

## Effects of gastric bypass surgery and weight loss on fertility of morbidly obese patients. Early case series

Efeitos da cirurgia de bypass gástrico e da perda de peso na fertilidade de pacientes com obesidade mórbida. Série inicial de casos

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### ABSTRACT

**Purpose:** The aim of this study was to assess initial outcomes of effects of large weight loss after gastric bypass surgery on male fertile profile. **Methods:** Eight male morbidly obese were submitted to Roux-en-y gastric bypass and assessed before and six months after the procedure with hormonal reproductive dosage and seminal analysis both compared with the BMI. The hormonal profile consisted in total testosterone (TT), follicle-stimulating hormone (FSH) and luteinizing hormone(LH). The points examined in seminal analysis were sperm concentration in million/ml and motility. **Results:** The results did not appoint to the perfect correlation of weight loss and seminal analysis. Otherwise, the sharp weight loss was responsible for the increasing on the TT levels in all patients submitted to the surgical treatment. No differences were observed on FSH and LH levels. **Conclusions:** Weight loss can improve the reproductive hormone profile, but this study showed that a greater number of cases to make the analysis more robust is need.

**Key words:** Gastroplasty. Roux-en-Y gastric bypass. Bariatric surgery. Male infertility. Testosterone. Morbid obesity.

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## RESUMO

**Objetivo:** O objetivo deste estudo foi avaliar os resultados iniciais de efeitos da perda de peso após cirurgia do bypass gástrico no perfil da fertilidade masculina. **Métodos:** Oito homens obesos mórbidos submetidos a bypass gástrico em Y de Roux foram avaliados antes e seis meses após o procedimentocirúrgico com a dosagem hormonal reprodutiva e análise seminal, em comparação com o IMC. O perfil hormonal consistiu na dosagem de testosterona total (TT), hormônio folículo-estimulante (FSH) e hormônio luteinizante (LH). Os pontos analisados na análise seminal foram a concentração de espermatozóides em milhões/ml e motilidade. **Resultados:** Os resultados não apontaram para a correlação perfeita de perda de peso e análise seminal. Entretanto, a perda de peso acentuada foi responsável por valores crescentes nos níveis de TT em todos os pacientes submetidos a tratamento cirúrgico. Não foram observadas diferenças nos níveis de FSH e LH comparando-se o pré e o pós-operatório. **Conclusões:** A perda de peso após cirurgia bariátrica pode melhorar o perfil hormonal reprodutivo. Para se conseguir uma análise mais acurada torna-se necessário o estudo de maior número de casos.

**Descritores:** Gastroplastia. Roux-en-Y bypass gástrico. Cirurgia bariátrica. Infertilidade masculina. Testosterona. Obesidade mórbida.

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## INTRODUCTION

There is a growing concern regarding the current high rates of infertility in the general population. Male factor is present in 20% of infertile couples and additionally contributes for poor fertility in almost 30-40% of the remaining cases<sup>1</sup>. It is well documented that hypothalamic and pituitary diseases, varicocele, infectious and genetic disorders can lead to male infertility, and there is a high percentage of infertile men where no apparent cause for infertility can be identified<sup>2,3</sup>.

Recent studies have also pointed out that excessive amount and distribution of body fat is related to fertility loss in men<sup>4,5</sup>, similarly to the negative impact on female gonadal dysfunction, as extensively demonstrated in women with obesity, insulin resistance and polycystic ovary syndrome<sup>6,7</sup>. Despite the existing results, the relationship between obesity and male infertility remains controversial. Some authors suggest that obesity in men can be associated with hypogonadotropic hypogonadism, and low serum gonadotropin and total testosterone concentrations. Other mechanisms could include the obesity-associated decrease in serum sex hormone binding globulin (SHBG), the increase in estrogen circulating level through aromatization in adipose

tissue, oxidative stress, excess of circulating leptin and also the hyperinsulinemia secondary to insulin resistance<sup>8-10</sup>.

