Effect of Atorvastatin on Postprandial Lipoprotein Metabolism in Hypertriglyceridemic Patients

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Running title: Atorvastatin and postprandial lipid metabolism

Abbreviations: apo, apolipoprotein; AUC, area under the curve; BMI, body mass index; LPL, lipoprotein lipase; TRL, triglyceride rich lipoprotein.
Abstract
Postprandial lipoprotein metabolism is impaired in hypertriglyceridemia. It is unknown how and to what extent atorvastatin affects postprandial lipoprotein metabolism in hypertriglyceridemic patients. We evaluated the effect of 4 weeks of atorvastatin therapy (10mg/day) on postprandial lipoprotein metabolism in 10 hypertriglyceridemic patients (age 40±3 years, BMI 27±1kg/m², cholesterol 5.74±0.34, triglyceride 3.90±0.66, HDL-cholesterol 0.85±0.05, LDL-cholesterol 3.18±0.23mmol/L). Patients were randomized to be studied either first with or without atorvastatin therapy. Postprandial lipoprotein metabolism was evaluated with a standardized oral fat load. Plasma was obtained every 2h for 14h. Large triglyceride-rich lipoproteins (TRL) (containing chylomicrons) and small TRL (containing chylomicron-remnants) were isolated by ultracentrifugation and cholesterol, triglyceride, apoB-100, apoB-48, apoC-III and retinyl-palmitate concentrations were determined. Atorvastatin significantly (p<0.01) decreased fasting cholesterol (-27%), triglyceride (-43%), LDL-cholesterol (-28%), and apoB-100 (-31%) and increased HDL-cholesterol (+19%). Incremental area under the curve (AUC) significantly (p<0.05) decreased for large TRL-cholesterol, -triglyceride, and -retinyl-palmitate, while none of the small TRL parameters changed. These findings contrast with the results in normolipidemic subjects where atorvastatin decreased AUC for chylomicron remnants (small TRL) but not for chylomicrons (large TRL). We conclude that atorvastatin improves postprandial lipoprotein metabolism in addition to decreasing fasting lipid levels in hypertriglyceridemia. Such changes would be expected to improve the atherogenic profile.

Supplementary keywords: triglyceride-rich-lipoprotein; chylomicrons; chylomicron-remnants; retinyl-palmitate
**Introduction**

Hypertriglyceridemia is a very common abnormality which particularly in the context of the diabetes confers a high atherogenic potential (1). To counter this, many hypertriglyceridemic diabetic patients are treated with HMG-CoA-reductase inhibitors and recent studies support that diabetic patients benefit from such treatment (2,3).

Despite increasing evidence of the importance of lipid-independent effects (pleiotropic effects) of statins, much of the beneficial effect may be related to changes in lipid metabolism. The inhibition of HMG-CoA-reductase leads to an upregulation of the LDL-receptor resulting in an increased catabolism of LDL-particles and thus lower LDL-cholesterol concentration (4). However, lipoproteins other than LDL, including postprandial triglyceride-rich lipoproteins (TRL) can also be internalized into hepatocytes via the LDL-receptor pathway (5-7). It is likely, therefore, that statins have profound effects on postprandial lipoprotein metabolism particularly in hypertriglyceridemic patients. Since the concentration of postprandial lipoproteins is an independent risk factor for cardiovascular disease (8-12), such changes in postprandial metabolism may be one of the mechanisms by which risk reduction is achieved with statin therapy.

We and others have previously shown that atorvastatin improves postprandial lipoprotein metabolism in normolipidemia, obesity, combined hyperlipidemia, and in patients with coronary heart disease (13-18). However, only few studies provided data on the mechanism by which such therapy improves postprandial lipoprotein metabolism. Furthermore, no data are available on hypertriglyceridemic patients, who have the most pronounced postprandial hyperlipidemia. In this study, we test the hypothesis that atorvastatin improves postprandial lipoprotein metabolism in patients with isolated hypertriglyceridemia. The primary end-point in this study was the apolipoprotein B-48 (apoB-48) response following a standardized fat challenge. We also wanted to evaluate whether or not the response to atorvastatin is similar to that observed in normolipidemic controls studied previously (13).
Methods

Ten otherwise healthy hypertriglyceridemic patients were recruited for this study. None were taking any medication. Participating patients (8 men, 2 women, age 40±3 years, BMI 27±1 kg/m²) were advised not to change their diet throughout the study. Postprandial lipoprotein metabolism was evaluated on two occasions, once without and once following 4 weeks of atorvastatin therapy 10 mg/day. Patients were randomized to be studied first either with or without atorvastatin therapy. Compliance was checked by pill-count. Liver function tests (ASAT, ALAT, γGT, alkaline phosphatase) and creatine-kinase were determined on and off atorvastatin therapy. The ethics committee of the Ludwig-Maximilians-University Munich approved the study protocol and all patients gave informed written consent.

