

CLINICAL STUDY

Drug usage analysis in pregnant women

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ABSTRACT

BACKGROUND: Drug usage in pregnant women is associated with a problem of possible negative influence on prenatal development. It is always necessary to judge the need for drug administration during pregnancy. **OBJECTIVE:** The aim of presented study was to analyse data about pregnant women hospitalized in the postpartum period.

METHODS: The study was designed as a retrospective observational study including 300 women hospitalized at the 2nd Department of Gynaecology and Obstetrics, University Hospital, Bratislava. Data were obtained through questionnaires in form of an interview.

RESULTS: The average age of women was 30.79 ± 4.40 years. Risk pregnancy occurred in 20.59 % of women. Chronic disorders before pregnancy required regular pharmacotherapy in 29.24 %. Drug usage analysis: I. trimester, 31 % used at least one drug, 52 % nutritional supplements, 63.3 % drug and/or nutritional supplement; II. trimester, 23 % used at least one drug, 45 % nutritional supplements, 58.3 % drug and/or nutritional supplement; III. trimester, 32 % used at least one drug, 67 % nutritional supplements, 75.3 % drug and/or nutritional supplement.

CONCLUSION: Drug usage during pregnancy requires great precaution at choosing pharmacotherapy. The benefit of pharmacotherapy should always outweigh the potential risk of administered drug (*Tab. 3, Fig. 3, Ref. 37*). Text in PDF www.elis.sk.

KEY WORDS: pregnancy, drug risk, prenatal development, analysis of pharmacotherapy.

Introduction

Drug administration during pregnancy represents a very specific and sensitive problem. On one side, there are fears from untreated disorder; on the other side, worry exists from possible risk of drug negative influence on healthy development of embryo and fetus (1). It is necessary to judge the need for drug administration, however rejection of pharmacotherapy during pregnancy is not always desirable. Untreated or inadequately treated maternal illness may cause teratogenic effects and worsen health of the woman (e.g. diabetes mellitus, epilepsy) or disrupt the adequate prenatal development (2).

Decision on safe drug usage during pregnancy is needed. Pregnant women are generally excluded from clinical trials due to ethical concerns about the possible effect of the drug on the embryo-fetal development (3). In particular, safety data are regularly obtained from findings of preclinical studies in animal models, published case studies, or national registries that were designed to evaluate the effect of the medicines in pregnancy (4). There exists

only limited data on the extent of risk not only in Slovakia but also in neighboring countries. The current situation offers only little information available on the drug effects during pregnancy (5). Risk overestimation can cause inadequate treatment, while underestimation is unwanted (6). Only a limited number of medicines are labeled as safe for use during pregnancy. The decision about drug prescription may be difficult and is based on information from FDA and EMEA databases on risk assessment of medicinal products in pregnancy (7, 8). In most of the summaries of product characteristics, standard information about the inadequacy of the drug administration during pregnancy can be found, but in fact, only a few drugs have a proven negative effect on embryo and fetus (9). When administering medicaments, the physiological changes that occur during pregnancy and significantly affect the pharmacokinetics should be taken into consideration, as well as gestation period during which the drug exposure occurred (10). The most vulnerable period for the development of birth defects is organogenesis during the first trimester. In the second and third trimester non-structural malformations such as growth retardation, central nervous system and immune system disorders can occur. Development of the central nervous system continues throughout the pregnancy and into infancy, leading to possible behavioral changes (11).

Methods

The study was designed as a retrospective observational study that included three hundred randomly selected women hospitalized

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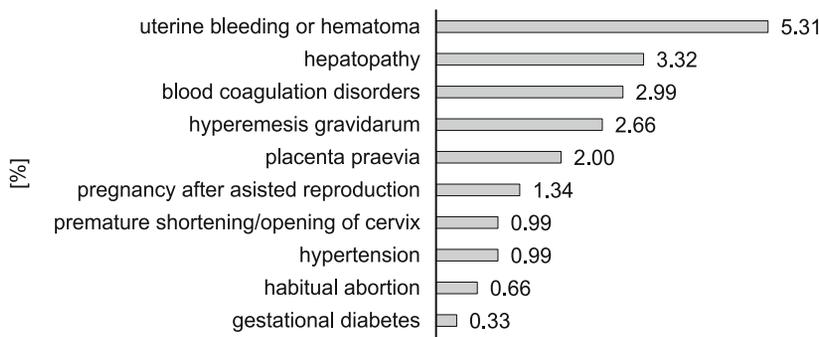


Fig. 1. Disorders complicating pregnancy (percentage of respondents, n = 300).

