Evidence for an Exaggerated Postprandial Lipemia in Chronic Paraplegia

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Abstract

Background/Objective: Excessive delay in triglyceride (TG) metabolism after ingestion of dietary fat represents a significant cardiovascular disease (CVD) risk. The objective of this study was to compare the postprandial lipemic responses of individuals with paraplegia with those of healthy nondisabled individuals.

Methods: The ability of 3 recreationally active individuals with paraplegia having normal fasting TG (mean = 103 mg/dL) to metabolize TG after ingestion of a high-fat test meal was compared with a previously published cohort of 21 recreationally active individuals without paraplegia (TG mean = 86 mg/dL) who underwent identical testing. The subjects with paraplegia had venous blood taken under fasting conditions, and then ingested a milkshake containing premium ice cream blended with heavy whipping cream (~92% of calories from fat). Additional blood samples were obtained at 2, 4, and 6 hours after ingestion. The area under the curve (AUC) for TG clearance for both subject groups was measured with an area planimeter.

Results: TG uptake for both groups was almost identical for the first 2 hours after ingestion. At 4 and 6 hours after ingestion, the TG levels were 50 and 35 mg/dL higher, respectively, in subjects with paraplegia than in nondisabled subjects. When corrected for small baseline differences in TG concentrations (16 mg/dL), the AUC was 46.5% greater for the group with paraplegia than in the nondisabled group. A near mirror association across time was observed between postprandial serum high-density lipoprotein cholesterol (HDL-C) and TG levels in subjects with paraplegia.

Conclusion: This case series finds an exaggerated postprandial lipemia (PPL) in persons with paraplegia with normal fasting TGs. This finding is the first evidence, in a small population, of an unreported potential CVD risk in persons with paraplegia.

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INTRODUCTION

Accelerated cardiovascular disease (CVD) is a widely recognized health risk for persons with spinal cord injuries (SCI; Refs. 1 and 2). CVD occurs earlier in life for individuals with SCI and can develop without overt clinical symptoms of impending cardiac damage (3,4). It may further impart atypical warning signs of imminent myocardial ischemia because of the interruption of

neurotransmission from afferent nerves that warn of cardiac damage (5). For all of these reasons, a full understanding of disease risks and methods for primary CVD prevention is essential if fullest life quality and longevity are to be attained by individuals with SCI.

A severely lowered presence of the cardioprotective high-density lipoprotein cholesterol (HDL-C) is the most common feature of dyslipidemia reported in persons with SCI (6–10). Low HDL-C as observed in individuals with SCI is widely reported in both clinical trial data and authoritative guidelines as an independent risk for accelerated CVD (11–13). In the process of studying

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causes for this risk, we observed persistence of elevated triglycerides (TG) in the blood of persons with SCI after ingestion of a high-fat test meal. This exaggerated postprandial lipemia (PPL), first described by Zilversmit in 1979 (14), is an important stimulus for atherogenic disease progression (15,16) because delayed removal of blood-borne TG-rich lipoproteins (TRLs) encourages direct deposition of lipoprotein remnants on the arterial wall (17) and increases the likelihood that low-density lipoprotein (LDL) cholesterol will undergo disease-accelerating oxidative modification (18). Because our observations were in persons with SCI who had normal levels of fasting TG, this risk may be insidious and be undetected by routine lipid testing. The objective of the study was to compare the postprandial lipemic responses of subjects with paraplegia with those of nondisabled individuals who had no evidence of CVD. This report describes the first evidence of and possible mechanisms for the CVD risk of PPL in persons with SCI who have normal fasting TG.

METHODS

Subjects

Three mesomorphic men aged 40 to 46 years with chronic complete motor function impairment from SCI (American Spinal Injury Association impairment scale grade A and B) below the T10 level were studied. The subjects were all in excellent health and recreationally active, but not involved in organized or self-initiated programs of exercise conditioning. Consent to undergo study was obtained with prior approval of the institutional Human Subjects Committee. Descriptive characteristics of the study subjects are shown in Table 1.

