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Influence of Obesity and Body Fat Distribution on Postprandial Lipemia and Triglyceride-Rich Lipoproteins in Adult Women*

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ABSTRACT

We know that upper body obesity is associated with metabolic complications, but we don't know how regional body fat distribution influences postprandial lipemia in obese adults. Thus, this study explored the respective effects of android or gynoid types of obesity and fasting triglyceridemia on postprandial lipid metabolism and especially triglyceride-rich lipoproteins. Twenty-four obese and 6 lean normotriglyceridemic women (control), age 24–57 yr, were enrolled. Among obese women with an android phenotype, 9 exhibited normal plasma triglyceride levels (mean: 1.38 mmol/L) (NTAO), and 7 displayed a frank hypertriglyceridemia (mean: 2.40 mmol/L) (HTAO). The 8 patients with a gynoid phenotype had normal triglyceride levels (mean: 1.00 mmol/L) (GO). All were given a mixed test meal providing 40 g triglycerides. Serum and incremental chylomicron triglycerides 0–7 h areas under the curve (AUCs) as well as triglyceride levels in apoB-48-containing triglyceride-rich lipoprotein (TRLs) or chylomicrons were significantly higher in HTAOs and NTAOs than in GOs and controls postprandially. The size of chylomicron particles was bigger in controls and GOs than in HTAOs and NTAOs postprandially. Android obese subjects showed abnormally elevated fasting apoB-48 and apoB-100 triglyceride-rich lipoprotein (TRL) levels. Most abnormalities that were found correlated to plasma levels of insulin and apoC-III. In conclusion, an abnormal postprandial lipid pattern is a trait of abdominal obesity even without fasting hypertriglyceridemia. (*J Clin Endocrinol Metab* **84:** 184–191, 1999)

IT IS well known that obese subjects have high risk of coronary heart disease (1, 2) that is potentially linked to the documented abnormalities in fasting plasma lipid and lipoprotein parameters (2). In addition, the regional distribution of body fat deposits (3, 4) plays a key role, abdominal adiposity considerably increasing disturbances in plasma lipid levels and cardiovascular risk (3–8). Accumulation of triglycerides in fasting plasma is highly incriminated (9), and in fact, over-production of hepatic very low density lipoprotein (VLDL) and/or reduced clearance of these particles from the plasma have been shown in obese subjects (10, 11). As extensively studied in diabetic subjects, one expects to find a central role of insulin resistance-hyperinsulinemia, which is exacerbated in obese subjects with abdominal fat depots (11–13). A reduced clearance capacity of triglyceride-rich particles from the plasma could be the result of reduced efficiency of endovascular lipolysis due to reduced levels of lipoprotein lipase (10, 14), abnormal lipoprotein particles (15), or elevated levels of apoC-III (16–18). Impaired receptor-mediated uptake of triglyceride-rich lipoprotein (TRL) remnant particles by the liver is also implicated (19).

Although fasting lipid and lipoprotein levels reflect steady-state lipid metabolism, even healthy subjects are in a state of postprandial hypertriglyceridemia most of the time, due to meal frequency (20), while in hyperlipidemic subjects the condition is even more extensive (21, 22). Indeed, abnormalities in postprandial lipid metabolism are increasingly incriminated in the etiology of atheroma deposition and cardiovascular disease (22–27), but the respective role of triglyceride-rich particles secreted by the liver or the small intestine is still an open question. Several studies have already shown disturbances in postprandial lipid and lipoprotein responses in diabetic subjects as reviewed (21), and the role of obesity on postprandial lipid metabolism has been studied in some occasions (28–34). At the time this paper was submitted, a study had been published (35) reporting exacerbated postprandial triglyceridemia and TRL responses in men with visceral obesity and elevated fasting triglycerides as compared to men with lower visceral adiposity and fasting triglycerides. Nevertheless, in these studies, the respective roles of android and gynoid obesity have not been evaluated separately from fasting hypertriglyceridemia.

In line with previous postprandial studies performed in our laboratory (20, 36), the aim of this study was to evaluate the respective roles of obesity, regional fat deposit, insulinemia, and fasting hyperlipidemia on the postprandial response after a standardized fat-containing mixed test meal. We were able to compare the 0–7 h postprandial lipid responses in four groups of women, two groups with android

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obesity, associated or not with fasting hypertriglyceridemia, one group with gynoid obesity and normal fasting lipemia, and a control group of lean normotriglyceridemic women. An abnormal postprandial accumulation of plasma triglycerides due to hepatically-derived and intestinally-derived triglyceride-rich particles was found in android obese women.

