METABOLIC ACTIVITY OF HUMAN CHORIONIC GONADOTROPIN (hCG) ON GLYCEMIA AND LEPTINEMIA IN CAFETERIA-FED DIET EXPERIMENTAL ANIMALS

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OBJECTIVE: The goal was to determine the modifications in plasmatic levels of adiponectins, glucose, and leptins in rats previously overfed with cafeteria diet. They were afterwards submitted to a hypocaloric diet combined with daily administration of either enteral or parenteral formulations of rhCG (recombinant) or uhCG (urinary) human Chorionic Gonadotropin (hCG).

Groups: 42 animals were selected for the study, and sorted as follows:

Group 0: control group.
Groups 1 to 6: fed with a hypercaloric and highly palatable cafeteria diet, as opposite to animals from group 0 which continued with standard laboratory diet.

- The amount of food provided with this diet was "ad libitum" and extended for a period of 45 days.
- After the fattening period, animals in group 1 to 6 were subjected to a restricted diet consisting in one-third of the average daily intake of balanced food for rats, calculated separately for both males and females.
- During the overfeeding period rats from groups 1 to 6 (group 0: standard diet) gained an average of 30% of their initial body weight. Thereafter, animals from groups 1 to 6 were administered a hypocaloric diet. Group 0 continued with standard diet.
- Animals in groups 2 to 6 received different hCG formulations – either urinary or recombinant – on a daily basis via intramuscular or intrarectal administration routes.

hCG administration: hCG was administered as follows during the five treatment weeks:

Group 0 did not receive any medication or diet, and continued with the standard diet throughout the course of the study.

Group 1 was submitted to a **hypocaloric diet, without hCG administration.**

Group 2 was submitted to a **hypocaloric diet** and received **125 International Units (IU) of hCG (urinary,** Massone Laboratories, Argentina) dissolved in normal saline (NaCl 0.9%), administered **intramuscularly,** daily, including Sundays (Injectable A).

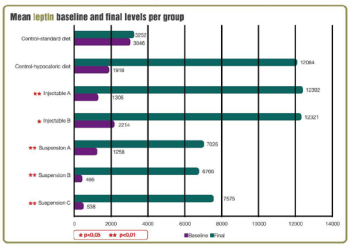
Group 3 was submitted to a **hypocaloric diet** and received **125 IU of r-hCG (Recombinant,** Ovidrel, Serono Laboratories) dissolved in normal saline (0.9% NaCl) administered **intramuscularly,** daily, including Sundays (Injectable B).

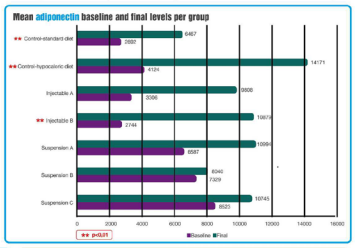
Group 4 was submitted to a **hypocaloric diet** and received **300 IU of hCG (urinary,** Massone Laboratories, Argentina) in **intrarectal emulsion containing 8 mg/ml of cyclodextrin** as enhancer, daily, including Sundays (Intrarectal Suspension A).

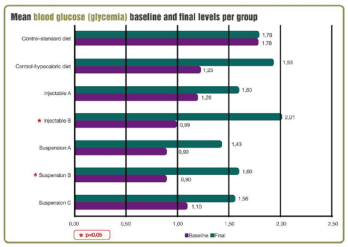
Group 5 was submitted to a **hypocaloric diet** and received **300 IU of hCG (urinary,** Massone Laboratories, Argentina) in **intrarectal emulsion containing 16 mg/ml of cyclodextrin** as enhancer, daily, including Sundays (Intrarectal Suspension B).

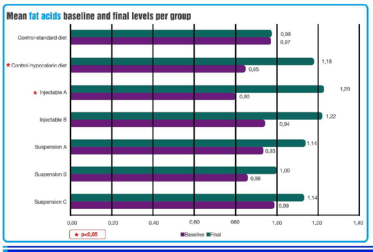
Group 6 was submitted to a **hypocaloric diet** and received **300 IU of r-hCG (Recombinant,** Ovidrel, Serono Laboratories) as **intrarectal emulsion containing 8 mg/ml of cyclodextrin** as enhancer, daily, including Sundays (Intrarectal Suspension C).

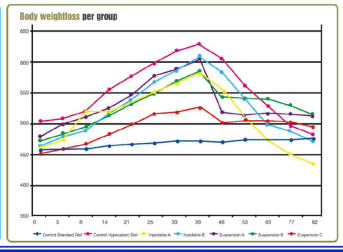
Assessments: Body weight determinations, as well as plasmatic glucose, adiponectin, leptin and non-esterified fatty acids (NEFA) determinations were assessed.











Leptin plays a key role in the regulation of energy metabolism. Serum leptin levels are increased in obesity in proportion to the amount of body fat. In disorders such as overweight and obesity, is found elevated in plasma, suggesting that resistance to its action determines an impairment of the regulation of adipose tissue metabolism.
Weight gain also determines the presence of hyperglycemia, a metabolic situation that clearly aggravates the underlying pathology (obesity).Selective leptin resistance contributes to obesity related hypertension and also contribute to other metabolic complications in obesity.

RESULTS

LEPTINS

At the end of the study, **leptinemia** levels were significantly higher in Control group: decreased in the group under hypocaloric diet and more noticeably in animals who received hCG.
1. The group treated with intrarectal Suspension B achieved the lowest values (analysis per dose).
2. The group treated with Injectable A/Intrarectal Suspension A/Intrarectal Suspension B groups displayed the lowest levels (analysis of the formulation).
3. Intrarectal Suspension A/B/C groups displayed the lowest levels (analysis of the pharmaceutical formulation).
No significant differences were observed between groups that did not receive hCG.

GLYCEMIA

At the end of the study, treated groups displayed lower significantly values, with lowest mean values in:
4. Animals treated with Intrarectal Suspension B (analysis per dose).
5. Animals treated with Injectable A/Intrarectal Suspension A/Intrarectal Suspension B (analysis of the formulation).
6. Animals treated with Intrarectal Suspension A/B/C (analysis of pharmaceutical form).

CONCLUSIONS

Experimental animals previously submitted to fattening cafeteria diet displayed a significant reduction on **glycemia and leptinemia** levels after of either enteral or parenteral hCG administration.
We conclude hCG may be considered a therapeutic approach for those pathologies associated with hyperglycemia and hyperleptinemia, such as obesity, type 2 diabetes and metabolic syndrome.
Regarding weightloss, no significant differences were observed in all tested groups.
No adverse pathologic events were observed even with the supraphamacological doses administered (up to 400 times the dose/kg of body weight administered in humans).
As far as we know, this is the first report demonstrating the enteral absorption and metabolic activity of either urinary (uhCG) or recombinant hCG (rhCG) on several plasmatic determinations related to obesity and its comorbidities.