Food intake and body weight response to long-term GLP-1 derivatives treatment in mice on a high fat /sugar diet

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Abstract. Mice fed a high-fat diet develop hyperglycemia and obesity. As a type II diabetes treatment drug, GLP-1 has been known to decreases appetite, losing body weight in diabetes host. To investigate the prevention therapeutic efficacy of GLP-1 derivate on obesity and insulin resistance in health mice on a high fat and high sugar diet. The mice were divided into 4 groups, high fat /high sugar diet treated (HFD+GLP-1) or untreated (HFD+PBS) with long-acting GLP-1 derivate (6.2), on regular diet treated (SD+GLP-1) or untreated (SD+PBS) with 6.2, their food intake and body weight were analyzed every day until 8 weeks. The result showed, control with the HFD+PBS group, the food intake, body weight decrease and the water intake increased in group HFD+GLP-1, there is no difference in the food intake, body weight between the group SD+GLP-1and SD+PBS. However, the water intake was statistically significant increase in group SD+GLP-1. The finding suggest the GLP-1 derivate can be used as obesity and insulin resistance prophylactic drugs, in addition, that are safe for the population on regular diet if they on this drug.

Keywords: Long acting GLP-1, Food intake, Body weight.

1. Introduction

Mice fed a high-fat diet develop hyperglycemia and obesity. Epidemiological and animal studies made on several environmental factors suggest that the high fat and high sugar diet is a major cause of obesity and insulin resistance. Indeed, various metabolic studies have confirmed the view that calories obtained from fat have a greater effect on obesity than energy per se.

GLP-1, a new type II diabetes treatment drug, has been known to slow or revert the progress of diabetes, to regulate multiple physiological processes including inhibiting stomach emptying, decreases appetite, losing body weight, cardiac protecting, lowing blood pressure and many others, and to interfere metabolism at multiple loci. However, the diabetic and obesity prevention therapeutic efficacy of Glp-1 derivate treatment in the not diabetes and obesity population with high fat-diet is unknown. Our previous research development a long-acting GLP-1 derivate, diabetes treatment efficacy has been proved. The work presented in this paper focuses in the response of food intake and body weight to the long-acting GLP-1 treatment in healthy mice fed high fat and sugar diet. Doing this work, we intend to reveal the potential indication of GLP-1 derivate as diabetes and obesity preventive medication.

2. Experimental

2.1. Materials and Equipment.

Animals and materials, BALB/c mice (7 weeks old) were obtained from experimental animal center (Guangzhou, China) and maintained at the animal facility at Jinan University of Medicine and Science. standard rodent diet (4% fat, 20% protein) provided by the Beijing HuaFuKang biological technology(China) and high fat/sugar diet (40% fat, 20% protein, 40% carbohydrates) provided by Shanghai SLAC laboratory animal center(,Shanghai, China).

Long acting GLP-1 derivate (6.2) were obtained in our molecular biology and biochemistry lab in Jinan University (China).

2.2 . Experiment.

