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Review Article

Effect of Obesity on the Reproductive System and the Exchange of Sex Hormones

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Abstract

Development of the female organism from birth to maturation and extinction of its functions is usually divided into separate periods, which are characterized by certain morphological and functional features. In any of these periods, obesity can have an adverse effect on the formation, development and function of the reproductive system.

Keywords: *Contraception; Miscarriage; Nutrition; Obesity; Reproduction*

In order for a woman to appear and have a normal menstrual cycle and, as a result, ability to bear birth, a minimal amount of fat should accumulate in her body, since the fat tissue participates in the regulation of the reproductive function. In analyzing the condition of the reproductive function [1]. In analyzing the condition of the reproductive function, women are judged for the premorbid background by the age of menarche, which has changed over the past 100 years and comes at an earlier age: the average age is 12.6 years.

Adolescents with obesity are formed either later or early menarche. Earlier menarche is due to acceleration, since there is a definite relationship between the average weight of the body at the time of menarche and the average age. How does the amount of fat affect the age of the menarche? To date, it is impossible to determine accurately, since the hypothalamus's reaction to the loss or accumulation of fatty body mass is ambiguous.

The development of menstrual function has a significant effect on the reproductive system, although the data on the features of its functioning in obesity are quite contradictory. Thus, with obesity, a longer reproductive life is associated with an earlier menarche and pleiotropic effect of the mutation of the p-3-AP gene on a number of physiological systems, including body mass index (BMI) and reproductive status. Some authors consider the early age of menarche to be not only a reproductive factor, but also an independent predictor of the growth of BMI and other obesity complications.

The influence of various factors on anabolic processes in the body is realized through the nervous and endocrine systems. It is established that the hypothalamus is the center of the energy balance, where signals from the periphery arrive. Complex neurohumoral links allow us to consider the hypothalamus as the main regulator in the reproductive system. The hypothalamus controls the energy expenditure through the autonomic nervous system, hormones of the pituitary gland, involving the entire endocrine system in this process. It is proved that activation of the hypothalamic-pituitary-adrenal axis is combined with obesity. The presence of obesity leads to violations of the reproductive function of women or aggravates already existing problems.

One of the earliest studies that showed a link between obesity and reproductive failure was published in the early twentieth century by Mitchell and Rogers (1922), following observations of obese women with anovulatory menstrual cycles and oligomenorrhea. After consultation of dieticians, the rhythm of menstruation was restored in the majority of thinner patients; those who did not manage to lose

weight, preserved oligomenorrhea [5]. Although these observations were relatively random, they laid the groundwork for subsequent studies of the association of obesity with anovulation.

In women of reproductive age with obesity, the menstrual cycle is irregular as a rule. As it is known, a key role in the regulation of the reproductive function is played by gonadotropic releasing hormones, and, possibly, the hypothalamus responds to changes in the level of estrogens. The relationship between the amount of adipose tissue and the content of estrogens has been revealed in a number of studies by P. Sinteri and P. McDonald (1981), who found that the aromatization of androgens occurs in adipose tissue and thus a third of circulating estrogens are formed.

Extremely often the former regular menstrual function is broken at one stage or another, and it can be difficult to restore it. Also, speaking about the state of the reproductive system, it should be noted that violations of the menstrual cycle (dysfunctional uterine bleeding at different ages, oligo and amenorrhea) are extremely frequent. There is also a high frequency of infertility.

Excess fatty tissue leads to the accumulation of steroids, and the amount and activity of estrogen circulating in the blood decreases. Violation of the hypothalamus leads not only to irregular menstrual cycles, but also to hypomenstrual syndrome and secondary amenorrhea. V.N. Serov (1995) in the study of menstrual function in women with postnatal obesity revealed a violation of tonic and cyclic secretion of gonadotropins, resulting in 63% of cases in the development of anovulatory bleeding with the subsequent development of hypomenstrual syndrome, or acyclic bleeding against the background of hyperplastic endometrial processes.

