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CLINICAL AND PHARMACOLOGICAL APPROACH TO THE USE OF CHOLIKINETIC AND HOLYRETIC DRUGS IN PREGNANT WOMEN

Resume: The use of the principles of clinical pharmacology in relation to the mother-fetus system makes it possible to better understand the features of pharmacokinetics during pregnancy.

The article presents the factors that determine these features associated with both changes in the body of the expectant mother and the presence of an additional fetoplacental circulatory system, the placenta itself and the developing fetus. These factors affect the results of drug treatment throughout the gestational period. Thanks to the rapid development of molecular technologies in the last decade, modern medicine opens up prospects for answering questions about the individual characteristics of pharmacokinetics and metabolism of drugs (drugs), about the presence of increased teratogenic risk due to the peculiarities of the genotypes of the mother and fetus.

Keywords: pharmacokinetics, drugs, pregnancy, placenta, mother-fetus system.

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КЛИНИКО-ФАРМАКОЛОГИЧЕСКИЙ ПОДХОД К ПРИМЕНЕНИЮ ХОЛИКИНЕТИЧЕСКИХ И ХОЛИРЕТИЧЕСКИХ ПРЕПАРАТОВ У БЕРЕМЕННЫХ

Резюме: Использование принципов клинической фармакологии применительно к системе мать-плод позволяет лучше понимать особенности фармакокинетики в период беременности.

В статье представлены факторы, которыми обусловлены эти особенности, связанные как с изменениями в организме будущей матери, так и с наличием дополнительного фетоплацентарного круга кровообращения, собственно плаценты и развивающегося плода. Эти факторы влияют на результаты медикаментозного лечения на протяжении всего гестационного периода. Благодаря бурному развитию в последнее десятилетие молекулярных технологий, у современной медицины открываются перспективы ответа на вопросы об индивидуальных особенностях фармакокинетики и метаболизма лекарственных средств (ЛС), о наличии повышенного тератогенного риска, обусловленного особенностями генотипов матери и плода.

Ключевые слова: фармакокинетика, лекарственные средства, беременность, плацента, система мать-плод.

Introduction. The use of medicines (drugs) in pregnant women is a very frequent phenomenon. According to international studies, more than 80% of women take at least one drug during pregnancy, an average of 4 names [60, 70]. In this regard, at least 5% of congenital malformations are caused by the effect of drugs on the fetus [1,6].

The problem of the safety of drug therapy for pregnant women has been the subject of close attention since the appearance in 1961 of reports on the teratogenic effects of thalidomide [3]. Currently, there are about 40 drugs or groups of drugs whose teratogenic or toxic effect has been proven: cytotoxic, antithyroid, hypoglycemic agents, ACE inhibitors, anticonvulsants, barbiturates, benzodiazepines, sex hormones (diethylstilbestrol, progestins, danazol),

anticoagulants, (warfarin), systemic retinoids, misoprostol, some antimicrobial drugs (tetracycline, streptomycin), and others [4].

However, only a few drugs are considered safe during pregnancy. Due to the fact that pregnant women are potentially excluded from clinical trials for ethical reasons, for most drugs there is no evidence of their effectiveness and safety during pregnancy and the use of drugs in this category of patients continues to be a poorly studied area of medicine — both in terms of risk and benefit [2].

The identification of teratogenic properties of drugs is complicated by the fact that there is a certain natural background of fetal malformations associated with other causes (gene and chromosomal abnormalities, infections, ecology); different species specificity does not allow extrapolating experimental data obtained from animals to humans. Many drugs cause behavioral, functional, delayed or rare adverse effects that remain unaccounted for [3,6].

Almost all drugs penetrate the placenta and can cause pharmacological effects in the fetus [4]. The consequences of taking drugs depend not only on the drug, dose and duration of treatment, but also on the duration of pregnancy, concomitant diseases and genetic characteristics of the mother and fetus. In the first trimester of pregnancy, drugs can cause malformations (teratogenic effect); in the second and third trimesters, they can affect the growth and development of the fetus, have a toxic effect on it, and when taken at the end of pregnancy or during childbirth, they can affect their course and the newborn [2,6].

Physiological changes during pregnancy, in turn, can lead to changes in the pharmacokinetics of drugs, which often leads to suboptimal dosing of drugs [5,7].

According to international recommendations, it is necessary to prescribe drugs to pregnant women only for strict indications, only if the expected benefit exceeds the possible risk to the fetus, using drugs only with established safety and long experience of use in pregnant women, and in minimal effective doses.

It is necessary, if possible, to avoid prescribing drugs in the first trimester of pregnancy, because none of the drugs should be considered absolutely safe for use in the early stages [6].

Often, taking drugs occurs either before a woman finds out about her pregnancy, or without consulting a doctor [58]. In addition, the actual practice of using drugs by pregnant women does not always correspond to medical prescriptions, which is confirmed in a number of studies [1].

In connection with the above, there is an obvious need for regular monitoring of the use of drugs during pregnancy and compliance of drug therapy with recommendations based on evidence-based medicine.

This pharmacoepidemiological study will allow us to obtain objective data on the practice of using drugs throughout pregnancy, to assess their compliance with modern recommendations. The results obtained will form the basis for the compilation of practical recommendations aimed at improving the quality and safety of pharmacotherapy for pregnant women.

