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Reproductive Function in Patients with Morbid Obesity after Bariatric Surgery

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Abstract

The present article examines the effectiveness of bariatric surgery in restoring reproductive health in patients with morbid obesity. The medical histories of 270 morbidly obese patients with reproductive dysfunction were studied. The patients were divided into two groups: 181 women and 89 men with a BMI of 45-65 kg/m2. The age of the operated women was 18 to 58 years; 7 patients (3.9% of the women) were in postmenopause. Of the 174 women, 45 were of childbearing age and complained of abnormal ovarian and menstrual function. The number of men was 89 persons aged from 18 to 60 years. The concentrations of hormones such as testosterone, estrogen, and progesterone were studied in the postsurgical period. The data obtained was with the initial figures. Surgical treatment of both sexes resulted in sustained positive results and improved quality of life. Due to bariatric surgery, the patients returned to normal indicators after a certain period, and their reproductive function improved. The reduction of visceral adipose tissue in patients led to the normalization of hormonal background, as evidenced by blood tests. As a consequence, the reproductive function was restored.

Keywords: Hormones, Reproductive function, Morbid obesity, Bariatric surgery

Introduction

Morbid obesity, which is widespread in modern society, leads to infertility in women and men alike (Broughton & Moley, 2017; Escobar-Morreale *et al.*, 2017). Abnormal fat deposition leads to the development of various pathologies and organ systems' malfunction. Obesity increases the content of adipose tissue in the body which can be regarded as an endocrine organ (Haghighi-Morad *et al.*, 2019; Mahassni & Bashanfar, 2019). The processes of transformation of substances occur with a developed network of capillary vessels in adipose tissue. As a result, the hormonal background of the body is changed and its endocrine regulation is disturbed. Obesity has a detrimental effect on the female reproductive system, disrupting the ovarian-menstrual cycle and reducing reproductive function (El Bardisi *et al.*, 2016; Luyssen *et al.*, 2018; Al-Nimr *et al.*, 2019). Progesterone deficiency affects the luteal phase, which can interfere with pregnancy (Escobar-Morreale *et al.*, 2017; Kjær *et al.*, 2017; Costa *et al.*, 2018). Male obesity is now a risk factor for erectile dysfunction, resulting in poor reproductive function. The well-vascularised adipose tissue in the male body enhances the transformation of testosterone into estrogen. As a result, the concentration of the main male sex hormone decreases. This affects spermatogenesis and the physical development of the patient (Aleid *et al.*, 2017; Escobar-Morreale *et al.*, 2017; Costa *et al.*, 2018). Gynecomastia, prostate diseases, and secondary hypogonadism are not uncommon. A strict thermal regime is required for various body processes. A deposit of fat can lead to an increase in temperature in the scrotum. This leads to the disruption of spermatogenesis. Besides, adipose tissue produces leptin and TNFα, which harm male sexual function (Mingrone & Cummings, 2016; Best *et al.*, 2017). To restore the fertility of patients, it is advisable to decrease their weight by reducing the amount of adipose tissue in the body. There are many ways to achieve this, but bariatric surgery is of particular interest because it has several important advantages: high efficiency, irreversible weight loss, and long-lasting results. After surgery, the patient's weight can be significantly reduced, and hormone levels can be restored (Autlev *et al.*, 2013; Makhmud, 2015; Cobourn & Dixon, 2016; Edison *et al.*, 2016; Barker *et al.*, 2018; Jakobsen *et al.*, 2018).

The Objective

To study the efficiency of bariatric surgery for the restoration of reproductive health in morbidly obese patients.

Materials and Methods

The medical histories of 270 morbidly obese patients with reproductive dysfunction were studied. The patients were divided into two groups: 181 women and 89 men with a BMI of 45-65 kg/m2. The age of the operated women was 18 to 58 years; 7 patients (3.9% of the 181 patients) were in postmenopause. Of the

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174 women, 45 were of childbearing age and complained of ovarian-menstrual dysfunction. The number of men was 89 patients aged 18 to 60 years **(Table 1)**.

