiafiltration in Diffusive and Convective Reduction Ratio

Thesis

Submitted for partial fulfillment of Master Degree
in Internal Medicine

By

May Abd Elaziz Abd Elaziz Elhashash

M.B.B.Ch
Cairo University

Supervised by

Prof. Hesham Mohamed Elsayed

Professor of Internal Medicine
Faculty of Medicine - Ain Shams University

Dr. Hussein Sayed Hussein

Assistant Professor of Internal Medicine
Faculty of Medicine - Ain Shams University

**Faculty of Medicine
Ain Shams University
2018**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgments

*First and forever, thanks to **Allah**, Almighty for giving me the strength and faith to complete my thesis and for everything else.*

*I would like to express my deepest gratitude and appreciation to **Prof. Hesham Mohamed Elsayed**, Professor of Internal Medicine, Faculty of Medicine - Ain Shams University, who initiated and designed the subject of this thesis, for his kindness, over available, fatherly attitude and untiring supervision, helpful criticism and support during the whole work,*

*My extreme thanks and gratefulness to **Prof. Eman Elgohary**, Professor of Clinical Pathology, Faculty of Medicine - Ain Shams University, I'm much grateful for her patience and strict supervision and revision of practical part of this work,*

*I would like also to thank with all appreciation **Dr. Hussein Sayed Hussein**, Assistant Professor of Internal Medicine, Faculty of Medicine - Ain Shams University, for the efforts and time he has devoted to accomplish this work,*

*Last but not least, I would like to thank all members of my family, specially my **Parents** and my **Husband**, for their care and support.*

 *May Abd Elaziz Abd Elaziz Elhashash*

List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Tables.....	iii
List of Figures	iv
Introduction	1
Aim of the Work.....	3
Review of Literature	
End Stage Renal Disease (ESRD).....	4
Hemodialysis Modalities	14
High Flux Dialyzer.....	32
Adequacy of Dialysis	44
Hemodiafiltration (HDF)	49
Patients and methods	77
Results.....	83
Discussion	95
Summary	101
References	103
Arabic Summary	—

List of Abbreviations

<i>Abbrev.</i>	<i>Full-term</i>
AGE	: Advanced glycation end-products
B2M	: Beta-2 microglobulin
BFRs	: Blood flow rates
Ca	: Calcium
CAVH	: Continuous arteriovenous hemofiltration
CAVHDF	: Continuous hemodiafiltration
CBC	: Complete blood count
CKD	: Chronic kidney disease
CRRT	: Contentious renal replacement therapy
CVVH	: Continuous venovenous hemofiltration
CVVHD	: Continuous venovenous hemodialysis
CVVHDF	: Continuous venovenous hemodiafiltration
DM	: Diabetes mellitus
DOPPS	: Dialysis Outcomes and Practice Patterns Study
EPO	: Erythropoetin
ESHOL	: On-line Haemodiafiltration Survival Study
ESKD	: End-stage kidney disease
ESRD	: End-stage renal disease
GFR	: Glomerular filtration rate
HD	: Hemodialysis
HEMO	: Hemodialysis

HE-OL HDF	: High-efficiency online hemodiafiltration
HPM	: High performance membrane
HTN	: Hypertension
IHD	: Ischemic heart disease
JSDT	: Japanese Society of Dialysis Therapy
K	: Potassium
KDIGO	: Kidney Disease Improving Global Outcomes
LF	: Low-flux
LVH	: Left ventricular hypertrophy
Na	: Sodium
PCR	: Protein catabolic rate
Qb	: Blood flow rate
Qd	: Dialysate flow rate
SCUF	: Slow continuous ultrafiltration
SCUF	: Slow Continuous Ultrafiltration
SD	: Standard deviation
SLED	: Slow low-efficiency diffusion hemodialysis
SPSS	: Statistical package for social science
TMP	: Transmembrane pressure
TNF-α	: Tumor necrosis factor- α
UF	: Ultrafiltration
UFR	: Ultrafiltration rate
URR	: Urea Reduction Ratio

