ROLE OF GHRELIN ON NITRIC OXIDE SECRETION AND IMPLANTATION IN MICE.

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During pregnancy maternal a Ghrelin (Ghr) concentration increases significantly, suggesting an important role of the peptide on the process. The objective of the present study was to evaluate the role of Ghr on implantation and nitric oxide (NO) secretion, a metabolite that is essential for placenta formation and function.

It was evaluated: 1) parameters related to implantation in pregnant female mice injected (s.c.) from Day 3 to Day 7 (peri-implantation period) with: Ghr (4 nmol/animal/day), an antagonist (Ant (D-Lys3)GHRP-6, 6 nmol/animal/day), a combination of both (Ghr+Ant) or isotonic solution (control); 2) the nitrite concentrations in the supernatant of pregnant female uterus (Day 8) incubated in a medium with arginine (for 1 h), with or without Ghr (10^{-9}M) and/or Ant (10^{-4}M). Results were analyzed by two-way ANOVA or repeated measures ANOVA respectively.

In experiment 1, not only hyperghrelinemia (Ghr group) but also endogenous Ghr inhibition (Ant group) decreased fetal weight (at gestation Day 18) and mothers weight gain during pregnancy. Ghrelin increased the percentage of embryo loss (Ghr=17.3±6.58 and Ghr+Ant=13.3±3.7 vs control=3.9±4.8 and Ant=6.7±4.0; n=9-12 females/group; p=0.045); Ghr and Ant augmented fetal atrophy (Ghr=71.4%, Ghr+Ant=44.4% and Ant=62.5% vs control=0%; n=7-10 females/group; p<0.01). In experiment 2, the addition of Ghr and/or Ant to the culture medium did not modify supernatant nitrite concentrations (22.5±1.1 µM, n=20). Experiments are actually being performed in order to evaluate nitrite concentration in uteri of pregnant females (Day 8) treated in vivo from Day 3 to Day 7 with Ghr and/or Ant.

These results suggest that Ghr has an important role on embryo implantation; nevertheless, do not support the hypothesis that the deleterious effects of hyper or hipoghrelinemia are associated to modification in NO secretion.