PPL Testing

Subjects refrained from alcohol and caffeine ingestion starting 24 hours before testing, and were studied in the postabsorptive state after a 10-hour overnight fast. Under antiseptic conditions, a 21-gauge Teflon catheter (Jelco) with multi-sample Luer connector was placed in a superficial arm vein. The catheter was kept patent with sterile physiological (0.9%) saline. PPL was assessed by measurement of blood plasma TG uptake and disposal after ingestion of a commonly described milkshake (19) consisting of heavy whipping cream and premium ice cream (1.3 g fat, 1.2 g carbohydrate, 0.2 g protein, and 76 kJ of energy; all per kilogram of body mass; Refs. 20,

21). Blood samples were collected in clot lysis activator (serum) and citrated Vacutainer tubes before intake of the test meal and at 2, 4, and 6 hours after the test meal. Blood samples were centrifuged at 8,000g for 30 minutes to isolate the serum. These isolates were assayed for TG concentration on a Roche Mira-Cobas Automated Chemistry Analyzer (Roche Diagnostic Systems, Basel, Switzerland), as we have described (7). Total HDL-C was measured using the same analyzer after poly ion precipitation of the apo B-containing lipoproteins (22).

Nondisabled Comparison Group

The comparison group was a cohort of 21 noncompetitive, recreationally active, mesomorphic men without disability, aged 21 to 39 years, whose responses to oral lipid loading had been previously published (23). Subjects in the comparison group were healthy, active persons who had undergone lipemic challenge under identical test conditions using the same high-fat meal formulation containing premium ice cream blended with heavy whipping cream (23).

Data Management

Data reflecting TG clearance were first plotted as a function of time. A second plot adjusted plasma TG concentrations to control for baseline TG concentrations occurring before ingestion of the test meal. The areas under the curves (AUC) for baseline-adjusted TG clearance for both groups were measured in triplicate using a handheld area planimeter (Koizumi, Niigata, Japan), and expressed as the average of these measurements.

RESULTS

Responses of both groups to high-fat intake are shown in Figures 1 and 2. Both groups had low fasting TG levels, with average TG concentrations of 103 mg/dL and 86 mg/dL in the paraplegic and control groups, respectively. After correction for a 16 mg/dL difference at baseline, the 2 study groups demonstrated nearly identical TG uptake for the first 2 hours of testing (Figure 2), with a TG difference at the second hour of 2 mg/dL. However, at 4 and 6 hours after ingestion, the TG levels were 50 mg/dL and 35 mg/dL higher in subjects with paraplegia, with peak TG concentrations of 228 mg/dL and 162 mg/dL in subjects with and without paraplegia, respectively. The AUC was 28.7% greater for

Table 1. Descriptive Characteristics of the Study Subjects

	Paraplegia		Nondisabled Controls	
	Range	Mean $\pm$ SD	Range	Mean $\pm$ SD
Age (y)	40–46	43.7 $\pm$ 1.2	21–39	27 $\pm$ 1.7
Level of injury	T10–L1			
Duration of injury (y)	3–8	5.7 $\pm$ 1.3	...	...

Figure 1. Responses of subjects with paraplegia and a nondisabled (ND) comparison group to ingestion of a high-fat meal.

Figure 2. Responses of subjects with paraplegia and a nondisabled (ND) comparison group to ingestion of a high-fat meal. Values are corrected to reflect changes from baseline TG concentrations.

Figure 3. Time-dependent effects of fat loading on concentrations of HDL-C and TG concentrations in subjects with paraplegia.

subjects with paraplegia when TG concentrations were left uncorrected for group differences observed at baseline. When corrected for baseline differences, the AUC was 46.5% greater for subjects with paraplegia than for the nondisabled subjects. A near mirror association across time was observed between postprandial serum HDL-C and TG levels (Figure 3).

