

Dyslipidemia: End Stage Renal Disease and Hemodialysis

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Citation

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Abstract

Chronic renal failure (CRF) is a pro-oxidant state and the degree of intracellular and extracellular oxidative stress is related to the severity of renal failure. The present study was taken up to evaluate Dyslipidemia in patients undergoing hemodialysis session. In our study, the hemodialysis patients were found to have Dyslipidemia as evidenced by HD can moderately attenuate the renal dyslipidemia. Accumulation of atherogenic lipoproteins could also play a role in the development of atherosclerotic complications in HD patients. This Dyslipidemia plays an important role in the development of atherosclerosis in hemodialysis

INTRODUCTION

Approximately 50% of patients with ESRD die from a cardiovascular event[1], which indicates a cardiovascular mortality that is 30 times higher in dialysis patients and 500 times higher in 25- to 34-year-old ESRD patients. Progressive renal failure is associated with characteristic alterations of lipoprotein metabolism and dyslipidemia [2]. Hemodialysis patients have a number of biochemical abnormalities including hyperlipidemia. The cardiovascular illness is an important cause of death in hemodialysis patients[1]. In many patients, the dyslipidemia may not be expressed as hyperlipidemia (i.e., elevated plasma levels of cholesterol and/or triglycerides). The renal dyslipidemia is reflected in an abnormal apolipoprotein (apo) profile and in the concentrations and composition of individual lipoprotein families [2, 3]. It is characterized by reduced concentrations of apoA-containing lipoproteins in high-density lipoprotein (HDL) and increased concentrations of intact or partially metabolized triglyceride-rich apoB-containing lipoproteins in VLDL, intermediate-density lipoprotein (IDL), and LDL [1, 3]. There is a preferential increase in the levels of IDL and small dense LDL [4,5].

Hyperlipidemia has been incriminated as a risk factor of atherosclerotic vascular disease in dialyzed patients[6]. Hemodialysis is associated with hypertriglyceridemia. The other dyslipidemias consist of (a) high serum lipoprotein levels (b) low serum high density lipoprotein. Plasma low density lipoprotein (LDL) cholesterol is usually not elevated[7,6,8]. The cause of hypertriglyceridemia is an increased production of Apo B protein and a marked

decrease in the metabolism of VLDL, primarily as a result of decreased endothelial cell delipidation of VLDL[6].

The principal disturbance of the lipoprotein metabolism appears to be a reduced catabolism and clearance of triglyceride-rich apoB-containing lipoproteins; the main contributing factors to a decreased catabolism include a reduced activity of lipolytic enzymes, compositional abnormalities of lipoproteins as substrates for lipolysis, and a decreased receptor-mediated uptake of lipoproteins [2]. Renal dyslipidemia was first described in hemodialysis (HD) populations, with elevated plasma triglyceride levels as the main characteristic finding. There are several possible ways in which dialysis treatment may modify renal dyslipidemia, including attenuation of uremic toxicity as well as specific effects of the dialysis modality. Lp(a) is structurally related to LDL and consists of a highly glycosylated subunit, apo(a), linked by disulphide bridges to the LDL particle.[9] The serum concentration is chiefly under genetic control.[10] Several studies have indicated that Lp(a) has both atherogenic and thrombogenic properties[11-14], the latter is due to sequence homology with plasminogen[15] and may be critical in increasing the risk of myocardial infarction (MI).[16] There is dispute, however, as to whether the risk of CHD conferred by raised Lp(a) is independent of LDL or apolipoprotein B[16-18]. The consequences of long-term dialysis on nutrition and the accompanying pharmacologic treatment may be additional contributing factors.

DISCUSSION

The initiation of renal replacement therapy as well as the

choice of dialysis modality may also influence the phenotypic characteristics of uremic dyslipidemia in patients with ESRD. However, the lipid and apolipoprotein profile that characterizes predialytic renal failure remains essentially unchanged during long-term hemodialysis (HD) [19,20]. Thus, HD patients usually display increased concentrations of intact or partially metabolized triglyceride-rich lipoproteins, reduced serum levels of HDL-cholesterol and elevated concentrations of Lp(a). Elevated Lp(a) in HD patients has been reported [21-24] but its role in the development of vascular complications or atherosclerotic death has yet to be fully proven. Our results are in agreement with increased Lp(a) levels. Whereas the subfractionation of apolipoprotein B-containing lipoproteins usually reveals a predominance of small, dense LDL particles [25]. The pathophysiological mechanisms that underlie the alterations in lipoprotein metabolism in HD patients are generally similar with those described in predialysis renal failure individuals. However, the dialysis procedure may result in additional defects in lipid homeostasis.

LIPID PROFILE IN ESRD

In patients with ESRD, dyslipidaemia is a common finding. This is caused by alterations in the metabolism and the composition of the plasma lipoproteins. The typical, traditional lipid profile in patients with ESRD is characterised by normal or low concentrations of LDL cholesterol, increased concentrations of triglycerides (TG) due to elevated levels of very-low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL) and decreased high-density lipoprotein cholesterol (HDL). The LDL composition is abnormal and characterised by the presence of small dense LDL particles. There are slight differences between patients treated with haemodialysis and those treated with peritoneal dialysis: levels of LDL cholesterol and small dense LDL are higher and levels of HDL cholesterol are lower in patients on peritoneal dialysis compared with patients on haemodialysis.[26-29] Most studies which describe the abnormalities in lipoproteins in ESRD focus on the 'absolute' levels of lipoproteins but do not mention possible alterations in the 'state' of these lipoproteins (e.g. oxidised or carbamylated), which may affect early onset of atherosclerosis.

