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BMI and Lipid Lowering – is there a Relation?

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Lipid lowering has become one of the major and efficient tools in cardiovascular primary and secondary disease prevention. The best understood causes of hyperlipidaemias are specific genetic changes such as “familial hypercholesterolaemia”, the inherited LDL-receptor defect, and mutations like ApoB3500 leading to decreased binding of ApoB containing lipoprotein particles to their eliminating receptors. But that does not explain hyperlipidaemia in most of our patients. We assume that present changes in the understanding of the “metabolic syndrome” will prove to be more important for that purpose. Obesity and especially visceral adipose tissue seem to play a central role in generating an increased “fatty acid flux” and a resulting “lipoprotein flux” towards the periphery which might increase the importance of minor underlying genetic variants and “weaknesses” in lipoprotein metabolism. In the present paper we outline the pathophysiological background of the importance of obesity and visceral fat and describe an increasing response to atorvastatin in hyperlipidaemic patients grouped by BMI. *J Clin Basic Cardiol* 2000; 3: 115–7.

Key words: HMG-CoA-reductase inhibitors, atorvastatin, obesity, drug action

Hyper- and dyslipidaemia are epidemiologically good predictors for life expectancy and cardiovascular morbidity (Framingham-Study). The “metabolic syndrome” (hyper-/dyslipidaemia, obesity, hypertension, glucose intolerance/diabetes mellitus, hyperuricaemia, hypercoagulability) which has often been discussed to improve our understanding of diabetes can help to better understand the role of lipids within other risk factors [1–4]. A big study in 1984 showed that improvements in the prediction of events can be reached by using obesity and fat distribution as co-variables (Table 1).

Independent of fat distribution, a high BMI is a risk factor for CVD; independent of BMI, a visceral fat distribution doubles the cardiovascular event rate and potentiates with overweight. Analysing stroke, visceral fat seems to be even more important. For mortality, both visceral fat and weight are strong determinants. Such close relations have to be analysed carefully for the underlying causes.

Dietary fat and hyperlipidaemia

Nutrients are well resorbed in the intestine and thence transported to liver and end organs (eg, muscle tissue) needing them for energy metabolism. Dietary fat is digested by intestinal triglycerid lipases. Resulting free fatty acids (FFA) are assembled to micelles and resorbed. The “microsomal triglyceride transfer protein” (MTP) uses ApoB48 to assemble the largest fatty acid particles, the chylomicrons.

Dietary fat reaches the liver and target organs via chylomicrons (or their predigested “remnants”) or as FFA, especially medium chain triglycerides (MCT) which can be transported without chylomicrons bound to albumin. In the liver MTP of the liver assembles VLDL particles using ApoB100, which is similar to the intestinal ApoB48. VLDL-

particles are degraded by vascular lipoprotein lipases and LDL-particles are the final product which has more or less to be taken up by receptor mediated processes. All nutrients therefore which are not circulating in the blood or needed for energy metabolism lead to storage of fat [6]. It is determined by sex and also seems to be genetically determined whether visceral or subcutaneous fat develops [7], which was also proven in identical twin studies [8]. The “fatty acid flux” is shown in Figure 1.

Visceral fat and hyperlipidaemia

Visceral and gynoid fat distribution are remarkably different in influencing lipoprotein metabolism and consecutive

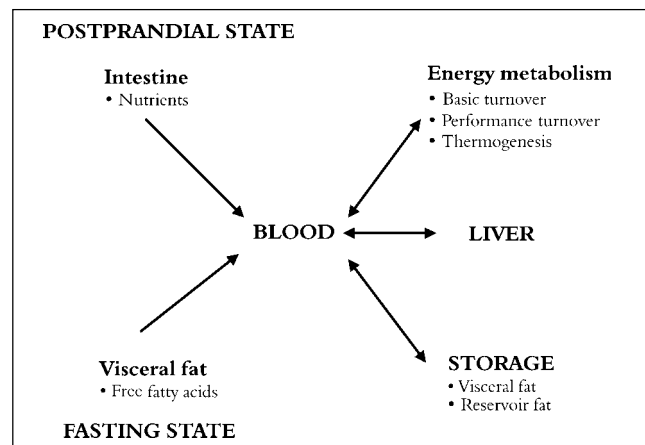


Figure 1. Uptake of nutrients into the body and their metabolic fate (simplified)

Table 1. Probability of macrovascular disease and death. Classification is done by tertiles of weight (BMI) vs tertiles of the waist to hip ratio (WHR), according to Larsson 1984 [5]

