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Rational Use of Medication in Pregnant Women

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Abstract

Introduction: the use of medication in pregnancy is a worldwide health challenge, since it can cause complications for both the pregnant woman and the fetus, and this risk is potentially increased in the first gestational trimester. **Objectives:** The objective of this article is to conduct a literature review on the rational use of medication in pregnant women. **Materials and methods:** The articles published from 2013 to 2019 in Portuguese - Brazil were used for the development of this literature review through an electronic search in the platforms: SCIELO - Scientific Electronic Library Online and Google Academic. **Results and Discussion:** 14 articles were analyzed, which showed a reflection on the effects of the use of drugs during pregnancy, where the perceptions of the authors were divergent, between the certainty that everything is harmful or everything is beneficial. **Conclusion:** Great variations were observed regarding the use of medication, in the same way, that the need for intervention promoting an increase in the rational use of medication is evident.

Keywords: Risk classification; Pregnancy; rational use of medication.

1. Introduction

The use of drugs by pregnant women became the subject of a great debate from the 1950, with the tragedy of thalidomide, a sedative drug used in the treatment of nausea and vomiting during pregnancy, which induced the birth of about 10,000 babies with phocomelia, a congenital malformation, which until that time was considered unusual. Only after this tragic event was it discovered that some drugs can cross the placental barrier [1]. The use of drugs during pregnancy consecutively represents a great challenge for health professionals, because it can cause a series of problems for both mother and baby, and this danger is exacerbated in the first 12 weeks of pregnancy, in the prenatal period it is necessary to deliberate on certain medications by professionals of basic care, to take care of the accommodated irregularities of the neural canal and anemia during pregnancy [2]. There is a great ethical challenge on the part of health professionals regarding clinical trials with pregnant women, doubts about the risks to the fetus, and insufficient scientific evolution, epidemiological drug research is of fundamental importance concerning the specific focus on the gestational period. The researches emphasize the value of individualized analysis of drugs used in pregnancy. For these factors the classification of risks on the use of drugs during the gestational period is adopted [3]. In the gestational period, there are several morphophysiological transformations due to the baby's generation. Consequently, the use of drugs by the mother is expanded to the baby who may suffer various types of reactions (death, abortion or malformation) this depends on the type of drug used in pregnancy, and also the constancy of doses used. For this reason, it should always take into account the risk-benefit regarding the use of drugs in the gestational period [4]. As a result, most of the drugs available on the market do not have a specific safety margin in human pregnancy. Until now, a small number of drugs have proven to be important teratogens, some of which have subtle effects on fetal development. And the consumption of drugs prescribed or not varies amazingly among social classes [5]. Although several drugs have records of teratogenic or malefic purposes when used in the gestational period, prescriptions of drugs for pregnant women are frequent. Although several factors determine the increased use of drugs prescribed during the gestational period, most of them for the treatment of chronic diseases. Another determining factor is the fact that most pregnancies are not targeted, which leads to the use of certain drugs even

before the woman knows she is pregnant [6]. One of the most important activities performed by the pharmacist is to analyze medical prescriptions, dosage, possible drug interaction, or with food or some pathology, therapeutic indication, route of administration, adverse effects to prevent and solve problems due to the use of drugs [7]. The irrational use of drugs in the gestational period can generate a negative impact on public health due to possible adverse reactions and microbial resistance. Research shows that adverse reactions reach 3.5% of hospital admissions. Causing an expenditure on health services of US$ 21 million per 100,000 inhabitants [8]. The objective of this article is to conduct a literature review on the rational use of drugs in pregnant women.

