A randomized controlled trial of the GLP-1 receptor agonist dulaglutide in primary polydipsia.

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4634739
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Year 2021
Title A randomized controlled trial of the GLP-1 receptor agonist dulaglutide in primary polydipsia.
Journal The Journal of clinical investigation
Volume 131
Number 20
Pages / **Article-Number** e151800
Keywords Addiction; Endocrinology; Homeostasis; Neuroimaging; Neuroscience
BackgroundPrimary polydipsia, characterized by excessive fluid intake, carries the risk of water intoxication and hyponatremia, but treatment options are scarce. Glucagon-like peptide 1 (GLP-1) reduces appetite and food intake. In experimental models, GLP-1 has also been shown to play a role in thirst and drinking behavior. The aim of this trial was to investigate whether GLP-1 receptor agonists reduce fluid intake in patients with primary polydipsia.MethodsIn this randomized, double-blind, placebo-controlled, 3-week crossover trial, 34 patients with primary polydipsia received weekly dulaglutide (1.5 mg, Trulicity) in one treatment segment and placebo (0.9% sodium chloride) in the other. During the last treatment week, patients attended an 8-hour evaluation visit with free access to water. The primary endpoint was total fluid intake during the evaluation visits. Treatment effects were estimated using linear mixed-effects models. In a subset of 15 patients and an additional 15 matched controls, thirst perception and neuronal activity in response to beverage pictures were assessed by functional MRI.RESULTsPatients on dulaglutide reduced their fluid intake by 490 mL (95% CI: -780, -199; P = 0.002), from 2950 mL (95% CI: 2435, 3465) on placebo to 2460 mL (95% CI: 1946, 2475) on dulaglutide (model estimates), corresponding to a relative reduction of 17%. Twenty-four-hour urinary output was reduced by -943 mL (95% CI: -1473, -413; P = 0.001). Thirst perception in response to beverage pictures was higher for patients with primary polydipsia than for controls, and lower for patients on dulaglutide versus placebo, but functional activity was similar among groups and treatments.CONCLUSIONSGLP-1 receptor agonists reduce fluid intake and thirst perception in patients with primary polydipsia and could therefore be a treatment option for these patients.Trial registrationClinicaltrials.gov NCT02770885.FundingSwiss National Science Foundation (grant 32473B_162608); University Hospital and University of Basel; Young Talents in Clinical Research grant from the Swiss Academy of Medical Sciences and the Gottfried & Julia Bangerter-Rhyner Foundation; Top-up Grant from the PhD Programme in Health Sciences, University of Basel.

ISSN/ISBN 1558-8238
Full Text on edoc ;
Digital Object Identifier DOI 10.1172/JCI151800
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/34473645