Subjects and Methods

Subjects

Twenty-four obese and 6 lean women, ages 24–57 yr, participated in the study. Fat distribution was assessed using the waist-to-hip ratio (WHR), which is the relation between the circumference of the waist at the level of the umbilicus and that of the hips at the level of the great trochanters and symphysis pubis. As shown in Table 1, among abdominal obese women with a WHR higher than 0.80 (3, 4), 9 had a slightly elevated but normal fasting triglyceridemia (NTAO group, mean WHR: 0.94), and 7 showed a hypertriglyceridemia (HTAO group, mean WHR: 0.92). Eight obese women had a WHR of less than 0.80 (mean WHR: 0.77) and a normal fasting triglyceridemia (GO group). The body mass indices (BMI) of obese women were in the range 35.3–39.8. The 6 lean women (mean BMI: 21.1) had a normal fasting triglyceridemia (control group). Mean ages of subjects were not significantly different in the 4 groups (Table 1), and all except one were premenopausal women. Mean fasting values of plasma total cholesterol, apoA-1, apoBs, nonesterified fatty acids (NEFA), and glucose levels were not different in the studied groups. Mean fasting plasma insulin and apoC-III levels (Table 1) were significantly higher in the HTAO group compared with the 3 other groups, which showed not different values. The allele distribution for apoE was not identical but close in the 4 groups (Table 1).

No subject suffered from any digestive or metabolic disease other than obesity as checked by medical history, clinical evaluation, and fasting blood parameters. The subjects had not taken medications that would interfere with lipid metabolism, nor had they taken vitamin A supplements, for months. All subjects participated in the study after giving written informed consent to a protocol approved by the local Medical Ethics Committee (Comité Consultatif pour la Protection des Personnes se prêtant à des Recherches Biomédicales, Marseille).

Test meal

After an overnight fast, in the morning (about 0800), the subjects were given as previously reported (20) a test meal containing 40 g triglycerides as sunflower margarine (50 g) and 50,000 UI retinyl ester in the form of a capsule of Avibon (Théraplix, Paris, France), together with 5 regular rusks, a 125 g nonfat yoghurt, half a hard boiled egg, 200 mL skimmed milk, and a decaffeinated coffee. The test meal provided 2841 kJ (680 kcal) with 11.5%, 61.8%, and 26.7% energy as proteins, lipids, and carbohydrates, respectively.

Analytical measurements and methods

Blood samples (15 mL) were collected, via a small forearm indwelling catheter just before the test meal (zero time) and every hour for 7 h after the meal, in tubes containing or not containing EDTA. Plasma and serum were immediately separated from whole blood by centrifugation (910 × 1 *g*, 4 C, 10 min).

The chylomicron fraction (Sf > 1000) was isolated from 1 mL plasma layered under 2 mL NaCl 0.9% by ultracentrifugation at 10 C for 15 min (1.310^6 *g* × min) in a Beckman, TL 100.3 rotor with a Beckman TL100 ultracentrifuge (Palo Alto, CA), as previously described (36). Chylomicron sizes were measured at 20 C on suspended, freshly prepared samples by Photon Correlation Spectroscopy (SEMATech, Nice, France) with a particle-size analyzer. We previously showed that the mean diameters obtained by using a particle-size analyzer are in good agreement with those obtained by the electron microscopy (37).

The TRL fraction (*i.e.* chylomicron fraction plus small remnants and VLDL particles; Sf 20–1000) was separated from whole plasma (fasting samples; pooled samples from 2, 3, and 4 h for representative peak values of all subjects; samples at 7 h) at a density of 1.019 kg/L and 16 C, at 412,000 × *g* for 3 h 30 min in a 100.3 rotor with TL100 ultracentrifuge (34). ApoB-100-containing TRL particles were subsequently separated from apoB-48-containing TRLs by affinity chromatography, using a 2G8 monoclonal antibody (Mona, Moscow, Russia) that does not cross-react with apoB-48 (38) according to a procedure described by Cohn *et al.* (39). Briefly, 1.2 mL of the 2G8 monoclonal antibody-coupled gel suspended in phosphate-buffered saline (PBS, pH 7.4, 0.02% NaN_3) was aliquoted in 1.5 mL Eppendorf (Fremont, CA) tubes. TRLs (300 μg protein) were added to the (0.5 mL) packed gel. After 1 h incubation at room temperature and centrifugation, about 0.5 mL supernate (unbound fraction) was aspirated. Then 2 × 1 mL PBS were added for washing purpose. Triglycerides were measured in about 2.5 mL pooled supernates (unbound apoB-48 fraction) and in the stacked gel (bound apoB-100 fraction) after appropriate validation. As checked by SDS-PAGE separation and quantitation (40), the unbound apoB-48-containing fraction contained minor amounts of contaminating apoB-100, *i.e.* 5–8% and 7–11% of total apoBs present in samples from control and hypertriglyceridemic patients, respectively. Thus, apoB-48-containing TRLs were, on the whole, overestimated by about 10%, which is in line with previous works (15, 39).

Triglycerides (41), total and free cholesterol (42), phospholipids (43), and glucose (44) were measured by enzymatic procedure with kits purchased from BioMerieux (Marcy l'Etoile, France). Retinyl palmitate was assayed in the chylomicron fraction obtained by ultracentrifugation using an HPLC method as previously used (20).