Reverse epidemiology is only one part of the story. The lack of an association between LDL cholesterol and cardiovascular risk may also be explained by the

contributions of other lipoproteins. As mentioned above, in patients with ESRD levels of IDL, small dense LDL and Lp(a) are increased. Several studies have reported a positive association between some of these lipoproteins and cardiovascular disease. In patients with elevated levels of IDL there is evidence of atherosclerotic disease. Moreover, Shoji et al. showed that IDL is an independent risk factor for aortic sclerosis in HD patients.⁴¹ In patients with ESRD Lp(a) is a risk factor for disease and mortality.[30-33] Finally, the highly atherogenic LDL subclass, small dense LDL, is present in HD patients.[28] In ESRD, these 'alternative' lipoproteins may fulfil a more important role in the development of cardiovascular disease than LDL. Therefore, it may be important to also focus on these nontraditional lipid parameters. Moreover, biochemical modifications of LDL, not reflected by total and LDL cholesterol levels, may offer another explanation for the increased cardiovascular risk in patients with ESRD. The most important process involves the oxidation of lipids.

cholesterol in patients with ESRD has become even more complicated since low-density lipoprotein (LDL) particles in these patients may be altered, and become 'ugly' through increased oxidative stress, which is characteristic for dialysis patients. This results in the formation of small, dense, oxidised LDL particles that are considered to be highly atherogenic and therefore play an important role in the development of atherosclerosis.[34,35]

LIPID PROFILE IN HD

Despite the neutral effect of dialysis on serum lipid profile, certain dialysis-related parameters may significantly affect lipoprotein metabolism and modify the features of dyslipidemia in HD patients. We found the results a significant increase in cholesterol levels, decrease in triglycerides comparing with pre and post dialysis. Thus, it has been shown that the use of high-flux polysulfone or cellulose triacetate membranes instead of low-flux membranes is accompanied by a significant reduction in serum triglyceride levels as well as by an increase in apolipoprotein AI and HDL-cholesterol levels [36,37]. In addition, the type of dialysate may also significantly affect the serum levels of lipoproteins in HD patients. Our results are found decrease HDL levels. Indeed, it has been shown that the use of bicarbonate dialysate may result in higher HDL-cholesterol concentrations than the use of acetate dialysate [38]. Another factor that can potentially affect lipoprotein metabolism in HD patients is the repeated use of heparin as an anticoagulant. Heparin releases lipoprotein

lipase from the endothelial surface and thus its chronic use may result in lipoprotein lipase depletion and defective catabolism of triglyceride-rich lipoproteins. However, the studies that tested the role of heparin in the pathogenesis of HD-induced dyslipidemia revealed contradictory results [39-41]. In addition, controversy exists as to whether low-molecular weight heparins have a more favorable effect on the lipid profile of HD patients compared to standard unfractionated heparin [42,43]. Finally, recent studies indicate that the use of the phosphate-binder sevelamer hydrochloride significantly reduces the concentrations of total cholesterol and apolipoprotein B in HD patients [44]. Our results showed a significant increase in cholesterol levels. Obviously, the cholesterol-lowering properties of this compound are irrelevant to phosphate reduction and can be mainly attributed to its bile acid sequestering properties.

Studies have indicated that the characteristic features of renal dyslipidemia remain essentially unchanged during long-term HD [2,45]. The apolipoprotein profile retains the main characteristics of the dyslipidemia observed in patients with less advanced renal failure [45]. Even in patients without hyperlipidemia, there is an increase in VLDL-cholesterol and a decrease in HDL-cholesterol levels [45,46]. Compared with patients before dialysis, HD patients have slightly lower concentrations of the triglyceride-rich lipoproteins, possibly representing an attenuation of the dyslipidemia [45]. The HD procedure includes factors that may influence the lipoprotein metabolism. The use of low-molecular weight heparins for anticoagulation have, in some, but not all studies, led to a moderate reduction of triglyceride levels in comparison with the use of unfractionated heparin. This may be related to the effect of low-molecular weight heparins on release and clearance of lipoprotein lipase. Studies on the influence of high-flux dialysis modalities, such as hemodiafiltration or hemofiltration, have yielded conflicting results [47-49]. However, recently one study shows that the choice of dialysis membrane does not influence the dyslipidemia [49].

CONCLUSION

Cardiovascular disease (CVD) is a major cause of mortality in patients with mild to moderate chronic kidney disease and end stage renal disease (ESRD). In this review, we summarise the data on serum lipid profile, Lp(a) as a possible cardiovascular risk factor. The principal features of renal dyslipidemia remain essentially unchanged during HD, but the expression of dyslipidemia can be moderately attenuated during long-term HD. Measurement of Lp(a) in

patients attending lipid clinics instead may be regarded as useful in indicating to clinicians the need for intensive treatment for other cardiovascular risk factors other than Lp(a) per se. Results from studies in non renal patients strongly suggest that the accumulation of atherogenic lipoproteins could also play a role in the development of atherosclerotic complications in HD patients.

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