Parameter	BMI 1 st Tertile			BMI 2 nd Tertile			BMI 3 rd Tertile		
	CVD	Stroke	Death	CVD	Stroke	Death	CVD	Stroke	Death
WHR 1 st Terz.	5.6	2.8	5.3	10.9	2.8	13.1	10.9	2.8	13.1
WHR 2 nd Terz.	6.4	3.5	8.8	12.5	3.5	13.1	12.5	6	13.1
WHR 3 rd Terz.	12.4	5	18.2	15.2	6.5	19	20.8	6.5	29.2

cardiovascular risk. The difference between patients with gynoid and visceral fat accumulation might be found in the postprandial state. The metabolic characteristics of patients with postprandial hyperlipidaemia and its relation to CVD has been long recognised [9]. Normally, lipids are elevated postprandially and rapidly normalise in absence of genetic “weaknesses” in lipoprotein elimination. Visceral adipose tissue is, in addition to the intestine (after meals), the source of FFA in the fasting state. Therefore lipoprotein synthesis is stimulated the whole day and lipids tend to be elevated independently of dietary fat. Additionally fatty acids stimulate cholesterol biosynthesis via HMG-CoA reductase which might be important for the assembly of VLDL-particles (Table 2).

Statin action in obesity

Statins exert their effect through their influence on HMG-CoA-reductase activity. In the absence of dietary fat and visceral adipose tissue the stimulation of this enzyme is done by “basal” lipid metabolism. Postprandially fat resorption and transport to the liver will stimulate this enzyme parallel to VLDL-production. Activity of the enzyme is therefore more or less driven by the genetic determinants and dietary fat within a meal. Visceral obesity through fatty acid production stimulates both HMG-CoA-reductase and VLDL-production throughout the day. Resulting hyperlipidaemia in patients with genetic “weaknesses” in lipoprotein metabolism might be higher in the fasting state and, even more likely, postprandially. Therefore especially statins with a long half life might also exert favourable effects in obese patients.

Atorvastatin efficacy and BMI

Atorvastatin is among the most potent HMG-CoA-reductase inhibitors on the market. The LDL-C lowering effect in the starting dose is around 40 %. Usually %-reductions are

Table 2. Metabolism of fat cells in gynoid and visceral obesity

	Visceral fat (android)	Adipose tissue (gynoid)
Kind of fat cell	Hypertrophic	Hyperplastic
Kinetics	Rapid	Slow
Lipolysis	High sensitivity	Low sensitivity
LDL-activity	High	Low
Glucocorticoid receptors	Many	Few

Table 3. BMI-distribution in 3557 Austrian patients receiving atorvastatin 10 mg

BMI (kg/m ²)	Weight classification	n	%
< 20	Underweight	37	1.04
20–24.9	Normal	925	26.01
25–29.9	Overweight	1879	52.83
30–39.9	Obesity	690	19.40
≥ 40	Morbid obesity	26	0.73

Table 4. BMI vs change in total cholesterol in 3557 Austrian patients receiving atorvastatin 10 mg

BMI (kg/m ²)	Weight classification	Untreated	Atorvastatin 10 mg	% change
< 20	Underweight	283	211	–25.7
20–24.9	Normal	281	212	–24.6
25–29.9	Overweight	288	212	–26.3
30–39.9	Obesity	282	208	–26.5
≥ 40	Morbid obesity	309	198	–36.0

given without describing BMI in the patient characteristics. In the present study we analysed the efficacy of atorvastatin 10 mg on blood lipids in 3557 Austrian patients in private practice (Table 3). Numbers of underweight and morbidly obese patients are low but reflect their prevalence in the population.

Total cholesterol

In general, total cholesterol values of the included patients were high with mean values considerably above 270 mg/dl with, as expected, the highest values in the morbidly obese patient group. With atorvastatin 10 mg treatment the mean total cholesterol values became similar in all groups, thus showing the best efficacy in the morbidly obese patient group (Table 4).

Triglycerides

Mean serum triglycerides are normal in underweight patients only and increased with BMI. That points to the fact that patients usually do not have elevated cholesterol levels only but also elevated triglyceride levels. Therefore, triglyceride lowering properties are important also with respect to treatment efficacy using HMG-CoA-reductase inhibitors. In our study the triglyceride lowering effect of atorvastatin increased with BMI (Table 5). This also points to a high stimulation of cholesterol biosynthesis in obese patients.