TABLE 1. Age, waist and hip circumferences, WHR, BMI, fasting blood parameters, and apo-E genotype of studied obese and lean women

	Control subjects (n = 6)	GO subjects (n = 8)	NTAO subjects (n = 9)	HTAO subjects (n = 7)
Age (yr)	33.4 ± 6.0	35.0 ± 3.0	40.7 ± 2.8	40.3 ± 6.0
BMI	21.1 ± 0.4 a	35.3 ± 2.7 b	38.3 ± 2.2 b	39.8 ± 2.9 b
Waist circumference (cm)		89.9 ± 3.0 a	111.8 ± 5.0 b	109.2 ± 5.9 b
Hip circumference (cm)		117.0 ± 2.8	120.2 ± 3.0	117.6 ± 5.4
WHR		0.76 ± 0.01 a	0.93 ± 0.02 b	0.91 ± 0.03 b
Glucose (mmol/L)	4.52 ± 0.27	4.58 ± 0.24	4.79 ± 0.14	5.49 ± 0.43
Insulin (pmol/L)	116.88 ± 21.5 a	127.36 ± 17.6 a	145.08 ± 15.3 a	249.62 ± 58.9 b
Triglycerides (mmol/L)	0.63 ± 0.08 a	1.00 ± 0.12 a,b	1.38 ± 0.14 b	2.40 ± 0.29 c
Total cholesterol (mmol/L)	5.00 ± 0.43	5.00 ± 0.27	5.78 ± 0.32	6.08 ± 0.44
ApoA1 (g/L)	1.2 ± 0.07	1.12 ± 0.09	1.02 ± 0.09	0.86 ± 0.16
AposB (g/L)	0.80 ± 0.08	0.80 ± 0.08	1.09 ± 0.06	1.05 ± 0.19
NEFA (mmol/L)	0.39 ± 0.09	0.72 ± 0.14	0.69 ± 0.09	0.70 ± 0.15
ApoE genotype	3/3 (n = 3)	3/3 (n = 3)	3/3 (n = 6)	3/3 (n = 4)
	3/2 (n = 2)	3/2 (n = 3)	3/2 (n = 1)	3/2 (n = 1)
	3/4 (n = 1)	3/4 (n = 2)	3/4 (n = 2)	3/4 (n = 1)

Values are mean ± SEM. Different letters indicate significant differences ($P < 0.05$) between groups. BMI, body mass index; WHR, waist-to-hip ratio.

Total plasma apoA-1 and apoBs were assayed by laser-immunonephelometry with commercial kits (Behring Werke A.G., Marburg, Germany) as before (36). ApoC-III concentrations were determined by an electro-immunoassay method using Hydragel LpC-III kit purchased from Sebia (Issy-Les-Moulineaux, France). ApoE genotyping was performed by PCR and *Hha*I-RLPF after DNA extraction from blood samples (45). Serum insulin was assayed by an immuno-enzymatic method (46) with commercial kits (Boehringer Mannheim, Germany). After the 7 h postprandial sampling, each subject was injected 50 U/kg heparin (Choay, Gentilly, France); 15 min after, a post-heparin blood sample was drawn for subsequent determination of lipoprotein lipase and hepatic lipase activities, according to the method of Krauss *et al.* (47).

Statistical analysis

Results are given as means ± SEM. Absolute postprandial changes are given as concentration values, and incremental postprandial variations were calculated by substracting the baseline values from the postprandial values. The 0–7 h area under the curve (AUC) was calculated by the trapezoidal method. Time effect was assessed by multivariate analysis of variance (MANOVA) using Wilcoxon test. Group effect and group-by-time effect during postprandial state were assessed by repeated measures analysis of variance (GLM). Pearson correlation coefficients were obtained from linear regression analysis. Data analysis was performed using the statistical SAS software program (SAS Institute, Inc., SAS/STAT 6.03 edition, (Cary, NC) at a significance level of $P < 0.05$ with Fisher's test.

Results

Postprandial serum and triglyceride rich-lipoprotein lipids

Absolute and incremental 0–7 h postprandial changes in serum triglyceride concentrations (mmol/L) are shown in Fig. 1. As expected, in the four groups of subjects serum triglycerides significantlly rose postprandially over baseline. Subjects in control (normolipidemic lean women) and GO (normolipidemic gynoid obese women) groups were not different and showed a moderate serum triglyceride rise postprandially, while subjects in the NTAO (normolipidemic android obese women) group showed a significantly higher rise, and subjects in the HTAO (hyperlipidemic android obese women) group showed an even higher, more marked rise (Fig. 1, *left panel*). The overall duration of the postprandial triglyceride rise over fasting level was expanded to 5 h in the HTAO group. The serum triglyceride 0–7 h AUCs (mmol/h/L) were lower in controls and GO subjects and markedly higher in NTAO and HTAO subjects (data not shown). Calculations of the incremental serum triglyceride responses over baseline at each time point (data not shown) or 0–7 h AUCs (Fig. 1, *right panel*) clearly showed two different patterns with comparably low responses given by subjects in control and GO groups and comparably higher ([mult] 3- to 4-fold) responses in subjects in groups NTAO and HTAO.

