

***Level of beta-2 Microglobulin in
chronic renal failure patients on
regular haemodialysis***

Thesis

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Contents

List of Tables.....	VIII
List of Figures.....	X
List of Abbreviations.....	XII
Introduction and Aim of Work.....	XV

Review of Literature

Chapter 1: Chronic Renal Failure.....	1
Chapter 2; Beta 2 microglobulin in renal diseases.....	16
Chapter 3: Renal Replacement Therapy	37
Patients and methods.....	69
Results.....	72
Discussion.....	81
Summary and conclusions.....	91
Recommendations.....	94
References.....	95
Arabic Summary.....	113

List of Tables

Tables of Review

Table (1): Normal Glomerular filtration rate (GFR) in children and adolescents.....	2
Table (2): CKD staging.....	3
Table (3): Primary Causes of CRF in children	5
Table (4): advantages and disadvantages of CRRT.....	61

Tables of results

Table (5): sex distribution among the study group.....	72
Table (6): Original renal disease in the study group.....	72
Table (7): Distribution of filter sizes in the study group.....	73
Table (8): Duration of dialysis session in hours.....	73
Table (9): Blood flow per dialysis session and erythropoietin therapy.....	74
Table (10): Comparison between blood pressure values (in mmHg) on high flux and low flux dialysis membranes.....	74
Table (11): The frequency of patients receiving antihypertensive drugs.....	76
Table (12): Weights of the study group.....	76

Table (13): Comparison between the weight of patients in relation to the type of dialysis membrane and timing of measurement whether pre or post dialysis.....	76
Table (14): Kt/V and blood cells during treatment with low flux and high flux dialysis membranes.....	77
Table (15): Comparison between low flux and high flux dialyzers' influence on routine lab investigations.....	78
Table (16): Comparison between low flux and high flux dialyzers' influence on the level of β 2 microglobulin.....	79

List of Abbreviations

A	Surface area
ACEI	Angiotensin converting Enzyme Inhibitor
AGE	Advanced Glycation End Product
AKI	Acute Kidney Injury
APD	Automated Peritoneal Dialysis
ARA	Angiotensin Receptor Antagonist
β 2 m	Beta 2 Microglobulin
BUN	Blood Urea Nitrogen
CAPD	Continuous Ambulatory Peritoneal Dialysis
CAVH	Continuous Arterio-Venous Hemofiltration
CAVHD	Continuous Arterio-Venous Hemodialysis
CAVHDF	Continuous Arterio-Venous Hemodiafiltration
CVVH	Continuous Veno-Venous Hemofiltration
CVVHD	Continuous Veno-Venous Hemodialysis
CVVHDF	Continuous Veno-Venous Hemodiafiltration
CKD	Chronic Kidney Disease
CML	Carboxy Methyl Lysine
CMS	Center of Medicare Services
CRF	Chronic Renal Failure
CRI	Chronic Renal Insufficiency
CRRT	Continuous Renal Replacement Therapy
CSF	Cerebrospinal Fluid
CT	Computerized Tomography
CTS	Carpel Tunnel Syndrome
CVS	Cardiovascular System

1,25 (OH) ₂ D ₃	1,25 dihydroxy cholecalciferol
DRA	Dialysis Related Amyloidosis
ESRD	End Stage Renal Disease
EPO	erythropoietin
FSGS	Focal Segmental Glomerular Sclerosis
GN	Glomerulonephritis
GFR	Glomerular Filtration Rate
GH	Growth Hormone
GHR	Growth Hormone Receptor
GIT	Gastrointestinal Tract
HD	Hemodialysis
HTN	Hypertension
HLA	Human Leucocytic Antigen
HRA	Hemodialysis Related Amyloidosis
I-125	Iodine 125
I-131	Iodine 131
IGF	Insulin Growth Factor
IHDF	Intermittent on line Hemodiafiltration
INF	Interferon
IL-1	Interleukin 1
IL-1 β	Interleukin -1beta
IL-6	Interleukin 6
KDa	Kilo Dalton
KoA	Mass transfer coefficient
MDP	Methylene Diphosphonate
MODS	Multi Organ Dysfunction Syndrome

MRI	Magnetic Resonance Image
MW	Molecular Weight
NKF	National Kidney Foundation
NAPRTCS	North American Pediatric Renal Transplant Cooperative Study
PTH	parathormone
PD	Peritoneal Dialysis
PS	Polysulphone
PAN	Polyacrylnitrile
PMMA	Polymethyl methacrylate
PUJ	Pelvi ureteric Junction
PUV	Posterior Urethral Valve
RAS	Renin Angiotensin System
Rh ($\beta 2$ m)	Recombinant Beta 2 Microglobulin
RO	Reverse Osmosis
RRT	Renal Replacement Therapy
SAP	Serum Amyloid P component
SCUF	Slow Continuous Ultra Filtration
SDS	Standard deviation scores
SPET.....	Single emission position tomography
STAT	Signal Transducer and Activation of Transcription
SD	Standard Deviation
TNF α	Tumor Necrosis Factor alpha
USRDS	United States Renal Data System
UTI	Urinary Tract Infection

