Potential Role of Direct K-ATP Channel Opening in the Anti-Diabetic Actions of Rimonabant and Ibipinabant

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Abstract

Background

Chronic treatment of Zucker rats with CB1 inverse agonists leads to improved insulinemia. In rodents this was linked with beta cell rest, independent effects of rimonabant and ibipinabant, also improves fed and fasting insulinemia, plasma insulin during a GTT and glycemia during a 10-week study in Zucker rats.

Acute in vivo and in vitro studies revealed a diazoxide-like effect of these drugs. Inhibitory acute treatments in either Zucker rats and eutomers of CB1 agonists and antagonists were equally effective in reducing insulin hypersecretion as well as CB1 like compounds might exhibit KCO activity. Improvements in beta cell function and glucose induced insulin secretion are facilitated by KCOs, directly inhibit GSIS, facilitating beta cell rest, lowering plasma insulin levels and reducing insulin hypersecretion in Zucker rats with CB1 inverse agonists and controls hyperinsulinemia as insulin appears to improve insulin signaling in muscle and glycemia, and these effects may combine with the actions at other cells to improve insulin sensitivity.

Conclusion

Further studies are needed to determine the extent to which the clinically observed anti-diabetic effects of rimonabant and ibipinabant are mediated through KCO actions on glucose-induced insulin secretion and insulin sensitivity associated with hyperinsulinemia.