Association of High Sensitive C Reactive Protein and Dialysis Adequacy with Uremic Pruritus In Hemodialysis Patients

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Neama Magdy Kamel

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List of Abbreviations

BFR	:	Blood flow rate
BUN	:	Blood urea nitrogen
Ca	:	Calcium
CBC	:	Complete blood picture
CKD	:	Chronic kidney disease
CKD-ap:	:	Chronic kidney disease associated pruritus
CNS	:	Central nervous system
CRP	:	C-reactive protein
CVD	:	Cardiovascular disease
CVC	:	Central venous catheter
DOPPS	:	Dialysis Outcomes and Practice Patterns Study
EDS	:	Excessive daytime sleepiness
ESA	:	Erythropoietin-stimulating agent
ESRD	:	End-stage renal disease
GSA	:	Guanidinosuccinic acid
HCV	:	Hepatitis C virus
HD	:	Hemodialysis
HMP	:	Hexose monophosphate shunt
hs-CRP	:	high-sensitive C-reactive protein
IL-6	:	Interleukin 6
K/DOQI	:	National Kidney Foundation's Kidney Disease Outcomes Quality Initiative
MG	:	Methyl guanidine
MRD	:	Maintenance renal dialysis
NADPH	:	Nicotinamide adenine dinucleotide phosphate
PCS	:	P cresol substance
PMMA	:	Polymethylmethacrylate
PROs	:	Patient reported outcomes
PTH	:	Parathyroid hormone
RBC	:	Red blood cell
TF	:	Tissue factor
TH	:	T helper

List of Abbreviations (Cont.)

Th-1	:	T-helper 1
Th2	:	T-helper 2
TNF-α	:	Tumor necrosis factor-α
UF	:	Ultrafiltration
URR	:	Urea reduction ratio
VAS	:	Visual analog scale
UP	:	Uremic pruritus

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Introduction

Uremic pruritus is one of the most common and complicated symptom affecting end-stage renal disease (ESRD) and hemodialysis (HD) patients **(Ko et al., 2013).**

The prevalence of uremic pruritus varies from 50% to 90% in various studies **(Narita et al., 2008)**.

Chronic pruritus can be persistent, distressing and have a significant impact on the quality of life, physical comfort and is accompanied by potential psychological, functional and social impacts as well as increased morbidity **(Grob et al., 2005).**

Uremic pruritus has many proposed mechanisms including xerosis, the presence of pruritogenic cytokines, secondary hyperparathyroidism and immune-inflammatory reactions **(Chiu et al., 2008)**.

However, the pathogenic mechanism of pruritus in these patients has not yet been clarified, which limits the use of effective treatment **(Ramonda et al., 2012).**

Previous studies demonstrated inflammatory reaction or inflammatory cytokines to be associated with uremic pruritus in ESRD patients **(Chen et al., 2010).** A few previous studies on hemodialysis (HD) patients with severe uremic pruritus showed that these patients had higher high-sensitive C-reactive protein (hs-CRP) levels (**Kimmel et al., 2006).**

Some studies had suggested that the aggravation of pruritus can be associated with inadequate dialysis (**Ko et al., 2013).**

It must be noted that uremic pruritus may be difficult to be differentiated from pruritus caused by non-renal diseases frequently associated with chronic kidney disease, such as liver diseases (hepatitis B and C infections) and endocrine disorders (hyperthyroidism) **(Manenti et al., 2009)**.

Aim of the study

To study the relationship between high sensitive C reactive protein and adequacy of dialysis with uremic pruritus in hemodialysis patients.

Dialysis Adequacy

Chronic kidney disease (CKD) describes abnormal kidney function and/or structure. It is common and often exists together with other conditions (for example, hypertension, cardiovascular disease and diabetes). CKD can progress to end stage Renal disease (ESRD) in a significant percentage of people. CKD is usually asymptomatic until the late stage, but it is detectable usually by measurement of serum creatinine or urine testing for protein **(Levey et al., 2009).**

Signs and symptoms of renal failure are due to metabolic derangements resulting from inability of failed kidneys to regulate electrolyte, fluid, and acid-base balance. They are also due to accumulation of toxic products of amino acid metabolism in the serum **(Xue et al., 2010).**

Hemodialysis (HD) is one of the most important methods of treatment in patients with CKD. Removal of the excess materials and maintaining the stability of the body's internal environment, are the goals of HD. It is also a process of removing the toxic and poisonous substances that cause permanent or fatal damages **(Tayyebi et al., 2012).** HD remains the major modality of renal replacement therapy **(Himmelfarb et al., 2010).**