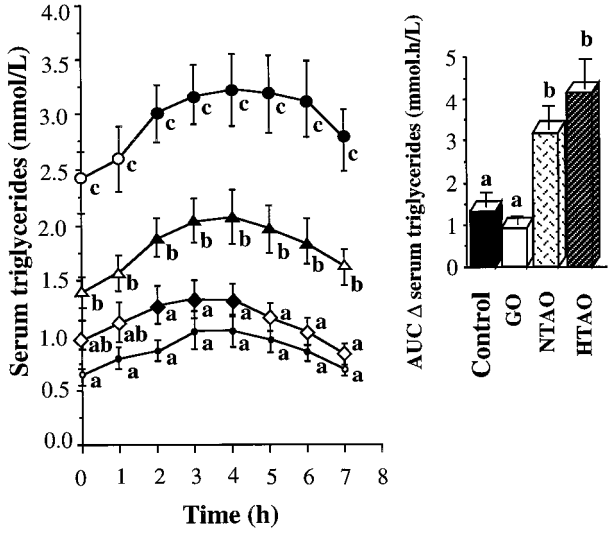

FIG. 1. Serum triglyceridemia (*left panel*) and incremental 0–7 h AUCs for serum triglycerides (*right panel*) for 7 h after test meal. Values are means ± SEM. Control lean women (∘); normotriglyceridemic android obese women (NTAO, △); hypertriglyceridemic android obese women (HTAO, ○); normotriglyceridemic gynoid obese women (GO, ◇). For a given group, a *filled symbol* indicates that the corresponding value was significantly different ($P < 0.05$) from the fasting (0 h) value. At a given time-point and for AUCs, *different letters* indicate a significant difference ($P < 0.05$) between groups.

Fasting serum total cholesterol, nonesterified cholesterol, and phospholipid concentrations were not different between groups, whereas only limited differences in postprandial responses were observed for these parameters. Serum phospholipid 0–7 h AUC (mmol/h/L) was higher in HTAO subjects (23.6 ± 0.5) than in controls (18.3 ± 1.1) and GO subjects (19.7 ± 1.4), with an intermediate mean value for NTAO subjects (20.8 ± 0.5). Serum free cholesterol 0–7 h AUC (mmol/h/L) was also higher in HTAO (13.2 ± 0.7) and NTAO (11.8 ± 0.9) subjects than in control (8.9 ± 0.6) and GO (9.3 ± 0.6) subjects.

The triglyceride concentrations in total TRL are shown in Fig. 2. In the fasting state, total TRL triglycerides were comparable in the control, GO, and NTAO groups, whereas much greater values were shown by the subjects in the HTAO group (Fig. 2A). Total TRL triglycerides were higher in the HTAO group at 2–4 h and 7 h postprandially too.

Hepatic and intestinal triglyceride rich-lipoproteins

We investigated the contributions of hepatically- and intestinally-derived TRL particles. Intestinally-derived TRLs were separated and quantified by either immunoaffinity method (apoB-48 particles) or by ultracentrifugation (chylomicrons).

As shown in Fig. 2B, the concentration of triglycerides in apoB-48 TRLs at baseline was low in both controls and GO subjects, significantly higher in NTAO subjects, and much higher in HTAO subjects. These differences were even more accentuated 2–4 h postprandially, and even 7 h after meal intake. ApoB-100 TRL triglyceride concentrations (Fig. 2 C) were not different in controls, GO and NTAO subjects at baseline, tended to rise after 2–4 h, and came back to fasting levels after 7 h. On the contrary, in HTAO subjects apoB-100-TRL triglyceride concentrations were significantly higher at baseline when compared to the other groups, tended to rise after 2–4 h, but continued to rise after 7 h, giving values significantly higher than in the other groups.

The relative proportions of triglycerides in apoB-48-containing TRL particles were calculated from raw data, thus giving 4–11% overestimated figures due to some uncontrolled apoB-100 contamination, as mentioned above. A higher proportion ($P < 0.05$) of fasting TRL triglycerides in apoB-48 particles was found in subjects in the HTAO group

