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EFFECTS OF THE USE OF HUMAN CHORIONIC GONADOTROPHIN ON THE METABOLIC PROFILE OF WISTAR RATS

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ABSTRACT

The modifications in the lifestyle have led to the increase in the number of overweight and obesity worldwide. Many are the medications, supplements or other products that promise a fast and easy weight loss and the use of Human Chorionic Gonadotrophin (HCG) is becoming very popular with this purpose. For these reasons, this study aimed to evaluate the effects of HCG on the metabolic profile, or Wistar rats fed a hypercaloric diet. Twenty male Wistar rats were treated with a hypercaloric diet and water *ad libitum* for four weeks. After this period, the animals were divided in, G1 that was treated with hypercaloric diet *and* water *ad libitum* for more four weeks; and G2, that was treated with hypercaloric diet water *ad libitum* for more four weeks and received 0.01mL of HCG (intraperitoneal route) for five consecutive days. Evaluation of body weight, visceral fat, glycemia, total cholesterol (TC), triglycerides (TG), Very Low-Density Lipoprotein (VLDL-c), High-Density Lipoprotein (HDL-c) (mg/dL), and atherogenic indices were performed. Our results showed that there was lower weight gain among the animals that received the HCG when compared to the control. However, no changes were observed in the food intake, lipid and glycemic profile of these animals. We may conclude that, although our results show some beneficial effects of HCG on the percentage of weight gain in the animals, no other favorable effects were observed. We suggest caution in the use of this medication because of the possible development of adverse effects.

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INTRODUCTION

The modifications in the lifestyle is a pattern observed in modern societies worldwide and have to lead to the increase in the number of overweight and obesity that have reached epidemic proportions. In many countries, such as Brazil and United States, the percentage of overweight and obesity affect more than half of the population.

The consequences of this condition include several health problems and relevant costs for the health systems (McLaughlin *et al.*, 2017; Krishna *et al.*, 2017; WHO, 2017; Umer *et al.*, 2017). The worrying scenario of obesity reaches children, adults and the elderly in all different income per capita. Concomitantly with the increasing of this health problem, there is a growing quest to achieve beauty standards, which are constantly changing, whether to fit a trend or to

adhere to a current physical biotype (Assunção *et al.*, 2017; Visser *et al.*, 2017). This dissatisfaction with the body weight leads many young people to insist on "easy" diets influenced by propaganda, by artists and individuals with sculptural bodies. The rapid weight loss resulting from unbalanced diets also encourages the desire to lose weight at any price. In view of this desire, diets with endogenous hormones have been used. These drugs normally are closely related to the metabolism, energy expenditure and appetite, promising fast results. One of these substances includes the Human Chorionic Gonadotrophin (HCG) (Will *et al.*, 2017; Rastogi *et al.*, 2017). HCG is a hormonal glycoprotein (38-kDa) produced by the syncytial trophoblastic cells in the placenta during pregnancy. It is the only hormone exclusive to this phase, conferring high accuracy in the diagnosis of gestation. Its main function is to maintain the *corpus luteum* that is responsible for assisting fetal development in the ovary during the first trimester of pregnancy. A second characteristic of the endogenous HCG is to ensure the supply of glucose to the fetus being, guaranteeing its development (Yang, Chien, Lin, 2017; Rastogi *et al.*, 2017; Thellesen *et al.*, 2014). Despite the lack of scientific evidence and security, it is noted that many young people have been using HCG to lose weight quickly. Therefore, the use of this method has gained prominence in the Brazilian media and has recently been used and indicated by physicians who believe in its power of losing weight. This use leads to an urgency of developing well-controlled studies to determine the effects of this hormone in weight loss and other biochemical parameters. For these reasons, this study aimed to evaluate the effects of HCG on the metabolic profile, or Wistar rats fed a hypercaloric diet.

METHODS

Group of Animals and Ethical Principle

This study was approved by the Animal Research Ethics Committee of the Medical School of Marilia (UNIMAR), Marília – São Paulo, Brazil. Twenty male Wistar rats (*Rattus norvegicus*), weighing 100g to 120g, were obtained from the Animal Experimentation Center - University of Marilia (UNIMAR), Marilia – São Paulo, Brazil. Seven days before the beginning of the experimental protocol, all the animals were acclimated to the laboratory conditions and were housed in plastic boxes at controlled room temperature (20°C to 25°C) and light/dark cycle of 12 hours. The males of the two groups were treated with a hypercaloric diet and water *ad libitum* for four weeks. After these four weeks, the animals were divided in G1 (n=10) and G2 (n=10) according to:

G1: Group treated with hypercaloric diet *and* water *ad libitum* for more four weeks;

G2: Group treated with hypercaloric diet water *ad libitum* for more four weeks and received 0.01mL of HCG (intraperitoneal route) for five consecutive days, a pause of 2 days and again the same process (The HCG was maintained in dilution in physiological saline and kept refrigerated). The weight of the animal and the consumption of rat feed and water were performed three times a week for the evaluation of the percentage of weight gain.