The postprandial studies were performed as previously described (13,19). Each postprandial study was performed following a 12h fast. After obtaining fasting blood patients received a fatty meal (1305 kcal, 87% from fat, 7% from carbohydrates and 6% from protein) enriched with 80000 units of vitamin A. Following the fat load blood samples were taken every 2h for 14 hours. During that time patients ate no calories but were allowed to drink water without restriction.

Blood samples were drawn in light-protected tubes containing EDTA-sodium. Ultracentrifugation was performed to obtain 2 fractions of triglyceride-rich lipoproteins (13). The fraction containing chylomicrons was called large TRL, the fraction containing chylomicron-remnants and VLDL was called small TRL. This corresponds to Svedberg flotation rate of Sf>400 for large TRL and Sf20-400 for small TRL. Cholesterol, triglyceride, apoB-100, apoB-48, and retinyl-palmitate concentrations were determined in plasma (not apoB-48) and in the TRL fractions.

Triglyceride and cholesterol concentrations were measured by using a commercial kit (Boehringer Mannheim, Mannheim, Germany). ApoB and apoC-III concentrations were
determined by immunonephelometry. Proteins of the TRL fractions were separated by polyacrylamide gel electrophoresis (5%) and stained with Comassie Blue (20). The protein bands corresponding to apoB-100 and apoB-48 were scanned by laser densitometry. ApoB-48 concentrations were estimated based on the assumption that apoB-100 and apoB-48 have the same chromogenicity. Retinyl-palmitate concentrations in plasma and the TRL fractions were determined by reverse phase HPLC as described previously (13,21).

Postprandial metabolism was quantified by calculating the area under the curve (AUC) using the 14h concentration data. The incremental AUC, the area between the plasma concentration and a baseline drawn between the concentrations observed at 0h and 14h was also calculated using the SAAM-II program (SAAM Institute Inc, Seattle, WA).

Results are presented as mean±SEM. Differences between parameters obtained before and during atorvastatin therapy were evaluated by paired t-test analysis. Associations between variables were identified with the Pearson’s product moment correlation coefficient. The results obtained from 10 normolipidemic subjects studied previously (13) are included for comparison purposes. All statistical tests were performed using the SPSS software (SPSS, Inc., Chicago, IL). The critical P value for significance was 0.05.
Results

All patients tolerated atorvastatin well and no side effects were reported. Furthermore, there was no change in liver function tests or CK. Fasting cholesterol (-27%), triglyceride (-43%), apoB-100 (-31%), LDL-cholesterol (-28%), large TRL-cholesterol (-65%), small TRL-cholesterol (-40%), small TRL-triglycerides (-46%), small TRL apoB-48 (-52%), and small TRL apoB-100 (-46%) concentrations decreased significantly and HDL-cholesterol (+19%) increased significantly during atorvastatin therapy (Table 1). In addition there was a non-significant decrease in plasma apoC-III (-23%), large TRL-triglyceride (-43%), large TRL-apoB-48 (-42%), large TRL-apoB-100 (-59%).

Figure 1 shows the mean triglyceride concentrations before and during atorvastatin therapy in plasma (panel A), large TRL (panel B), and small TRL (panel C). The total AUC for plasma, large and small TRL measurement variables, with the exception of large TRL-apoB-48 and small TRL-retinyl-palmitate (p=0.061), decreased significantly on atorvastatin therapy. The incremental AUC decreased significantly for large TRL-triglyceride, cholesterol, apoB-100, and retinyl-palmitate. In contrast, small TRL-triglyceride, cholesterol, retinyl-palmitate and apoB-48 incremental AUC did not change with atorvastatin therapy. Incremental AUC for plasma retinyl-palmitate and large TRL apoB-48 were lower on atorvastatin treatment although this failed to reach statistical significance (Table 2).