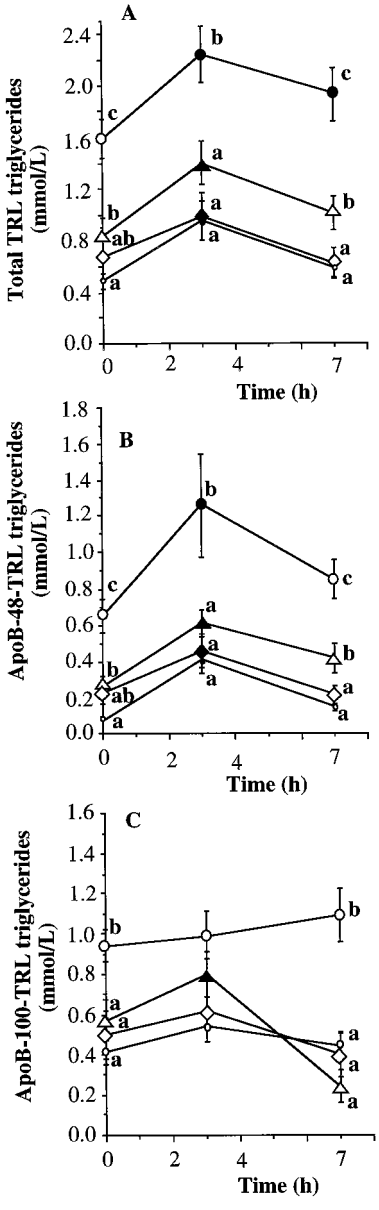

FIG. 2. Triglyceride concentrations in A, total TRLs; B, apo-B48-; and C, apo-B100-containing TRLs. Values are means ± SEM. As discussed in *Subjects and Methods*, apo-B48 triglyceride values are somewhat overestimated (4–11%) and thus, apoB-100 triglyceride values are underestimated. Control lean women (◦); normotriglyceridemic android obese women (NTAO, △); hypertriglyceridemic android obese women (HTAO, ○); normotriglyceridemic gynoid obese women (GO, ◇). For a given group, a *filled symbol* indicates that the corresponding value was significantly different ($P < 0.05$) from the fasting (0 h) value. At a given time-point, *different letters* indicate a significant difference ($P < 0.05$) between groups.

(40.4 ± 2.2%) and to a slightly less extent in the NTAO group (32.8 ± 2.7%) compared with those in the GO group (28.8 ± 6.1%) and, more markedly, with those in the control group (16.8 ± 1.4%). At 2–4 h postprandially, no difference in the proportion of triglycerides in apoB-48 TRLs was found among all four groups (range: 42–53%). Conversely, after 7 h, the three groups of obese women showed significantly higher values (range: 37–43%) than those in lean control ones (25.3 ± 2.5%).

In a more classical approach, we measured the occurence in the serum of chylomicron (CM) triglycerides isolated by ultracentrifugation as shown in Fig. 3. In control and GO groups, chylomicron triglycerides moderately increased 3–4 h postprandially and returned back to baseline 6–7 h after meal intake (Fig. 3A). Conversely, chylomicron triglycerides in the NTAO and HTAO groups markedly increased after 3 and 4 h and were still different from fasting values after 6 h in the HTAO group. As a result (Fig. 3A, *insert*) the incremental chylomicron triglyceride 0–7 h AUCs in subjects in both the NTAO and HTAO groups were markedly higher than those in subjects in the control and the GO groups.

As shown in Fig. 3B, fasting chylomicrons present in limited amounts had a small size, which was not different in the four groups of subjects (range: 51–69 nm). During the first 3 h

