BANTAO Journal 3 (2): p 53; 2005

Prealbumin and Inflammatory Markers in Dialysis Patients

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Introduction

Inflammation is one of the main causes of high mortality and morbidity rates in patients with chronic renal failure treated with dialysis methods[1]. In these cases, the use of anthropometric or biochemical markers alone, is not enough. It is very important to use the combination of them, in order to have more reliable assessment[1]. Further studies in this area, are required to examine the association between markers of visceral protein stores, inflammatory markers and clinical outcomes, in dialysis patients [2].

Prealbumin is a visceral protein with short half-life (2-3 days), a rapid turnover and a simple method exists to measure serum levels[3]. It is an earlier nutritional marker compared with serum albumin and more responsive to immediate changes in nutritional intake and clinical status than albumin. Although prealbumin is considered as a more sensitive index compared with albumin[4], it is not commonly used and its associations with other inflammatory and nutritional indices, during End Stage Renal Disease (ESRD), have not been well documented[4].

Inflammation is a key determinant of serum prealbumin (an acute phase protein) [4]. However, a few studies support that prealbumin is a reliable marker of inflammation but still more studies are required to confirm this hypothesis[2].

The aim of this study is to evaluate serum prealbumin as an inflammatory and nutritional marker and determine whether there is an association between prealbumin and other anthropometric and biochemical markers. Furthermore, this study will compare the nutritional and inflammatory status between HD and PD patients, through prealbumin and other indices.

Methods

The study is performed at the Outpatient Dialysis Unit at "Laikon" General Hospital (Athens, Greece). A total of 30 dialysis patients of whom 15 were on HD and 15 on PD participate in the study. Moreover, only clinically stable patients are included in this study.

An Ethical approval is granted from University of Surrey Roehampton ethics committee and approval from the director of Laikon General Hospital of Athens.

The investigated anthropometric and biochemical measurements of the study are body weight (BW), Body Mass Index (BMI), percentage body fat derived from skinfold thickness measurements (%BF) and serum prealbumin, albumin, transferrin, C - reactive protein (CRP), creatinine, ferritin, Interleukin-6 (IL-6), cholesterol, Iron (Fe) and Prognostic Inflammatory and Nutritional index (PINI). The investigated variables of this study are compared with the outcome goals for dialysis patients based on Kidney Disease Outcome Quality Initiative (K/DOQI). Inflammatory markers are compared with the laboratory reference ranges.

BMI (in kilograms per meter²) is calculated from patient height and dry body weight. This study considers undernourished patients as those with BMI< 18.5 Kg/m².

The same observer takes anthropometric measurements, immediately before the dialysis session (weight empty of dialysis fluid). Skinfold measurements are taken at 4 sites in triplicate (triceps, biceps, superilliac and subscapular skinfolds) using Harpenden callipers (Baty, British Indicators CE 0120). Percentage body fat is calculated using Durnin and Womersley equation.

Non-fasting blood samples are taken before dialysis treatment for serum prealbumin, albumin, creatinine, ferritin, transferrin, IL-6, CRP, cholesterol and iron. All these parameters, apart from prealbumin and IL-6 immunoassays, are analysed on the day of sampling at the Department of Clinical Chemistry Laboratory at "Laikon" General Hospital. IPrealbumin and IL-6 mmunoassays are performed at the laboratory for Experimental Surgery and Surgical Research "Christeas Hall". Serum prealbumin is measured by a photometric enzyme-linked assay (ELISA, Immune Diagnostic, Cat. No: K 6331) and serum albumin is determined with a photometric method (bromcresol method, BCG-Olympus). Cholesterol is analysed by a photometric enzyme-linked assay with Olympus analysers (RA-XT 1000). Serum transferrin, iron and ferritin are analysed by Tholosimetry (Hitachi 912). CRP is analysed by nephelometry (SEAC, RADIM GROUP, DELTA) and High-Sensitive IL-6 is analysed by a photometric enzyme-linked assay (ELISA, Quantikine HS, Cat. No: HS 600B).

The PINI value is calculated using markers from the biochemical tests, in the following equation: (C-reactive protein $_{X}$ alpha (1)-acid glycoprotein): (albumin x transthyretin) [16].

The statistical programme SPSS for Windows (version 11.5) is used for data analysis. Results are presented as mean ± standard deviation (Mean ± SD). A P-value of <0.05 is considered statistically significant.

Results

There are no significant differences in age, duration of dialysis, dry weight and BMI between patients on HD or PD. There is a large variation in the duration of dialysis in both patient groups. Results are shown in table 1.

Prealbumin: Mean prealbumin levels are not significantly different between patients on HD or PD, but there is a

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definite trend towards significance (336.1±113.6 and 273.3±144.0, P=0.053 for HD and PD respectively). Potential relationships between prealbumin and the other investigated variables are also examined. In HD patients prealbumin levels negatively correlated with ferritin (r=-0.665, P=0.07). However, no significant correlation for prealbumin and any other investigated parameter is found in the HD or PD group.

