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Serum Cholesterol as a Marker of Nutrition in End-stage Renal Failure Patients on Renal Replacement Therapy

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Abstract: To elucidate whether and how in patients with uremia on Hemodialysis (HD) the level of CRP as the marker of inflammation correlate with serum cholesterol, which is an index of nutrition in HD patients. The study was conducted on patients with End-Stage Renal Disease (ESRD), who were undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. After 12 h fasting, levels of serum cholesterol (Chol) and serum creatinin were measured. The total patients were 36 (F = 15, M = 21). The median patient's age was 43 years. The median length of the time patients had received hemodialysis 19 months. The median serum CRP was 8 mg L^{-1}. The median serum cholesterol was 115 mg dL^{-1}. In this study a significant inverse correlation of serum cholesterol with serum CRP was seen. It may be concluded that using the antilipid drugs in hemodialysis patients might be limited to specific cases and secondly more attention to use bio-compatible dialysis membranes which has a lower complement system activation to avoid more inducing the inflammation as well as more attention to the nutrition of HD patients needs.

Key words: Cholesterol, hemodialysis, end-stage renal failure, C-reactive Protein (CRP)

INTRODUCTION

Malnutrition due to poor food intake is a common clinical problem in patients with End-stage Renal Disease (ESRD) (Aparicio *et al*., 1999; Bergström, 1995a) and is associated with an increase in morbidity and mortality in patients on haemodialysis treatment (Bergström, 1995b). In dialysis patients, malnutrition is an independent factor causing morbidity and mortality. Both inadequate alimentation and metabolic alterations, which involve nitrogen and energy metabolism, contribute to malnutrition (Aparico *et al*., 1999; Bergström, 1995a;b). About 40% of patients undergoing maintenance dialysis suffer from varying degrees of protein-energy malnutrition. This is a problem of substantial importance because many measures of nutritional status correlate with the risk of morbidity and mortality (Fox *et al*., 2004; Bossola *et al*., 2004). The nutrient intake of patients receiving maintenance dialysis also is often inadequate and several lines of evidence suggest that toxins that accumulate with renal failure suppress appetite and contribute to nutritional decline once patients are on maintenance dialysis (Fox *et al*., 2004; Bossola *et al*., 2004). In end-stage renal failure, dyslipidemia is linked to risk of cardiovascular disease (Nasri and Baradaran, 2004). Increased concentrations of triacylglycerol-rich, Very Low Density Lipoproteins (VLDL) and decreased concentrations of High Density Lipoproteins (HDL) are usual, whilst total cholesterol and Low Density Lipoprotein (LDL) concentrations are not increased (Nasri and Baradaran, 2004; Gillet *et al*., 2004). In the general population, hypercholesterolemia is a known risk factor for cardiovascular morbidity and mortality. Among lipid components, increased serum levels of Low Density Liproprotein (LDL) and non-high-density lipoprotein cholesterol appear to have the strongest predictive value for poor cardiovascular outcome, whereas HDL-cholesterol is generally considered protective in the general population (Nasri and Baradaran, 2004; Gillet *et al*., 2004; Kalantar-Zadeh *et al*., 2003). In hemodialysis patients hypercholesterolemia appear to be a protective feature that are associated with a greater survival among dialysis patients. This finding is in contrast to the well-known association between over-