The aim of the study the aim of the study is to improve the clinical and pharmacological approach to the use of cholekinetic and holyretic drugs in pregnant women

Materials and methods. A retrospective descriptive pharmacoepidemiological study was conducted on a sample of 298 case histories of pregnant women admitted to RSO-A hospitals in 2023 with the threat of termination of pregnancy.

To enter the data, an individual registration card of the pregnant woman was developed, which reflected demographic data, pregnancy period, diagnosis, as well as all drugs prescribed to the pregnant woman during the period of hospitalization, indicating the route of administration, dosage regimen and duration of use. The drugs were encoded in accordance with the Anatomical Therapeutic Chemical Classification (ATS) recommended by WHO.

Results and discussion. 298 medical records of pregnant women (average age 27.6±5.67 years) were analyzed, of which 160 (53.7%) had this pregnancy first, 56 (18.8%) had the second, 38 (12.8%) had the third, 24 (8.1%) had the fourth, 10 (3.4%) – the fifth, 5 (1.7%) – the sixth, for 5 (1.7%) women it was the seventh – eleventh pregnancy. For the majority of women – 184 (61.7%), the upcoming birth was the first, for 74 (24.8%) – the second, 31 (10.4%) – the third, 7 (2.3%) – the fourth, 2 (0.7%) – the fifth. 40 (13.4%) women had a history of 1 to 6 spontaneous abortions; 43 women (14.4%) – from 1 to 6 medical abortions.

Somatic anamnesis in 82 (27.5%) pregnant women was burdened with extragenital diseases: 27 (32.9%) had pathology of the cardiovascular system (CCC) (most often – vegetative–vascular dystonia), 23 (28%) - endocrine system (most often – obesity), 33 (40.2%) pregnant women – there were diseases of the urinary tract (most often – chronic pyelonephritis), in 10 (12.2%) – diseases of the digestive tract (most often – gallstone disease), in 3 (3.7%) – diseases of the ENT organs and respiratory organs.

Complications of the gestational period were present in all women: in 290 (97.3%) – the threat of termination of pregnancy, in 57 (19.1%) – anemia, in 19 (6.4%) – fetal hypoxia and fetoplacental insufficiency, in 8 (2.7%) – dropsy of pregnant women, in 3/4 (1/1.3%) – polyhydramnios /lack of water, in 1 (0.3%) nephropathy of pregnant women.

As a result of studying the medical records of pregnant women, it was found that drug therapy was used in 100% of cases. A total of 2665 drug prescriptions have been studied. In 1,365 (51.2%) cases, drugs were prescribed parenterally, 1,071 (40.2%) – orally and in 229 (8.6%) cases topically. 97 different names of drugs from 37 PBX groups were used for the treatment of pregnant women.

The average number of drugs prescribed to a pregnant woman during the period of hospitalization was 8.89 ± 2.91 (from 3 to 17 names). Attention is

drawn to the fact that only in 24 (8.1%) cases less than 5 medications are prescribed to pregnant women at the same time, while 200 (67.1%) women received from 6 to 10 drugs at the same time during the hospitalization period, 66 (22.1%) – from 10 to 15 drugs and 8 (2.7%) – 16-17 HP (Fig. 1).

Most often, based on the data obtained, plasma–substituting and perfusion solutions were prescribed – (10.5%), systemic antibiotics – (9.5%), antianemic drugs (8.4%), multivitamins (7.4% of prescriptions), drugs for the treatment of gastrointestinal diseases – (9.5%), sedatives and hypnotics - (7.4%), hemostatics – (3.2%), hormonal drugs for the treatment of threatened miscarriage – (2.1%), cardiovascular drugs – (9.5%), antimicrobials for intravaginal use – (3.2%), immunomodulators – (4.2%), antihistamines – (3.2%), drugs for the treatment of urological diseases – (1%), systemic GCS – (2.1%) (Fig. 2).

According to the FDA classification of the total number of drugs, 11.3% of drugs (such as sorbifer, dufalac, iodomarin) belonged to category A, category B – 12.4% (cephalosporins, monural, curantil), category C – 8.2% (dexamethasone, ascorbic acid, amlodipine), and 68% were drugs with an unspecified risk for pregnant women (cocarboxylase, mildronate, actovegin, essentiale, etc.) (Fig. 3).

Analysis of the results of the study showed that the frequency of drug use during pregnancy is extremely high – 69.8% of women received more than 5 drugs at one time. At the same time, a serious problem is not only the number of drugs prescribed to pregnant women at the same time, but also the structure of prescriptions – 76.2% of medicines recommended by doctors for treatment in the second trimester belonged to category C and drugs with unknown consequences of use and could lead to serious consequences for the health of the mother, fetus and newborn. It is necessary to conduct educational work with pregnant women, monitor the intake of all drugs during pregnancy.

Conclusions. This pharmacoepidemiological study will allow us to obtain objective data on the practice of using drugs throughout pregnancy, to assess

their compliance with modern recommendations. The results obtained will form the basis for the compilation of practical recommendations aimed at improving the quality and safety of pharmacotherapy for pregnant women.

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