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Atorvastatin and fenofibrate exert opposite effects on the vascularization and characteristics of visceral adipose tissue

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Background.Statins may precipitate the onset of type 2 diabetes (T2D) in high-risk patients. In contrast, only the subset of individuals with insulin resistance (IR) and/or diabetes receives cardiovascular benefits with fibrates. The mechanism responsible of such effects may be related with visceral adipose tissue (VAT). In this context, previous observations have suggested that atorvastatin induced an increase of VAT whereas fenofibrate had the opposite effects in rabbits.

Purpose. To determine the mass, morphology and vascularization of VAT in New Zealand white rabbits that received of atorvastatin or fenofibrate during two months.

Methods. New Zealand white rabbits (n=6 per group) received by oral gavage during 2 months, 0.33 mg/Kg of atorvastatin or 2.6 mg/Kg fenofibrate. The control group received 0.5 mL of vehicle. Plasma lipids were monitored. The visceral adipose tissue (VAT) was dissected and quantified. The expression of genes related with vascularization, VEGF-A and TGF-ß, FGF2 as well as TNF-a were determined by qPCR in VAT. Histological slices were stained by hematoxilin and eosin to determine the size of adipocytes. The marker of angiogenesis, PECAM-1, was determined by immunohistochemistry.

Results. As expected, the cholesterol from atorvastatin was lower after treatment while triglycerides decreased in fenofibrate group. The mass of VAT from fenofibrate group was 46% lower compared with the controls meanwhile atorvastatin was associated with a larger diameter of adipocytes (+65%) than that of the control and fenofibrate groups. FGF2 gene expression was lower in fenofibrate than in control group (-54%). By contrast, VEGF-A gene expression in fenofibrate-treated rabbits was 110% higher than in control group. TGF-ß and TNF-a remained comparable among groups. In agreement with the gene expression, the marker of angiogenesis PECAM-1 was slightly but significantly higher (+10%) in rabbits treated with fenofibrate than in controls, as determined by immunohistochemistry.

Conclusion. Fenofibrate enhanced the VEGF-A gene expression, PCAM-1 in VAT whereas decreased its total mass. In contrast, atorvastatin increased the adipocyte size without any effect on vascularization markers. These results suggest that fenofibrate is associated with a favorable remodeling of VAT, in contrast with atorvastatin, which induced a non-favorable remodeling of VAT. These results may be related with the cardiovascular benefits of fenofibrate and the increased risk of T2D in high-risk subjects induced by atorvastatin.