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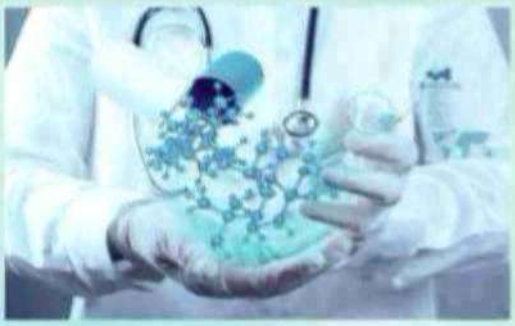

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PERSONALISED APPROACH TO CONTRACEPTIVE USE IN WOMEN WITH SOMATIC DISORDERS

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✓ ***Rezyume***

Modern contraception offers a wide range of methods for preventing unwanted pregnancy, but the selection of the optimal method for women with somatic pathology requires special attention. The purpose of this work is to consider the principles of a personalized approach to choosing contraceptives, taking into account the individual clinical and functional characteristics of women suffering from somatic diseases. Particular attention is paid to the interaction of hormonal contraceptives with chronic diseases of the cardiovascular, hepatobiliary, endocrine and autoimmune systems, as well as to the assessment of risks and contraindications. The article presents modern clinical guidelines, algorithms for choosing a contraceptive method and approaches to counseling patients taking into account their age, reproductive plans, the presence of risk factors and drug interactions. A personalized approach can increase the safety and effectiveness of contraception, as well as improve the quality of life of women with somatic disorders

Key words : Obesity, Reproductive health, personalized approach physical activity, medication, contraindications to contraception, risk assessment, medical eligibility criteria (MEC, WHO)

ПЕРСОНАЛИЗИРОВАННЫЙ ПОДХОД К ИСПОЛЬЗОВАНИЮ КОНТРАЦЕПТИВОВ У ЖЕНЩИН С СОМАТИЧЕСКИМИ РАССТРОЙСТВАМИ

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✓ ***Резюме***

Современная контрацепция предоставляет широкий выбор методов предупреждения нежелательной беременности, однако подбор оптимального средства у женщин с соматической патологией требует особого внимания. Целью данной работы является рассмотрение принципов персонализированного подхода к выбору контрацептивных средств с учётом индивидуальных клинико-функциональных особенностей женщин, страдающих соматическими заболеваниями. Особое внимание уделено взаимодействию гормональных контрацептивов с хроническими заболеваниями сердечно-сосудистой, гепатобилиарной, эндокринной и аутоиммунной систем, а также оценке рисков и противопоказаний. Представлены современные клинические рекомендации, алгоритмы выбора метода контрацепции и подходы к консультированию пациенток с учётом их возраста, репродуктивных планов, наличия факторов риска и лекарственных взаимодействий. Персонализированный подход позволяет повысить безопасность и эффективность контрацепции, а также улучшить качество жизни женщин с соматическими расстройствами

Ключевые слова. Ожирение, репродуктивность, персонализированного подхода физическая активность, медикаментозный, противопоказания к контрацепции, оценка риска, медицинские критерии приемлемости

SOMATIK KASALLIKLARGA CHALINGAN AYOLLARDA KONTRATSEPTIV VOSITALARDAN FOYDALANISHGA SHAXSIY YONDASHUV

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✓ ***Resume***

Zamonaviy kontratseptsiya istalmagan homiladorlikning oldini olish uchun keng ko'lamli usullarni taklif etadi, ammo somatik patologiyasi bo'lgan ayollar uchun optimal usulni tanlash alohida e'tibor talab qiladi. Ushbu ishning maqsadi somatik kasalliklarga chalingan ayollarning individual klinik va funktsional xususiyatlarini hisobga olgan holda kontratseptiv vositalarni tanlashga individual yondashuv tamoyillarini ko'rib chiqishdir. Gormonal kontratseptivlarning yurak-qon tomir, gepatobiliar, endokrin va otoimmun tizimlarning surunkali kasalliklari bilan o'zaro ta'siriga, shuningdek, xavf va kontrendikatsiyalarni baholashga alohida e'tibor beriladi. Maqolada zamonaviy klinik ko'rsatmalar, kontratseptsiya usulini tanlash algoritmlari va bemorlarga ularning yoshi, reproduktiv rejalari, xavf omillari mavjudligi va dorilarning o'zaro ta'sirini hisobga olgan holda maslahat berish usullari keltirilgan.