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nutrition and poor outcome in the general population. The association between under-nutrition and adverse cardiovascular outcome in dialysis patients, which stands in contrast to that seen in non-ESRD individuals, has been referred to as reverse epidemiology (Kalantar-Zadeh *et al*., 2003; 2005). C-reactive Protein (CRP) is an acute phase protein whose synthesis in the liver is regulated by different cytokines, particularly interleukin 6 (IL-6). Plasma levels of CRP in the absence of active disease are low, but can rise up to 1000 fold in patients with an inflammatory reaction. Besides being a marker of inflammation, CRP itself may have proinflammatory properties since it can activate the complement system (Wolbink *et al*.,1996; Morrow and Ridker, 2000). Thus elevated plasma concentrations of CRP, a sensitive marker of underlying systemic inflammation (Morrow and Ridker, 2000; Clyne and Olshaker, 1999). Serum CRP concentrations have also been found to be significantly elevated in hemodialysis patients (Clyne and Olshaker, 1999; McIntyre *et al*., 1997; Haubitz *et al*., 1996) and reflects chronic inflammation and as an acute-phase reactant, is a sensitive and independent marker of malnutrition (Haubitz *et al*., 1996). Regarding the present data, studies concerning the association of (CRP), as a marker of malnutrition and serum cholesterol a marker of nutrition could show the importance of serum cholesterol in maintaining the hemodialysis patients. Therefore, the aim of the present study was to elucidate whether and how in patients with uremia on hemodialysis the level of CRP as the marker of inflammation correlate with serum cholesterol.

MATERIALS AND METHODS

Patients: This cross-sectional study was carried out in hemodialysis section of Hajar Medical, Educational and Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord of Iran in June and July of 2005.

The study was conducted on patients with End-stage Renal Disease (ESRD), who were undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. According to the severity of secondary hyperparathyroidism, each patient being treated for secondary hyperparathyroidism was given oral active vitamin D3 (Rocaltrol), calcium carbonate and Rena-Gel capsules at various doses. According to the severity of anemia, patients were under IV iron therapy with Iron sucrose (venofer) at various doses after each dialysis session, all patients were under treatments of 6 mg folic acid daily, 500 mg L-carnitine daily, also 2000U IV Eprex (recombinant human erythropoietin (rHuEPO) and also oral Vitamin B-complex tablet daily after each dialysis session routinely. Exclusion criteria were antilipid drugs taking or drugs affect serum lipids.

Laboratory methods: After 12 h fasting, levels of serum pre and post dialysis Blood Urea Nitrogen (BUN) and also Cholesterol (Chol) and serum creatinin were measured. For the adequacy of hemodialysis the Urea Reduction Rate (URR) was calculated from pre- and Post-blood Urea Nitrogen (BUN) data (Haubitz *et al*., 1996). Duration and dosages of hemodialysis treatment were calculated from the patients' records. The duration of each hemodialysis session was 4 h.

Statistical analysis: Results are expressed as the mean±SD and median values. Statistical correlations were assessed using partial correlation test. All statistical analyses were performed using SPSS (version 11.5.00). Statistical significance was determined at a $p<0.05$.

RESULTS AND DISCUSSION

Table 1 shows that the total patients were 36 (F = 15, M = 21). The median patient's age was 43 years. The median length of the time patients had received hemodialysis 19 months. The median serum CRP was 8 mg L^{-1}. The median serum cholesterol was 115 mg dL^{-1}. In this study a significant inverse correlation of serum cholesterol with serum CRP ($r = -0.35$, $p = 0.045$; Fig. 1) (adjusted for age, duration and doses of dialysis was seen.

In this study we found a significant inverse correlation of serum cholesterol with serum CRP was seen. In a study conducted by Fox *et al*. (2004) on 812 incident hemodialysis found a 40% prevalence of hyperlipidemia in patients. To compare 46 hemodialysis patients with 56 healthy subjects in the aspect of serum lipids, Gillett *et al*. (2004) showed that, total and LDL-cholesterol were unchanged, triacylglycerols and free cholesterol were raised and HDL-cholesterol concentrations were

Table 1: Mean±SD, minimum and maximum of age, duration and doses of hemodialysis and also laboratory results of patients

Total patients n = 36	Minimum	Maximum	Mean±SD	Median
Age (years)	16	80	46±16	43
DH* (months)	2	156	32±36	19
Dialysis dose sessions	36	1584	294±393	156
URR (%)	39	76	59±9	57.5
Creat (mg dL^{-1})	3	18	9±3	9.5
BUN (mg dL^{-1})	30	180	82±33	78
Chol (mg dL^{-1})	59	211	117±40	115
CRP (mg L^{-1})	3	40	8.7±6.6	8