2. Methodology

It is an exploratory study of literature, elaborated through scientific articles already published. It aims to approach in a qualitative way the subjects related to the rational use of medicines in pregnant women. The data survey was conducted through the search in electronic platforms: SCIELO - *Scientific Electronic Library Online* and Google Academic. Articles in Portuguese-Brazil were included, published between 2013 and 2019, which was adapted to the subject. Thus, articles paid for outside the established period were excluded, as well as those that escaped the proposed theme. The terms were used: Rational Use of Drugs, Pregnant Women, Risk Classification. The analysis of the results was carried out through the reading and rigorous analysis of the chosen articles taking into consideration the inclusion and exclusion criteria defined, where the necessary information was extracted for the preparation of the article. Thus, since it was a research carried out with literary materials, the present article did not need to be submitted for approval with the Committee of Ethics in Research, according to the National Health Council (CNS) resolution 466/2012.

3. Results and Discussion

After the research, 14 articles were selected that fit the objectives and inclusion criteria, according to table 1.

Table 1: Articles used in this research

Quantity		Year of publication
04	Articles	2013
05	Articles	2014
01	Articles	2016
02	Articles	2017
01	Articles	2018
01	Articles	2019

The first weeks of pregnancy it is the most delicate period and the one of greater risk of harmful occurrences for the embryo, it is in this stage that the fundamental embryological modifications take place, being indispensable the redoubled care in the use of medicines during the gestation season [12]. The use of any medicine during pregnancy should always prioritize risk-benefit for mother and fetus. Where the drug of choice has to be the one that has no teratogenic purpose or functional transformation13. To provide guidance, the American Food and Drug Administration (FDA) mentions the drugs used in pregnancy, as well as classifies the risks presented by them in the first trimester of pregnancy into 5 categories (A, B, C, D and X) shown in Tables 2 and Table 3 [12].

Table 2: Risk Classification of Drugs for Use in Pregnancy according to the FDA.

Risk Category A	Studies on women showed no risk for the fetus in the first and another trimester:
Risk Category B	Studies in animals have not shown fetal risk, but there are no studies in humans;
Risk Category C	Reports in animals have revealed adverse effects on the fetus. There are no controlled studies in women and animals. Drugs should be administered only if the benefit justifies the teratogenic potential;
Risk Category D	There is positive evidence of fetal and human risk, but the benefits of use in pregnant women may be acceptable;
Risk Category X	Studies on animals or human beings have revealed deleterious effects on the fetus that outweigh the benefits.

Table 3: Pharmacological classes of drugs and their respective indications for use in pregnancy and lactation.

Pharmacological class	**Drugs**	**Indication and Classification according to FDA**
Antibiotics	Azithromycin, Erythromycin, Clindamycin; Cephalexin; Nitrofurantoin;	Risk Category B, being used only with medical guidance;
Anti-inflammatories	Acetylsalicylic acid, Nimesulide;	Category C risk, presenting a high degree in teratogenics in the fetus;
Antihypertensives	Captopril, Methyldopa, Nifedipine, Atenolol;	They present category C and D, with high toxicity degree and others cannot rule out the possibility of damage to the fetus;
Antianemic	Folic acid;	Category A recommended for use during pregnancy.
Pharmacological class	**Drugs**	**Indication and Classification according to FDA**
Anticoagulants	Warfarina	Category X, causing malformation of children.
Antipsychotics	Haloperidol	Category C, no significant increase in abnormalities.
Diuretics	Hydrochlorothiazide, Furosemide, Spironolactone;	Categories B, C and D respectively, with risks and damages that may outweigh the benefits, such as inhibition of birth or lactation;
Corticoids	Prednisone;	Category B, being able to cross the placental barrier and also to pass to the maternal milk.
Antigases	Simethicone	Category C, however, there is not enough information in the literature to prove any teratogenic effect;
Antifungals	Cetoconazol	It crosses the placenta and can cause fetal problems during the first trimester of pregnancy. It is recommended not to prescribe it during pregnancy and lactation.
Antiparasitic	Mebendazole	Category C. Possible risks associated with the prescription of Mebendazole during pregnancy should be weighed against the expected therapeutic benefits.
Retinoids	Isotretinoin	Category D, causing teratogenic effect, and generation of permanent defects in the fetus.
Antidepressants	Amitriptyline	Category C, the possible benefits should be confronted against the possible risks for mother and child.