Atorvastatin treatment of the hypertriglyceridemic patients affected the maximum peak height in both TRL fractions and reduced the time to peak in large TRL (triglycerides: 5.8±1.0h vs. 6.8±1.9h, p=0.1) with the exception of retinyl-palmitate. We also noted (before and during atorvastatin therapy) that the retinyl-palmitate curve peaks later than any other measurement variables in both TRL fractions (data not shown).

The fasting triglyceride concentration was correlated with incremental AUC of large TRL-triglycerides (r=0.63, p<0.05) and small TRL-triglycerides (r=0.64, p<0.05). As
expected, these associations were also significant when total AUC was used in the analysis. There was, however, no significant correlation between atorvastatin induced LDL-cholesterol or triglyceride reduction and any of the AUC at baseline or changes in AUC with atorvastatin.
Discussion

The cholesterol lowering effect of atorvastatin is widely acknowledged. This study was performed to assess the effect of atorvastatin on postprandial lipoprotein metabolism in hypertriglyceridemia. In addition to significantly decreasing fasting cholesterol, triglycerides, and LDL-cholesterol and increasing HDL-cholesterol, atorvastatin also decreased the incremental area under the curve of large TRL (containing chylomicrons) triglyceride, cholesterol, and retinyl-palmitate following an oral fat load and reduced the time to peak of large TRL-triglyceride and apoB-48 concentration. Atorvastatin treatment did not change any incremental AUC’s in the small TRL fraction (containing chylomicron-remnants). This contrasts with results in normolipidemic subjects, where using the same experimental protocol, atorvastatin only decreased the AUC’s in the chylomicron-remnant fraction (13).

In our study, the decrease in fasting plasma triglyceride concentration was profound but within the limits previously described in hypertriglyceridemic patients (17,22,23). Atorvastatin’s triglyceride lowering effect is believed to be related to the strong inhibition of cholesterol biosynthesis, which also reduces the secretion of lipoproteins (24,25). Triglyceride reduction may also be related to the fact that VLDL and LDL compete for the same removal mechanisms (6,7), thus, a profound reduction in the number of LDL may also increase the removal of VLDL. Statins also reduce apoC-III (26), a protein that inhibits LPL-mediated hydrolysis (27). This reduction is thought to occur via the PPAR-α effect of statin on the AI/CIII/AIV gene cluster, leading to decreased apo-CIII mRNA and presumably protein concentrations (26). This is in good agreement with recently published studies indicating that atorvastatin does not affect LPL mass (28) but increases LPL activity (29). This increased LPL activity results in a more effective hydrolysis of fasting and postprandial triglyceride rich lipoproteins. Evidence for this improvement comes not only from the reduced incremental AUC of large TRL but also the shorter time to peak concentration, a feature consistent with increased turnover of chylomicrons.

Although initial studies (30-35) evaluating the effect of statins on postprandial
lipoprotein metabolism have shown conflicting results, recent studies using atorvastatin have uniformly shown positive effects on postprandial lipoprotein metabolism (13-18). In patients with mild hypertriglyceridemia (plasma triglyceride concentration 2.4±0.9mmol/L) pravastatin did not affect postprandial lipoprotein metabolism determined from a single triglyceride concentration measured 8h after a standardized meal (32). In contrast, lovastatin decreased the AUC of retinyl-palmitate in the chylomicron and chylomicron-remnant fractions in 5 patients with elevated triglycerides (2.3±0.3mmol/L), but did not affect the postprandial response in normolipidemic subjects (30). In patients with coronary heart disease Schaefer and colleagues showed that atorvastatin (40 mg/d), which almost normalised fasting triglycerides also normalized remnant like particle concentration following a standardized meal (17). In patients with combined hyperlipidemia it was shown that atorvastatin causes reductions of postprandial plasma concentrations of all triglyceride-rich lipoproteins (15,16,18). In one study atorvastatin therapy reduced cholesterol-ester transfer from HDL to TRL, a pathway that is enhanced in untreated combined hyperlipidemia (15). The same investigators demonstrated that the initial rise of the chylomicron concentration curve following a standardized mixed meal was not affected by atorvastatin, indicating a lack of effect on chylomicron secretion. This is in good agreement with our previous study in normolipidemic subjects (13) and the current study in hypertriglyceridemic subjects.