In the setting of an increasing prevalence of morbidly obese and super obese individuals<sup>11,12</sup> where there is a growing rate of surgical treatment for obesity, it is plausible to investigate the potential benefit of weight loss induced by surgical treatment on male fertility. Particularly in relation to these categories of more severe obesity, there is no accurate published data on the male fertility, as well as possible changes resulting from intense weight loss achieved with the available surgical treatment options. In this paper, the authors report a case series of morbidly obese men (body mass index > 40 kg/m<sup>2</sup>) undergoing gastroplasty, specifically focusing on the assessment of reproductive function before and after surgery, in order to establish possible effects of surgery induced weight loss on male fertility.

## **METHODS**

A prospective study was performed at the Hospital Universitário Onofre Lopes, Natal-RN, Brazil, from December, 2008 to June, 2011. The study was approved by the Institutional Ethics Committee (protocol number 240/08) and all volunteers signed an informed consent term. The inclusion criteria were: men between 18 and 40 years old and sexually active, body mass index (BMI) above 40 kg/m<sup>2</sup>, and candidates to perform surgical treatment for obesity. Initially, we selected 36 individuals who were assessed for the presence of other factors causing infertility in order to exclude possible confounding factors as infections, hyperprolactinemia, testis cancer, radiotherapy, chemotherapy, cryptorchidism and other causes not associated with obesity. A sample of eight volunteers completed the study protocol and was included in the current case series.

All patients underwent clinical examination consisting of measurement of body mass (kg), height (m), waist and hip circumferences and blood pressure measurements. The BMI was calculated by the formula weight (kg) / height<sup>2</sup> (m<sup>2</sup>) and expressed as kg/m<sup>2</sup>. In addition, urological examination was performed consisting of inspection and palpation of the genitals, with emphasis to palpation and measure of testis and look for varicocele or another special situation that could be etiology to infertility.

Venous blood samples were collected between 08:00 and 10:00h, after a 12h fasting for measurement of hormonal parameters. Levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (TT), free testosterone (FT), prolactin and estradiol were determined by chemiluminescence method, using the equipment *IMMULITE 2000* (Diagnostic Products Corporation, Los Angeles, CA, USA).

The sperm evaluation was performed in the preoperative period, and repeated after 6 months of surgical treatment for obesity, all patients operated by the same surgeon. The semen samples were collected by self-masturbation

of each man in an appropriate local at BIOS- Center of Human Reproduction in Natal- Brazil. The samples were liquefied for 60 minutes at 37<sup>0</sup>C and. After that, analyzed by an oil immersion with bright light at 1000x about sperm concentration and motility, according to World Health Organization guidelines (WHO,1999).The samples about the azoospermic man were repeated before and after the surgery.

A Roux-en-Y gastric bypass was performed in all patients who were followed postoperatively by the same multidisciplinary team. A specifically designed questionnaire was used to obtain information on variables related to clinical data, biochemical and hormonal parameters, and assessment of sperm function. The main variables considered for analysis were: BMI before and after gastroplasty, levels of reproductive hormonal parameters, and semen analysis including sperm concentration (in millions/ml) and the percentage of sperm motility of type A and B, ie, sperm that show progressive movements fast (A) and slow (B).

A literature review was conducted using the SciELO, PubMed and Web of Science databases and adopting the following keywords: gastroplasty, gastric bypass surgery, bariatric surgery, male infertility, testosterone, and morbid obesity.

## **RESULTS**

The group consisted of eight patients with a BMI ranging from 44.0 to 55.0 kg/m<sup>2</sup>. Four of them were classified as super-obese (BMI above 50 kg/m<sup>2</sup>). Table 1 summarizes the clinical and patients anthropometric data. It is observed that all patients experienced significant reduction in body weight after surgery (mean BMI 48.3 kg/m<sup>2</sup> to 35.3 kg/m<sup>2</sup>; for preoperative and post-operative periods, respectively).

**Table 1** – Individual clinical and laboratory parameters of a case series of morbidly obese men submitted to surgical treatment of obesity.

