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

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We appreciate your interest and comments on our article entitled "The Effect of DPP-4 Inhibitors on Metabolic Parameters in Patients with Type 2 Diabetes," which was published in *Diabetes & Metabolism Journal* 2014;38:211-9 [1].

In our study, we showed the different effects of 24-week dipeptidyl peptidase-4 (DPP-4) inhibitor (sitagliptin and vildagliptin) treatments on serum glucose and lipid parameters. The glucose lowering efficacy was not significantly different between both groups, but vildagliptin showed augmented total cholesterol and triglyceride reduction than sitagliptin group. Although it is not clear whether the lipid-lowering effect of DPP-4 inhibitors is the result of direct DPP-4 inhibition or indirect metabolic effects of medication, other studies have also shown the lack of correlation between the reduction of total cholesterol and reduction in blood glucose levels. This suggests that the effects of DPP-4 inhibitors on lipid parameters might be independent of their blood glucose lowering effect. In addition, the direct effect of DPP-4 inhibitors on lipid biosynthesis has been reported in mice model [2]. Regarding body weight change, no significant weight change was observed in both treatment groups (data not shown). Considering that DPP-4 inhibitors have no effect on body weight in general, as reported in many other studies [3-6], it is unlikely that the change in blood lipid profile is due to weight loss. Unfortunately, we did not measure insulin levels at follow-up visit, and hence we could not calculate homeostatic model assessment-insulin resistance as an index of insulin resistance.

In general, all DPP-4 inhibitors are reported to have an effect on postprandial lipid levels [7]. One meta-analysis study reported that vildagliptin and alogliptin could have a greater lipid lowering effect than sitagliptin [8]. A recent observation study showed that a greater reduction in total cholesterol was achieved with vildagliptin (–24 mg/dL) than with sitagliptin (–11 mg/dL) and saxagliptin (–3.6 mg/dL) [9]. These studies are in line with our study and suggest the differential DPP-4 inhibitor effects on blood cholesterol levels. A potential reason for this difference may be due to the pharmacokinetics of vildagliptin versus sitagliptin. Vildagliptin interacts with DPP-4 as a kind of substrate blocker, with vildagliptin continuously binding to DPP-4 as long as vildagliptin levels are adequate. In contrast, sitagliptin, a competitive DPP-4 antagonist, inhibits its activity in a dose-dependent manner [10]. However, further and larger clinical studies and functional studies are needed to better establish the impact of different DPP-4 inhibitors on dyslipidemia *in vivo* and *in vitro*.

Lastly, although it would be interesting to identify the difference between the patients who showed lipid lowering response to DPP-4 inhibitors and those didn't, we did not assess external factors such as diet or exercise. Instead, we analyzed the effect of statin medication and showed the result in Sup-

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plementary Table 1 [1], and found that there was a difference between sitagliptin and vildagliptin on lipid profile change regardless of the use of statin. We would like to thank Dr. Lee for the interest in our study and for your thoughtful comments.

CONFLICTS OF INTEREST

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

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