Intuitively, we expected that atorvastatin in hypertriglyceridemic patients would also decrease AUC of small and possibly large TRL. Our finding that atorvastatin primarily decreases AUC of large TRL (containing chylomicrons), while not affecting small TRL (containing chylomicron-remnants) was somewhat surprising. Potential mechanisms of action of atorvastatin on postprandial lipoprotein metabolism in normolipidemic and hypertriglyceridemic patients are shown in Fig. 2. In normolipidemia, lipolysis of chylomicrons proceeds normally and chylomicron metabolism is not stimulated with atorvastatin although atorvastatin modulated an improvement in chylomicron-remnant metabolism due to less competition from VLDL particles for removal via a receptor-mediated process (6,7). In hypertriglyceridemia increased turnover of the chylomicron-
remnants is coupled to an increased conversion of chylomicrons to chylomicron-
remnants. The combined effect of these processes would negate any observable changes
in small TRL incremental AUC. Thus, although the mechanism by which atorvastatin
affects postprandial lipoprotein metabolism is similar in normolipidemia and
hypertriglyceridemia, the observed changes differ because of differences at baseline.

Our finding of differential effects on small and large TRL contrasts with a recently
published study showing an equivalent effect of 40mg atorvastatin/d on all postprandial
TRL in patients with combined hyperlipidemia (18). However, in contrast to that study,
our patients are characterized by isolated hypertriglyceridemia and received only 10mg
atorvastatin/d. Although it has been shown that increasing atorvastatin from 10 to 80mg/d
has no significant effect on fasting triglycerides (23), higher doses of atorvastatin may
have a more pronounced effect on postprandial lipoprotein metabolism. Finally, the
differences between studies may be related to differences in the methodology (isolation
of different TRL fractions; collecting data over 6h vs. 14h).

Compared with 10 normolipidemic men (13) studied, using the same protocol, the
incremental AUC for plasma, large and small TRL triglycerides were significantly
(p<0.05) higher in the hypertriglyceridemic patients. On treatment, plasma and large TRL
triglycerides, were lower but still remained elevated compared with the normolipidemic
subjects. In contrast, small TRL triglycerides were not different between the treated
hypertriglyceridemic and normolipidemic subjects. Thus, atorvastatin therapy improves
but does not normalize postprandial lipoprotein metabolism (figure 3). This contrasts
with previous findings described by Schaefer (17), who described normalization of
fasting and postprandial lipoprotein metabolism with atorvastatin 40 mg/d. However, it
should be noted that the normolipidemic subjects used for comparison here and shown in
figure 3 represent a somewhat different population as they were younger (30 ± 2 years),
leaner (BMI 22±3 kg*m⁻²) and included only males, factors that may affect postprandial
lipoprotein concentrations independently of the underlying hypertriglyceridemia. The
optimal group for comparison would have been an age and BMI matched control group. As discussed above, it is also unclear whether higher doses of atorvastatin can further normalize postprandial lipoprotein metabolism and whether the effect on postprandial lipoprotein metabolism is a class effect of statins, is specific to atorvastatin or is linked to the effect on fasting triglycerides.

Although we intended to isolate chylomicrons and chylomicron-remnants/VLDL the presence of apoB-100 in the chylomicron fraction suggested this fraction also contained large VLDL particles (table 2). Thus, the ultracentrifugation method used does not separate lipoprotein fractions containing chylomicrons and chylomicron-remnants but rather heterogenous particle populations containing apoB-100 and apoB-48 that we have called large and small TRL, respectively. This contamination with apoB-100 containing particles, however, has little impact upon our key finding that atorvastatin affects incremental AUC of large TRL more than that of small TRL. It is also of interest that apoB-100 concentration is not constant, but increases following the oral fat load. This has been observed previously (18) and is consistent with the concept that apoB-100 and apoB-48 containing particles compete for the same removal mechanisms. In addition, the increased flux of substrate in the postprandial state may also affect the secretion of apoB-100 containing lipoproteins from the liver.

The effects of atorvastatin on the total AUC were much more pronounced than on incremental AUC reflecting the strong effect of atorvastatin on fasting lipids. These changes in fasting values are probably more important from a clinical point of view, particularly since fasting values and postprandial values correlate. However, in order to further understand postprandial lipoprotein metabolism and in particular whether, and to what extent, statins affect these pathways it is important to focus on incremental AUC.