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Frequency of Primary Disease causing End-Stage Renal Disease	8
Table (2):	Comparison of techniques	31
Table (3):	Dialyzer classification.....	37
Table (4):	Classification of solutes molecular weight.....	40
Table (5):	Relative advantages and disadvantages of fluid reinfusion site.	64
Table (6):	Demographic characteristics of the studied cases	83
Table (7):	Basal laboratory findings of the studied cases	84
Table (8):	Serum β_2 microglobulin ($\mu\text{g/ml}$) among the studied cases	85
Table (9):	Blood Urea (mg/dl) among the studied cases....	87
Table (10):	Blood pump (Qb), dialysate flow(Qd) and TMP among the studied cases	89
Table (11):	Correlation between serum β_2 microglobulin reduction and other variables among the studied cases	92

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	A CKD population study performed in Morocco presenting percentiles for repeated estimates of GFR	6
Figure (2):	The latest overview about kidney health care in all regions of the world	6
Figure (3):	Prognosis of CKD by GFR and albuminuria categories	7
Figure (4):	An integrated care continuum for CKD that is consistent with the chronic care model.....	9
Figure (5):	A proposed step-by-step approach to help prepare patients for dialysis.	10
Figure (6):	Movement of solutes by diffusion, convection and adsorption	17
Figure (7):	Blood and dialysate circuits	21
Figure (8):	Effect of increasing blood flow on solute clearance	23
Figure (9):	Different Hemodialysis Techniques	27
Figure (10):	Cross Section of a Dialyzer	33
Figure (11):	Scanning electron microscopy of a conventional low-flux-membrane hollow fiber (Panel A).....	42
Figure (12):	A synthetic high-flux-membrane hollow fiber (Panel B).....	43

List of Figures

Figure (13): Distribution of the use of various forms of dialysis therapy.	50
Figure (14): Classic HDF	59
Figure (15): On-Line hemodiafiltration	59
Figure (16): Push-pull HDF.....	60
Figure (17): Double high-flux HDF and paired filtration dialysis with endogenous reinfusion.....	60
Figure (18): Mid-dilution HDF	65
Figure (19): Pre-dilution and Post-dilution HDF	65
Figure (20): Mixed-dilution HDF	66
Figure (21): Benefits of online hemodiafiltration.....	74
Figure (22): Serum β_2 microglobulin among the studied cases	86
Figure (23): Blood Urea among the studied cases	88
Figure (24): Blood Pump among the studied cases	90
Figure (25): Dialysate flow among the studied cases	90
Figure (26): TMP among the studied cases	91
Figure (27): Correlation between β_2 microglobulin reduction and its predialysis level in HF group	93
Figure (28): Correlation between β_2 microglobulin reduction in HF group and predialysis blood BUN	94
Figure (29): Correlation between β_2 microglobulin reduction in HDF group and predialysis blood BUN	94

Abstract

Background: Several epidemiological studies performed in recent decades based on large databases suggest that convective treatments may be superior at reducing morbidity and mortality in dialysis patients. HDF has also been reported to improve beta2- microglobulin (β_2 -m), phosphate and urea removal. Some others studies have reported better anaemia correction and lower inflammation when using HDF. The main disadvantages of HDF are its cost and the loss of albumin. **Aim of the Work:** The objective of the study is to compare between efficiency of dialysis sessions of high flux dialysis and HE-OL HDF in diffusive and convective reduction ratio of urea and β_2 microglobulin by using them as an indicators. **Patients and methods:** This observational cross sectional study was conducted on 22 prevalent hemodialysis patients attending at hemodialysis unit of Ain Shams University specialized hospital. The included patients are clinically stable on thrice weekly hemodialysis sessions for 4 hours per session, performing both high flux hemodialysis sessions alternating with high efficiency online hemodiafiltration sessions. **Results:** The study showed that There was more significant reduction ratio in serum β_2 microglobulin in HDF session ($82.2 \pm 3.4\%$) than in HF session ($67.4 \pm 6.5\%$) with (p value < 0.001). Also, there was more significant reduction ratio in blood urea in HDF session ($82.2 \pm 5.0\%$) than in HF session ($76.0 \pm 5.9\%$) with p value < 0.001 **Conclusion:** The results of this study confirm the experience of other investigators that routine on-line hemodiafiltration can be performed safely in a large group of patients. Our results also show that hemodiafiltration provides superior solute removal to high-flux hemodialysis over a wide range of solute sizes for blood flow rates in the range of 250 to 400 ml/min. **Recommendations:** Further studies on a larger scale of patients are needed to confirm the results obtained by this work.

