

Fenofibrate and Orlistat, Alone or In Combination, Do Not Alter Plasma Visfatin Levels in Subjects with Metabolic Syndrome

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Visfatin (pre-B cell colony-enhancing factor) is a cytokine highly expressed in visceral fat which exhibits insulin-mimetic properties [1]. We recently showed that overweight and obese patients with metabolic syndrome (MetS) exhibit significantly higher plasma visfatin levels compared with subjects without MetS [2]. We next investigated the effect of fenofibrate and orlistat, alone or in combination, on visfatin levels in obese subjects with MetS. To the best of our knowledge this is the first time that the effect of orlistat or orlistat plus fenofibrate combination on plasma visfatin levels is reported.

Patients with MetS, without known CVD or T2DM, were prescribed a low-fat low-calorie diet and were randomly allocated to receive orlistat 120 mg three times daily (n=28, O group), micronized fenofibrate 200 mg/day (n=28, F group) or both (n=27, OF group) for 6 months [3]. Plasma visfatin concentrations were measured using an enzyme-linked immunosorbent assay (EIA) kit (Phoenix Pharmaceuticals, Belmont, California, USA).

All groups experienced a significant weight loss, as well as a significant improvement in lipid profile and parameters of carbohydrate metabolism [3]. Visfatin levels ~~did~~ were not changed significantly in the 3 groups [from 29.1 (16.5-46.0) to 28.1 (18.9-47.3) ng/mL in O group, from 29.0 (15.4-46.0) to 26.9 (17.0-51.0) ng/mL in F group and from 28.7 (13.4-43.0) to 27.6 (15.5-48.0) in OF group, all p=NS (Figure)].

It has been reported that massive weight loss with gastric binding results in a significant decrease of visfatin levels [4]. In our study orlistat-induced weight loss was not accompanied by a decrease in visfatin levels in all patients (Figure). Similar results were reported in the study of Manco et al [5], in which visfatin decrease did not occur in all morbidly obese women after massive weight loss. Furthermore, in another study visfatin was actually increased after massive weight loss with gastroplastic surgery in morbidly obese women [6]. It seems that visfatin does not decrease uniformly in all patients after weight loss, which suggests that neither fat mass nor insulin sensitivity consist the only predictors of visfatin levels.

Choi et al [7] examined the expression of visfatin in visceral fat depots of fenofibrate-treated Otsuka Long-Evans Tokushima fatty (OLETF) rats. The expression of visfatin mRNA in visceral fat deposits was significantly elevated by fenofibrate treatment when compared to untreated OLETF rats. In our study fenofibrate did not alter plasma visfatin levels. This discrepancy may be due to the fact that the fenofibrate dose per body weight given in the OLETF rats was much higher compared to the dose given in human studies. Moreover, a recent study also showed that fenofibrate did not change plasma visfatin levels in hypertriglyceridemic male subjects [8]. These results suggest that peroxisome proliferator-activated receptor alpha (PPAR alpha) agonists may not be powerful regulators of plasma visfatin expression and concentration in vivo.

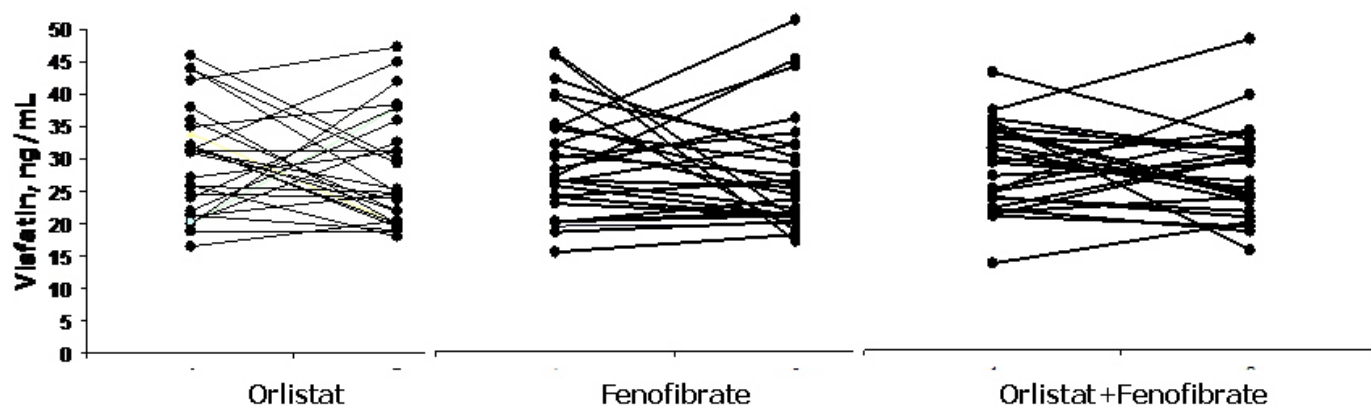


Figure. Plasma visfatin levels before and after intervention treatment.

We recently showed that fenofibrate and orlistat combination is useful in terms of weight loss, improvement of lipid profile as well as of parameters of carbohydrate metabolism [3]. Plasma visfatin levels were also uniformly changed in this combination group. Our findings suggest that either orlistat or fenofibrate do not act directly to plasma visfatin levels or that visfatin, an insulin mimetic agent, possibly needs a co-factor in order to act during weight loss. Studies investigating the effect of weight loss and pharmaceutical improvement of lipid profile and insulin sensitivity on plasma visfatin levels are inconclusive. It seems that visfatin may be only one of different pathways to fat reduction and that the regulation of plasma visfatin levels does not depend only on insulin sensitivity and is much more complicated than the original paper investigating visfatin [1] suggested.

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