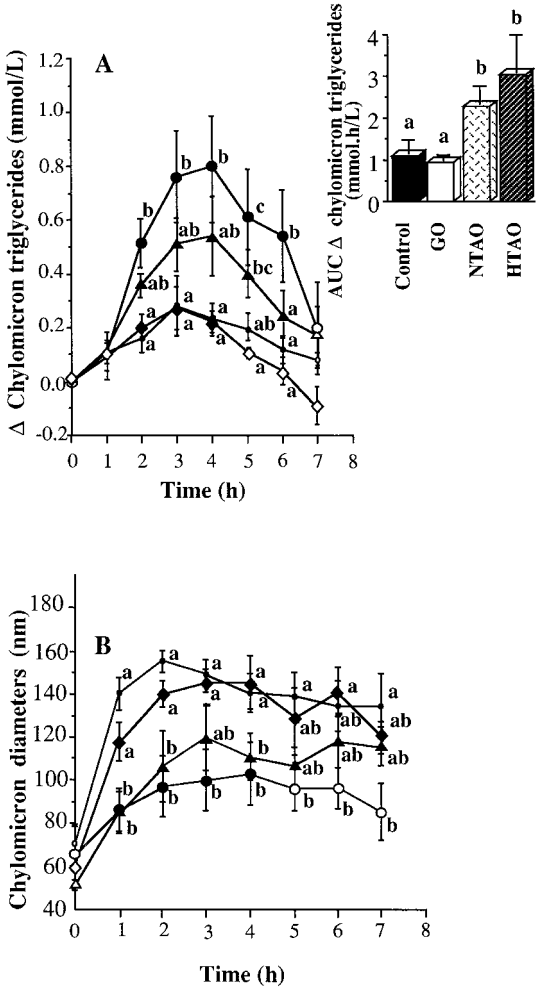

FIG. 3. Postprandial changes in chylomicrons. A, Incremental chylomicron triglyceride responses (concentration changes (△) from fasting values) for 7 h to the test meal and 0–7 h AUCs (*insert*). B, chylomicron sizes (nanometers, diameters) measured for 7 h after meal intake. Values are means ± SEM; n = 6 for Control and NTAO groups, n = 5 for HTAO and GO groups. Control lean women (◦); normotriglyceridemic android obese women (NTAO, △); hypertriglyceridemic android obese women (HTAO, ○); normotriglyceridemic gynoid obese women (GO, ◇). For a given group, a *filled symbol* indicates that the corresponding value was significantly different ($P < 0.05$) from the fasting (0 h) value. At a given time-point, *different letters* indicate a significant difference ($P < 0.05$) between groups.

postprandially, the mean chylomicron size sharply increased in controls and GO subjects (up to 146–156 nm) and only slightly decreased until 7 h. Conversely, in the HTAO subjects, the size of chylomicrons increased significantly more slowly and to lower values. In the NTAO subjects, the increase in chylomicron size was close to that observed in the HTAO subjects during the first 3 h.

As shown in Table 2, a comparable dramatic rise in chylomicron retinyl palmitate levels was observed in all four groups of subjects after 2–4 h. After 7 h, retinyl palmitate levels tended to decline in controls and GO subjects, whereas these figures continued to rise in NTAO subjects and more markedly in HTAO ones.

Lipases, apoC-III, and insulin

Mean values for post-heparin plasma activities of lipoprotein lipase and hepatic lipase were not different in all four groups of subjects, as shown in Table 3. Conversely, fasting and 2–4 h postprandially apoC-III levels were significantly higher in subjects in the HTAO group than in the three other groups, which showed comparable values (Table 3).

As shown in Table 1, fasting serum insulin level was not different in control, GO, and NTAO subjects, whereas values in HTAO subjects were significantly higher. Insulin concentrations rose from baseline to maximum values 1 h after meal intake in all four groups (Fig. 4), with a significantly higher value in the HTAO subjects. The mean insulin incremental 0–2 h AUC (pmol/h/L) was higher in the HTAO subjects (1170.24 ± 284.13) than in others (263.32 ± 123.4, 370.23 ± 137.86, and 571.13 ± 190.85, in control, GO, and NTAO groups, respectively).

Discussion

The aim of this study was to evaluate the respective role of obesity, regional body fat repartition, and fasting hyperlipidemia on the postprandial lipidemic response to a fat-containing meal. The test meal used was very close to physiological conditions in its composition and had been previously validated in healthy subjects (20, 36). The main finding was that this response was exacerbated in obese females with an android morphotype in comparison with a gynoid one despite comparable BMIs and levels of fasting plasma triglycerides. This postprandial response was amplified in patients combining android obesity and fasting hypertriglyceridemia.

Until now, few studies have delt with postprandial lipemia in obese subjects (28–33). One study (34) compared hypertriglyceridemic men with abdominal fat depots with normolipidemic men with desirable weight, showing an amplified postprandial triglyceridemia in the fist ones. Very recently, a study reported (35) an exacerbated postprandial triglyceridemia response in men with visceral obesity and elevated fasting triglycerides compared with others with lower visceral adiposity and fasting triglycerides.

Our present demonstration of an amplified and prolonged postprandial lipidemic response completes the long list of metabolic and vascular abnormalities associated with abdominal obesity in the framework of the so called "X syndrome" (12) related to a marked increase in coronary heart disease incidence (2, 3–8). Exacerbation of postprandial hyperlipidemia has previously been associated with various physio-pathological conditions,such as fasting hypertriglyceridemia (21, 23, 24, 27), noninsulin-dependent diabetes (21), or previous myocardial infarction (25), that lead to a high risk for coronary heart disease . In the present study, it is noteworthy that the abnormal postprandial pattern found in android obesity can be detected even in the absence of fasting hypertriglyceridemia, suggesting that it could be a better predictor of cardiovascular risk than fasting parameters (25, 26, 28). In contrast, increased fasting levels of apoB-48-containing lipoproteins were found in android obese subjects, as already reported in noninsulin-dependent diabetes patients (21, 48, 49). We found that BMIs ($r = 0.59$, $P < 0.001$), waist circumferences ($r = 0.47$, $P < 0.05$), and WHRs ($r = 0.69$, $P < 0.004$) were positively correlated to fasting apoB-48 triglycerides.

Positive correlations between BMI or intra-abdominal fat and postprandial triglyceridemia has already been reported in some studies (50, 34, 35). This association was also found in the present study with overall comparable figures given by BMI, waist circumference, or WHR with postprandial triglyceridemia or TRL-triglycerides. In contrast, no correlation was found between ages of subjects and postprandial responses.

