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Editorial

Possible pleiotropic effects of alogliptin on cardiovascular and renovascular system

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Dear Editors

Alogliptin is a newer agent of the class dipeptidyl peptidase-4 inhibitor which has higher affinity for the enzyme being more specific for DPP-4. Alogliptin produces a quick and sustained inhibition of DPP-4 which leads to significant reduction in postprandial plasma glucose levels in patients with type 2 diabetes mellitus (T2DM).[1,2] The selectivity of alogliptin, a DPP 4 inhibitor is more than 10,000 times than other related proteases. Alogliptin administration in the dose range of 25 to 800 mg, orally has 93 to99 % mean DPP 4 inhibition range.[2,3] The indications of alogliptin in patient with T2DM is as an adjunct to diet and exercise leading to improved glycaemic control.[3]

Its clinical efficacy and safety have demonstrated reducing patients glycosylated haemoglobin by 0.4-1.0% in 26 week.[4] Alogliptin was showed to be safe and effective in more than 10000 patients with T2DM as monotherapy, with metformin as well as pioglitazone. Treatment of T2DM with DPP-4 inhibitors involves a variety of extra pancreatic effects that include renal protection which occur either by the incretin-independent as well as incretin-dependent mechanisms.[5]

The cardiovascular protective effects results from multiple factors that include insulin resistance, oxidative stress, dyslipidaemia, adipose tissue dysfunction, dysfunctional immunity and anti-apoptotic properties in the heart and vasculature.[6]

DPP-4 has shown to be involved in the inflammatory signalling pathway, stimulation of vascular smooth cell proliferation, and the stimulation of oxidative stress in various cells, they ameliorate these pathophysiologic processes. In recent randomized clinical trials in high-risk patients with T2DM, DPP-4 inhibitor therapy led to sympathetic activation and neuropeptide Y-mediated vascular responses and did not show any cardiovascular protective effect, but further studies are warranted to characterize the cardiovascular effects of DPP-4 inhibitor.[7]

In T2DM, nephropathy is associated with increased reactive oxygen species (ROS) along with hyperglycaemia, activation of the intrarenal renin angiotensin system (RAS), and high blood pressure. ROS or the peroxidation of lipids leads to glomerular injury with hyperglycaemia inducing acyl glycerol and activating protein kinase C, increased levels intrarenal angiotensinogen (AGT) and ROS formation accelerates onset of diabetic nephropathy. DPP-4 inhibitors have shown to improve the marker of oxidative stress in the kidney and Reno protective effect.[8]

1. Conclusion

Alogliptin appears to be safe and efficacious as monotherapy or adjunct therapy with other hypoglycaemic agents with

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treatment significantly reducing fasting blood glucose, glycosylated haemoglobin. Recent studies suggest a possible cardioprotective role and Reno protective role independent of its glucose lowering effect, but further studies are warranted to explicitly recommend it for the other role.

2. Conflict of Interest

None.

References

1. Feng J, Zhang Z, Wallace MB, Stafford JA, Kaldor SW, Kassel DB, et al. Discovery of alogliptin: a potent, selective, bioavailable, and efficacious inhibitor of dipeptidyl peptidase IV. *J Med Chem.* 2007;50:2297–300.
2. Covington P, Christopher R, Davenport M, Fleck P, Mekki QA, Wann ER, Karim A. Pharmacokinetic, pharmacodynamic, and tolerability profiles of the dipeptidyl peptidase-4 inhibitor alogliptin: a randomized, double-blind, placebo-controlled, multiple-dose study in adult patients with type 2 diabetes. *Clin Ther*. 2008;30(3):499–512.
3. Christopher R, Covington P, Davenport M, Fleck P, Mekki QA, Wann ER, et al. Pharmacokinetics, pharmacodynamics, and tolerability of single increasing doses of the dipeptidyl peptidase-4 inhibitor alogliptin in healthy male subjects. *Clin Ther*. 2008;30(3):513–27.
4. Ndefo UA, Okoli O, Erowele G. Alogliptin: A new dipeptidyl peptidase-4 inhibitor for the management of type 2 diabetes mellitus. *Am J Health Syst Pharm*. 2014;71(2):103–9.
5. Makino Y, Fujita Y, Haneda M. Dipeptidyl peptidase-4 inhibitors in progressive kidney disease. *Curr Opin Nephrol Hypertens*. 2015;24(1):67–73.
6. Aroor AR, Sowers JR, Jia G, DeMarco VG. Pleiotropic effects of the dipeptidylpeptidase-4 inhibitors on the cardiovascular system. *Am J Physiol Heart Circ Physiol*. 2014;307(4):H477–92.
7. Wang H, Liu J, Zhao H. Emerging options for the treatment of type 2 diabetes in Chinese patients: focus on arterial function and alogliptin. *Drug Des Devel Ther*. 2015;9:683–6.
8. Kim NH, Yu T, Lee DH. The nonglycemic actions of dipeptidyl peptidase-4 inhibitors. *Biomed Res Int*. 2014;2014:368703.

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