List of Figures

Figures of Review

Figure (1): Uremic frost.....	7
Figure (2): Etiology of growth retardation in children with CRF.....	9
Figure (3): Radiological findings in renal osteodystrophy.....	10
Figure (4): Bone cysts in the wrists of CRF patients suffering from DRA.....	28
Figure (5): Amyloid may build up in the wrist and cause bone cysts or carpal tunnel syndrome.....	30
Figure (6): A sagittal reconstructed CT scan shows destruction of the vertebral bodies with some developing kyphosis at the upper level and retropulsion of bone into the spinal canal.....	31
Figure (7): Hemodialysis machine.....	37
Figure (8): Semi permeable membrane.....	38
Figure (9): Scanning electron microscopy of a conventional low-flux- membrane hollow fiber and a synthetic high-flux-membrane hollow fiber.....	48
Figure (10): An arteriovenous graft	54
Figure (11): A radio cephalic fistula	54

Figures of Results

Figure (12): Sex distribution among study group.....	72
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Figure (13): distribution of Original renal disease in the study group.....	73
Figure (14): Comparison between low flux and high flux regarding blood pressure.....	75
Figure (15): Distribution of hypertensive patients on low flux.....	75
Figure (16): Distribution of hypertensive patients on high flux.....	76
Figure (17): Comparison of weight reduction on low and high flux dialyzers.....	77
Figure (18): Comparison between low flux and high flux regarding hematocrite level.....	78
Figure (19): Comparison between low flux and high flux regarding creatinine and phosphorus.....	79
Figure (20): Comparison between low flux and high flux regarding $\beta 2$ microglobulin.....	80

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Abstract

Dialysis associated amyloidosis or β 2 microglobulin- derived amyloidosis is a unique type of amyloidosis that has been described in individuals with ESRD on chronic dialysis. It has been associated with serious complications that significantly add to the morbidity of long term dialysis patients. Its clinical expression in terms of arthralgias, destructive arthropathies and carpal tunnel syndrome is often associated with amyloid deposits, which are mainly composed of β 2m fibrils which is related to elevated plasma β 2m that is characteristic of CRF. Also a visceral form with systemic organ involvement has been also described. Diagnosis of DRA is through conventional non invasive diagnostic techniques, i.e. clinical evaluation, joint ultrasonography or X ray, CT or MRI as well as conventional bone scans in addition to scintigraphy with radiolabelled serum amyloid P component (SAP) or with radiolabelled A β 2m precursor protein

One of the risk factors that contribute to the development of DRA is the type of HD membranes. High flux dialysis membranes have been shown to remove and adsorb β 2m more efficiently than the cellulosic membranes.

This study represents a group of 20 CRF patients' ages between 10-15 years undergoing regular HD in the center of nephrology and kidney transplantation. Blood samples were taken while they were on low flux dialysis membranes to measure the level of β 2 microglobulin in the patients' sera then they were shifted to high flux dialysis membranes for 3 months and after that period blood samples were withdrawn again to measure and the level of β 2 microglobulin in the sera of these patients to compare them with the previously measured levels. The results of this

study showed that the levels were significantly lower on high flux dialysis membranes than on low flux ones.

Key words: Chronic renal failure- Dialysis related amyloidosis- Beta 2 microglobulin- Hemodialysis- Membrane flux

Introduction

Hemodialysis is the major modality of renal replacement therapy for patients with ESRD who are waiting for or not suitable for undergoing renal transplantation. Adequate dialytic treatment has prolonged the survival of patients with good quality of life.

However many long term complications may affect CRF patients who are on regular HD therapy. One of these complications is DRA which is a major cause of morbidity in CRF patients manifesting as carpal tunnel syndrome, arthropathy, and bone cysts resulting in fractures or other systemic manifestations. DRA was found to be caused by amyloidogenic β 2-microglobulin which is a middle sized molecule with a molecular weight of 11,800. Increased clearance of β 2-microglobulin leads to decreased incidence of DRA. This could be achieved by using high flux (high permeability) membranes which have larger pore sizes than low flux one i.e they are capable of removing middle sized molecules (β 2 microglobulin) more than low flux ones. Current evidence suggests that high-flux, polysulphone, biocompatible membranes i.e. with low complement activation such as polyacrylonitrile significantly delay amyloidosis development compared with low flux complement activating membranes such as cuprophane, High flux membranes were found to be characterized by β 2 microglobulin clearance $>20\text{ml/min}$ while low flux membranes $< 10\text{ml/min}$

Aim of work

The aim of the present study is to compare the ability of high flux and low flux dialysis membranes to eliminate B-2 microglobulin from the sera of CRF patients on regular hemodialysis and to prove that high flux dialysis membranes are capable of eliminating these medium sized molecules more than low flux ones and thus decreasing the incidence of DRA (dialysis related amyloidosis) and related complications