Letter

Diabetes Metab J 2014;38:317-318
http://dx.doi.org/10.4093/dmj.2014.38.4.317
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

The Effect of DPP-4 Inhibitors on Metabolic Parameters in Patients with Type 2 Diabetes (*Diabetes Metab J* 2014;38:211-9)

Seung-Hwan Lee

Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea College of Medicine, Seoul, Korea

Incretin-based therapies are now widely used for the treatment of type 2 diabetes mellitus. Beyond its glucose-lowering effect, the pleiotropic actions of the glucagon-like peptide-1 (GLP-1) analogue and dipeptidyl peptidase-4 (DPP-4) inhibitors are being discovered, raising the possibilities for their role in the management of various comorbidities associated with diabetes mellitus [1,2]. Another point of interest is whether or not the different DPP-4 inhibitors exert the same glycemic and nonglycemic effects [3].

In the article entitled "The effect of DPP-4 inhibitors on metabolic parameters in patients with type 2 diabetes," Choe et al. [4] compared the effects of sitagliptin and vildagliptin on glucose and lipid parameters. They described that there were no differences in the glucose- and lipid-lowering efficacy between two agents. However, when compared with the baseline data, patients in the vildagliptin-treated group showed significant improvements in their total cholesterol and triglyceride (TG) levels after 24 weeks of follow-up, but no differences were observed in sitagliptin-treated group. This interesting article merits much attention, although some points need to be discussed.

Firstly, it is unclear whether the lipid-lowering effect of DPP-4 inhibitors is a direct phenomenon of DPP-4 inhibition per se or not. Previous experimental studies showed that infusion of GLP-1 or inhibition of DPP-4 activity acutely decreases postprandial TG and apolipoprotein B (ApoB)-48, supporting the direct role of GLP-1 in lipoprotein synthesis and secretion [5,6]. However, because many other factors may affect lipid homeostasis, it would be helpful to provide information regarding whether there were any changes in body weight or the degree of insulin resistance in the study subjects.

Secondly, whether the significant improvements of lipid parameters in patients treated with vildagliptin but not in those treated with sitagliptin can be explained by the differences in their pharmacologic profiles remains elusive. A 4 week, randomized study in patients with type 2 diabetes receiving vildagliptin (50 mg twice daily) demonstrated improvements in postprandial plasma TG and ApoB-48-containing TG-rich lipoprotein particle metabolism in response to a fat-rich test meal [7]. Similarly, a 6-week, cross-over study using 100 mg/day of sitagliptin also showed a significant reduction in the circulating levels of postprandial TG, ApoB-48, and free fatty acid [8]. Although the results are inconsistent across trials, a meta-analysis indicated possible beneficial effects of DPP-4 inhibitors on the total cholesterol and TG levels, suggesting that incretins modulate lipid metabolism [9]. Interestingly, when the effect of individual DPP-4 inhibitors was analyzed, a significantly lower total cholesterol level was observed in subjects treated with vildagliptin and alogliptin, but not sitagliptin or saxagliptin. This data is in line with the observation by Choe

Corresponding author: Seung-Hwan Lee
Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea College of Medicine, 222 Banpo-daero, Seocho-gu, Seoul 137-701, Korea
E-mail: hwanx2@catholic.ac.kr

et al. [4], although further studies are needed to clarify this issue.

Lastly, it seems that the changes in the total cholesterol levels from baseline to the end of the study varies greatly among subjects. It would be interesting to identify the differences between the patients who showed reductions in their lipid levels and the patients who did not. Some external factors such as diet, exercise, and use of other medications also should be considered.

Accumulating evidence suggest a promising view for DPP-4 inhibitors in controlling some well-recognized cardiovascular risk factors, including dyslipidemia. Although the questions raised above might not be answered by a single study, further investigations are warranted to enhance our understanding on the benefits of incretin-based therapies.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Ussher JR, Drucker DJ. Cardiovascular biology of the incretin system. Endocr Rev 2012;33:187-215.
2. Aroor AR, Sowers JR, Jia G, DeMarco VG. Pleiotropic effects of the dipeptidylpeptidase-4 inhibitors on the cardiovascular system. Epub 2014 Jun 13. DOI: http://dx.doi.org/10.1152/ajpheart.00209.2014.
3. Deacon CF, Holst JJ. Dipeptidyl peptidase-4 inhibitors for the treatment of type 2 diabetes: comparison, efficacy and safety. Expert Opin Pharmacother 2013;14:2047-58.
4. Choe EY, Cho Y, Choi Y, Yun Y, Wang HJ, Kwon O, Lee BW, Ahn CW, Cha BS, Lee HC, Kang ES. The effect of DPP-4 inhibitors on metabolic parameters in patients with type 2 diabetes. Diabetes Metab J 2014;38:211-9.
5. Qin X, Shen H, Liu M, Yang Q, Zheng S, Sabo M, D'Alessio DA, Tso P. GLP-1 reduces intestinal lymph flow, triglyceride absorption, and apolipoprotein production in rats. Am J Physiol Gastrointest Liver Physiol 2005;288:G943-9.
6. Hsieh J, Longuet C, Baker CL, Qin B, Federico LM, Drucker DJ, Adeli K. The glucagon-like peptide 1 receptor is essential for postprandial lipoprotein synthesis and secretion in hamsters and mice. Diabetologia 2010;53:552-61.
7. Matikainen N1, Manttari S, Schweizer A, Ulvestad A, Mills D, Dunning BE, Foley JE, Taskinen MR. Vildagliptin therapy reduces postprandial intestinal triglyceride-rich lipoprotein particles in patients with type 2 diabetes. Diabetologia 2006;49:2049-57.
8. Tremblay AJ, Lamarche B, Deacon CF, Weisnagel SJ, Couture P. Effect of sitagliptin therapy on postprandial lipoprotein levels in patients with type 2 diabetes. Diabetes Obes Metab 2011;13:366-73.
9. Monami M, Lamanna C, Desideri CM, Mannucci E. DPP-4 inhibitors and lipids: systematic review and meta-analysis. Adv Ther 2012;29:14-25.