Drugs during lactation accenting boron exposure

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Abstract

OBJECTIVES: The benefits of breastfeeding are generally accepted. Risk of drug usage for baby due to lactation is well assessed minimally in certain cases. However, information given about drugs are often insufficient, frustrating, and not recommending lactation. In Czech Teratology Information Service (CZTIS) counselling we use these information.

RESULTS: We have given advice in 58 cases inquiring the CZTIS about the risk of drug exposure during lactation. The most frequent queries were on chronic disease treatment following the drug exposure during pregnancy. Remaining cases were associated with acute infections. Mothers suffered from idiopathic bowel disease and psychiatric patients want to be informed before delivery about possibility to breastfeed their babies. Treatment of epilepsy, another frequent disease, is associated with better level of knowledge of both, neurologists and patients. Breastfeeding is recommended according to management in care of epileptic women.

CONCLUSION: In our counselling we consider the factors which are involved in drug transfer in the milk and mechanisms and steps of transfer as well. We follow the classification of drugs during lactation by their effect on infants: absolutely contraindicated, temporary cessation of breastfeeding, drugs of special concern and drugs compatible with breastfeeding.

We would like to dedicate this paper the memory of ***Prof. Richard Jelínek, MD., DSc.*** *(1934–2008)*

CASE REPORT

INTRODUCTION

The benefits of breastfeeding are generally accepted. The problem appears if mothers are exposed to drugs due to acute or chronic diseases that has to be treated. There is only little information about prescribing medications and their level in milk. Lack of information is done due to insufficient research on this field. Studies on experimental animals are connected with technical problems. Composition of milk varies in different species, volume is small in laboratory animals. Milk composition also changes during lactation. Clinical trials on lactating women are not acceptable due to ethical problems. Studies dealing with this problem are rare. Therefore, the risk estimation for clinicians is difficult.

It depends on chemical structure and properties of the drug that may be different in similar drugs. Passage of medications into mother´s milk depends on these factors:

a) Physico-chemical properties of drugs: molecular weight, ionization, lipid solubility, protein binding.
b) Pharmaco-kinetical parameters of drug: oral bioavailibility, volume of distribution, half-life (Begg, 1996).

SUBJECT AND METHODS

Czech Teratology Information Service (CZTIS) gives answers to the queries about risk of drug exposure during pregnancy. We analyzed consultations on drug exporure during 11 year long period (1997–2007). Questions were solved after phone or e-mail request. Answers were given to the health care providers, only. Informations were based on data from relevant databases (AISLP at *www.aislp.cz*; Micromedex, 2007; Medline), experiences of the other members of the European Network of Teratology Information Services (ENTIS) and monographies (Briggs *et al*., 2005; Bennet, 1996; Schaefer, 2001). We analyzed time of question and groups of drugs used. Except for the analysis of our consultations during last years, we give an example of problems that have to be solved.

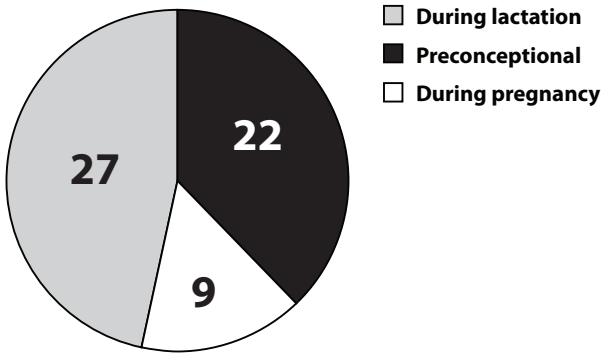

Figure 1. Majority cases were queries still before birth (during pregnancy and preconceptional together) for chronic diseases, questions during lactation were for acute illnesses, mostly.

RESULTS

We obtained 1351 questions during mentioned period. Except for queries on exposure during pregnancy, 58 cases were the drug exposure during lactation. Majority of them were questions about drugs that has been used chronically just before birth. They were joined many times with quiery on drug exposure during pregnancy (Figure 1). The most frequent were the question on psychotropic drugs – 18 cases (psychiatric diseases and epilepsy) or disorders of immunity, autoimmune as well as alergic diseases – 13 cases. The questions on the treatment of acute infection diseases by antibiotics were also frequent (9 cases). Remaining queries were on beta-blockers, vaccination, and also cytostatic treatment of malignant tumors and immunosuppresion for kidney transplantation (Figure 2). In comparison with Slovak centres offering consultation, we had higher number of exposures to the psychotropic drugs and lower to the antibiotics (Tisoňová *et al*., 2006).

In our paper we present information about problems that have to be solved. We may documented it on case report answered by our TIS.

Query: Is it possible to use vaginal globules with boric acid during lactation for the treatment of yeast vaginitis?

Boric acid is bacteriostatic drug for local treatment used in different forms on skin, eye, vagina, or oral cavity. According to the provider recommendation, drugs with boron are allowed in the form of eye drops and dermatologic drugs during pregnancy and with exception for local nipple treatment during lactation as well. Vaginal treatment is not allowed during lactation for possible toxicity.