five days in postpartum period at 2nd Department of Gynaecology and Obstetrics, University Hospital, Bratislava. All women gave informed consent to participate in the study. Respondents answered anonymously pre-prepared questions in the form of interview. The same physician for all respondents participating in the study conducted the questionnaires. During the interview, the socio-demographic characteristics and the pharmacotherapy used during pregnancy were investigated. The characteristics of the patients included: age, pregnancy order and possible abuses – smoking, alcohol and coffee consumption. At the same time, they were asked about acute diseases that appeared during pregnancy and chronic illnesses from which they suffered before. Data were collected for the individual trimesters. The research was conducted with the approval of the Head of the Department as well as the Hospital Management. The Ethics Committee of the University Hospital Bratislava agreed to conduct the study.

Results

Analysis of participants' basic data

The analyzed group consisted of 300 respondents who were randomly selected from hospitalized patients in the postpartum period. Age of woman was in range 17–45 years, the average age was 30.79 ± 4.40 years, the majority was 31–35 years old (Tab. 1). More than half of women (52 %) were primiparae. None of the interviewed women worked in risky environment (noise, vibration, chemical and biological substances, ionizing and non-ionizing radiation). None of them reported consumption of alcohol during

Tab. 1. Age of pregnant women (percentage of respondents, n = 300).

Age (years)	17–25	26–30	31–35	36–40	41–45
%	12.3	34.4	40	11.6	1.7

Tab. 2. Comparison of smoking before and during pregnancy (percentage of respondents, n = 300).

Cigarettes per day before pregnancy	≤ 2	≤ 5	≤ 10	≤ 20	≤ 40
% of smoking women	14	27	35	21	3
% of all women	1.54	2.97	3.85	2.31	0.33
Cigarettes per day during pregnancy	≤ 2	≤ 5	≤ 10	≤ 20	≤ 40
% of smoking women	3	3	–	–	–
% of all women	0.33	0.33	–	–	–

pregnancy. Smoking before pregnancy was reported in 11 % of women: up to 40 cigarettes daily (0.33 %), up to 20 cigarettes daily (2.31 %), up to 10 cigarettes daily (3.85 %), up to 5 cigarettes daily (2.97 %), up to 2 cigarettes daily (1.54 %). Almost all women stopped smoking after pregnancy and only 0.66 % of them continued with smoking during pregnancy, but maximally 5 cigarettes daily (Tab. 2). About half of the women consumed coffee during pregnancy: one third of them one cup of coffee daily, the others two cups of coffee daily.

High-risk pregnancy occurred in 20.59 % of women, most commonly due to hyperemesis gravidarum, uterine bleeding or hematoma, placenta praevia, blood coagulation disorders, pregnancy after assisted reproduction, premature shortening and opening of the cervix, habitual abortion, hepatopathy, hypertension and gestational diabetes (Fig. 1). Approximately one third of mothers (29.24 %) required regular pharmacotherapy due to following chronic diseases before pregnancy: allergies, varicose veins, hypothyroidism, bronchial asthma, anemia, migraine, depression, diabetes mellitus (Fig. 2).

Analysis of pharmacotherapy during pregnancy

Women were asked about pharmacotherapy in each trimester of pregnancy. In the I. trimester of pregnancy 31 % of women used at least one drug, 52 % used nutritional supplements (vitamins, folic acid, magnesium, iron) and 63.3% used drug and/or nutritional supplement (Fig. 3). The most frequently applied pharmacological groups during this period were analgesics, hormonal preparations, anticoagulants, antimicrobials, antiemetics and antihistamines. Among nutritional supplements dominated vitamins and folic acid (Tab. 3). In the II. trimester at least one drug used 23 % of women, 45 % used nutritional supplements and 58.3 % used drug and/or nutritional supplement (Fig. 3). During the II. trimester the most commonly used drugs were analgesics, hormonal preparations, anticoagulants, antimicrobials, antihistamines, and antihypertensives. The main nutritional supplements were iron and vitamins (Tab. 3). During the III. trimester 32 % of women used at least one drug, 67 % used nutritional supplements

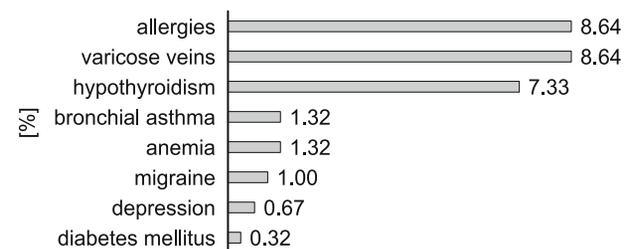


Fig. 2. Chronic diseases before pregnancy (percentage of respondents, n = 300).

