Study of the Ameliorative Effect of Naltrexone/Bupropion, Liraglutide or Food Restriction On β-Cell Regeneration and Insulin Resistance in Obese Diabetic Male Albino Rats

Thesis

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ABSTRACT

Background: insulin resistance, characterized by impaired cellular response to insulin, plays a central role in the development of type 2 diabetes mellitus and obesity.

Aim of work: The aim of this work is to assess the effects of naltrexone/bupropion on body weight, β-cell regeneration, cardiovascular outcomes and the mechanism by which they can affect some selected parameters. Also, to compare the effect of naltrexone/bupropion on these parameters with both caloric restriction and liraglutide in obese type 2 diabetic male albino rats.

Methodology: This study is a comparative study which was conducted in the animal house of faculty of medicine, Fayoum university, Egypt. It

included 50 male albino rats who were divided into 5 groups; group I: normal control group in which rats continued on standard commercial chow diet, group II: obese diabetic control group, group III: caloric restricted group in which rats subjected to dietary restriction of about 50% of the food intake of normal control group, group IV: (NTX+BUP) treated group (by a ratio of 1 NTX / 10 BUP, orally) and group V: liraglutide treated group (0.3mg/kg/day, S.C). Body weight, blood pressure, fasting

glucose, fasting insulin, β-arrestin-1 were measured. Body mass index (BMI), homeostatic model assessment of insulin resistance (HOMA-IR) and of beta-cell function (HOMA- β) were calculated. Hematoxylin and eosin (H&E), anti-insulin antibodies and Ki-67 staining for histopathology of the pancreas was done.

Results: The results demonstrated significant improvement in insulin resistance, serum lipid profile and systolic blood pressure across all intervention groups compared to obese diabetic control group (P<0.05). Weight reduction was significantly higher in treatment with (NTX+BUP) treated group than liraglutide treated group and insignificantly higher than caloric restriction group. β-cell regeneration (assed through Ki-67 and anti-insulin Abs) was significantly higher in liraglutide treatment than caloric restriction and (NTX+BUP) treated groups however caloric restriction group was significantly higher than (NTX+BUP) treated group regarding β-cell regeneration. There were no statistically significant differences between treated groups according serum insulin level, serum lipid profile, HOMA-IR, HOMA-β, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure (MAP) or atherogenic indices. There was no significant correlation between β-arrestin-1 and serum glucose, serum insulin, HOMA-IR or HOMA- β. There was a positive correlation between MAP and atherogenic index of plasma (AIP).

Conclusion: our study highlights the potential benefits of (NTX+BUP), liraglutide and caloric restriction in ameliorating insulin resistance and

promoting weight loss in diabetic obese male albino rats. Furthermore, (NTX+BUP) promising effect on glycemic control and systolic blood pressure reduction suggesting potential therapeutic approach for weight reduction in obese hypertensive diabetic patients but its role in β-cell regeneration was minor.

Keywords: Naltrexone/Bupropion, Liraglutide, Caloric restriction, β-cell regeneration, Obesity, Type 2 diabetes, Rats.