Boron is a trace element essential for plants but also for animals and bacterias. Boron affects expression of hox genes by inhibition of DNA deacetylation (Di Renzo *et al*., 2007). It may have by that way an effect on development and metabolism (Yazici *et al*., 2008). Sources of boron are food, especially plants, milk or water. Vegetarians have higher intake (Rainey *et al*., 1999). Boron is also used in cosmetics, for example in tooth creme. Boron compounds are resorbed only as boric acid. Acute poisoning is manifested by emesis, skin irritation, depresion of CNS, seizures or hyperthermia. Local toxicity is manifested by irritation of skin or mucous membranes. Threshold for chronical toxicity is about 0.45 mg/kg/day (Fail *et al*., 1998) Chronic toxicity may be caused by profesional exposure by inadequate hygienic conditiones on the work place. Studies conclude that typical exposure in human is under treshold level that may have an impact on reproduction (Moore, 1997; Narotsky *et al*., 1998; Price *et al*., 1998). Boron intake should be limited especially in children. They are more sensitive than adult and higher dose may be danger for them. Degree of boric acid ionization is

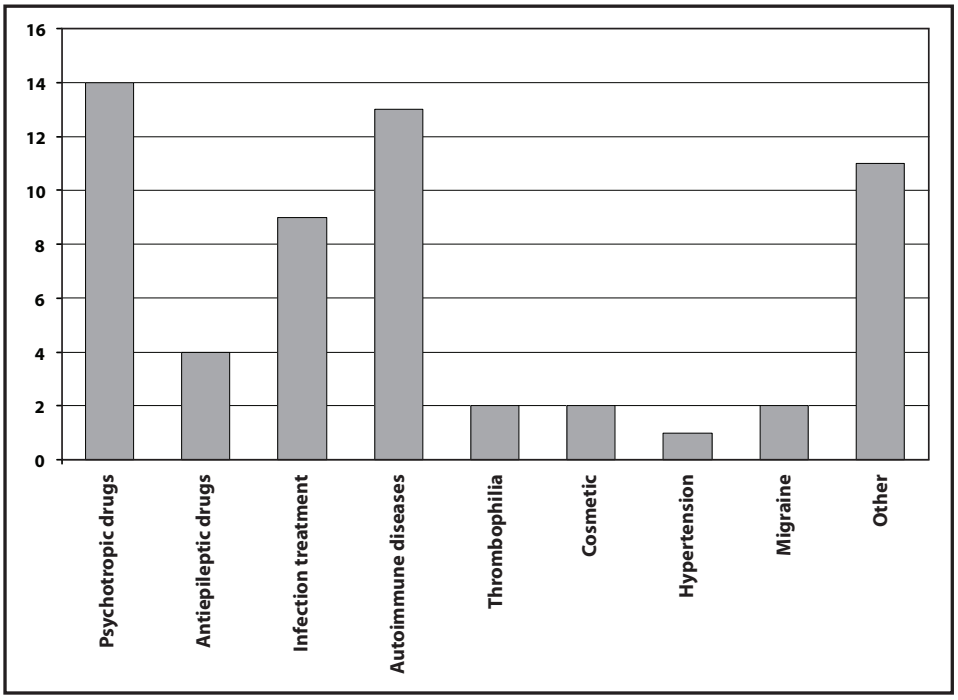

Figure 2. The highest number of questions was for psychotropic drugs and for treatment of chronic autoimmune diseases. Very frequent were also queries for acute infectious illnesses and their treatment by antibiotics. Women were treated by combination of drug in many cases.

low in vagina. Therefore it is not resorbed and plasma level is very low. Higher level of ionisation is by oral intake and resorption by this way facilitating resorption is also higher. Boron is actively secreted to the milk, but concentration in milk is very low and relatively steady (30 μg/L), probably under metabolic control (Anderson, 1992; Hunt *et al*., 2005).

Epidemiological studies did not confirm reproductive toxicity after vaginal treatment. It is rationale, if usage for the nipple treatment is not permit. Per-oral dose may be relatively high, poisoning was described. There is no reason for higher impact during lactation and lower or no during pregnancy. Borax exposure should be restricted during first trimestr, in reality for tentative caution/vigillance. Breasfeeding restriction shoud be taken in consideration if mother is poisoned. We suppose that there is no reason for any prohibition of the usage, if it is used for vaginal treatment, only.

In general, there are following medications considered fundamentally problematic during breastfeeding: antineoplastic drugs, radionuclides, combination therapy with several psychoactive or antiepileptic drugs, iodine containing contrast media, expectorans, and disinfectants. On the other hand, many antibiotics are acceptable. The dose for child is lower than 1% therapeutic dose based on weight. Plasma level is then only minimal if can be detected. It does not reach bacteriostatic level and it cannot affect bacterial growth and composition. However in this group of drug are these, which are contraindicated during lactation and are not acceptable for the treatment as for example chloramphenicol, and quinolones. Aminoglycosides may be used only if it is strongly indicated for mother treatment because of their ototoxicity. Other groups contraindicated during breastfeeding are antiinflamatory drugs (COX inhibitors, pyrazolone and phenylbutazone derivates), allopurinol for gout treatment, hormones (antiestrogenes, androgenes, and antiandrogenes). An accidental intake of a single dose does not require an interruption of breastfeeding, however treatment should not be continued. Medication that affect lactation perform the special group of drugs. There are drugs reducing production of milk (bromocriptine, cabergolin, dopamine agonists, amphetamines, diuretics) as contrast to the drugs stimulating secretion of prolactin followed by milk secretion increase (metoclopramide, alpha-methyldopa, phenothiazine, sulpiride and other drugs with antidopamine effect) (Schaefer, 2001).

CONCLUSIONS

When we solve problems with treatment during breastfeeding, we must find out all the data regarding appropriate drug. Risk for baby due to lactation should be correctly assessed using available data. Rules for drug treatment during lactation are the same as during pregnancy. It means that drugs should be used only if it is indicated and rather these drugs that are proved as safe. If necessary, breastfeeding may be stoped temporarily or permanently.

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