

Evaluations of Inflammatory Status in Chronic Renal Failure Patients Undergoing Hemodialysis and Conservative Treatment

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Abstract

Introduction: - Chronic inflammation is a basic feature of end stage kidney disease and is associated with increasing risk of mortality and morbidity in patients undergoing dialysis. **The aim:** - the study aimed to evaluate white blood cells and IL-6 in patients undergoing hemodialysis and without hemodialysis. **Methods and Subjects:-** The study was designed on 106 patients with chronic renal failure age range (20-69years). The patients divided in two groups according to treatment, 40 patients with conservative treatment and 66 patients with hemodialysis treatment. IL-6 were determined by using a commercially available ELISA Micro wells kit. Total white blood cells count and differential count were determined by using an automated hematology autoanalyzer XT2000i. **Results:-** showed a significant ($p < 0.05$) decrease of total white blood cells count, neutrophils, lymphocytes, monocytes, eosinophils and basophils in hemodialytic group when compared with conservative group. But IL-6 levels was higher significantly ($p < 0.01$) in hemodialytic group when compared with conservative group. **Conclusion:** - hemodialysis session impaired immune system and activated anti-inflammatory factors.

Keywords: - Hemodialysis, Conservative treatment, Chronic inflammation

Introduction

Chronic kidney disease (CKD) is a life-threatening disorder often related with hypertension, kidney dysfunction, progression to kidney fibrosis, and eventual chronic renal failure [1,2]. Chronic inflammation is a basic feature of end stage kidney disease and is associated to an increasing risk of mortality and morbidity in patients under hemodialysis [3, 4, 5]. Patients with hemodialysis treatment, have an increased susceptibility to infectious diseases compared with healthy subjects [6, 7]. White blood cells play important function in host defense mechanism against infectious diseases [8].

The three mechanisms stimulation of the pro-inflammatory system may be occurs in hemodialytic patients: inflammatory response stimulated by bio-incompatible dialysis membranes, contact to local fistula and graft infections and contact to contaminated

dialysate containing cytokine-inducing substances such as endotoxins [5]. On the other hand, membrane adsorption of cytokines and clearance through HD session may be change circulating cytokine levels [9]. Some of inflammatory marker could be used in medical practice that include interleukin-6 secreted from activated endothelial cells, monocytes, adipocytes, fibroblasts and macrophages as a result to several stimuli, such as bacterial endotoxins, IL-1b, tumor necrosis factor (TNF-a), oxidative stress and physical exercises. The main effects of IL-6 are result of its level in the circulation and take place at distinct positions and far from its origin [10]. The possible causes of raised IL-6 levels in ESRD diseased people may be belong to the losing of renal function and some factors are related with hemodialysis [11].

The aim: the aim of this study to evaluate white blood cells and IL-6 in patients undergoing hemodialysis and without hemodialysis.

Subjects and Methods

The study conducted on on 106 patients with chronic renal failure age range (20-69years).

The patients divided in two groups according to treatment, 40 patients with conservative treatment (12Males and 29Females) and 66 patients with hemodialysis treatment (44Males and 22Females). IL-6 were determined in serum of all patients by using a commercially available ELISA Micro wells kit from Diaclone France. Total with blood cells count and differential count in whole blood of all patients were determined by using an automated hematology autoanalyzers XT2000i (from sysmex, Japan).

Statistical Analysis

SPSS version 20 was used as Statistical analysis. The results comparison assessed by student t-test.

Results

The results illustrated total white blood cells count, neutrophils, lymphocytes, monocytes, eosinophils, and basophils showed the normal range ($4-10 \times 10^9 / L$, $2-7 \times 10^9 / L$, $1-3 \times 10^9 / L$, $0.2-1 \times 10^9 / L$, $0.0-0.5 \times 10^9 / L$ and $0.0-0.1 \times 10^9 / L$) respectively in conservative group ($7.7 \pm 0.3 \times 10^9 / L$, $4.8 \pm 0.3 \times 10^9 / L$, $1.9 \pm 0.1 \times 10^9 / L$, $0.5 \pm 0.0 \times 10^9 / L$, $0.2 \pm 0.0 \times 10^9 / L$, $0.0 \pm 0.0 \times 10^9 / L$) and in hemodialytic group ($5.7 \pm 0.2 \times 10^9 / L$, $3.6 \pm 0.1 \times 10^9 / L$, $1.4 \pm 0.0 \times 10^9 / L$, $0.4 \pm 0.0 \times 10^9 / L$, $0.1 \pm 0.0 \times 10^9 / L$, $0.0 \pm 0.0 \times 10^9 / L$) respectively. However total white blood cells count, neutrophils, lymphocytes, monocytes, eosinophil and basophils decrease significantly ($p < 0.05$) in hemodialytic group when compared with conservative group. IL-6 levels were in conservative group (16.4 ± 3.4 pg/ml) and in hemodialytic group (26.0 ± 5.96 pg/ml), rise than the upper limit of the normal rang ($5-15$ pg/ml), The IL-6 level was higher significantly ($p < 0.01$) in hemodialytic group when compared with conservative group. As showed in table below.

