Can anticholinergics influence insulinotropic actions of incretins?

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Background: The mode of action of glucagon-like peptide-1 (GLP-1) remains speculative, as only a fraction of secreted GLP-1 actually reaches the beta cells via the pancreatic arteries, following first-pass of the portal circulation. This suggests the role for a neurally-mediated stimulation of beta cells, wherein the enteric cholinergic pathways may play a modulatory role. Accordingly, this study was undertaken to examine the effect, if any, of cholinergic blockade on plasma glucose (PG) and insulin following an oral glucose load.

Method: Ten subjects with impaired glucose tolerance (IGT; age, 49.4 ± 16.1 yrs, body mass index [BMI], 28.8 ± 2.3 kg/m²) and normal glucose tolerance (NGT; age 45.6 ± 13.5 yrs, BMI, 23.00 ± 0.80 kg/m²) underwent an oral glucose tolerance test (OGTT, 75g), in the absence (Day 1) and presence of hyoscine butyl-bromide (HBB, 20 mg, PO) at Day 4. The PG and insulin levels were serially estimated at 30-min increments for 2-h. Changes monitored included 30-min incremental AUC (iAUC-30), 0-120 min total AUC (tAUC 0-120), along with indices of early (insulinogenic index, IGI_{0-30} = Δinsulin_{0-30}/ΔPG_{0-30}) and late (insulin/PG_{AUC 60-120}) beta-cell activity.

Results: In the IGT group, HBB significantly decreased insulin iAUC-30 at t = 60-90 min (p = 0.023). However, in the NGT group, a bimodal trend was observed, as insulin iAUC-30 increased at t = 30-60 min (p < 0.001) but decreased at t = 90-120 min (p < 0.05). With regard to insulin tAUC 0-120, HBB caused a significant reduction only in the NGT group (p = 0.031). Although HBB had a minimal impact on early beta-cell activity (IGI_{0-30}), it significantly attenuated the late activity (insulin/PG_{AUC 60-120}) in IGT (24.00 ± 1.12 vs. 20.70 ± 0.72 pM/mM, p = 0.023) and NGT (39.4 ± 1.79 vs. 30.27 ± 2.34 pM/mM, p = 0.006) groups.

Conclusion: In the NGT group, hyoscine attenuated the insulin patterns, whereas in the IGT group, who possibly have an attenuated prandial GLP-1 response, the effect was minimal, substantiating that anticholinergics modulate the insulinotropic actions of incretins.