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P-575 Application of biomarkers in obese infertile women: a genetic tool for a personalized treatment

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Study question: Investigate CART and Leptin gene expression, FSH Receptor Asn680Ser polymorphism, and reproductive hormones in patients suffering from obesity under 40, facing infertility, undergoing bariatric surgery.

Summary answer: The present study proposes that variations in CART, leptin expressions, and the Polymorphism Asn680Ser on the FSH Receptor, may influence the response to IVF treatment.

What is known already: Obesity, presents a multifaceted challenge with profound implications for fertility, particularly concerning hormonal disruptions in reproductive hormones. Research has shown that Asn680Ser polymorphism of FSH Receptor has a pivotal role in infertility. Notably identified as a singular factor sufficient for infertility, this polymorphism influences the response of the FSH receptor to follicle-stimulating hormone (FSH). Leptin activates the expression of CART neuropeptide, indicating a significant interplay between these two regulatory factors. In ovarian granulosa cells (GCs) of obese patients, elevated CART levels have been observed, with leptin stimulation increasing CART expression and subsequently inhibiting GC aromatase expression and steroidogenesis.

Study design, size, duration: A total of 29 women were included in the study. An hormonal profile along with a detection of CART and Leptin gene expression was evaluated before and after bariatric surgery. Additionally, the presence or absence of Asn680Ser of FSHR gene was studied.

Participants/materials, setting, methods: Participants had suffer from obesity and experiencing infertility, with a body mass index (BMI) equal to or greater than 40 kg/m². Only women below 40 were included. Blood samples were collected from all women before surgery and 6 months later. Total RNA was extracted from blood samples. To assess the gene expression of

Leptin and CART, we utilized Real-time Polymerase Chain Reaction (RT-PCR). The FSHR polymorphism was detected by using the RFLP method.

Main results and the role of chance: Following bariatric surgery, a mean reduction in BMI (16.03 kg/m²) was observed in all women, reaching high statistical significance ($p < 0.001$). The intervention also yielded significant differences ($p < 0.001$) in hormone levels and gene expressions post-surgery, with FSH, LH, E2, and AMH displaying noteworthy variations. Further investigations explored associations between CART and leptin gene expression before and after the intervention, coupled with the detection of the Polymorphism Asn680Ser on the FSH Receptor. Elevated CART expression before treatment correlated with lower expression after treatment ($r_s = 0.51$, $p = 0.005$), and a similar significant correlation was noted for leptin ($r_s = 0.75$, $p < 0.001$). Genetic analysis revealed that 27.6% of patients were homozygous for the polymorphism, 44.8% were heterozygous, and it was absent in 27.6%. An ongoing statistical analysis is realized to establish a potential relationship between the presence/absence of the polymorphism and CART and Leptin expression.

Limitations, reasons for caution: The study's limitations encompass a small patient cohort, exclusively pre- and post-bariatric surgery assessments. Expanding the sample to include diverse groups—infertile women with lower BMI and high BMI women without fertility issues—would enhance validity. Furthermore, examining gene expression in all participants one year post-surgery could provide valuable insights.

Wider implications of the findings: Our results underscores the positive impact of bariatric surgery on BMI decrease and possible link between surgical intervention, genetic markers, and hormonal alterations and consequently with infertility issues. These significant correlations may be applied for personalized therapeutic approaches, offering a valuable genetic tool for improved fertility outcomes in obese individuals.

Trial registration number: not applicable