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Short communication

Pharmacovigilance system role in safe use of medicines in pregnancy and breastfeeding

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Introduction

Lack of drugs safety information can negatively affect the optimal treatment of pregnant and lactating women. At the same time certain diseases, without proper treatment, pose a risk to the health of mothers or the fetus. In addition, breastfeeding may be discontinued due to a specific illness diagnosed to mothers who are facing unavoidable need for appropriate treatment. Lack of information obtained both from properly designed and conducted clinical trials, as well as from postmarking surveillance often averts healthcare professionals and patients from the decisions for treatment of underlying condition. In some cases, this can result in increased harm for mother and fetus beside appropriate treatment is available.

Spontaneous reporting of adverse reactions is insufficient to routinely detect fetal risks caused by medicine use during pregnancy. Therefore, there is a growing need for active involvement of pharmacovigilance activities in the process of monitoring of drugs utilization during pregnancy, nationally and globally. In order to establish appropriate guidelines and recommendations for drug use during lactation, there is a need to monitor the use of drugs in breastfeeding woman.

Despite the lack of safety information, drug use in pregnant and lactating women is widespread with estimates of prevalence between 40 and 96% of women receiving at least one prescribed drug during pregnancy (Cleary et al., 2010).

Materials and methods

Relevant European, American and Macedonian legislation was reviewed, in particular, Directive 2010/84/EU, Regulative (EU) 1235/2010, rulebooks, as well as PubMed, Medline and other relevant web sites for articles with empirical analysis, evaluating the impact of European and non-European regulatory activities.

Results and discussion

Safety data obtained in the pre-authorization phase are limited, due to the restrictions of clinical trials in terms of size, time, duration of follow-up and the inclusion/exclusion criteria for selecting participants. That rises the need for pharmacovigilance guidance for the use of medicinal products in different patient population including pregnancy and lactation. This should be considered in the wider context of women of childbearing potential as pregnancy may be unplanned, treatment may be started at young age or long before the woman is considering pregnancy, so the effects of the medicine on pregnancy and the need to avoid pregnancy or for preconception counselling may have to be taken into account by the prescribing physician and the patient (GVP, 2019). Women need to be provided with effective and safe treatment during pregnancy and lactation. Their health, as well as the life and health of their fetuses/newborns, may be endangered due to improper prescription of drugs, unsuccessful dosing of drugs and in general, failure to provide safe and effective treatment. The monitoring and

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evaluation of drugs used during pregnancy and lactation is and the consequent effect on the fetus/newborn is essential for obtaining reliable data for pregnancy-related clinical pharmacology. Ongoing studies identifying commonly used drugs in pregnancy are important in prioritizing the study of birth defects with major implications for public health. (*Report of a WHO Global Survey*.Geneva,2005). A safety monitoring mechanism and stabile capacity of pharmacovigilance system needs to be established in order to provide reliable information for promotion of safe and effective treatment during pregnancy. Successful recruitment of an adequate number of pregnancies exposed to medicines, together with comprehensive monitoring during pregnancy and accurate determination outcomes in newborns form medicine treated mothers are key elements in creating a well-designed registry or database as a reliable source of information for drug utilization during pregnancy and breastfeeding. Having this approach is crucial in building capacity for improved maternal and neonatal care within the overall health care system.

Depending on the available evidence for the product in the areas of pregnancy and breastfeeding, the risk management plans (RMPs) will reflect the measures considered necessary to identify, characterize and minimize a medicinal product's important risks. Spontaneous reporting during the post-authorization phase is one primary source of information on adverse reactions occurring following exposure in utero or during breastfeeding. Signal detection on spontaneously reported adverse reactions in the post-authorization phase specific for pregnant women should be taken into account. Identified signals related to women who are of child-bearing potential, planning a pregnancy, are pregnant or breastfeeding are communicated with healthcare professionals or patients in order to keep them informed when making therapeutic decisions. The evaluation of data in the PSUR may be one way of further characterizing risks of medicine use during pregnancy and breastfeeding. For medicines where safety data relating to use of a medicine in pregnancy and breastfeeding are limited, additional pharmacovigilance activities may be warranted. It is considered when use of the product cannot be discontinued during pregnancy due to the disease, when a disorder arises during pregnancy that needs treatment, or where changes in treatment during pregnancy are associated with risks for the pregnant woman and/or the fetus; Additionally, this approach is necessary if a potential risk to the child has been suggested by non-clinical data, when a signal based on the chemical or pharmacological properties of the medicine where the medicine is used to treat conditions that occur commonly in women of child-bearing potential or if measuring compliance with risk minimization measures (RMM) in place regarding pregnancy or breastfeeding is required. The RMMs are aiming at avoiding exposure *in utero* for drugs with identified teratogenic properties, avoiding the unplanned pregnancy by discontinuing, switching or changing the dosage route of administration the drug where possible. Concerning the breastfeeding woman, the RMMs should enable minimal exposure to breast milk by optimized timing of medicine intake, discontinuation or even avoiding of breastfeeding.

All important information could be appropriately distributed to the HCP and patients with approved educational material by regulatory agencies. The educational material also contains information related to encouragement of healthcare professionals and pregnant women to report exposure and pregnancy outcomes or suspected adverse reactions in a (breastfed) child to, as appropriate, a pregnancy registry with follow-up into breastfeeding.

Sometimes well-established epidemiological studies, such drug utilization studies, medicines safety studies and Studies to evaluate the effectiveness and broader impact of RMM are needed, and the use of drugs in pregnancy and/or breastfeeding have to be provided in these studies. Sometimes additional pharmacovigilance activities such data collection from pregnancy registry are justified as well as evaluation of long-term pregnancy outcomes, especially as some adverse events and health outcomes become apparent many years after exposure.

Conclusion

In order to ensure adequate treatment with drugs with a positive benefit / risk ratio in pregnant and breastfeeding women and their children, it is necessary to provide appropriate information and their implementation within the framework of the law. Regulation of the national level should be harmonized with regulation and rulebooks for good pharmacovigilance practice in pregnancy and breastfeeding adopted and implemented EU.

References

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