Effect of Central Dialysis Fluid Delivery System (CDDS) on IL6 & CRP Levels in Prevalent Haemodialysis Patients

Thesis

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List of Abbreviations

Abb.	Full term
AAMI	*Advancement of Medical Instrumentation*
AGEs	*Advanced glycosylated end-products*
AMP	*Adenosine MonoPhosphate*
BCM	*Biocompatible membrane*
CCDS	*Central concentrates delivery systems*
CDDS	*Central Dialysis Fluid Delivery System*
CFUs	*Colony-forming units*
CKD	*Chronic kidney disease*
CRP	*Serum reactive protein*
CVD	*Cardiovascular disease*
ESRD	*End-stage Renal disease*
ET	*Endotoxin*
ETRFs	*Eendotoxin retentive filters*
FADS	*Fully Automated Dialysis System*
GFR	*Glomerular filtration rate*
gp130	*Glycoprotein 130*
HD	*Hemodialysis*
HDF	*Hemodiafilteration*
HPA	*Hypothalamic-pituitary-adrenal axis*
IFEHD	*Internal Filtration-Enhanced Dialysis*
IL-1	*Interleukin-1*
IL-6	*Interleukin-6*
IL-6R	*Iinterleukin-6 receptor*
Jak	*Janus kinase*
JSDT	*Japanese Society for Dialysis Therapy*
LRVs	*Logarithmic reduction values*
MCO	*Medium cut-off*
NHANES	*National Health and Nutrition Examination Survey III*
OS	*Oxidative stress*
PD	*Peritoneal dialysis*
PDGF	*Platelet derived growth factor*
PEW	*Protein-energy wasting*

List of Abbreviations cont...

Abb.	Full term
pg/mL	*Picogram per millilitre*
PTFE	*Polytetrafluoroethylene*
RAK	*Rapidly Accelerated Fibrosarcoma*
RAS	*Rapidly Accelerated Sarcoma*
RO	*Reverse Osmosis*
SOCS	*Suppressor of cytokine signalling proteins*
SPDDS	*Single patient dialysis fluid delivery system*
STAT	*Signal transducer and activator of transcription*
TNFalpha	*Tumor necrosis factor alpha*
Tyk2	*Tyrosine Kinase*
μg/mL	*Microgram per millilitre*

INTRODUCTION

End-stage kidney disease (ESKD) is a significant and growing public health problem, associated with high morbidity, mortality and diminished quality of life. ESKD also generates disproportionately high costs to the health care system as patients require renal replacement therapy, for long-term survival ***(Li et al., 2018).***

Incidence of ESRD is increasing worldwide at an annual growth rate of 8%, far more than the population growth rate which is of 1.3%. Only about 15% of those with ESRD are receiving hemodialysis worldwide, with about 80% being treated in Europe, North America, and Japan ***(Sanyaolu et al., 2018).***

In the 2015 Global Burden of Disease Study, kidney disease was the 12th most common cause of death, accounting for 1.1 million deaths worldwide. Overall CKD mortality has increased by 31.7% over the last 10 years, making it one of the fastest rising major causes of death ***(Neu et al., 2017).***

Millions die each year because they do not have access to affordable treatment, Over 2.5 million people worldwide currently receive treatment, yet this number may only represent 10% of people who actually need treatment to live ***(Couser et al., 2015).***

Despite recent advances in end-stage renal disease (ESRD) management, morbidity and mortality in this population remain exceptionally high. Dialysis is considered as a chronic inflammatory state, as there is increased production and decreased clearance of pro-inflammatory cytokines, oxidative stress and acidosis, chronic and recurrent infections, including those related to dialysis access where extracorporeal factors, such as impurities in dialysis water, microbiological quality of the dialysate, and bioincompatible factors in the dialysis circuit play an additional role ***(Akchurin & Kaskel, 2015).***

In patients with renal failure, the systemic concentrations of both pro-inflammatory and anti-inflammatory cytokines are several times higher than that in healthy individuals. HD results in activation of cytokines, which can induce protein catabolism and promote apoptosis. In HD patients, inflammatory mediators, such as IL-1, IL-6, and tumor necrosis factor alpha, cause synthesis and release of C-reactive protein (CRP), decreased albumin, prealbumin, and increased homocysteine and endothelin I ***(Raj et al., 2007).***

IL-6 increases during HD and is associated with cardiovascular mortality, malnutrition, and resistance to erythropoietin (EPO) in haemodialysis patients. It is considered a prognostic marker in these patients ***(Hasuike et al., 2009).***

In hemodialysis, more than 90% of the dialysate delivered to the dialyzer is water, so water purity for dialysis is of critical importance for patient health and outcome, as hemodialysis patients are exposed to more than 400 L of water per week. Contrast this with a person with normal kidney drinking only less than 15 L of water per week and this purification depends on water treatment systems which decrease water contamination ***(Ahmad, 2005)***.

Water contamination can lead to anemia, alterations in blood pressure and acid-base balance, neurological issues, bone disease, increased levels of inflammatory indices on long run and more, and patients may suffer acute or chronic problems from exposure to substandard dialysate ***(D'Amato-Palumbo et al., 2013)***.

Currently available dialysis fluid delivery systems include the single-patient dialysis fluid delivery system (SPDDS) (or individual dialysis fluid delivery system) and central concentrates delivery systems (CCDS), as well as the CDDS (central dialysis fluid delivery systems) ***(Hideki et al., 2016).***

In SPDDS, the patient monitor contains a dialysis fluid supply equipment. Presently, it is considered as the global standard for dialysis treatment. Many of its models require separate water treatment equipment. Aside from the advantage of the relatively free location, SPDDS allows for the

individualization of dialysis fluid composition in order to meet unique patient needs ***(Hideki et al., 2016).***

The central dialysis fluid delivery system (CDDS) simplifies the maintenance and supervision involved by enabling the combined management of dialysis fluid for multiple persons, preparation of cleaning and antiseptic solutions, and delivery of these to each patient monitor. It is a cost-effective, laborsaving, time-tested system with good microbial safety, which has been used for 45 years**.** Reliability is required in CDDS systems, as a single abnormality can affect multiple patients negatively ***(Hideki et al., 2016).***

The CDDS has been used exclusively in Japan since 1960s. Approximately 88 % of dialysis machines are patient monitors with CDDS. It is widely known that the survival rate of Japanese hemodialysis patients is the highest in the world. This is mainly due to the development of dialysis and blood purification devices and development of the dialysis system. The introduction of the central dialysis fluid delivery system (CDDS) in the 1960s enabled the provision of stable dialysis conditions for all patients, which made a marked contribution to the field of dialysis ***(Takahashi et al., 2016).***

AIM OF THE WORK

It is to compare the effect of central dialysis fluid delivery system (CDDS) versus single-patient dialysis fluid delivery system (SPDDS) in purification of water that used in dialysate, and its effect on inflammatory markers (CRP & IL-6) levels in prevalent hemodialysis patients.

Chapter 1

INFLAMMATION IN CHRONIC KIDNEY DISEASE

End-stage kidney disease (ESKD) is a significant and growing public health problem, associated with high morbidity, mortality and diminished quality of life. ESKD also generates disproportionately high costs to the health care system as patients require renal replacement therapy, for long-term survival ***(Li et al., 2018).***

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