Shaxsiylashtirilgan yondashuv kontratseptsiya xavfsizligi va samaradorligini oshirishi, shuningdek, somatik kasalliklarga chalingan ayollarning hayot sifatini yaxshilashi mumkin

Kalit so'zlar: semizlik, reproduktiv salomatlik, shaxsiy yondashuv jismoniy faoliyat, dori-darmonlar, kontratseptsiya uchun kontrendikatsiyalar, xavfni baholash, tibbiy muvofiqlik mezonlari (MEC, JSST)

Relevance

The choice of a contraceptive method for women with somatic diseases is a complex clinical task that requires an individual approach. Standardized schemes for prescribing hormonal agents do not always take into account the presence of chronic pathologies, such as arterial hypertension, diabetes mellitus, liver disease, autoimmune and thrombophilic conditions, which can increase the risk of side effects and complications when using certain contraceptives.

Against the background of increasing prevalence of somatic diseases among women of reproductive age, especially in the context of urbanization, stress and growth of comorbidity, the need for personalized choice of contraception is becoming increasingly important. In addition, modern approaches to medicine suggest not only effective, but also safe for overall health reproductive behavior, which is especially important for women with a burdened medical history. [1,2,4].

The availability of a wide range of contraceptives requires a thorough assessment of risks and benefits, individualization of the patient management strategy taking into account age, the nature of the somatic disease, the degree of compensation and the potential impact of the drug on the course of the underlying disease. This makes the topic of a personalized approach to contraception in women with somatic pathology particularly relevant both from the point of view of reproductive health protection and in the context of improving the quality of life and preventing complications.

Materials and methods

In Uzbekistan, 25.2% of women (15-49 years old) are overweight, 15.5% of women are obese, according to a study conducted in 2017 by the United Nations Children's Fund (UNICEF) and the Ministry of Health of Uzbekistan. The study surveyed 3,874 housewives in all regions of the country. The survey included 251 pregnant women and 2,269 women of reproductive age (WRA). Among girls aged 15-19, 10.7% are overweight or obese. The number of overweight people is increasing progressively. This growth is 10% of their previous number every 10 years.

It is estimated that if this trend continues, then by the middle of the current century the entire population of economically developed countries will suffer from obesity. It should be especially emphasized that obesity causes such serious diseases as type II diabetes , arterial hypertension, coronary heart disease, gallstone disease, uterine and mammary gland tumors [1,2]. Obesity is the

trigger for the “deadly” quartet of metabolic syndrome: arterial hypertension, insulin resistance, visceral obesity, dyslipidemia.

Women with increased body weight are diagnosed with ovulatory menstrual cycles, infertility, miscarriage, complicated pregnancies. Thus, we consider obesity not only as a risk factor for the development of various diseases, but also as a reproductive barrier. The problems associated with the obesity pandemic result in significant economic and social costs. Lifestyle modifications have limited effect because they do not significantly improve end goals such as pregnancy, ovulation, or regular menstrual cycles, with the exception of reducing the risk of preeclampsia and shoulder distance. Current literature data confirms expert predictions that obesity will continue to increase. The close relationship between obesity and reproductive disorders makes this issue relevant. At the same time, there is sufficient evidence that obesity not only reduces fertility, but also complicates pregnancy and childbirth.

Overweight women are 4 times less likely to seek contraception than women of normal weight are, and the frequency of abortions in this group is no less. Do young overweight women need reliable contraception? Of course they do! Every unplanned pregnancy that ends in abortion may be the last, since obese women have an increased risk of infertility.