Although the AUC of TRL is a function of lipoprotein production and clearance, there is no evidence, that atorvastatin affects the secretion of postprandial lipoproteins from the intestine (36,37). Since the secretion and composition of postprandial lipoproteins is
mostly driven by dietary lipid components it is unlikely that the decrease in HMG-CoA-reductase activity alters the secretion of postprandial lipoproteins.

In summary, 10mg atorvastatin per day for 4 weeks improves, but does not normalize, postprandial lipoprotein metabolism in hypertriglyceridemic patients. Together with previous studies, it is clear that atorvastatin improves fasting and postprandial lipoprotein metabolism in normolipidemia, hypertriglyceridemia and combined hyperlipidemia.
Acknowledgements

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**Figure legends**

**Fig. 1:** Lipid concentrations following the oral fat load before and during atorvastatin therapy. Plasma triglycerides (Panel A), large TRL-triglycerides (Panel B), and small TRL-triglycerides (Panel C) are shown as means (±SEM). Open and closed symbols represent data obtained before and during atorvastatin therapy, respectively; * indicates significant (p<0.05) differences compared to the situation without atorvastatin.

**Fig. 2:** Potential mechanisms of action of atorvastatin on postprandial lipoprotein metabolism in normolipidemic subjects and hypertriglyceridemic patients. Atorvastatin modulates LDL receptor activity and VLDL apoB secretion. As a result the VLDL pool is reduced, thus decreasing competition for clearance mechanisms and hence improving chylomicron remnant (CR) clearance. Furthermore, a reduced VLDL pool decreases apoC-III concentration. In normolipidemic subjects LPL activity can either not be further stimulated by lower apoC-III or is not rate limiting for CM metabolism, while in hypertriglyceridemia an increased LPL activity results in an enhanced hydrolysis of chylomicron particles (CM) particles. This increased conversion of CM to CR balances the increased catabolism of CR.

**Fig. 3:** Incremental AUC (mean±SEM) of plasma, large TRL, and small TRL triglycerides in normolipidemic subjects (open bar, 10 subjects, reference 13) and in hypertriglyceridemic patients without (grey) and with (black) atorvastatin. a indicates significantly (p<0.05) different compared with normolipidemic subjects, b indicates significantly (p<0.05) different compared to treated hypertriglyceridemic patients.
Table 1: Fasting lipid parameters before and after 4 weeks of atorvastatin therapy (10 mg/day)

<table>
<thead>
<tr>
<th></th>
<th>Without atorvastatin</th>
<th>With atorvastatin</th>
<th>change (^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol mmol/L</td>
<td>5.74 ± 0.34</td>
<td>4.14 ± 0.26</td>
<td>-27 (^b)</td>
</tr>
<tr>
<td>Triglyceride mmol/L</td>
<td>3.90 ± 0.66</td>
<td>1.91 ± 0.26</td>
<td>-43 (^b)</td>
</tr>
<tr>
<td>LDL-cholesterol mmol/L</td>
<td>3.18 ± 0.23</td>
<td>2.28 ± 0.15</td>
<td>-28 (^b)</td>
</tr>
<tr>
<td>HDL-cholesterol mmol/L</td>
<td>0.85 ± 0.05</td>
<td>0.98 ± 0.05</td>
<td>+19 (^c)</td>
</tr>
<tr>
<td>Apo-B mg/L</td>
<td>1200 ± 210</td>
<td>830 ± 170</td>
<td>-31 (^b)</td>
</tr>
<tr>
<td>ApoC-III mg/L</td>
<td>211 ± 23</td>
<td>168 ± 26</td>
<td>-23</td>
</tr>
<tr>
<td>large TRL-cholesterol mmol/L</td>
<td>0.30 ± 0.10</td>
<td>0.07 ± 0.03</td>
<td>-65 (^b)</td>
</tr>
<tr>
<td>large TRL triglyceride mmol/L</td>
<td>1.04 ± 0.39</td>
<td>0.40 ± 0.14</td>
<td>-43</td>
</tr>
<tr>
<td>large TRL-apoB-100 mg/L</td>
<td>34 ± 17</td>
<td>12 ± 5</td>
<td>-58</td>
</tr>
<tr>
<td>large TRL-apoB-48 mg/L</td>
<td>4.7 ± 2.4</td>
<td>2.5 ± 1.2</td>
<td>-42</td>
</tr>
<tr>
<td>small TRL-cholesterol mmol/L</td>
<td>0.99 ± 0.15</td>
<td>0.39 ± 0.05</td>
<td>-40 (^b)</td>
</tr>
<tr>
<td>small TRL-triglyceride mmol/L</td>
<td>1.78 ± 0.22</td>
<td>0.91 ± 0.12</td>
<td>-46 (^b)</td>
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<tr>
<td>small TRL-apoB-100 mg/L</td>
<td>122 ± 7</td>
<td>66 ± 3</td>
<td>-46 (^b)</td>
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<tr>
<td>small TRL-apoB-48 mg/L</td>
<td>13 ± 2.5</td>
<td>6.1 ± 1.2</td>
<td>-52 (^b)</td>
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Mean ± SEM, \(^a\) change refers to mean percentage change, \(^b\) indicates \(p < 0.01\), \(^c\)
indicates $p < 0.05$. 
Table 2: Incremental AUC following an oral fat load before and after 4 weeks of atorvastatin therapy (10 mg/day)

