Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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LETTER TO THE EDITOR

Potent antiatherosclerotic effects of alogliptin in addition to its potent antidiabetic effects

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy
10 May 2012
Number of times this article has been viewed

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To the editor

I read with great interest the article by Andukuri et al in a recent issue of your journal.[1] The article makes compelling reading. Interestingly, research over the past few years has shown that in addition to its significant diabetic-modulating effects, alogliptin also exerts significant direct antiatherosclerotic effects.

For instance, alogliptin decreases plasma nonesterified fatty acid levels by 11%.[2] It simultaneously has an attenuating effect on serum triglyceride levels, decreasing them by almost 24%. Similarly, Monami et al in a recent meta-analysis reported that alogliptin is associated with a significant attenuation in total serum cholesterol.[3] Alogliptin also significantly decreases postprandial very low-density lipoprotein and chylomicron levels.[4] Alogliptin mediates its antiatherosclerotic effects by decreasing expression of interleukin-1β and interleukin-6, which is typically enhanced in diabetes.[5] It also has an attenuating effect on extracellular signal-regulated kinase-mediated expression of metalloproteinases 1 and 12.[6] This exerts a significant inhibitory effect on macrophage-modulated inflammation and thereby attenuates vascular atherosclerosis.

Interestingly, these hypolipidemic effects of alogliptin are markedly enhanced when used in combination with pioglitazone. For instance, alogliptin with adjunctive pioglitazone therapy decreases plasma nonesterified fatty acid levels by 25%–48% and serum triglyceride levels by 67%–77%.[2,7] Alogliptin clearly exerts significant antiatherosclerotic and hypolipidemic effects, and may go a long way towards attenuating atherosclerosis-related morbidity and mortality in patients with diabetes as well as the metabolic syndrome.

References

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Author's response

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The letter by Dr Kapoor points out useful data in animal models. The current long-term cardiac outcome trials of alogliptin will be essential to determine the effect of this agent on the atherosclerotic process in man.