شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

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HANAA ALY

HIGH FLUX VERSUS HEMODIAFILTRATION IN REMOVAL OF INDOXYL SULPHATE

Thesis

Submitted for partial fulfillment of MD degree in internal Medicine

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الاستصفاء الدموي الترشيحي مقابل الاستصفاء الدموى باستخدام فلاتر عاليه التدفق في ازاله سم اندوكسيل الكبريتات

رسالة

توطئة للحصول علي درجة الدكتوراة في أمراض الباطنة العامة

مقدمة من

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Contents

List of Abbreviations

AhR..... **:**Aryl hydrocarbon receptor.

CC-HDF ..... **:**Convective-controlled double high-flux hemodiafiltration.

CKD..... **:**Chronic kidney disease

CRP ..... **:**C-reactive protein.

CVD..... **:**Cardiovascular disease

ELISA..... :Enzyme linked immunosorbent ssay

EPC..... **:**Endothelial progenitor cell.

ESKD..... **:**End-stage kidney disease.

ESRD..... **:**End Stage Renal Disease

FGF-23 ..... **:**Fibroblast growth factor-23.

GFR ..... **:**Glomerular filtration rate

GI tract..... **:**Gastrointestinal tract.

HD..... **:**Hemodialysis

HDF ..... **:**Hemodiafiltration

HF ..... **:**High flux.

hs-CRP ..... **:**High sensitivity C-reactive protein.

IAA ..... **:**Indole acetic acid

ICAM-1 ..... **:**Intercellular Adhesion Molecule-1.

IL ..... **:**Interleukein

IS RR..... **:**Indoxyl sulfate reduction ratio.

IS..... **:**Indoxyl sulfate

LF ..... **:**Low flux.

LPS ..... **:**Lipopolysaccaride

MAPKs..... **:**Mitogen-activated protein kinases.

MCP-1 ..... **:**Monocyte chemoattractant protein-1.

MMW ..... **:**Middle molecular weight.

mRNA..... **:**Messenger Ribonucleic acid.

MW..... **:**Molecular weight

NADPH ..... **:**Nicotinamide adenine dinucleotide phosphate.

NF ..... **:**Nuclear factor

NF-κB ..... **:**Nuclear factor-κB.

NO..... **:**Nitric oxide

OATs ..... **:**Organic anion transporters.

PAA ..... **:**Phenylacetic acid

PAI-1 ..... **:**Plasminogen activator inhibitor-1.

PBTs ..... **:**Protein-bound toxins

PBUTs ..... **:**Protein bound uremic toxins.

PCS ..... **:**P-cresyl sulfate

PD ..... **:**Peritoneal dialysis.

PTH ..... **:**Parathyroid hormone.

RAS..... **:**Renin–angiotensin system

ROS ..... **:**Reactive oxygen species

SCFA ..... **:**Short chain fatty acid.

SF ..... **:**Super flux.

TGF ..... **:**Transforming Growth Factor

TGF-β1 ..... **:**Transforming growth factor-β1.

TMAO ..... **:**Trimethylamine n-oxide

TMP..... **:**Transmembrane pressure.

TNF-α ..... **:**Tumor necrosis factor α.

VSMC..... **:**Vascular smooth muscle cell.

WSCs..... **:**Water-soluble compounds.

β2M..... **:**B2-microglobulin.

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ABSTRACT

- **BACKGROUND:** protein-bound compounds such as the p-cresol conjugates p-cresyl sulphate (p-CS) and Indoxyl sulphate (IS) have attracted most interest in recent years due to their poor clearance by conventional dialysis and their potential toxicity. **Aim of the study:** To compare removal of indoxyl sulphate toxin during single session between low flux, high flux hemodialysis and hemodiafiltration. **METHODS:** Cross sectional study was concluded upon 60 randomly selected ESRD patients on regular hemodialysis from nephrology Department in Ain Shams University Hospitals. Serum indoxyl sulphate was measured (pre dialysis and post dialysis) using low flux, high flux hemodialysis and hemodiafiltration. **Results:** 60 test subjects were randomly selected had mean age 43.95 (±11.91 years) in low flux HD group, 48.35 (±13.25 years) in high flux HD group and 45.10 (±18.56 years) in HDF group, were males 66.67 % (n=40) and females 33.33% (n=20). The mean indoxyl sulphate reduction ratio using low flux filter was 13.5% (±9.52), using high flux 19.7% (±14.31) and in hemodiafiltration 24.2% (±10.73). There was a statistically significant difference between low flux HD group and HDF group as regard indoxyl sulphate reduction ratio **(**P value 0.015). There was no statistically significant difference between high flux HD group and HDF group as regard indoxyl sulphate reduction ratio.

  Conclusion: Removal of indoxyl sulphate by hemodiafiltration is higher than hemodialysis using low flux membrane and there is no difference between hemodiafiltration and high flux hemodialysis.

Keywords: p-cresyl sulphate (p-CS), Indoxyl sulphate (IS), End Stage Renal Disease (ESRD), Chronic kidney disease (CKD), Hemodiafiltration (HDF), Hemodialysis (HD), peritoneal dialysis (PD)

INTRODUCTION

Indoxyl sulfate, a uremic toxin, is accumulated in the serum of chronic kidney disease (CKD) patients. A part of the dietary protein-derived tryptophan is metabolized into indole by tryptophanase in intestinal bacteria. Indole is absorbed into the blood from the intestine, and is metabolized to indoxyl sulfate in the liver. Indoxyl sulfate is normally excreted into urine. In CKD, however, an inadequate renal clearance of indoxyl sulfate leads to its elevated serum levels ***(Niwa, 2010)***

The imbalance in gut microbiota associated with alterations in colonic epithelium contributes to the accumulation of gut-derived uraemic toxins. Toxic gases, indoxyl sulphate (IS), p-cresyl sulphate (p-CS), amines, ammonia and trimethylamine n-oxide (TMAO) as well as precursors for lipopolysaccharides (LPS) may be absorbed into the bloodstream and be responsible for systemic inflammation ***(Mafra & Fouque, 2015).***

Indoxyl sulfate stimulates progression of both tubulointerstitial fibrosis and glomerular sclerosis by increasing the expression of transforming growth factor-b1, a tissue inhibitor of metalloproteinase-1 and proa1 (I) collagen, leading to a further loss of nephrons ***(Niwa, 2010)***

Indoxyl sulphate accumulates in the blood of patients with ESRD. Moreover, Indoxyl sulphate cannot be efficiently removed by conventional hemodialysis because of its high binding affinity for albumin. The role of Indoxyl sulphate as a uremic toxin was first revealed by its accelerating effects on the progression of CKD. Recently, it has been reported that Indoxyl sulphate may also act as a vascular toxin. In endothelial cells, Indoxyl sulphate has been shown to induce oxidative stress by modifying the balance between pro- and antioxidant mechanisms stimulate the release of endothelial microparticles and blunt endothelial healing ability. Furthermore, Indoxyl sulphate directly stimulates vascular smooth muscular cell proliferation in a concentration dependent manner ***(Barreto et al., 2009)***.

Retained Indoxyl sulphate in renal failure is also associated with several detrimental effects on other organs such as altered thyroid function, endothelial dysfunction, vascular smooth muscle cell proliferation and an increased risk of atherosclerosis ***(Lekawanvijit et al., 2010)***

It was found that serum IS levels are significantly higher in the presence of coronary artery disease and correlate with the severity of the disease and coronary atherosclerosis scores, which suggest that increased serum IS may be involved in the pathogenesis of coronary atherosclerosis ***(Hsu et al., 2014)***