Source: Ribeiro, 2013 [12]

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The literature points out that the most prescribed drugs for pregnant women are dipyrone sodium, butylscopolamine, cephalothin, Tenoxicam and ferrous sulfate. The most cited classes were those of action on the central nervous system, gastrointestinal tract, and anti-infectives for systemic use, analgesics are also cited, and antibacterial for systemic use [14, 16, 17]. In contrast, the FDA reports that the pharmacological class of drugs most used and those less used in pregnancy and lactation and their respective indications for use are the Antianemic, such as folic acid, which is included in "category A" due to its beneficial effect. The same study points out that the anticoagulants: Warfarin, antifungals: ketoconazole, Retinoids: isotretinoin and diuretics: Hydrochlorothiazide, Furosemide and Spironolactone are the drugs less used, due to their teratogenic effect, which can cause poor formation in newborns, which are included in categories C, D, and X [12]. The cited authors say that this difference is a reflection of the characteristics of health care services, where public health problems and cultural differences between the places studied. The same argument of these authors could explain the differences between the cities involved in the study. However, going further, one could propose that the use of drugs would not only reflect but also be part of these differences [1, 2, 12]. There are situations where the lack of clinical trials, whether due to operational obstacles or important ethical limitations, cooperates to a dangerous lack of definition. The empirical use of drugs in pregnancy can be seen as a much less justifiable "experiment" because when not very conservative, they can expose the concept and mother to situations that often lead to unknown outcomes [16]. In some studies, different situations are analyzed, which in specific situations, with solid information, the therapeutic intervention, with fetal exposure, presents itself in a safer way than the lack of exposure due to the possible morbid consequences of the pathological condition of the mother. An example in this sense is the use of corticoids for the maturation of the fetal lung between the 24th and 34th weeks of gestation, in case of risk of premature birth. Another example is antibiotic therapy to combat chronic infections during pregnancy and intrapartum [4, 6]. The problems related to pregnancy have been discussed for a long time, this issue has become a worldwide concern, because of the diseases that affect the pregnant woman as well as the fetus, concerning the disease process that results in high-cost treatments, determining an impact on the economy of the country. Among the clinical pathologies that characterize high-risk pregnancy are Gestational Hypertensive Syndrome, Diabetes Mellitus (DM) and syphilis. In these cases, the use of medication becomes indispensable for the health of mother and baby [13, 14, 15]. These questions are preponderant, so that, crucially, few studies are unequivocal about the compliance of the therapeutic regimen by the patients under study. Since in certain specific cases, drug treatment is used for curative purposes, and in others, drugs can be used indiscriminately, as a protocol for all, such as in the use of anti-anemic and multivitamin preparations, which are used in a prophylactic manner, because they provide cost-effective advantages, but the literature shows no evidence of benefit [16]. Therefore, studies on the effects of exposure are indispensable, such as the determination of the "risk window" appropriate to the risk that follows an exposure. Analyzing, the greater or lesser probability of showing possible effects or the absence of them. To have an effective risk window it is also essential to have a comprehensive knowledge of the distinctions arising from exposure to the substance or substances in question, as well as the phenomenon to be studied [17]. Another public health factor that may affect pregnant women is self-medication, where part of the researches discusses the problem, whose

organizational structure represented by the Unified Health System (SUS) did not reach a sufficiently efficient level, favoring self-medication, in the classes that depend on the system. These studies show that guidance on the risks of certain drugs during pregnancy is below ideal [15, 17].

4. Final Considerations

The use of medication in pregnancy involves and exposes the future of both mother and concept, creating great ethical and technical challenges. Since there is no way to abstain pregnant women from the risks of drug therapy, which in some cases would be inappropriate and irrational because, like most of the population, women in the gestational period are subject to complications that require drug intervention. The danger in question arises not from the use of medication, but self-medication and unassisted use of therapy. To overlap this practice, it is proposed the responsible involvement of health professionals, such as pharmacists, with intervention measures, and that stimulate the rational use of medicines. In the same way, the studies have shown that there is a lack of clinical grounds, focused on obstetrics.

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