Key words: high flux dialysis, high efficiency online hemodiafiltration, diffusive, convective reduction ratio

Introduction

Although it was not until 1960s that long term dialysis in a clinical setting become a reality, dialysis as a treatment for renal failure had been the focus of interest for some time, it is difficult now to imagine that less than 50 years ago patients with ESRD had only one prognosis, death. Dialysis Involves bidirectional movement of molecules across a semipermeable membrane (*Ahmad, 2009*).

Hemodialysis (HD) is a dynamic process, which occurs during movement of low molecular weight water soluble substances through a semipermeable membrane, Transport across the membranes of low-flux (LF) dialyzers is based mainly on diffusion and through the membranes of high-flux (HF) dialyzers, diffusion and convection (*Sobaszek-Pitas et al., 2014*).

The mortality rate of patients on maintenance dialysis remains alarmingly high, at approximately 15-20 % per year. Increasing dialyzer urea clearance has not been shown to improve survival and hence interest has shifted towards convective therapies, such as hemodiafiltration (HDF) which can remove middle molecular weight uremic toxins, which have been suggested to increase mortality in patients with end-stage kidney disease (*Basile et al., 2017*).

Because of incomplete removal of uremic toxins, 90% of hemodialysis patients reveal symptoms of pathologic amyloidosis caused by β_2 microglobulin after five years of dialysis (*Oshvandi et al., 2014*).

HDF combines diffusion and convection. The large convective volumes that are generated using high-flux membranes are replaced with substitution fluid, from either commercially available bags or using ultrapure dialysis fluid in a technique known as online HD (*Vilar et al., 2009*).

HDF is a treatment designed to remove accumulated metabolic products from blood by a combination of diffusive and convective transport through a semi-permeable membrane of high-flux type. Fluid is removed by ultrafiltration and the volume of filtered fluid exceeding the desired weight loss is replaced by sterile, pyrogen-free infusion solution. HDF provides a solute elimination of high molecular weight molecules better than HD (*Tattersall & Ward, 2013*).

Aim of the Work

The objective of the study is to compare between efficiency of dialysis sessions of high flux dialysis and HE-OL HDF in diffusive and convective reduction ratio of urea and β_2 microglobulin by using them as an indicators.

End Stage Renal Disease (ESRD)

Chronic kidney disease (CKD) is a global health problem. CKD patients are widely prevalent, and the number of end-stage kidney disease (ESKD) patients is still increasing (*Kimura, 2016*).

ESKD patients require cost-prohibitive kidney replacement therapy. Moreover, CKD patients are highly vulnerable, and the risk of cardiovascular events and death increases with the progression of CKD stages. Thus, it is critical to predict their risk for the progression to ESKD in CKD patients to avoid these unfavorable situations (*Kimura, 2016*).

DEFINITION

CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health.

The addition of ‘with implications for health’ is intended to reflect the notion that a variety of abnormalities of kidney structure or function may exist, but not all have implications for health of individuals, and therefore need to be contextualized (*KDIGO, 2012*).

Mechanism (pathophysiology)

Nephrons are generated in weeks 12–36 of gestation in humans, with a mean of 950,000 nephrons per kidney (with a range of ~200,000 to >2.5 million) (*Bertram et al., 2011*).

No new nephrons can be generated after this period. During growth, the available nephrons increase in size to accommodate increased renal demands. Furthermore, GFR decreases with age (*Brenner et al., 1982*).

Nephron loss, for example owing to injury or donation of one of the kidneys, can have hypertrophic effect on the remaining nephrons (*Brenner et al., 1982*).

This nephron adaptability allows for continued normal clearance of plasma solutes. Plasma levels of substances such as urea and creatinine start to show measurable increases only after total GFR has decreased to 50% (*Schnaper, 2014*).

The plasma creatinine value will approximately double with a 50% reduction in GFR. For example, a rise in plasma creatinine from a baseline value of 0.6 mg/dL to 1.2 mg/dL in a patient, although still within the adult reference range, actually represents a loss of 50% of functioning nephron mass (*Schnaper, 2014*).

Aging and renal function

The GFR peaks during the third decade of life at approximately 120 mL/min/1.73 m²; it then undergoes an annual mean decline of approximately 1 mL/min/y/1.73 m², reaching a mean value of 70 mL/min/1.73 m² at age 70 years (*Hallan, 2012*).