The method of choice for contraception for women with obesity may be purely progestin contraceptives, especially since according to the WHO acceptance criteria; this is category I for such a contingent of patients. However, the high frequency of intermenstrual bleeding limits the use of this method of contraception.

The correct selection of an effective and safe contraceptive for overweight women should be based on an understanding of the mechanisms of excess weight formation and the effect of hormonal contraceptive components on key links in eating behavior and lipogenesis. In addition, one should be guided by the WHO medical criteria for the acceptability of contraceptive methods.

WHO Medical Eligibility Criteria for Contraceptive Use

WHO attaches primary importance to increasing access to quality contraceptive services. One aspect of improving the quality of services is the development of medical criteria for contraceptive acceptability. In 1994-95, participants in workshops held by the World Health Organization (WHO) developed a classification system. According to this classification, various contraceptive methods are assessed in terms of the ratio of possible health risks to the benefits of their use in the presence of certain conditions. The concept of “condition” includes the biological characteristics of the woman (age or reproductive history) and any known current diseases (for example: hypertension, obesity, etc.), bad habits (smoking). [225]WHO experts proposed classifying conditions that affect the acceptability of the method into 4 categories (Table 1). The importance of some procedures for the safe and effective use of hormonal contraception (Table 2).

Class ≪ A ≫ : Are essential for the safe and effective use of contraceptive methods and are mandatory in all cases.

Class ≪ B ≫ : Significantly contribute to the safe and effective use of the method. However, if it is not possible to carry out a particular examination or test, then in this case the possible risks of not using the examination methods and tests should be carefully weighed against the advantages that the use of this contraceptive method will provide.

Class ≪ C ≫ : Not essential for the safe and effective use of the method.

Absolute contraindications to the use of COCs (category IV) are: history of thromboembolic conditions; thrombogenic mutations; surgery with prolonged immobilization; arterial hypertension; migraine with aura; diabetes mellitus with vascular complications or duration of more than 20 years; liver disease in the stage of decompensation; liver tumors; uterine bleeding of unknown etiology; pregnancy; breastfeeding up to 6 months after childbirth; current breast cancer; smoking more than 15 cigarettes per day at the age over 35 years.

Program for calculating the acceptability of combined oral contraception in obese women

Despite the fact that WHO and CDC experts have formulated medical criteria for the acceptability of contraceptive methods for women suffering from obesity; the use of modern low- and micro-dose estrogen-containing drugs as part of combined oral contraception for this group of patients has been poorly studied.

Using the Eligibility Calculator combined oral contraception in women with obesity will improve the safety of using modern hormonal contraceptives in women with various types of obesity based on the study of eating behavior, obesity biomarkers, lipid and carbohydrate spectrum of the blood, and endothelial dysfunction.

Results and discussions

Based on the data obtained, a point assessment calculation of the acceptability of the combined oral contraception was conducted at 40 women with obesity.

0-5 points - *minor metabolic disorders* . Combined oral contraceptives containing drosperinone can be taken by obese women without restrictions. At the same time, it is recommended to change eating behavior and increase physical activity.

6-15 points - *moderate degree of metabolic disorders* . Combined oral contraceptives containing drosperinone can be recommended, but under the supervision of a doctor and laboratory parameters. The benefits of using the contraceptive method exceed risk.

16-34 points – *high degree of metabolic disorders* . Combined oral contraceptives are not recommended. The risk of using the contraceptive method exceeds the benefit.

Criteria for inclusion in the group, hosts hormonal contraceptives:

- the patient's desire and written consent to use hormonal contraception;
- absence of contraindications for taking sex hormone preparations within six months prior to the start of the study.
- overweight or obesity

Exclusion criteria :

- the presence of standard contraindications to taking combination
- oral contraceptives;
- hypothyroidism, hyperprolactinemia, hypercorticism, adrenal
- hyperandrogenism

The control group consisted of 50 overweight and obese women (25 women with the gynoid type and 25 with android type of obesity) who did not use any contraception. The purpose of observing these women was to assess the dynamics of obesity during its natural course.