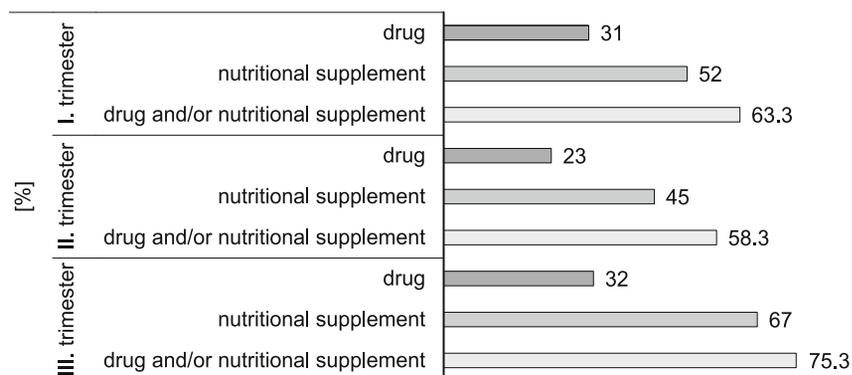


Fig. 3. Comparison of drug and nutritional supplement use in each trimester (percentage of respondents, n = 300).

and 75.3 % used drug and/or nutritional supplement (Fig. 3). In the last trimester of pregnancy predominantly used medicaments were analgesics, anticoagulants, hormonal preparations, antimicrobials, antihistamines, antihypertensives and drugs for liver diseases. The main nutritional supplements were iron supplements (Tab. 3). During the whole pregnancy at least one drug used 45.7 % of women, 37.7 % of all respondents used both, drug as well as nutritional supplement and only 10.6 % of women did not use any drug and/or nutritional supplement. The most commonly used drug during the whole pregnancy was paracetamol (22.7 %) and iron as nutritional supplement (52.3 %).

Discussion

The study was conducted as an interview with established questions. This method is generally used in pharmacoepidemiology and pharmacovigilance (12).

In Slovakia, as in the most of European countries, a trend of postponing parenthood to higher age is seen in recent years (13). This is in agreement with data obtained from present study. The majority of women were between 31–35 years old. It is relatively high age, taking into consideration that around half of them were primiparae. Higher age of pregnant women is associated

Tab. 3. Use of specific drugs and nutritional supplements in each trimester (percentage of respondents, n = 300)

Drugs	I. trimester	II. trimester	III. trimester
	[%]	[%]	[%]
Hormones	20.7	11.7	8.7
Analgesics	13.7	11.2	8.7
Anticoagulants	8.7	10.1	10.1
Antimicrobials	3.7	5.1	7.3
Antihistamines	1.7	3.1	3.1
Antihypertensives	–	1.4	2.7
Drugs for liver diseases	–	–	3.3
Nutritional supplements			
Vitamins	26.3	17	15
Folic acid	20.3	8	8.3
Iron	7.3	19.3	47.7
Magnesium	3	11	23

with increased incidence of risk pregnancies, assisted reproduction, occurrence of chronic diseases with necessity of regular pharmacotherapy (14). In the present study about one fifth of respondents had risk pregnancy and almost one third of respondents suffered from chronic disease with necessity of regular pharmacotherapy. Women with chronic diseases requiring medication should have a pre-conception consultation that would allow a thorough discussion of the impact of their disease on pregnancy, as well as the risks and benefits of continuing a medication during pregnancy (15). There are differences between chronically ill women

and healthy women in peri- and prenatal variables as well as birth outcomes on the population level. However, they are less frequent than expected (16).

It is a favorable signal that only 11 % of women reported smoking before pregnancy, and after conception their number decreased radically to 0.66 %. On the other hand, it is alarming that there are mothers who continue despite pregnancy. Smoking during pregnancy is in relationship with premature birth and lower birth weight of the newborn. Premature labor leads to severe complications such as respiratory insufficiency and insufficient maturation of the gastrointestinal system, as well as delayed development of the nervous system. Low birth weight may increase mortality and morbidity in the neonatal age (17). Regarding consumption of caffeine, almost half of all women in this study reported consumption of coffee during pregnancy, what is a relatively high amount. A meta-analysis of seven studies in 1998 has demonstrated a significant increase in low birth weight linked with caffeine intake during pregnancy (18).