Table: Inflammation Status Parameters in Conservative and Hemodialytic

Biomarker	Normal range	Conservative (n=42) Mean \pm SE	Hemodialysis (n=66) Mean \pm SE	t-test P value
IL-6	5-15pg/ml	16.47 \pm 3.43	26.08 \pm 5.96	0.022S
WBC	$4-10 \times 10^9/L$	7.74 \pm 0.35	5.70 \pm 0.24	0.001S
NEU	$2-7 \times 10^9/L$	4.88 \pm 0.31	3.68 \pm 0.19	0.001S
LYM	$1-3 \times 10^9/L$	1.98 \pm 0.11	1.40 \pm 0.06	0.001S
MON	$0.2-1 \times 10^9/L$	0.57 \pm 0.03	0.42 \pm 0.02	0.001S
EOS	$0.02-0.5 \times 10^9/L$	0.26 \pm 0.02	0.18 \pm 0.02	0.029S
BAS	$0.0-0.1 \times 10^9 / L$	0.03 \pm 0.00	0.01 \pm 0.00	0.001S

IL-6 Interleukin-6, W.B.C White Blood Cells, N.E.U Neutrophil, L.Y.M Lymphocytes, M.O.N Monocytes, E.O.S Eosinophil, and B.A.S Basophil.

Discussion

Our current study shows white blood cells count and differential count decreased significantly in hemodialytic patients, but they were within normal ranges. That uremia related to immune dysfunction has been seen in some researches. However, abnormal immune dysfunction are recorded because of uremic toxins [12]. Prevalence of the studies focused on the abnormal dysfunction of WBC. Minnaqanti and Cunha pointed that subjects showed renal disorders impair defense of host [13]. Baqdasarian et al showed subjects with kidney disease on dialysis counter with infection which is a major cause of mortality and morbidity [14]. The studies revealed that there is an relationship between renal disorder and infection. Hayder et al., reported that total WBCs were decreased significantly at the ages 40-60 years of 111 CRF on dialysis, while total WBCs reduced statically in 50 CRF of HD patients [15]. Suresh et al., has been perceived that the total white blood cells are decreased in HD patients than the control. The specific mechanism by which chronic renal disease leads to a slight decrease in total white blood cells count is not clear. The possible hypothesis is as follows in chronic kidney failure patients undergoing dialysis, in the dialyzer, exposure of blood to artificial membranes may result in complement activation in vivo [16]. Agrawal et al., have recorded that antigen presentation dendritic cells decreased in uremia [17]. Decreasing number of B lymphocytes capacity for producing antibody have been recorded in uremic subjects by Pahl et al., [18]. Depleting of naïve and memory T cells in uremic cases has been recorded by Moser et al [19]. The total and differential count showed significant differences but values were within limit of the normal ranges that normal total and differential WBC count in one study was seen in majority of cases (28 cases 87.5%). Four cases (12.5%) revealed increased WBC count and neutrophilia, that the etiology of chronic renal failure was included type-II diabetes mellitus 8 cases (25%) obstructive uropathy 5 cases (15.62%), hypertension 3 cases (9.37%) and renal tuberculosis 1 case each (3.125%) and in remaining 14 cases etiology was not known [20]. While Agarwal and Light had reported that Patients with CKD had more eosinophils and granulocytes and less lymphocytes. Over time, granulocytes rise and lymphocytes reduced in those with and without CRD. In addition, in those with CRD, over time monocytes increased and eosinophils

decreased [21].

IL-6 were as an immunological Parameters that cytokines are released in the course of HD session mainly by monocytes, and factors responsible for monocytes activation include endotoxins that may be present in dialysate fluid, activated complement and dialyzer membrane itself [22]. The physical interaction between artificial dialyzer membrane and some compounds in dialysate fluid leads to activation of alternative pathway of complement. The type of dialyzer membrane is critical in this course [23]. Our results of study showed serum concentrations of IL-6 are increased in hemodialysis patients. Several studies reported unchanged serum IL-6 during HD concurrent with increased clearance or membrane adsorption of these cytokines [24]. The reasons for this phenomenon maybe depend on cytokine kinetics. The half-life of IL-6 (3-7 min), are seem to be short..Plasma cytokines are quickly bound to cell surface receptors, this suggests that stable plasma concentrations are achieved by a continuously high production rate. As a consequence, the entire amount of cytokines potentially removed via hemodialysis is maybe significantly lower when compared with the endogenous production [25]. It is not unlikely that the serum concentrations of cytokines serve as target of feedback mechanisms, since their endocrine function has been displayed, apart from paracrine functions [26]. Thinking that adsorption of cytokines happens mainly in the first minutes of HD and may not reflect a substantial amount of cytokine elimination [25]. HD membranes may rise cytokine production by activating mononuclear cells [27].

Conclusion - hemodialysis session impaired immune system and activation anti-inflammatory factors.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Bilad AlRafidain University College and all experiments were carried out in accordance with approved guidelines.

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