*Duration of hemodialysis treatment

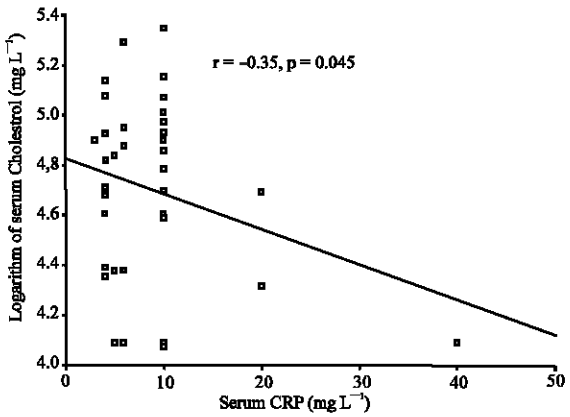

Fig. 1: Significant inverse correlation of serum CRP with serum cholesterol (r = − 0.35, p = 0.045)

significantly decreased compared to controls. Previously we showed that on thirty-six patients with the mean of ages of 47.5 years old, the mean cholesterol level was 153.4±31.3 mg dL^{-1}, also the mean triglyceride level was 135.1±66.1 mg dL^{-1} (Nasri and Baradaran, 2004). Concerning these results, studies showed that cholesterol levels is inversely associated with mortality in dialysis patients. This paradox may be explained by systemic inflammation and/or malnutrition, which are associated with lower cholesterol levels and higher mortality (Liu *et al*., 2004). In fact dialysis patients have a high risk of atherosclerotic cardiovascular disease, but dialysis patients with higher serum cholesterol have lower mortality rates (Fox *et al*., 2004). Uremic malnutrition and chronic inflammation often coexist in ESRD patients. A recent study by Stevinkel *et al*. (1999) demonstrated this relationship in advanced chronic kidney disease patients not yet on maintenance dialysis. Out of 109 patients with advanced chronic renal failure, 44% had moderate to severe protein-calorie malnutrition and 32% had signs of inflammation, as determined by elevated CRP concentrations. Most importantly, 53% of the patients with malnutrition had signs of inflammation and 72% of the patients with inflammation had signs of malnutrition. A similar association is observed in chronic hemodialysis patients. Qureshi *et al*. (1998) have demonstrated that chronic hemodialysis patients with severe malnutrition display signs of chronic inflammation (CRP>20 mg L^{-1}) approximately four times that of well-nourished chronic hemodialysis patients. Recently, markers of chronic inflammation have also been associated with adverse clinical outcome in chronic renal failure patients. CRP is a significant predictor of mortality as well as morbidity in both chronic hemo and peritoneal dialysis patients (Ikizler *et al*., 1999; Zimmermann *et al*., 1999; Yeun *et al*., 2000). Similarly, increased levels of proinflammatory cytokines are associated with increased risk of mortality in ESRD patients (Stenvinkel *et al*., 2002; Bologa *et al*., 1998). Whereas these two unfavorable conditions independently predispose ESRD patients to increased risk of morbidity and mortality (Warner *et al*., 2002), when uremic malnutrition and chronic inflammation coexist, they have an exponential relationship to morbidity and mortality, i.e., a small increase in the severity of either condition leads to significant worsening of morbidity and mortality (Caglar *et al*., 2002). In a study conducted by Fujino *et al*. (2005) on 389 HD patients, significant negative correlations were seen between fat mass changes and CRP was mentioned. Taken together, we showed an inverse association between CRP level and serum cholesterol. Regarding the previous mentioned data and this result, it may be concluded that using the antilipid drugs in hemodialysis patients might be limited to specific cases and secondly more attention to use bio-compatible dialysis membranes which has a lower complement system activation to avoid more inducing the inflammation as well as more attention to the nutrition of HD patients needs.

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