HDL-cholesterol

HDL-cholesterol decreases with weight and exhibits the activity of the “reverse cholesterol transport”. In our study there was an increase in HDL-cholesterol in all treatment groups with exception of the morbidly obese patients (Table 6). There was also a strong tendency to better effects on HDL-C in overweight and obese than in normal and underweight patients.

Taking total to HDL-C ratios as an important determinant of cardiovascular risk shows that all treatment groups considerably improved (data not shown).

Discussion and conclusion

Obese patients usually are undertreated due to the fact “that they should start with diet”. The present data on the other hand point out that atorvastatin was efficient in lipid lowering in normal and overweight hyperlipidaemic patients. The

Table 5. BMI vs change in triglycerides in 3557 Austrian patients receiving atorvastatin 10 mg

BMI (kg/m ²)	Weight classification	Untreated	Atorvastatin 10 mg	% change
< 20	Underweight	201	153	–24.0
20–24.9	Normal	247	171	–30.7
25–29.9	Overweight	284	193	–32.0
30–39.9	Obesity	320	207	–35.2
≥ 40	Morbid obesity	465	221	–52.5

Table 6. BMI vs change in HDL-C in 3557 Austrian patients receiving atorvastatin 10 mg

BMI (kg/m ²)	Weight classification	Untreated	Atorvastatin 10 mg	% change
< 20	Underweight	53	57	+7.0
20–24.9	Normal	47	51	+8.6
25–29.9	Overweight	43	49	+12.6
30–39.9	Obesity	42	48	+14.4
≥ 40	Morbid obesity	45	41	–9.2

treatment effect was even increasing with the extent of obesity. That might be due to the fact that FFA levels stimulate HMG-CoA-reductase resulting in more pronounced hyperlipidaemia. Atorvastatin proved to counteract such stimulation by a pronounced decrease in both cholesterol and triglyceride containing particles suggesting a decreased assembly of VLDL-particles. Increasing HDL-C levels furthermore suggest a reduction in reverse cholesterol transport due to the decreased particle number of ApoB-containing particles.

Previous studies have shown that atorvastatin has the highest triglyceride lowering potency of statins due to its distinct properties [10]. Thus further studies with other statins are needed which investigate these effects.

In conclusion, lipid lowering therapy is at least as effective in obese patients and should not be started at the end but at the beginning of dietary therapy to efficiently reduce cardiovascular risk in that high risk patient group.

References:

1. Reaven GM. Role of insulin resistance in human disease. *Diabetes* 1988; 37: 1495–516.
2. Reaven GM. Role of insulin resistance in human disease (syndrome X): an expanded definition. *Annu Rev Med* 1993; 44: 121–31.
3. DeFronzo RA, Ferrannini E. Insulin resistance in human disease. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; 14: 173–94.
4. Jahnke K, Daweke H, Liebermeister H, Schilling WH, Thamer G, Preiss H, Gries FA. Hormonal and metabolic aspects of obesity in humans. In: Östmann J (ed). *Diabetes. Proceedings of the sixth congress of the International Diabetes Federation*. Excerpta Medica Foundation, Amsterdam, 1969; 533–9.
5. Toplak H. Fat distribution and risk. *Acta Med Austriaca* 1998; 25: 131–2.
6. Lechleitner M, Hoppichler F. Bewertung von Genetik und Umwelt für die Entstehung von Übergewicht. *Acta Med Austriaca* 1998; 25: 129–30.
7. Bouchard C, Rice T, Lemieux S, Desprez JP, Perusse L, Rao DC. Major gene for abdominal visceral fat area in the Quebec Family Study. *Int J Obes* 1996; 20: 420–7.
8. Bouchard C, Tremblay A, Desprez JP, Nadeau A, Lupien PJ, Thierault G, Dussault J, Moorjani S, Pinault S, Fournier G. The response to long-term overfeeding in identical twins. *N Engl J Med* 1990; 322: 1477–82.
9. Patsch JR, Miesenböck G, Hopferwieser T, Mühlberger V, Knapp E, Dunn JK, Gotto AM, Patsch W. Relation of triglyceride metabolism and coronary artery disease. Studies in the postprandial state. *Arterioscler Thromb* 1992; 12: 1336–45.
10. Jones P, Kafonek S, Laorora I, Hunninghake D, for the CURVES investigators. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (CURVES-Study). *Am J Cardiol* 1998; 1: 582–7.

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