Table 1. Medical history of patients with morbid obesity and reproductive dysfunction

	Groups:	State of reproductive function
N=270	1. 89 men aged 18 to 60 years	
270 patients (BMI 45-65 kg/m2)	2. 181 women aged 18 to 58	7 patients (3,9%) in postmenopause (n= 181)
		45 patients (25,9%) in childbearing age (n = 174)

In the postoperative period, the hormone concentrations of testosterone, estrogen, and progesterone were studied. The obtained data were compared with the initial figures. The patients were treated by bariatric surgery methods (biliopancreatic diversion (BPD), longitudinal gastric resection (LGR), and adjustable gastric banding (AGB). For objective evaluation of the results, the patients underwent blood tests for hormones, and the physiological state of the reproductive system was examined. Measurements were taken before and after surgical intervention after a certain period. Patients were divided into two main groups: group 1 — BMI 45 to 54.9 kg/m2, group 2 — BMI 55 to 65 kg/m2. In group 1, 62 patients underwent BPD, 68 patients underwent AGB, and 36 patients underwent LGR. Patients were followed up for five years after the surgical interventions, with one year of monitoring the preoperative and postoperative laboratory values. In group 2, 38 patients underwent BPD, 32 patients underwent AGB, and 34 patients underwent LGR. An electrochemiluminescence immunoassay (ECLIA) method was used to determine estradiol and progesterone concentrations using automated analyzers. The measuring range for progesterone was 0.095-191.0 nmol/l and for estradiol 18.4-15,781 pmol/l. Testosterone hormone concentrations were determined using the Elecsys Testosterone II test system, based on a competitive monoclonal antibody assay. The test system is capable of calculating the testosterone concentration in each sample (optionally in ng/ml, ng/dl, or nmol/l). The measurement range was 0.087-52.0 nmol/l. Timing of blood processing and delivery to the laboratory is following GOST R 53079.4-2008. Statistical software and Microsoft Excel were used to statistically process the research results. Quantitative indicators with an asymmetrical distribution were assessed using the median and percentile. For parametric normally distributed indicators, the arithmetic mean and standard deviation were used. Spearman's method for calculating the correlation coefficient (r) and significance level (p) was used to describe the statistical relationship between quantitative or qualitative characteristics. Mann-Whitney's test was used to compare two independent groups. Wilcoxon's test was used to compare two dependent groups for a quantitative or qualitative feature with a level of statistical significance ($p<0.05$; $p<0.01$; $p<0.001$).

Results and Discussion

The hormones tested in patients control the reproductive system. Oestradiol is a hormone that controls many processes in the female body. Progesterone is responsible for initiating the development of endometrial tissue, thereby, regulating the ovarian-menstrual cycle. Low doses of testosterone may be present in the female body, but its increase may indicate the development of a pathological process (Cobourn & Dixon, 2016; Costa *et al.*, 2018; Fleming *et al.*, 2018). Symptoms of ovarian-menstrual cycle disorders can be divided into three groups **(Table 2)**.

Table 2. Ovarian-Menstrual Cycle Disorders

Patients of childbearing age (n=45)		
Cycle more than 35 days	Lengthening the menstrual cycle	The presence of menorrhagias
39 (87%)	34 (76%)	14 (31%)
Cycle normalization	Normal menstrual bleeding duration	Disappearance of menorrhagias
36 (92% от n=39)	31 (91% от n=34)	11 (79% от n=14)