<table>
<thead>
<tr>
<th>Incremental AUC</th>
<th>without atorvastatin</th>
<th>with atorvastatin</th>
<th>change ((%))</th>
<th>p-value</th>
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<tr>
<td>plasma triglyceride (mmol/L*h)</td>
<td>29.4 ± 4.6</td>
<td>19.8 ± 2.6</td>
<td>-17</td>
<td>0.131</td>
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<td>cholesterol (mmol/L*h)</td>
<td>3.01 ± 0.68</td>
<td>2.25 ± 0.14</td>
<td>-21</td>
<td>0.380</td>
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<td>retinyl-palmitate (µg/dL*h)</td>
<td>1198 ± 210</td>
<td>600 ± 112</td>
<td>-27</td>
<td>0.061</td>
</tr>
<tr>
<td>large TRL triglyceride (mmol/L*h)</td>
<td>24.0 ± 4.0</td>
<td>13.0 ± 2.3</td>
<td>-40</td>
<td>0.018</td>
</tr>
<tr>
<td>apoB-48 (mg/L*h)</td>
<td>103 ± 22</td>
<td>60 ± 13</td>
<td>-19</td>
<td>0.116</td>
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<tr>
<td>apoB-100 (mg/L*h)</td>
<td>122 ± 27</td>
<td>55 ± 10</td>
<td>-34</td>
<td>0.028</td>
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<tr>
<td>cholesterol (mmol/L*h)</td>
<td>2.66 ± 0.50</td>
<td>1.31 ± 0.22</td>
<td>-41</td>
<td>0.021</td>
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<tr>
<td>retinyl-palmitate (µg/dL*h)</td>
<td>972 ± 156</td>
<td>443 ± 88</td>
<td>-38</td>
<td>0.023</td>
</tr>
<tr>
<td>small TRL triglyceride (mmol/L*h)</td>
<td>5.6 ± 0.88</td>
<td>4.4 ± 0.65</td>
<td>8</td>
<td>0.458</td>
</tr>
<tr>
<td>apoB-48 (mg/L*h)</td>
<td>3.34 ± 0.70</td>
<td>3.61 ± 0.58</td>
<td>0</td>
<td>0.736</td>
</tr>
<tr>
<td>apoB-100 (mg/L*h)</td>
<td>3.8 ± 2.0</td>
<td>9.5 ± 5.4</td>
<td>-1.5</td>
<td>0.340</td>
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<tr>
<td>cholesterol (mmol/L*h)</td>
<td>0.97 ± 0.34</td>
<td>1.25 ± 0.26</td>
<td>10</td>
<td>0.79</td>
</tr>
<tr>
<td>retinyl-palmitate (µg/dL*h)</td>
<td>196 ± 35</td>
<td>112 ± 21</td>
<td>-17</td>
<td>0.107</td>
</tr>
</tbody>
</table>

Mean ± SEM; \(a\) change refers to mean percentage change.
Atorvastatin

- VLDL secretion ↓
- LDLr ↑
- VLDL catabolism ↑

VLDL pool ↓

ApoCIII ↓

LPL activity ↑ in HTG, but not rate limiting in NTG (i.e., no effect on catabolism in NTG)

CM (large TRL) + HTG CR (small TRL) + HTG

+ HTG + HTG and NTG

Figure 2