Metabolic improvement by telmisartan beyond angiotensin receptor blockade: role of adipokines

Melhora da função metabólica ocasionada pelo telmisartan além do bloqueio do receptor da angiotensina: papel das adipocinas

Amirhossein Sahebkar[1]

Recently, there have been promising findings on the protective effects of telmisartan against insulin resistance and related complications. Notably, amelioration of diet-induced obesity, insulin resistance, and fatty liver caused by telmisartan treatment have recently been reported in *AT1a*-deficient mice, implying that these effects could be exerted independent of angiotensin II type 1 receptor (AT1) blockade (1). As for the mechanisms behind observed metabolic improvements, adipose tissue has been suggested as a potential target for the insulin-sensitizing effect of telmisartan. Based on this, I would like to propose an important mechanism by which adipose tissue might be involved in the observed AT1-independent effects of telmisartan.

Over the past decade, the attitude toward adipose tissue has changed from a sole energy storage organ to an active endocrine organ capable of expressing and secreting different adipokines with important metabolic activities (2). Adiponectin is an adipocyte-derived hormone that possesses interesting beneficial impacts on different metabolic processes. Numerous studies have reported the anti-obesity actions of adiponectin, as well as the improvement of multiple obesity-associated metabolic disorders, such as insulin resistance, type 2 diabetes, nonalcoholic fatty liver disease, dyslipidemia, and cardiovascular disease (2,3). Hypoadiponectinemia has been proposed as a risk factor for a number of those metabolic disorders (3). Particularly, telmisartan has been found to clinically increase plasma concentrations of adiponectin, high molecular weight (HMW) adiponectin – which is the major bioactive isoform of the hormone – and HMW-adiponectin/total adiponectin ratio (4-6). Besides, there is evidence indicating that telmisartan treatment stimulates adiponectin transcription in adipocytes (7,8).

Tumor necrosis factor-α (TNF-α) represents another important adipokine that has been shown to be critically involved in the development of insulin resistance, *diabetes mellitus*, lipid metabolism, nonalcoholic fatty liver disease, and obesity. Adipocyte expression and circulating levels of this cytokine have been reported to be elevated in obese or diabetic subjects. In a previous clinical study in patients with type 2 diabetes and metabolic syndrome, treatment with telmisartan was reported to significantly reduce serum levels of TNF-α (9). Although the impact of telmisartan on adipocyte-derived TNF-α needs to be clarified, it appears that this drug could change the TNF-α/adiponectin balance in favor of adiponectin.

Telmisartan has also been shown to reduce serum levels of resistin in obese mice, as well as in type 2 diabetic patients with metabolic syndrome (10,11). Resistin is another adipokine hypothesized to link obesity, insulin resistance and type 2 diabetes. Finally, telmisartan has been demonstrated to stimulate the release of visfatin from adipocytes (12). Considering the physiological effects of visfatin, its boosted release may result in insulin-sensitizing, antidiabetic and cardioprotective effects.

[1] Cardiovascular Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences (MUMS), Mashhad, Iran. Biotechnology Research Center and School of Pharmacy, MUMS, Mashhad, Iran I

Correspondence to:
Amirhossein Sahebka
sahebkarah811@mums.ac.ir

Received on Feb/10/2011
Accepted on Jun/3/2011

Taken together, AT1-independent, beneficial metabolic effects of telmisartan against obesity, insulin resistance and fatty liver may be, at least in part, attributed to the alteration of adipokine levels (including adiponectin, resistin and TNF-α) produced by this drug.

Disclosure: no potential conflict of interest relevant to this article was reported.

REFERENCES

1. Rong X, Li Y, Ebihara K, Zhao M, Naowaboot J, Kusakabe T, et al. Angiotensin II type 1 receptor-independent beneficial effects of telmisartan on dietary-induced obesity, insulin resistance and fatty liver in mice. Diabetologia. 2010;53:1727-31.
2. Fasshauer M, Paschke R. Regulation of adipocytokines and insulin resistance. Diabetologia. 2003;46:1594-603.
3. Sowers JR. Endocrine functions of adipose tissue: focus on adiponectin. Clin Cornerstone. 2008;9:32-8.
4. Makita S, Abiko A, Naganuma Y, Moriai Y, Nakamura M. Potential effects of angiotensin II receptor blockers on glucose tolerance and adiponectin levels in hypertensive patients. Cardiovasc Drugs Ther. 2007;21:317-8.
5. Makita S, Abiko A, Naganuma Y, Moriai Y, Nakamura M. Effects of telmisartan on adiponectin levels and body weight in hypertensive patients with glucose intolerance. Metabolism. 2008;57:1473-8.
6. Satoh M, Tabuchi T, Minami Y, Takahashi Y, Itoh T, Nakamura M. Prospective, randomized, single-blind comparison of effects of 6 months of treatment with telmisartan versus enalapril on high--molecular-weight adiponectin concentrations in patients with coronary artery disease. Clin Ther. 2009;31:2113-25.
7. Moriuchi A, Yamasaki H, Shimamura M, Kita A, Kuwahara H, Fujishima K, et al. Induction of human adiponectin gene transcription by telmisartan, angiotensin receptor blocker, independently on PPAR-γ activation. Biochem Biophys Res Commun. 2007;356:1024-30.
8. Yamada S, Ano N, Toda K, Kitaoka A, Shiono K, Inoue G, et al. Telmisartan but not candesartan affects adiponectin expression in vivo and in vitro. Hypertens Res. 2008;31:601-6.
9. Derosa G, Cicero AFG, D'Angelo A, Ragonesi PD, Ciccarelli L, Piccinni MN, et al. Telmisartan and irbesartan therapy in type 2 diabetic patients treated with rosiglitazone: Effects on insulin--resistance, leptin and tumor necrosis factor-α. Hypertens Res. 2006;29:849-56.
10. Derosa G, Fogari E, D'Angelo A, Cicero AF, Salvadeo SA, Ragonesi PD, et al. Metabolic effects of telmisartan and irbesartan in type 2 diabetic patients with metabolic syndrome treated with rosiglitazone. J Clin Pharm Ther. 2007;32:261-8.
11. Araki K, Masaki T, Katsuragi I, Tanaka K, Kakuma T, Yoshimatsu H. Telmisartan prevents obesity and increases the expression of uncoupling protein 1 in diet-induced obese mice. Hypertension. 2006;48:51-7.
12. Storka A, Vojtassakova E, Mueller M, Kapiotis S, Haider DG, Jungbauer A, et al. Angiotensin inhibition stimulates PPARγ and the release of visfatin. Eur J Clin Invest. 2008;38:820-6.