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

Thesis
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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 D3…. 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-1β …….. 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 Uretheral Valve

RAS …….. Renin Angiotensin System

Rh (β2 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

TNFα …… Tumor Necrosis Factor alpha

USRDS ……. United States Renal Data System

UTI ……....Urinary Tract Infection

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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 β2m 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 Aβ2m 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 β2m 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 carpel tunnel syndrome, arthropathy, and bone cysts resulting in fractures or other systemic manifestations. DRA was found to be caused by amyloidogenic β2-microglobulin which is a middle sized molecule with a molecular weight of 11,800. Increased clearance of β2-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 (β2 microglobulin) more than low flux ones. Current evidence suggests that high-flux, polysulphone, biocompatible membranes i.e. with low complement activation such as polyacrilonitrile significantly delay amyloidosis development compared with low flux complement activating membranes such as cuprophane, High flux membranes were found to be characterized by β2 microglobulin clearance>20ml/min while low flux membranes< 10ml/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