Other parameters: Albumin is significantly lower in the PD group, whereas, transferrin and total cholesterol are significantly greater in the HD group (Table 2). The duration of dialysis does not have a significant influence on the above parameters.

In the HD group, albumin is negatively correlated with CRP (r=-0.65, P=0.009) and creatinine is negatively correlated with %BF (r=-0.532, P=0.041). In the PD group, only albumin is positively correlated with IL-6 (r=0.604, P=0.029).

Prevalence of inflammation and malnutrition: The prevalence of inflammation is identified from 3 inflammatory markers (CRP, IL-6 and ferritin), based on their laboratory upper normal values. A higher percentage of the HD patients have inflammation with CRP>5g/l and IL-6>8.8ng/ml compared with the PD patients. Results are shown in table 3.

The prevalence of malnutrition based only on prealbumin levels shows that a much higher percentage of PD patients are severely malnourished with prealbumin <200mg/ml compared to the HD patients (Table 4). In table 5, the prevalence on malnutrition based on the other investigated variables is presented.

Malnutrition and inflammation: Malnutrition indices are analysed against inflammation indices. In the current study, a patient is characterised as malnourished if he/she is found malnourished for at least one nutritional marker. Moreover, a patient is considered to have inflammation if he/she is found to have values above the cut-off points for of the inflammatory markers. A higher percentage of PD patients have both malnutrition and inflammation compared with the HD patients as shown in table 6.

Conclusions

Prealbumin levels are not significantly different between the two groups but there is a trend towards significantly greater levels in HD patients (Table 2). Beto and Bansal (2004) supported that prealbumin<300 mg/dl indicates the presence of malnutrition. Therefore, 69% of the PD patients and only 13% of the HD patients could be considered as malnourished according prealbumin values (Table 4).

Gender, age and duration of dialysis have no influence on prealbumin levels, in both groups. However, Koople et al (2002) concluded that serum prealbumin is significantly affected by age[4], which age groups were studied compared with current study. Moreover, Chertow et al (2000) concluded that prealbumin is significantly affected from the gender in HD patients[5]. Qureshi et al (1998) agrees with our findings that duration of dialysis has no influence on

The Pearson correlation test showed that prealbumin is significantly negative correlated with ferritin, only in the HD group. Cano et al (1987) found that serum prealbumin was significantly correlated with body weight, triceps skinfold and serum creatinine[6] in HD patients. Herziq et al (2001) and Owen and Lowrie (1998) found a significant negative correlation between CRP and prealbumin[7, 8]. The current study has relatively few subjects for correlation analysis when separated into PD and HD groups.

A meta-analysis by Goldwasser et al (2002), in dialysis patients found that 100% of PD patients had prealbumin levels>300 mg/ml and 75% of HD patients had prealbumin levels >300 mg/ml [9]. However, this meta-analysis does not seem to agree with our findings since PD patients are presented with lower levels of prealbumin than HD patients.

Furthermore, mean albumin levels are significantly higher in the HD group than the PD group (Table 2). This finding agrees with previous studies about albumin in dialysis patients. Particularly, a meta-analysis supports that albumin is higher in HD patients compared with PD patients due to the great renal albumin losses during peritoneal dialysis[9]. Moreover, previous studies found that inflammatory markers, such as CRP and IL-6, are inversely correlated with creatinine, but not with albumin[10].

Serum transferrin is significantly different between the two groups, while iron and ferritin are not (Table 2). Transferrin is reduced during inflammation, where ferritin, usually, is increased[10]. Moreover, reduced transferrin levels in the HD group of this study, are not caused from the elevated CRP levels but probably, the elevated IL-6 levels cause the reduction in transferrin levels.

Prevalence of inflammation and malnutrition: Prevalence of inflammation seems to be higher in the HD group compared with the PD group, using CRP and IL-6 cut off points as the only markers, while using ferritin, the prevalence is higher in the PD group than in the HD group (Table 3). Malnutrition is more prevalent in the PD group compared with the HD group, based on albumin, BMI and %BF (in females), as the only markers (Table 5). None of the patients either in HD group or in PD group is well nourished based on our study criteria of being below one marker of malnutrition (Table 6). 73% of the HD patients and 80% of the PD patients have malnutrition and inflammation at the same time.

According to the present study, prealbumin levels are lower in the PD group compared with the HD group (definite trend towards significance) but it is not significantly correlated with any of the investigated parameters, apart from ferritin, in the HD group. Moreover, further analysis showed that patients are malnourished independently if they have inflammation or not. None of the patients have inflammation without being malnourished at the same time.

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