General clinical and anthropometric methods of research were carried out . To determine the type of obesity (android, hypoid), waist circumference was measured. *Laboratory studies* : Blood serum lipids, glucose and insulin concentration in the blood serum before the start and at the end (after 6 months) of the contraceptive course.

The average age of the patients was 26.2 ± 2.2 years, with fluctuations from 18 to 35 years. There were 88 (62.9%) women with hyoid obesity - subgroup A (WC ≤ 82 cm), and 37.1% with android obesity - subgroup B (WC ≥ 82 cm). The average body mass index in subgroup A was 33.1 ± 0.7, in subgroup B - 32.5 ± 0.8 ($p > 0.05$), in the control group - 33.3 ± 0.2. That is , all groups examined were homogeneous By BMI.

Of the total number of examined main subgroups of patients, 101 were city residents (72.1%), 39 were rural residents (27.9%). When studying the anamnesis, attention is drawn to a large number of diseases and surgeries suffered in childhood, puberty, in adulthood: 97.1% of patients had childhood infections, 41.1% had infectious diseases in adulthood, 30% had diseases of the urinary system, 20% had respiratory diseases, 10.7% - diseases of the gastrointestinal tract.

28 (20%) women in the past underwent various surgical interventions due to gynecological diseases and obstetric situations: ovarian cysts, tubal pregnancy, ovarian apoplexy, cesarean section, two examined women underwent conservative myomectomy. Operations for acute appendicitis and cholecystitis were performed in 41 patients. (29.3%) patients. In 17 (12.1%) patients, in addition to obesity, there was concomitant somatic pathology: hypertension, hypothyroidism, chronic pyelonephritis, chronic bronchitis. 86 (61.4%) had concomitant iron deficiency anemia. In 66 patients (47.1%), the examination revealed the presence of concomitant genital pathology, of which almost half had chronic inflammatory processes of the genitals.

Thus, all patients of reproductive age with excess body weight have an unfavorable premorbid background, pronounced manifestations of the underlying disease, and the presence of additional somatic pathology in some women.

All patients had their eating behavior studied using a short dietary questionnaire developed by Blok, including 24 items, and consisting of 2 parts: Part 1 evaluates the frequency of fat consumption (15 items); Part 2 evaluates the frequency of consumption of plant products (9 items). The questionnaire is designed for self-completion and calculation of the accumulated points by the respondent. Eating behavior was assessed before and during (6 months) hormonal contraception using special questionnaires. After studying the questionnaires, all patients were given recommendations on a balanced diet and increased physical activity. Blood serum lipids were determined before and at the end (6 months) of the contraceptive course.