DISCUSSION

The findings of this small sampling of persons with chronic paraplegia show delayed clearance of dietary TG in blood after ingestion of a high-fat meal. Delayed metabolism of TRLs is strongly associated with a constellation of atherogenic and thrombogenic lipoprotein changes (24). These include an increased plasma concentration of intestinally derived chylomicrons and their remnants; increased levels of hepatic very low-density lipoproteins and their remnants; and decreased LDL cholesterol size, which is associated with heightened susceptibility of LDL-C to undergo atherogenic oxidative modification. Postprandial TRLs are also potentially thrombogenic, and are associated with increased pro-coagulant activated factor VII activity and increased levels of the antifibrinolytic mediator, plasminogen activator inhibitor-1.

Experimental results and clinical trial data suggest that plasma accumulation of remnant lipoproteins in the fed or fasted state is not only an associated feature of an atherogenic lipoprotein profile, but that TRL remnants themselves contribute to the pathogenesis of atherosclerosis. For these reasons, an exaggerated PPL is viewed as an independent risk for accelerated CVD (24); thus,

resolution of PPL is an aggressively targeted goal for reducing CVD risk and slowing vascular disease progression in humans without SCI (20,25,26).

This report conveys the first finding of an exaggerated PPL in persons with SCI. Although the mechanisms underlying this observation are incompletely understood, they are, in many respects, consistent with effects of physical deconditioning and changes in muscle physiology accompanying SCI. Physical deconditioning accompanying SCI reportedly lowers skeletal muscle lipoprotein lipase activity, which would slow TG extraction from the blood after oral intake (15). Persons with SCI also lose sublesional muscle mass that might otherwise more substantially metabolize postprandial TG as a fuel source (27). Sublesional muscle also transforms to faster myosin heavy chain isoforms that preferentially metabolize carbohydrates, not TG, as a source of muscle energy (21,28,29). Notwithstanding a defined cause for the observations of this case series, the PPL was observed in patients who had fasting TG levels stratified in the “low risk” range. This suggests that PPL in persons with SCI may occur silently and go undetected during routine lipid screening for CVD.

The inverse lowering of HDL-C concentrations during periods of elevated postprandial TG is both an interesting observation and an apparent paradox in lipid metabolism. Similar findings have been reported in persons without disability after high fat intake (24), and are associated with an increase in TG content of the HDL complex (24,30). Presumably, the decrease in HDL-C is mediated by the action of cholesteryl ester transfer protein, which causes the net transfer of cholesterol

esters from HDL to the TRLs, and the reverse transfer of TG from the TG-containing lipoproteins to HDL (31). The increased transfer of cholesteryl esters from HDL to the TRL during the elevated PPL may lead to a greater production of atherogenic TRL remnant particles, the generation of the atherogenic small, dense LDL particles, and accelerated catabolism of HDLs (32), further exacerbating the dyslipidemia associated with SCI. Because TG levels were still elevated above baseline by 80 mg/dL at 6 hours after ingestion of the high-fat test meal, these data do not rule out the possibility that excessive PPL may contribute to the low HDL-C commonly reported in persons with SCI. Whether similar persistence of elevated TG would also accompany a more typical high-fat meal, such as found in "fast food," is an intriguing possibility worthy of study.

The findings of this case series are especially compelling for several additional reasons. Subjects undergoing study were relatively young, had injuries at spinal levels sparing adrenergic functions, had motor loss fully sparing the upper extremities and part of the trunk, and abstained from tobacco use. By contrast, nearly half of individuals living with SCI will have higher levels of injury and adrenergic dysfunction than did participants in this study. Because PPL in persons without disability is worsened by health concerns common to individuals with SCI, including advancing age (33), truncal obesity (34), imprudent diet (35), physical inactivity (36), reduced fasting HDL (37), and type 2 diabetes (38), it is plausible that the subjects in this case series were an ideal, rather than typical, representation of the population (39). Individuals with paraplegia who are older, more sedentary, obese, or diabetic may indeed fare worse (40).

We conclude that exaggerated PPL may accompany the CVD risk profile of persons with SCI, although this early finding requires corroboration in a larger study sample. The risk for PPL in the current instance poses a heretofore undescribed and insidious risk that may partially cause and explain the elevated incidence of CVD in persons with SCI.

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