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Original Contribution

THE INFLUENCE OF THE VERY LOW CALORIE DIET ON THE HYPERGLYCAEMIC EFFECT OF EPINEPHRINE IN NEW ZEALAND WHITE RABBITS

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ABSTRACT

In this study we investigated whether long lasting Very Low Calorie Diet (VLCD) decreased hyperglycaemic potential of epinephrine. For 80 days a group of New Zealand White (NZW) rabbits received 120 g of standard commercial pellets, as Control, while another group received 30 g VLCD. At the end of the experiment 15µl/kg BW epinephrine was administered as intravenous bolus to both groups. One hour after administration blood glucose level increased significantly both in the VLCD ($p<0.05$) and the Control ($p<0.001$) groups without significant differences between them. Glycogen in VLCD hepatocytes was reduced but not fully exhausted. We concluded that in VLCD hyperglycaemic effect of epinephrine remained almost unaltered compared to Control group and this prevented VLCD treated subjects from hypoglycaemia.

Key words: VLCD, hyperglycaemia, glycogen, hypoglycaemia

INTRODUCTION

The beneficial effect of the Very Low Calorie Diet (VLCD) on insulin resistance motivates its therapeutic use but little is known about the related health hazards The decreased glycogen storages could alter the hyperglycaemic potential of the body in stress situation and provoke hypoglycaemic episodes. The epinephrine infusion could be used for stress modelling. In normal dogs epinephrine resembles some physiological effects of the stress and increases endogenous glucose production (1). Epinephrine is important for the neural metabolic regulation (2) by stimulating lipolysis, ketogenesis, thermogenesis, gluconeogenesis and glycogenolysis (3) and increases blood glucose levels. Epinephrine venous levels 410-680 pmol/l activate its lipolytic and thermogenic activity and levels 550-1090 pmol/l – its glycaemic, ketogenic and glycogenolytic effects being in the physiological ranges of 50-1200 pmol/l in unstressed conditions (4). Epinephrine, glucagon, and neural stimulation are capable of activating liver glucose production and their partial contribution to hyperglycaemia depends on diet (5). There is a relationship between sympathoadrenal system activity and insulin levels (6) and VLCD can change sympathoadrenal activity (7) and thus modulate insulin secretion. The aim of our study was to examine how VLCD impacts hyperglycaemic potential of the epinephrine and to draw conclusion about changes of stress reactivity in VLCD treated patients.

METHODS

For 80 days a group of mail New Zealand White (NZW) rabbits (VLCD; n=7) received 30 g of standard commercial pellets, and another group (same gender and age - Control; n=8) received 120 g of the same pellets daily (PROVIMI, Stara Zagora, Bulgaria - energy content 2648.38 kcal/kg; crude protein 19%; fat 3.3%; carbohydrates 29.8%). The animals were housed in individual stainless steel cages (size 40/60

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cm) under light cycle conditions (12h:12h) at 22±2^0 C and had free access to tap water. The chow was removed 12 h before the experiments. All tests and measurements were performed in the morning hours (08.00-11.00 h). Guide for the care and use of laboratory animals (8) were followed and our institutional Ethical Committee approved the study protocols.

At the end of the feeding procedure we measured blood glucose levels in animals of both groups. Then we administered 15 μl /kg epinephrine as intravenous bolus to all animals in both groups. Again, we measured blood glucose levels in each animal, using the Glucomer Elite (Bayer®). The animals continued feeding for additional 72 h and then were sacrificed by haemorrhage under urethane narcosis. Cryostat sections for histochemical glycogen determination (PAS reaction) were prepared from the liver tissue.

Statistical comparison between the two groups was performed by means of unpaired Students t-test. Non-parametrical Wilcoxon signed rank test for paired comparison between pretest and posttest blood glucose was performed in both groups. Variations were considered statistically significant when $p < 0.05$.

RESULTS

Despite equal initial physiological states, rabbits after the diet VLCD had significantly lower body weight (3534 g±220) than Control group (4374 g±163; p=0.00001). Significant reduction in glycogen content of the liver, heavier around central vein than in periphery was found in hepatocytes from VLCD compared to Control (**Figure 1**). In both groups epinephrine caused a significant increase in blood glucose 1 h after its application. Despite blood glucose in VLCD increased from 7.28 mmol/l±1.20 to 8.8 mmol/l ±1.89 (p=0.025), and in Control this increment was from 7 mmol/l ±0.97 to 9.38 mmol/l ±1.32 (p=0.0005); blood glucose levels between both groups did not differ significantly before (p=0.65) and an hour after epinephrine infusion (p=0.53).

DISCUSSION

Our experiment confirmed pre-existing expectations that VLCD reduced significantly body weight and glycogen storages but despite heavy calorie restriction some glycogen storages still persisted. The glycogen localization was supposed to be of alimentary origin. Obviously, VLCD decreased significantly gluconeogenetic ability of the liver but the glucose uptake from the liver was probably increased in peripheral hepatocytes, which absorb almost fully glucose from portal circulation and prevent glucose uptake from central hepatocytes. Thus we suppose an existence of a physiologic mechanism for preservation of minimal quantities of glycogen in case of heavy calorie restriction. Maybe during starvation this mechanism helps glycogenolysis and liver glucose production in acute stress responses. The nature of the supposed mechanism is not clear but it has obvious advantages for stress reactivity in nature. For medical practice the glycogen saving mechanism in VLCD prevents patients from heavy hypoglycaemia but the exhaustion of liver glycogen depots proposes that VLCD should be accompanied with limited physical activity to prevent full glycogen exhaustion.

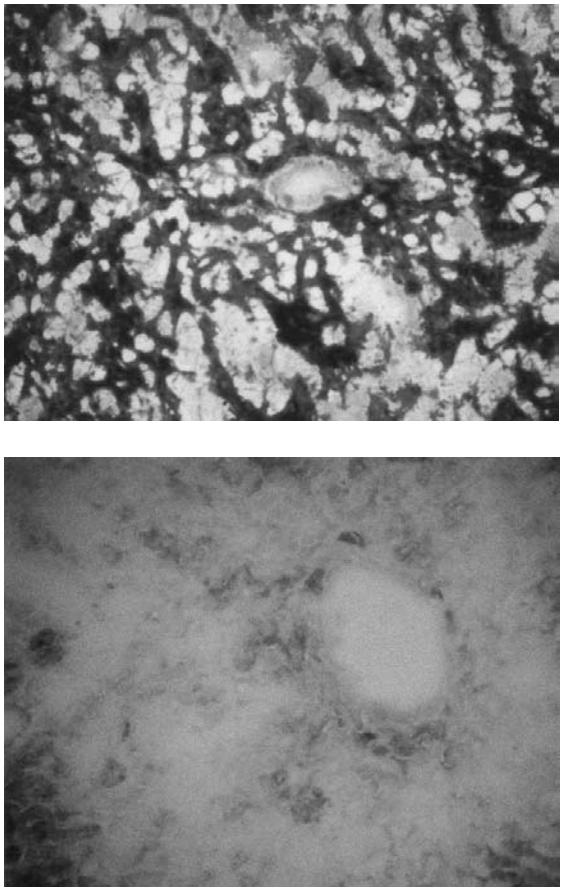

Figure 1: *The glycogen content in the liver (a – Control; b – VLCD)*

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