No	*Indicators*	*Main characteristics*	*Points*
1	**BMI**	BMI> =18.5 < 2.5 kg / m^2	0
		BMI > =25,1 < 30 kg/ m^2	1
		BMI > =30.1 < 40 kg / m^2	2
2	**Waist circumference**	up to 82 cm	0
		82.1 cm and more	2
3	**Systolic blood pressure**	up to 120-140 mm Hg	0
		141-160 mm Hg	1
		161 mmHg or more	2
4	**Diastolic blood pressure**	up to 91 mm Hg	0
		91-100 mmHg	1
		101 mm Hg and more	2
5	**Pathology of the mammary glands**	No	0
		Benign neoplasms of the mammary gland	1
		Malignant neoplasms of the mammary gland	2
6	**Pathology of the cardiovascular system**	No	0
		Ischemic heart disease	1
		History of thrombosis and embolism	2
7	**Varicose veins**	No	0
		Varicose veins of the superficial veins	1
		Varicose veins of the deep veins	2
8	**Headaches due to migraine**	No migraine	0
		Migraine with typical headache attacks	2
9	**Smoking**	Non-smokers	0
		Stopped smoking over 1 year ago	1
		Smokers or quit smoking less than 1 year ago	2
10	**Liver diseases**	No	0
		Chronic hepatitis	1
		Liver tumors and active viral hepatitis	2
11	**Homocysteine**	10-20 µmol/l	0
		21-29 µmol/l	1
		30 µmol/l and more	2
12	**Leptin**	1.1-27.6 ng/ml	0
		27.7 – 35.5 ng/ml	1
		35.6 ng/ml or higher	2
13	**Cholecystokinin**	5-800 ng/l.	0
		801 ng/L and more	1
14	**Low density lipoproteins**	up to 3.9 mmol/l	0
		above 4.0 mmol/l	1
15	**High-density lipoproteins**	0.75-1.67 mmol/l	0
		above 1.68 mmol/l	2
16	**Insulin- HOMA index - IR)**	up to 22.5	0
		22.6 and above	1
17	**Eating behavior according to questionnaire 1**	Total points up to 25	0
		Total score 26-30	1
		Total score over 31	2
18	**Eating behavior according to questionnaire 2**	Total points up to 25	0
		Total score 26-30	1
		Total score over 31	2
19	**Liver ultrasound (non-alcoholic fatty liver disease)**	No	0
		Eat	1

Based on the implementation of the eligibility calculation program combined oral contraception in women with obesity will justify in practice the need for a detailed examination of patients before prescribing hormonal contraception and further dynamic monitoring with mandatory determination of obesity biomarkers, vascular endothelial function, lipid spectrum and insulin resistance index.

The use of the program will allow the widespread use of modern micro- and low-dose drugs in obese female patients for at least six months without the risk of weight gain, significant disturbances in serum lipid levels and carbohydrate metabolism indicators.

The implementation of the program in practical healthcare will allow developing an algorithm for the tactics of managing patients with excess body weight and obesity in the process of contraception based on the study of the characteristics of the eating behavior of women with obesity. This program provides for the need for dynamic determination of obesity biomarkers, blood lipid spectrum, insulin resistance indicators and endothelial function in the process of hormonal contraception, taking into account the metabolic effects of micro- and low-dose combined oral contraceptives in women with feminine and android types of obesity. [6,7,9].

Combined oral monophasic estrogen-gestagen drugs registered in Uzbekistan were used as hormonal contraceptives: Mediana (GedeonRichter , Plc . Hungary)

- for patients who have completed their reproductive function - and Yarina Plus (Bayer , AG , Germany) - for patients in the process of pre-pregnancy preparation. [5].

The drugs are low-dose COCs and are characterized by common estrogenic (ethinyl estradiol) and gestagen (drospirenone) components and their identical doses - 0.03 mg and 3 mg, respectively. [4]. COCs were prescribed according to the generally accepted cyclic 21-day scheme: from the 5th day of the menstrual cycle, 1 tablet 1 time per day, at the same time, for 21 days, followed by a 7-day break. Drosperinone, which is part of the drugs, has an antimineralocorticoid property and is able to prevent weight gain, reduce edema associated with estrogen-dependent fluid retention. [6,7].

Conclusion

Pregnancy and termination of pregnancy are the most significant health risks that women face in their reproductive years. "Reproductive health is a state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity, in all matters relating to the reproductive system and its functions and processes" - WHO. The choice of a contraceptive method plays a huge role in maintaining reproductive health , allowing for the regulation of fertility, mainly by preventing unwanted pregnancy, which makes it possible to reduce maternal mortality from induced abortions by 25-50%, as well as from complications of pregnancy, childbirth and the postpartum period. Currently, at least 200 million women worldwide prevent unwanted pregnancy using combined oral contraceptives (COCs). Rational use of modern contraceptives is today considered not only as the main opportunity to improve the health of mother and child, but also as one of the reproductive rights of a person.

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