In the postprandial state, circulating triglycerides originate from intestinal absorption of digested fat and hepatic synthesis (39). Accordingly, we investigated metabolic changes from the two origins during fat assimilation by three converging approaches. The three complementary approaches used— chylomicron isolation by ultracentrifugation (20, 36), immunoaffinity separation of apoB-100 and apoB-48-containing TRLs (15, 39), and retinyl palmitate measurement (20, 28)—demonstrated that intestinally-derived TRLs accumulated more markedly in the serum of both groups of subjects with android obesity. In contrast, the pattern found in subjects with gynoid obesity was never different from that observed in the lean control subjects. Postprandial accumulation was particularly evident after 7 h: a clearance index calculated as the 2–4/7 h ratio of chylomicron retinyl palmitate (20) was comparable in lean controls

TABLE 2. Chylomicron retinyl palmitate concentrations at fasting and postprandially

	Retinyl palmitate (μg/mL)			
Time-point	Control subjects (n = 6)	GO subjects (n = 6)	NTAO subjects (n = 6)	HTAO subjects (n = 6)
Fasting	0.0003 ± 0.0002	0.0004 ± 0.0001	0.002 ± 0.001	0.0006 ± 0.0004
2–4 h	0.16 ± 0.1*	0.24 ± 0.09*	0.11 ± 0.07	0.1 ± 0.03*
7 h	0.10 ± 0.04 a	0.12 ± 0.05 a,b	0.18 ± 0.05 b*	0.41 ± 0.03 c*

Chylomicrons were prepared by ultracentrifugation. Values are mean ± SEM. Different letters indicate significant differences ($P < 0.05$) between groups. * indicates a difference ($P < 0.05$) from fasting value in a given group.

TABLE 3. Post-heparin lipoprotein and hepatic lipases, fasting and postprandial apoC-III levels

	Control subjects (n = 6)	GO subjects (n = 8)	NTAO subjects (n = 9)	HTAO subjects (n = 7)
Post-heparin lipoprotein lipase (μmol/mL/h)	0.19 ± 0.03	0.36 ± 0.12	0.37 ± 0.04	0.33 ± 0.06
Post-heparin hepatic lipase (μmol/mL/h)	1.00 ± 0.09	1.35 ± 0.09	1.26 ± 0.11	1.22 ± 0.15
ApoC-III (mg/L)				
Fasting	16.6 ± 2.4 a	19.7 ± 1.2 a	20.3 ± 2.7 a	30.4 ± 3.0 b
2–4 h	16.8 ± 3.3 a	18.8 ± 1.9 a	22.8 ± 2.3 a	31.3 ± 3.1 b

Values are mean ± SEM. Different letters indicate significant differences ($P < 0.05$) between groups. * indicates a difference ($P < 0.05$) from fasting value in a given group.

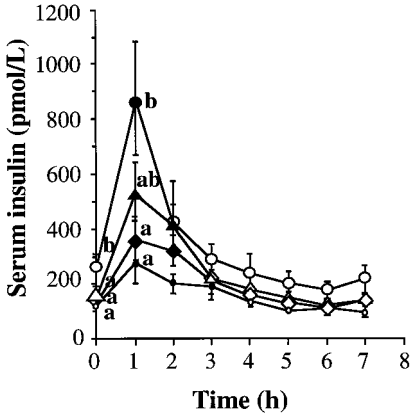

FIG. 4. Serum insulin for 7 h after meal intake. Values are means ± SEM. Control lean women (°); normotriglyceridemic android obese women (NTAO, △); hypertriglyceridemic android obese women (HTAO, ◯); normotriglyceridemic gynoid obese women (GO, ◇). For a given group, a *filled symbol* indicates that corresponding value is significantly different ($P < 0.05$) from fasting (0 h) value. At a given time-point, *different letters* indicate a significant difference ($P < 0.05$) between groups.

(1.6) and gynoid obese subjects (2.0), but was markedly lower in NTAO (0.61) and HTAO (0.45) obese subjects.

During the absorptive phase, intestinally-derived apoB-48 TRLs and hepatically-derived apoB-100 TRLs were shown to contribute equally to the total plasma triglyceride level, while apoB-100-containing particles provided most (*i.e.* at least 60–85%) fasting triglycerides, in agreement with previous data obtained in healthy subjects (15, 39). This postprandial accumulation of intestinally-derived TRLs likely led to an increase in apoB-48-containing TRLs in the postabsorptive state in android obese patients. In the case of preexisting fasting hypertriglyceridemia an amplified competition for the clearance of the two kinds of TRL particles led to exagerated levels of apoB-100 TRLs after 7 h in these subjects. An amplified postprandial accumulation of medium and small TRLs in men with visceral obesity and hypertriglyceridemia has recently been reported (35).

To elucidate some mechanisms underlying the change in lipoprotein pattern induced postprandially by android obesity, some parameters susceptible to control TRL clearance directly or undirectly were investigated.