Dialysis delivery should be adequate to not only improve quality of life, but also to prolong survival. The aims of dialysis are thus, to decrease morbidity, increase quality of life, and prolong life span. To achieve these aims, dialysis must be performed effectively. Effective HD is one of the important factors that plays a role in decreasing morbidity and mortality of patients **(Borzou et al., 2009).**

In 1990s, certain biocompatible features and the desire to remove amyloidogenic (B2-microglobulin) led to the popularity of high-flux dialysis. During 1990s, the use of high-efficiency and high-flux membranes steadily increased and use of conventional membrane declined. In 1994, a survey by the Centres for Disease Control showed that high-flux dialysis was used in 45% and high-efficiency dialysis in 51% of dialysis centres in United States. Despite the increasing use of these new haemodialysis modalities the clinical risks and benefits of high-performance therapies are not well defined **(Weber et al., 2011).**

The goal of dialysis in patients with ESRD is to restore body's extracellular and intracellular composition to that of normal to the greatest extent possible. The surrogate marker for this physiological achievement of dialysis in clinical practice is the measurement of "adequacy of dialysis". Inadequate dialysis is responsible for the high mortality of patients with ESRD. Apart from duration of dialysis and blood flow rates, body surface area of the patient, composition of diet and nutritional status may also influence the adequacy of dialysis **(Rocco et al., 2011).**

According to European Best Practice Guideline, three definitions of dialysis adequacy are:

(1) The amount of dialysis needed to achieve optimum patient survival.
(2) The amount of dialysis needed to ensure that complications in dialysis patients are not caused by insufficient blood purification or ultrafiltration.
(3) The amount of dialysis needed to ensure a survival rate in dialysis patients equal to that of an undialyzed population.

(Dombros et al., 2005).

Adequacy of dialysis can be evaluated by improvement of signs and symptoms of uremia like tiredness, weakness, nausea or poor appetite, loosing body weight, malnutrition and anemia but monitoring the patient's symptoms alone is also insufficient, since the combination of dialysis plus erythropoietin to correct anemia can eliminate most uremic symptoms although the patient may be under dialyzed. Thus, in addition to symptoms, patient nutrition and survival appear to best reflect dialysis adequacy **(Abed et al., 2013).**

One method of assessing dialysis dose is calculation of Kt/V. This index reflects the efficiency of dialysis, and correlates with mortality and morbidity rate of patients. Dialysis dose can also be assessed measuring the urea reduction ratio (URR). Many factors can increase Kt/V and URR, including use of high level of dialyzers, increasing blood flow rate (BFR), increasing flow of dialysate, and dialysis time **(Borzou et al., 2009).**

Factors affecting HD adequacy:

The results of many surveys show that achieving a Kt/V of 1.2 or more and URR of 60% or more is effective in improving prognosis of patients on dialysis. Therefore, achieving this goal remains one of the aims of dialysis. Many factors can increase Kt/V and URR including use of high level dialyzers, increasing blood flow rate (BFR), increasing flow of dialysate, and dialysis time (**Cigarran et al., 2004)**

1-Effect of blood flow rate:

The blood clearance increases in direct proportion to blood flow rate (range from 250 to 350 ml/min), given that clearance is

computed as the blood flow rate times percentage reduction across the dialyzer in the BUN level. This is only partially true. As the blood flow rate increases, the dialyzer is unable to remove urea with the same degree of efficiency. As a result, the plasma urea nitrogen level at the dialyzer outlet rises **(Borzou et al., 2009).**

2- Effect of dialysis solution flow rate:

Clearance of urea depends on the dialysis solution flow rate as well. A faster dialysis solution flow rate increases the efficiency of diffusion of urea from blood to dialysate; however, the effect is usually not large. The usual dialysis solution flow rate is 500mL/ minute. Increasing the dialysate flow rate from 600 to 800 ml/min would result in only a 4% increase in urea clearance for a blood flow rate of 400 ml/min and a hematocrit of 35%, and when a high efficiency dialyzer is used **(Ward et al., 2006& Ronco et al., 2006).**

3- Frequency of Dialysis:

Increasing the frequency of dialysis can also be of benefit. Similarly, blood pressure control and quality of life improved with more frequent, dialysis. Patients acted as their own controls, and total weekly Kt/V was kept constant. Blood pressure control and quality of life both improved.

Another approach to reducing urea is by nocturnal hemodialysis, where both the duration and frequency of dialysis are increased. This technique was pioneered in Canada, but is now practiced widely in other centers, including Australia and the