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Dialysis modalities and dyslipidemia

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Dialysis modalities and dyslipidemia. Progressive renal failure is accompanied by dyslipidemia, which is reflected in an abnormal apolipoprotein profile. It is characterized by increased concentrations of intact and partially metabolized triglyceride-rich apoB-containing lipoproteins. They occur preferentially in very-low density lipoprotein (VLDL) and low-density lipoprotein (LDL) as a result of impaired metabolism and clearance. Hemodialysis can moderately attenuate the renal dyslipidemia. In contrast, peritoneal dialysis is associated with further aggravation, including an increase of cholesterol-rich apoB-containing lipoproteins.

RENAL DYSLIPIDEMIA

Progressive renal failure is associated with characteristic alterations of lipoprotein metabolism and dyslipidemia [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 [1, 2]. 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 [3, 4], but little change in the concentrations of cholesterol-rich apoB-containing lipoproteins. A significantly decreased plasma apoA-I to apoC-III ratio is the hallmark of the altered lipoprotein composition in renal disease. It is detected at the early asymptomatic stages of renal insufficiency and will become further accentuated as renal failure develops [5, 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 [1]. The pathophysiologic links to loss of renal function are still not clearly defined, but changes in insulin-mediated processes and insulin resistance appear to be of significance [1].

Treatment with dialysis is effective for amelioration of uremic symptoms and certain features of uremic toxicity. An important question is to what extent can dialysis and the choice of dialysis modality influence the expression of dyslipidemia in patients with renal failure? 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. The consequences of long-term dialysis on nutrition and the accompanying pharmacologic treatment may be additional contributing factors.

HEMODIALYSIS AND DYSLIPIDEMIA

Studies have indicated that the characteristic features of renal dyslipidemia remain essentially unchanged during long-term HD [1, 7]. Depending on the criteria, up to 70% of HD patients have hyperlipidemia, mainly a moderate elevation of plasma triglycerides. The apolipoprotein profile retains the main characteristics of the dyslipidemia observed in patients with less advanced renal failure, including reduced apoA-I and apoA-II levels, moderate elevations of apoB and apoE, and a significant increase of apoC-III concentrations [7]. Even in patients without hyperlipidemia, there is an increase in apoC-III and VLDL-cholesterol and a decrease in HDL-cholesterol levels [7, 8]. The increase of apoC-III occurs preferentially among the apoB-containing lipoproteins [7]. By measuring individual, apolipoprotein-defined lipoprotein families, we have found that there is little change in the

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levels of lipoprotein B (LpB), the characteristic cholesterol-rich lipoprotein of LDL [7]. In contrast, there is an increase in the levels of triglyceride-rich apoB-containing lipoproteins, which, in addition to apoB, also contain apoC and/or apoE, resulting in a marked increase of apoB-containing lipoproteins in IDL [9]. The distribution of apoC-III in lipoprotein fractions is similar to that occurring in patients before dialysis [3, 6]. Compared with patients before dialysis, HD patients have slightly lower concentrations of the triglyceride-rich lipoproteins, possibly representing an attenuation of the dyslipidemia [7].

Recent studies have shown that VLDL and IDL from HD patients do not differ from VLDL and IDL from predialysis patients in respect to reactivity to lipoprotein lipase [10]. The increased content of apoC-III in apoB-containing lipoproteins appears to be an important factor associated with decreased reactivity to lipoprotein lipase [1, 6].

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 [11, 12, 13]. However, we have recently shown that the choice of dialysis membrane does not influence the dyslipidemia [13].

It is of interest to note that treatment of hyperphosphatemia with the resin sevelamer hydrochloride (HCl) has resulted in a significant decrease in the levels of plasma cholesterol and apoB in hemodialysis patients [14]. Sevelamer HCl is known to bind bile acids, as well as phosphate, and therefore has a cholestyramine-like effect in addition to controlling serum phosphate. It is likely that the use of sevelamer would result in a similar cholesterol-lowering effect in both predialysis and peritoneal dialysis (PD) patients.

In summary, the principal features of renal dyslipidemia remain essentially unchanged during HD, but the expression of dyslipidemia can be moderately attenuated during long-term HD.

PERITONEAL DIALYSIS AND DYSLIPIDEMIA

In contrast to studies in HD patients, there are fewer studies of dyslipidemia in PD patients. Hyperlipidemia is more prevalent in PD patients than in HD patients [7, 9, 15–18]. In addition to hypertriglyceridemia there is also an increase of plasma cholesterol and LDL-cholesterol levels [7, 9, 15–18]. The apolipoprotein profile of PD patients is characterized by a proportionately greater increase in the levels of apoB, apoC-III, and apoE than in HD patients [7, 9, 16]. In addition to elevated levels of triglyceride-rich apoB-containing lipoproteins, there is also an elevation of cholesterol-rich apoB-containing lipoproteins, as reflected by increased levels of both IDL and LDL [7, 9, 16]. The characteristic reduction of apoA-containing lipoproteins in HDL of patients with less advanced renal failure and HD patients is also shared by PD patients [7, 9, 15, 16].

We have shown in a recent study that PD patients have significantly higher levels of both cholesterol-rich and triglyceride-rich apoB-containing lipoproteins than HD patients [7]. In view of the documented atherogenic potential of both triglyceride-rich and cholesterol-rich apoB-containing lipoproteins, it appears that the already unfavorable lipoprotein profile in HD patients is further aggravated in PD patients.

There are several features of the PD treatment that may directly affect lipoprotein metabolism. The significant absorption of glucose from the dialysis fluid provides a substrate for increased lipoprotein synthesis that may result in elevated plasma lipid concentrations [16]. In support of this, modification of the PD procedure with the use of icodextrin-containing dialysis solutions instead of glucose for the overnight dwell results in a moderate reduction of plasma cholesterol [19]. The failure to demonstrate a direct correlation between glucose absorption and lipid levels may be due to the fact that almost all patients have a significant absorption of glucose in a range that does not permit correlation analysis [16]. The peritoneal protein clearance may, in addition to albumin, include apolipoproteins and HDL, and possibly other lipoprotein regulatory substances, which may trigger mechanisms that resemble those operative in nephrotic syndrome, particularly an increase of cholesterol-rich lipoproteins [7, 9, 20].

In summary, in PD patients, the renal dyslipidemia also retains its characteristic profile. However, in contrast to HD, the increase of atherogenic lipoproteins is more pronounced.

CONCLUSION

The dialysis modality may, to a certain extent, influence the expression of renal dyslipidemia in patients with end-stage renal disease. There is a moderate attenuation of the dyslipidemia in HD patients in contrast to its aggravation observed in PD patients. The clinical significance of renal dyslipidemia is not yet established but is awaiting conclusive interventional studies. However, results from studies in nonrenal patients strongly suggest that the accumulation of atherogenic lipoproteins could also play a role in the rapid development of atherosclerotic complications in dialysis patients.

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