Hypercaloric diet

The hypercaloric diet was manufactured by mixing commercial rat feed and condensed milk (395g of condensed milk/500g of rat feed). This mixture was remodeled, pelletized and dried (65 ° C) for 6 hours. Each 20 g of the condensed milk contains 11 g of carbohydrates, 1.4 g of proteins and 1.8 g of lipids, totaling a caloric content of 85 grams. This product is widely used in Brazil and many countries as the composition of cakes, candies and other confectionery products.

Blood collection

At the end of the experimental protocol, the rats were anesthetized with thiopental (200mg/kg). After death, blood samples were collected to evaluate the biochemical profile: glycemia, total cholesterol (TC), and triglycerides (TG), Very Low Density Lipoprotein (VLDL), and Low Density Lipoprotein (LDL) (mg/dL).

Atherogenic Index

Atherogenic Index (AI), Atherogenic Coefficient (AC), Cardiac Risk Ratio 1 (CRR1), Cardiac Risk Ratio 2 (CRR1), and non-HDL-c levels were calculated according to AI = log (TG/HDL-c); AC = (TC – HDL-c)/HDL-c; CCR1 = TC/HDL-c; non-HDL-c = TC – HDL-c (Munshi *et al.*, 2014; Ahmadvand *et al.*, 2016; Ikewuchi, 2012).

Statistical analysis

For the Statistical analysis, ANOVA and T Student test was performed. Variables were shown as a mean and standard deviation, adopting a 5% level of significance.

RESULTS

Significant changes were observed in mean weight gain in animals before and after treatment (p=0,035) (Figure 1).

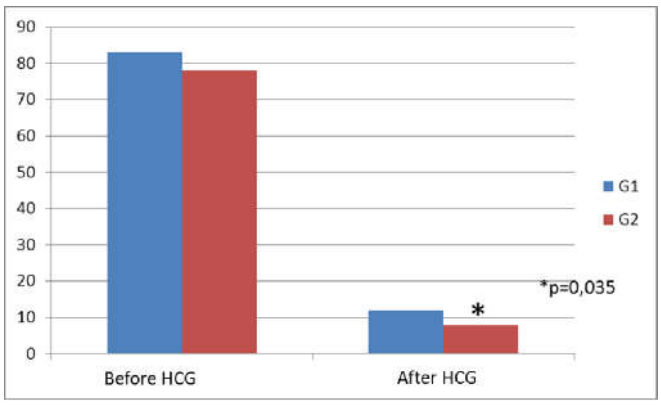

Figure 1. Weight gain in the animals of Control Group (G1) and in the treated group (G2) before and after the use of HCG

Table 1 shows that there were no significant modifications in results for the biochemical parameters after the use of HCG.

Table 1. Biochemical parameters of the animals of the the control group (G1) and the group treated with HCG (G2) at the end of the experimental protocol

Parameter	G1	G2	p-value
Glucose	291.4±81.32	316.22±137.90	0.32
Cholesterol	62.9±7.29	62.56±8.00	0.46
Triglycerides	155.3±43.09	189.33±64.74	0.10
HDL-c	39.7±5.66	38.78±608	0.37
Non-HDL-c	23.3±7.23	21.4±8.32	0.61

HDL-c: High-density lipoprotein; VLDL-c: Very Low-density lipoprotein; LDL-c: Low-density lipoprotein; Non-HDL-c: non-HDL- cholesterol.

No significant differences were found for the visceral fat between the groups after the use of HCG (Figure 2).

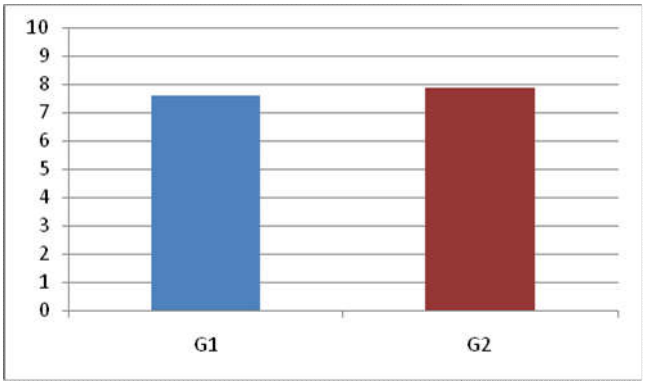

Figure 2. Visceral fat before and after the use of HCG in the Control Group (G1) and the group treated with HCG (G2).

No significant differences were found for the intake between the groups before and after the use of HCG (Figure 4).