First, patients in whom the cycle lengthens more than 35 days (39 patients — 87% of the group). Second, women patients whose menstrual cycle becomes longer than 6 days because they are overweight (34 patients — 76% of the group). Women in the third group suffer from menorrhagia (14 patients — 31% of the group). The following signs of clinical improvement in the reproductive system were found. Thirty-six patients (92%) had normalization of cycle length. Thirty-one patients (91%) reported a return to normal menstrual bleeding duration. In the last group, menorrhagia disappeared in 11 patients (79%). The treatment led to the normalization of hormone concentrations. The values of oestradiol decreased to 462±128.4 pmol/l after a year of the postoperative period ($p<0.01$). Similarly, testosterone levels decreased to 0.89±0.71 nmol/l ($p<0.01$). Progesterone content increased to 43±8.3 nmol/L ($p<0.01$). In 89 male patients with morbid obesity, there was an abnormal sex hormone background in the form of hypostosteroneemia to 5.34±1.91 nmol/l, hypoprogesteroneemia 0.12±0.09 nmol/l, and hyperestrogenemia 278±53.8 Pcmol/l. At the laboratory examination a year after surgery, the values were as follows: 1.53±0.92 nmol/l to 5.34±1.91 nmol/l ($p<0.01$). Similarly, progesterone increased from 0.12±0.09 nmol/l to 2.31±0.83 nmol/l ($p<0.01$). Importantly, oestradiol, a product of testosterone aromatization and the female sex hormone, decreased significantly, amid a decrease in adipose tissue in the patients. Initially, the oestradiol concentration was 278±53.8 Pcmol/l, the hormone content decreased to 72.3±21.2 Pcmol/l ($p<0.01$). Surgical treatment of both sexes resulted in lasting positive results and improved quality of life (Dirinck *et al.*, 2016; Donkin *et al.*, 2016; Aleid *et al.*, 2017; Moslehi *et al.*, 2017). Due to bariatric surgery, female patients returned to normal indicators after a certain period, and reproductive function was also restored (Edison *et al.*, 2016; Chiofalo *et al.*, 2017; Milone *et al.*, 2017; Reinehr *et al.*, 2017). Reducing visceral adipose tissue in patients resulted in the normalization of hormonal levels, as shown by laboratory blood tests. As a consequence, the reproductive function was restored. This is demonstrated by the normal duration of the

ovarian menstrual cycle and the elimination of menorrhagia. The surgeries also had a positive effect on the health of male patients. The improvement in reproductive function can be judged by the concentration of hormones in the blood. In the male body, a significant proportion of estrogens is formed as a result of testosterone aromatization. Thus, the synthesis and metabolism of these hormones are closely linked, and they have a joint effect on the regulation of processes in the body. An overabundance of female hormones in men affects reproduction and redistributes body fat, as well as leads to gynecomastia and prostate diseases. Progesterone is normally synthesized in small quantities but has a significant effect on the body. Changes in hormone concentrations in patients as a result of bariatric surgery show their high efficacy. The normalization of the duration of the ovarian-menstrual cycle was observed in 92% of female patients after bariatric surgery. The duration of menstrual bleeding normalized in 91% of the patients and menorrhagia disappeared in 79% of the women. Changes in blood hormone content similarly occurred, leading to normalization of the values. The study of oestradiol in the blood of patients showed a steady decrease of the hormone to 462±128.4 pmol/l ($p < 0.01$). Similarly, the concentration of testosterone reduced to 0.89±0.71 nmol/l ($p < 0.01$). The content of progesterone in the studied samples increased to 43±8.3 nmol/l ($p < 0.01$). After one year in the men who underwent the operation, the concentration of hormones was found to be normal, the plasma tests showed an increase in testosterone from 1.53±0.92 to 5.34±1.91 nmol/l ($p < 0.01$).

In modern scientific literature, the topic of changes in sex hormones arising after bariatric surgery is extremely rare, traditionally only the issues of hormonal levels in men and women with various degrees of obesity are considered (Dirinck *et al.*, 2016; Donkin *et al.*, 2016; Reinehr *et al.*, 2017). Our results show a positive effect of bariatric surgery on the sexual health of men and women, which improves their fertility and increases their quality of life.

Conclusion

As a result of bariatric surgery in morbidly obese patients with reproductive dysfunction, we can conclude about the normalization of hormonal background in the postoperative period and a decrease in adipose tissue as a consequence of positive endocrine regulation. Surgical treatment in people with morbid obesity and metabolic syndrome has good results. Modern surgery can solve infertility problems caused by excess adipose tissue and distorted hormones. That is why, when planning a pregnancy, one should consider the characteristics of their body.

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