Nutritional supplements may have a protective effect on embryo-fetal development. Commonly, physicians recommend usage of prenatal vitamins and minerals. In this study prenatal vitamins were used mostly by women in the I. trimester, in the II. and III. trimesters the number slightly decreased. Although, in the presence of sufficient diet, such supplementation may lead to an upper limit for reference doses (19). Many micronutrients in excessive doses are related to health risks (20). Animal studies suggest that intrauterine exposure to high levels of vitamins and minerals increases susceptibility to obesity and metabolic abnormalities in the offspring (21).

In the I. trimester, the most frequently used supplement was folic acid, which is important for adequate fetal development during the prenatal period. Its clear importance in pregnancy lies in the process of developing the brain and the nervous system, especially in the prevention of neural tube defects (22). In Slovakia, 5 per 10,000 live-born children are affected by congenital malformations of the central nervous system. Some drugs, in particular folic acid antagonists (anticonvulsants, trimethoprim and others), significantly increase the risk of neural tube defects in children of women during the critical period of development (23).

Iron was used mainly in the III. trimester. Iron deficiency is the leading cause of anemia in pregnancy with an estimated worldwide prevalence of 20–80 %. In addition to the general consequences of anemia, there are specific risks to the mother and fetus during pregnancy, such as intrauterine growth retardation and preterm birth (24). Much attention is given to conditions of iron deficiency and iron deficient anemia, because of the high global prevalence estimated in this vulnerable life stage. Preliminary evidence demonstrates a U-shaped risk at both low and high iron status for birth and infant adverse health outcomes including growth, preterm birth, gestational diabetes, gastrointestinal problems, and neurodegenerative diseases during aging (25).

At least one drug (not including nutritional supplements) was used by 45.7 % of women during pregnancy (26). Compared to other developed countries, this number is similar. In a retrospective study including more than 19 000 women, about 90 % were taking at least one medication (either prescription drug or over-the-counter drug) during the pregnancy (27).

In the present study, hormonal preparations were the most frequently administered drugs. In the first trimester 20.7 % of women used dydrogesterone and levothyroxine. Dydrogesterone reduces the risk of miscarriage and is mostly used at the beginning of pregnancy (28). Thyroid hormones are necessary for healthy fetal development (29). Decreased thyroid activity before pregnancy and regular pharmacotherapy with levothyroxine reported 7.32 % of respondents. Levothyroxine has no evidence for drug-induced teratogenicity or foetotoxicity in humans at recommended doses (29). The second most frequently used medicaments in present study were analgesics, predominantly paracetamol (acetaminophen). In study performed by Werler et al (2005) paracetamol, as an over-the-counter medication, was used at least 65 % of the time (30). Paracetamol is the safest antipyretic and analgesic medicine for nociceptive pain in pregnancy, while it should be used short-term and at the lowest effective dose (31).

Since from varicose veins suffered 8.64% of women before conception, to often prescribed drugs belonged fraxiparine as anticoagulant. Low-molecular weight heparins are preferentially administered in pregnancy, since they do not cross the placental barrier (32). Many times infectious diseases cannot be avoided in pregnancy (33). Anti-microbial agents prescribed in this study were predominantly beta-lactam antibiotics (penicillins and cephalosporins), which have long-term good experience with regard to possible teratogenicity (34). Allergic diseases before conception were reported by 8.64 % of women surveyed. Both asthma and atopic conditions may worsen, improve or remain the same during pregnancy. Intranasal and inhaled steroids are relatively safe to continue during pregnancy (e.g. budesonide), preferred are the second-generation antihistamines as cetirizine and loratadine (35).

The results of present study suggest that in Slovakia there is sufficient education in the area of drug risk in pregnancy. A certain number of mothers even completely eliminate the medication during pregnancy because of the fear of disturbed fetal development. Results of a multinational European study conducted in 15 European countries show that the most women used medications classified as safe, only about one-third used medications classified

as risky, and 3% used medications with no classification available (36). The benefit of pharmacotherapy applied in pregnancy must always outweigh the risks it carries, but only few recently approved pharmaceuticals by FDA contain human data in their pregnancy section (37). On the other hand, the disease itself can be teratogenic. Therefore, to absolutely avoid the use of drugs in pregnancy is not desirable.

Conclusion

In pharmacotherapy during pregnancy, the drug is applied to the mother, while embryo and fetus become an undesirable recipients and its effect is manifested as unwanted. It is necessary to minimize the risk on prenatal development and in treatment of acute or chronic diseases of pregnant women are preferred drugs that have long-term experience over the newer ones. Obtained results through surveys represent a suitable way how to collect information on drug usage in pregnancy that can be helpful in formation of national databases.

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