A striking observation was that android obese females showed a markedly reduced size of chylomicron particles. This morphological modification is likely associated to an increased number of intestinally-derived particles (51). It has already been reported that high density lipoprotein (HDL) or low density lipoprotein (LDL) particles with altered sizes are present in subjects with disturbed lipid metabolism (21). We have no direct explanation for this observation, but the most likely hypothesis might be that amplified competition for clearance between VLDL and chylomicrons leads to an increased residence time in the circulation and thus, a more extensive triglyceride lipolysis of the particles in these subjects. Alternatively, the small intestine could secrete chylomicrons of reduced size. It has already been shown that bigger particle sizes (51–53) and/or reduced particle number (51) are associated with faster endovascular triglyceride lipolysis and/or uptake from the circulation. Thus, a reduced chylomicron size in subjects with android type of obesity is logically associated with a reduced clearance from plasma and an exacerbated accumulation postprandially as observed herein. This is illustrated by regression analyses that indicate that chylomicron particle size in the postprandial state is negatively related to fasting serum triglycerides ($r = -0.79$, $P < 0.0001$) and postprandial insulin response ($r = -0.50$, $P < 0.05$).

Post-heparin lipoprotein lipase and hepatic lipase activities were not different in the four groups of women. Some studies have shown a defect with variable extent in lipoprotein lipase activity in obesity (10, 29, 35), and the enzyme activity may be negatively correlated with the degree of insulin resistance; but this finding remains controversial (10).

Fasting levels of apoC-III were significantly increased in hypertriglyceridemic android obeses only. We found that fasting apoC-III levels were positively correlated with fasting ($r = 0.74$, $P < 0.0001$) and postprandial serum triglycerides ($r = 0.67$, $P < 0.0001$) as well as postprandial chylomicron triglycerides ($r = 0.57$, $P < 0.001$). Other data have shown that fasting plasma triglyceride levels are correlated to plasma apoC-III concentration (16, 54) or apoC-III/apoE ratio (55). In fact, apoC-III has been shown to inhibit *in vitro* the activity of both lipoprotein and hepatic lipases (56) and to inhibit *in vivo* the clearance and hepatic uptake of triglyceride-rich lipoprotein and their remnants (18, 57). In addition, apoC-III level has been correlated with insulin level in some studies (17) as herein ($r = -0.38$, $P < 0.05$). Thus, one can point out that higher levels of apoC-III, which is assumed to reduce the clearance of triglyderide-rich lipoproteins and remnants, is a detrimental characteristic of obese subjects with the android type of obesity.

The potential role of hyperinsulinemia linked to insulin resistance deserves special attention given its implication in disturbances of lipid metabolism (2, 12, 58). Indeed, fasting insulinemia was markedly elevated in android obeses with hypertriglyceridemia only. In the postprandial state, the insulin responses were close in controls and gynoid obeses and moderately or markedly higher in android obeses without or with hypertriglyceridemia. Regression analysis indicates

that fasting insulin was positively related to fasting apoB-48 triglycerides ($r = 0.44$, $P < 0.05$) only, while the 0–2 h postprandial insulin response was positively correlated to postprandial serum triglycerides ($r = 0.59$, $P < 0.0001$), chylomicron triglycerides ($r = 0.59$; $P < 0.0001$), apoB-48 triglycerides ($r = 0.47$; $P < 0.01$), and apoB-100 triglycerides ($r = 0.44$, $P < 0.05$). Thus, fasting and postprandial hyperinsulinisms were clearly associated to defects in clearance of all kinds of TRL particles whatever their origin, endogenous or exogenous. This is in line with data obtained in nonobese normolipidemic men (59). In fact, insulin resistance could, at the same time, limit the stimulation of endothelial lipase expression and activity (10, 29, 31) and reduce the normal down-regulation by insulin of adipocyte hormone-sensitive lipase, especially in visceral depots, as well as limit the down-regulation of the secretion of apoB-100 TRLs (*i.e.* VLDL) by the liver. These three combined phenomena may markedly reduce the rate of lipolysis of intestinally-derived apoB-48 particles and may exacerbate the competition for lipolysis of various TRL particles. Thus, as already shown by others in different conditions, insulin resistance and impregnation, especially in the postprandial state, is likely to play a key detrimental role regarding accumulation in the circulation of both hepatically- and intestinally-derived TRLs. In this respect, the android type of obesity seems directly implicated in postprandial disturbances, whereas the gynoid type is not, or only marginally.

To summarize, the accumulation of both intestinally- and hepatically-derived triglyceride-rich lipoproteins in the circulation postprandially, and consequently in the fasting state, in obese women with android type could basically be due to the combination of increased insulin response linked to insulin resistance, high apoC-III levels and reduced chylomicron size. A direct link thus appears between abdominal obesity, postprandial lipemia and atherogenesis (22, 25, 26, 27), in line with epidemiological observations (1, 2, 5–9, 12). Thus, we suggest that abnormal postprandial lipemia is to be added as an important metabolic disturbance to the X syndrome.

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