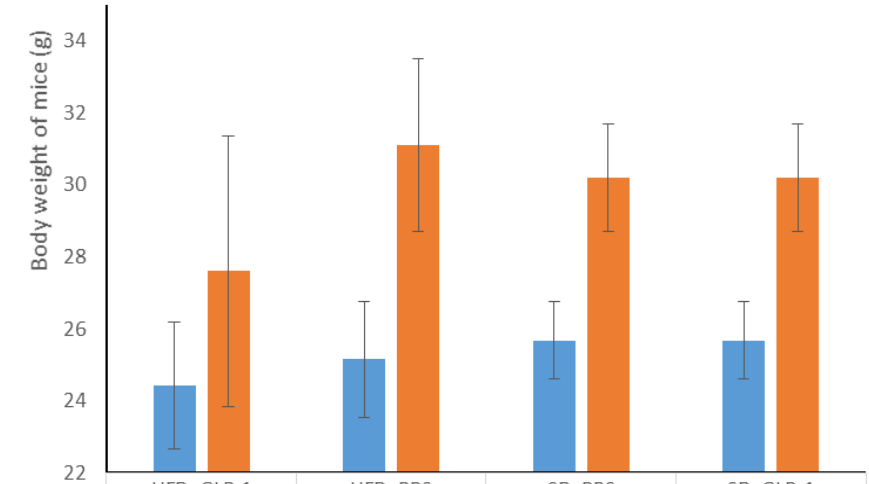
The mice were divided in to 4 groups, 12 mice/ group, group HFD+GLP-1 were fed high fat/sugar diet and peritoneal injection with 6.2 everyday (1800μg/kg of body weight), group HFD+PBS were fed high fat/sugar diet and peritoneal injection with PBS buffer (0.2ml/mice) every day, group SD+GLP-1 ad libitum on a standard rodent diet and peritoneal injection with 6.2 everyday (1800μg/kg of body weight), group SD+PBS ad libitum on a standard rodent diet and peritoneal injection with PBS buffer(0.2ml/mice) every day.

Body weight water and food intake of each group mice were weight out every day for 8 weeks.

3. Results and discussion

3.1. Effects of 6.2 on body weight in mice on high fat/sugar diet and standard rodent diet.

The initial body weight of mice in each group is similarly, the difference was not statistically significant (Fig 1). The body weight of HFD+GLP-1 group mice was significantly lower than that of HFD+PBS group ($p < 0.05$), in addition, the final weight has no statistically difference between SD+GLP-1 group and SD+PBS group. Compared with HFD+PBS group, HFD+GLP-1 mice showed a significant increase in body weight ($p<0.05$). The weight gain has no significant difference between HFD+GLP-1 and SD group. The result showed that GLP-1 can decrease body weight gain in mice on high fat/sugar diet, however has no influence on body weight gain in mice fed standard diet. It indicate that GLP-1 drugs slow body weight gain by reducing fat and sugar absorption or intake in mice.



	HFD+GLP-1	HFD+PBS	SD+PBS	SD+GLP-1
0 weeks	24.41	25.15	25.68	25.68
8 weeks	27.6	31.1	30.2	30.2

Fig. 1 Effect of 6.2 on body weight in mice fed different diet

3.2 Effect of 6.2 on food and water intake in mice on different diet.

The food intake in the HFD+GLP-1 group mice was significantly less than HFD+PBS group ($p<0.05$).The Food intake has no significant difference between SD+GLP-1 group and SD+PBS group. The water intake in HFD+GLP-1 group was almost same with HFD+PBS group. Interestingly, the water intake in SD+GLP-1 group is significantly higher than SD+PBS group (Table 1). Combined with 3.1 conjecture, we confirm that GLP-1 drugs slow body weight gain in mice by reduce the intake for high fat and sugar diet. However, injected with GLP-1 drug in mice on standard rodent diet, the mechanism of water intake increased remains to be established.

Table 1 Three Scheme comparing

Groups	Food intake (g/day/mice)	Water intake (ml/day/mice
HFD+PBS	3.49±0.38a	3.15±0.49a
HFD+GLP-1	3.33±0.34b	3.35±0.55a
SD+PBS	3.82±0.41c	4.57±0.59b
SD+GLP-1	3.81±0.34c	5.85±0.95c

4. Conclusion

The result do not imply the mechanism of GLP-1 drugs causing water demand increased in mice on standard rodent diet. However our data provide long acting GLP-1 slow the body weight gain in mice on high fat/sugar diet by decrease food intake. Furthermore, under GLP-1 drug treatment, there is no difference in the food intake and body weight gain in mice fed standard rodent diet. The finding suggest the GLP-1 derivate can be used as obesity and insulin resistance prophylactic drugs, in addition, that are safe for the population on regular diet if they on this drug.

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