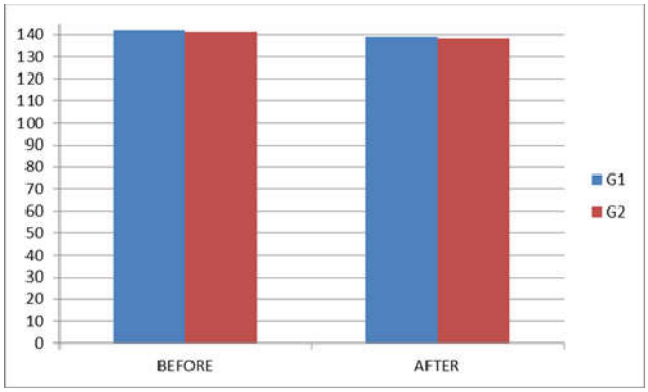

Figure 3. Ingestion of food before and after the use of HCG in the Control Group (G1) and the group treated with HCG (G2).

Table 2 indicates that there were no significant differences in atherogenic indices for the groups. Table 2. Atherogenic Coefficient (AC), Atherogenic Index (AI), and Cardiac Risk Ratio 1 (CCR1) of the animals of the control group (G1) and group treated with HCG (G2).

Parameter	G1	G2	p-value
AC	0.55±0.20	0.60±0.12	0.50
AI	0.56±0.18	0.66±0.22	0.22
CCR1	0.44±0.13	0.37±0.18	0.44

AC = (TC – HDL-c)/HDL-c; AI = log (TG/HDL-c); CCR1 = TC/HDL-c and

DISCUSSION

Despite the concern of the population with the physical biotype, the overweight or obesity is far from being only an aesthetic problem, but it is a pathology that requires treatment once it is related to several comorbidities. The control of the body weight may improve biochemical parameters and, for this reason, may avoid several illness conditions such as cardiovascular diseases that are among the major death causes worldwide (Yao *et al.*, 2017; Muredda *et al.*, 2017; McCuen-Wurst *et al.*, 2017).

We have observed a recent revival of losing weight based on the use of HCG. This hormone is produced during the pregnancy and as pointed before, has specific purposes in this condition. Normally, β-HCG levels are linked to raising in germ cell tumors. As a drug, it may be used in the treatment of infertility or to induce endogenous testosterone and anabolism in men, but there are no substantial or conclusive studies associating its use with weight loss. The "HCG Diet" is advertised in several and leading to the main global application of therapeutic HCG besides the risk of developing some kinds of cancer. (Wong *et al.*, 2016; Butler, Cole, 2016; Cunningham, 2010). Formulations of HCG preparations vary in purity. Dietary HCG supplement may be found as pills or nasal drops, and authors have questioned if these preparations of the hormone have enough, very little or no immunological action. Another issue is if this different kind of administration, would reach the blood and promote the desirable effects (Butler, Cole, 2016).

Our results showed that there was lower weight gain among the animals that received the HCG when compared to the control (both treated with a hypercaloric diet), indicating that this hormone may affect the weight control of Wistar rats. However, no changes were observed in food intake, lipid and glycemic profile of these animals. The lipids in the circulation play a major role in the prevention of cardiovascular diseases and, for this reason, these molecules are important targets for decreasing the development of cardiac risks. In abnormal conditions, it is observed low levels of HDL-c levels and increased levels of total cholesterol, triglycerides, and LDL-c. This scenario increases the risk of hypertension, metabolic syndrome, and cardiovascular complications. Elevated levels of blood glucose are also associated with this increased risk of cardiac complications. There is a tight link of hyperglycaemia and the production of oxidative species and increase in the inflammatory processes (Li *et al.*, 2017; Hernandez-Perez *et al.*, 2017; Ornellas *et al.*, 2017; Wang *et al.*, 2017). Nevertheless, in our study, the use of HCG did not bring improvements in these biochemical parameters.

The evaluation of the atherogenic indices showed that no differences were produced with the use of HCG. The indices increase the chances of developing coronary heart disease. Conditions such as inflammation and oxidative stress may also increase the atherogenic indices. The overweight/obesity are known as low chronicle inflammation process that may be related to several other disorders such as diabetes, metabolic syndrome, hypertension, and cancer. (Muredda *et al.*, 2017; Stolarczyk *et al.*, 2017; Moghadam *et al.*, 2016; Munshi *et al.*, 2014). Further studies should be performed evaluating long term effects of HCG in order to recommend this hormone to treat obesity or overweight. As its use may be related to the development of cancer, authors have suggested that preparations with this hormone need to be submitted to a very tight control (Butler, Cole, 2016).

Conclusion

Although our results show beneficial effects of HCG on the percentage of weight gain in the animals treated with a hypercaloric diet, no other favorable effects were observed in the abdominal fat and the biochemical parameters. We suggest caution in the use of this medication because of the possible development of adverse effects.

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