Variables	Patients							
	1	2	3	4	5	6	7	8
Preoperative BMI	50	44	53	46	46	52	50	46
Post-operative BMI	28	33	31	34	36	42	42	37
Preoperative sperm concentration (*106/ml)	38	0	0	95	15	60	0,5	60
Post-operative sperm concentration (*106/ml)	25	0	1,2	32	30	48	52	67
Preoperative sperm motility (% A + B)	20+23	0	0	25+25	20+30	28+28	0+10	25+25
Post-operative sperm motility (% A + B)	18+32	0	0	18+38	20+30	27+27	26+24	25+25
Preoperative testosterone level (ng/dL)	120	145	161	160	235	373	186	260
Post-operative testosterone level (ng/dL)	270	282	391	441	457	722	564	878
Preoperative FSH level (mIU/ml)	7,6	3,8	2,49	2,4	2,7	2,0	3,7	2,9
Post-operative FSH level (mIU/ml)	3,8	?	8,09	1,8	3,3	1,7	6,2	2,3
Preoperative LH level (mIU/ml)	8,3	4,5	4,09	4,8	4,9	2,4	3,8	5,9
Post-operative LH level (mIU/ml)	4,2	?	3,9	2,8	1,5	2,9	12,5	3,0

Before surgery, the sperm analysis was abnormal in four of eight patients. In the sixth postoperative month, 2 patients with previous abnormal sperm analysis improved their sperm parameters after weight loss induced by surgery. On the other hand, one patient (4) showed a significant reduction in sperm concentration, but without impairment of sperm motility.

Regarding the hormonal profile, we observed the increase in serum total testosterone concentration in all patients. Except for two cases (2 and 5), in all others the serum level of total testosterone more than doubled. Additionally, the serum LH level was reduced in five of seven patients analyzed.

## DISCUSSION

As obesity has assumed epidemic proportions in the world, the curiosity about anything related to the topic assumes the same proportions. Fertility now assumes a degree of importance among the complications. Studies are still recent, so that the mechanisms by which obesity affects the reproductive system are partially understood and their results are still conflicting, requiring further investigation, according to a review article<sup>13</sup>. However, the literature

points to multifactorial causes, such as: the action of aromatase produced by the adipose tissue, the involvement of changes in the endocrine hypothalamus-pituitary-gonadal axis, insulin resistance and erectile dysfunction.

The key which seems to explain the possible changes goes through hormonal changes. The total testosterone is the main involved hormone and some studies have pointed out to its elevation in cases of patients undergoing marked weight loss after gastric bypass surgery<sup>9,10</sup>. As it is known, testosterone has an important role in spermatogenesis acting at the tissue level and indirectly in stimulation of Sertoli cells that work with nurturing immature sperm cells.

The excess of adipose tissue is accompanied by increased levels of aromatase, this enzyme is responsible for converting androgens into estrogens. Increasing its activity results in hypotestosteronemia and hyperestrogenism. The estrogen derived from this peripheral conversion will act on the hypophysis by inhibiting the hypothalamic-pituitary axis, resulting in the decreasing production of gonadotropins (LH and FSH) and deficit in the gonadal stimulus. This process will result once again in the decreasing of testosterone levels, but this time due to the hypogonadismo<sup>10,11,12</sup>. This seems to be a plausible explanation for the rise of testosterone in these patients. The other hormonal findings do not seem to have yet, as shown in other studies, a clear correlation with this testosterone increase. It is known from the hypothalamic-pituitary-gonadal regulations axis that they come from them.

The main contribution of our research was to evaluate sperm before and after the gastroplasty. In 2005, di Frega<sup>18</sup> was the first and the only one who presented an initial series of cases of men who had already become father and became azoospermic after weight loss from the bariatric surgery, but without examinations.

In our analysis, we studied basically the sperm concentration and motility of A and B types. It was not possible to establish a correct profile of the trend of improvement or worsening of the default because there were variations in both directions. However, we observed that in extreme cases of infertility there was improvement and appearance of sperm in the semen sample, revealing that if it is the causative agent, it can be reverted with a proper treatment.

We have opened a search path through the seminal analysis in this specific population. We have been going on improvements in our research, but it is necessary to have more studies in the long term, and with a greater number of patients in order to find more convincing answers.

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