Obesity is often combined with amenorrhea and infertility, but the mechanism of the occurrence of menstrual irregularities is not well understood, but to restore the cycle of menstrual function, it is often enough to reduce body weight by 10 - 15%.

According to most researchers, menstrual irregularities are secondary and are a consequence of obesity. With postnatal obesity, the frequency of spontaneous abortion is increased [2]. When alimentary obesity is 6 times more frequent violations of menstrual function and almost 2 times more often - primary infertility. There is a direct relationship between the increase in body weight and the severity of violations of ovarian function, which are accompanied by anovulation, inferiority of the luteal phase of the cycle and a decrease in the number of pregnancies.

Any clinician considers a complex group of patients with obesity. First, it is difficult for both diagnosis and treatment to treat the reproductive system pathology in women with normal body weight. In a patient with obesity, it sometimes need to double the dose of drugs, it is even more complicated. Secondly, a woman with an overweight can give an inadequate response to the appointment of a particular treatment. In case of pregnancy, the doctor meets with various complications, such as the threat of termination of pregnancy, often fetal hypotrophy, the development of gestosis, up to severe form - eclampsia and fetal death [3]. Therefore, patients with obesity are at risk for the occurrence of a variety of complications of the reproductive process. These are complications in childbirth and the puerperium: violations of labor, premature or delayed discharge of amniotic fluid, and hence a high incidence of surgical interventions. It is often necessary to perform delivery by cesarean section with a very high frequency of reproductive losses.

Timely correction of body weight leads to normalization of the cycle, in many patients even without the use of any additional therapy, and restoration of fertility. One of the frequent mistakes in the management of this contingent of patients is the fact that before the appointment of treatment for obesity, the function of the ovaries is stimulated [7]. With prolonged stimulation of ovulation without weight loss, the syndrome of premature ovarian depletion may develop.

The results of the effect on the reproductive function of a gradual decrease in body weight in the treatment of obesity are encouraging. If a woman treats menstrual dysfunction and obesity, treatment should first be aimed at weight normalizing. In this case only we can hope for success. The appointment of hormonal treatment can exacerbate the pathological condition. M. Hollmann and C. Galletly (1988) report that against a background of weight loss, menstrual function was restored in 80% of women without prescribing any other therapy

and 29% of them had a pregnancy without stimulation of ovulation. These results indicate the need to begin treatment of patients with weight loss.

In gynecological endocrinology, there is almost no syndrome that would not be associated with obesity. Examples are: postpartum neuro-exchange-endocrine syndrome, one of the symptoms of which is an increase, sometimes very significant, in body weight; polycystic ovary syndrome (PCOS), almost in all patients accompanied by an increase in body weight or metabolic disorders that occur in obesity [4,6]; Amenorrhea caused by obesity, in addition, menopausal syndrome, and in particular the postmenopausal metabolic syndrome that develops against it, and finally the neuroendocrine syndrome of puberty, or the so-called youthful basophilism. If the last syndrome is put on the first place, then it is clearly seen that all violations of the endocrine system from the period of puberty to menopause are closely related to obesity.

In most neuroendocrine syndromes, the clinical picture is largely determined by metabolic disturbances. Firstly, dyslipidemia of varying degrees is often observed, an increase in the coefficient of atherogenism (KA), a violation of carbohydrate metabolism of a very different nature, a violation of glucose tolerance, insulin resistance, which is observed in the syndrome of polycystic ovaries particularly.

Adrenal adiposity is considered the main risk factor for PCOS, as the peripheral conversion of androgens to estrogens occurs predominantly in adipose tissue. In the majority of patients, PCOS manifests itself in the adolescent period as irregular menstruation [4]. Hirsutism and acne, like other common symptoms of the disease, also appear in the adolescent period. In 60% of patients obesity develops at the age of 20 - 30 years. Often there are signs of insulin resistance, including acanthosis nigricans, hyperpigmentation of the skin around the neck, etc. Irregular, anovulatory menstrual cycles lead to infertility, and hyperestrogenia increases the risk of hyperplasia and endometrial cancer.

