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Glucagon-Like Peptide-1 Analogues: A New Way to Quit Smoking? SKIP – a Randomised Controlled Study
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Background: Cigarette smoking is the leading preventable cause of premature death. Despite dedicated programs, quit rates remain low due to barriers such as nicotine withdrawal syndrome or post-cessation weight gain. Glucagon-like peptide-1 (GLP-1) analogues reduce energy intake and body weight and seem to modulate addictive behavior. These GLP-1 properties are of major interest in the context of smoking cessation. The aim of this study was to evaluate the GLP-1 analogue dulaglutide as a new therapy for smoking cessation.

Methods: This was a placebo-controlled, double-blind, parallel group, superiority, single-center randomized study including 255 patients. The intervention consisted of a 12-week treatment phase with dulaglutide 1.5 mg or placebo injected subcutaneously at a weekly study visit, in addition to standard of care (behavioral counselling and pharmacotherapy with varenicline).

Point-prevalence abstinence rate at week 12 as primary outcome was assessed by self-reported smoking status and biochemical confirmation by end-expiratory exhaled carbon monoxide measurement. We further investigated weight gain and changes in the glucose homeostasis at week 12. In a substudy (n = 71), we compared behavioral (i.e., nicotine craving measured by a Visual analogue Scale from 1-7) and brain activity changes in response to smoking cue videos using functional magnetic resonance imaging (fMRI) at baseline and week 12.

Results: The point-prevalence abstinence rate after 12 weeks of treatment was 80/127 (63%) in the dulaglutide group and 82/128 (65%) in the placebo group (difference in proportions [95% CI] -1.9% [-10.7, 14.4], p=0.859).

We observed an increase in weight in the placebo (+1.8kg [SD 2.4]) and a decrease in the dulaglutide group (-0.7kg [SD 3.3]) between baseline and week 12; baseline-adjusted difference in weight change [95% CI] -2.5kg [-3.3, -1.7], p<0.001.

Craving in response to smoking cue videos decreased from baseline to week 12 (estimated mean difference [95% CI] -3.0 [-3.7, -2.3], p<0.001), with no difference between dulaglutide and placebo (estimated mean difference [95% CI] 0.4 [-1.2, 2.0], p=0.6). Similarly, no difference in whole brain functional activity was seen between the two treatments, at both time points and between baseline and follow up.

Conclusion: In this study, an exceptional high point prevalence abstinence rate in both groups was observed, most probably due to the very close (weekly) supervision of the patients. Our data provides no evidence that dulaglutide modulates nicotine craving or smoking cessation rates. Nevertheless, GLP-1 analogues such as dulaglutide may be a promising treatment during smoking cessation as it may avoid post-cessation weight gain.

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