In women with obesity and anovulation, the concentrations of estrone, estradiol and / or free estradiol are significantly higher than in the early follicular phase in women with obesity and preserved ovulation, as well as in women with normal body weight. The Edman and McDonald report (1989) on the same aromatase activity in women with a normal menstrual cycle and in women with oligomenorrhea that had comparable body weight suggests that higher estrogen concentrations in obese women with oligomenorrhoea depend on enhanced production of precursors of estrogens, i.e. Androgens. It is believed that the chronic effect of estrogens, observed in women with obesity and oligomenorrhea, is the main factor in the development of PCOS. Tonic increase in the level of estrogen formed as a result of the peripheral conversion of androgens, by the mechanism of positive feedback acts on the pituitary gland. Increased release of biologically active luteinizing hormone (LH) leads to stimulation of production of androgen stromal ovaries. Formed in elevated concentrations, androgens are additional precursors for subsequent aromatization and conversion into estrogens in adipocytes - so the “vicious circle” closes.

Particularly important is the problem of obesity during the menopause. A number of large epidemiological studies clearly demonstrate that after the onset of menopause, 60% of women have an increase in body weight of 2.5 - 5 kg or more, and in addition, accumulation and redistribution of adipose tissue in the abdominal-visceral region.

As noted earlier, adipose tissue is the place of conversion of bioactive estrogens from androgen precursors [2]. Therefore, it is believed that such manifestations of climacteric disorders, such as menopausal syndrome or osteoporosis, develop less often in obese women. However, a number of studies have shown that in obese women, the increase in FSH levels and the decrease in estrogen concentration occurs on average 4 years earlier, therefore in women aged 40 - 44, obese, “hot flashes” are observed more often compared with women who have a normal body weight, and by 50 - 55 years, these differences are erased. Menopause in women with insulin-dependent diabetes mellitus occurs earlier, and the age of menopause is clearly correlated with the age at which the disease was diagnosed. It has been established that insulin resistance has a significant effect on ovarian function, while changes in the activity of factors such as insulin-like growth factor-1 and leptin may be important [4].

In studying the changes in heart and vascular function, the hemostasis system, as well as the metabolism of lipids and carbohydrates, it is proved that all these changes are interrelated and many of them are also risk factors for CVD, and on this basis the researchers introduced the term "menopausal metabolic syndrome" (MMS). The main etiological factor of MMC is the deficiency of sex hormones. The main components of MMC: abdominal obesity, insulin resistance, hyperinsulinemia, dyslipoproteinemia and increased content of blood clotting factors.

Thus, the redistribution of adipose tissue and its accumulation in the abdominal-visceral region in women during the period of age-related decline in ovarian function sharply increases the risk of CVD and is associated with the development of various metabolic, endocrine, psychoemotional and other disorders.

Despite the variety of syndromes accompanied by obesity, there is a separate nosological unit - amenorrhea caused by obesity. The fatty tissue contains enzymes: aromatase and 5a-reductase. Aromatase turns androgens into estrogens; when aromatase is present in excess, as in obesity, estrogens are constantly produced in increased amounts, causing a violation of normal ovulation. The excess amount of 5a-reductase, converting testosterone to dehydrotestosterone (DHT), leads to an increase in DHT production, causing the development of hirsutism and acne. Obesity treatment leads to the restoration of normal reproductive function.

Conclusion

At every stage of a woman's life, we are faced with such a complex pathological process as obesity. Currently, there are great opportunities for therapy, but in gynecological practice, we often do not take into account the fact that in the treatment of almost all diseases accompanied by obesity, the first phase of women should be activities aimed at weight reducing.

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