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Breastfeeding and risk classification of medications used during hospitalization for delivery: 2015 Pelotas Birth Cohort

Classificação de risco dos medicamentos usados na internação para o parto na amamentação: coorte de nascimentos de Pelotas/2015

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ABSTRACT: ***Objective:*** To classify the drugs used during childbirth in relation to risks in breastfeeding, by using different sources of information and determining their disagreements. ***Methods:*** Cross-sectional study, within the 2015 Pelotas Birth Cohort. Information about the use of drugs was collected, classified and compared regarding risk according to: 1) Brazil Ministry of Health Manual (MS), 2) World Organization (WHO), 3) Newton and Hale's classification and 4) American Academy of Pediatrics (AAP). ***Results:*** A total of 1,409 mothers participated, and they had used 14,673 medicines, with 143 different drugs, of which 28 showed discordant classification with regard to breastfeeding risk. These 28 drugs included the following: morphine (64%), classified by AAP and WHO as compatible and as judicious use use by MS and Newton and Hale; hyoscine (23%), classified as judicious use by MS and compatible (A) by AAP; and metoclopramide (18%), classified as compatible by MS, of effects unknown (D) by AAP, and should be avoided according to WHO. Of the total drugs, 49.7% were classified as compatible during breastfeeding. Almost all women used oxytocin (97.4%), followed by lidocaine (75%), ketoprofen (69%), cephalothin (66%) and diclofenac (65%), which were classified as compatible. ***Conclusion*:** There was extensive use of drugs by mothers in labor during admission, most of the drugs being classified at the same risk and almost half classified as compatible with breastfeeding. However, there was disagreement between the sources for 19.6% of the drugs analyzed, which could endanger the infant's health or leave doubts about the use of the drug or breastfeeding.

Keywords: Breastfeeding. Pharmaceutical preparations. Adverse drug reactions. Lactation. Drug utilization.

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RESUMO: ***Objetivo:*** Classificar os medicamentos usados durante o parto quanto aos riscos na amamentação, utilizando diferentes fontes e verificando suas discordâncias. ***Métodos:*** Estudo transversal inserido na coorte de nascimentos de Pelotas de 2015. Coletaram-se informações sobre o uso de medicamentos, classificando-os quanto ao risco de acordo com: manual do Ministério da Saúde (MS), Organização Mundial da Saúde (OMS), classificação de Newton e Hale e Academia Americana de Pediatria (AAP). ***Resultados:*** Participaram 1.409 mães, utilizando 14.673 medicamentos, sendo 143 fármacos diferentes, dos quais 28 tiveram classificação de risco na amamentação discordante. Entre aqueles com classificação discordante estão morfina (64%), classificada pela AAP e OMS como compatível e pelo MS e por Newton e Hale como criterioso; hioscina (23%), criterioso pelo MS e compatível (A) pela AAP; e metoclopramida (18%), compatível pelo MS, de efeitos desconhecidos (D) pela AAP e evitado de acordo com a OMS. Do total de medicamentos, 49,7% foi classificado como compatível com a amamentação. Quase a totalidade das mulheres utilizou ocitocina (97,4%), seguida de lidocaína (75%), cetoprofeno (69%), cefalotina (66%) e diclofenaco (65%), classificados como compatíveis. ***Conclusão:*** Houve amplo uso de medicamentos pelas mães durante a internação para o parto, a maioria deles classificada no mesmo grau de risco, e quase a metade classificada como compatível com a amamentação, porém houve discordância entre as fontes para 19,6% dos medicamentos analisados, o que pode colocar em risco a saúde do lactente ou deixar dúvida quanto ao uso do medicamento ou à prática da amamentação.

Palavras-chave: Aleitamento materno. Medicamento. Efeitos adversos. Lactação. Uso de medicamentos.

INTRODUCTION

The use of medications in the immediate postpartum period is very common, occurring in almost all postpartum women[1], which may be a reason for not breastfeeding. The World Health Organization (WHO) recommends breastfeeding for at least 2 years of age and exclusively until the sixth month[2], as breastfeeding is related to several nutritional, immunological, cognitive, psycho-affective, economic and social advantages[3], but breastfeeding time in Brazil and in several other countries does not meet this recommendation[4]. According to Victora et al.[5], if breastfeeding was extended to an almost universal level, it could prevent 823,000 deaths of children under 5 years each year and 20,000 deaths from breast cancer, with the additional benefit of saving 300 billion dollars.

Care should be taken when making a decision about whether a medication taken during breastfeeding is safe, where the risk to the baby and the benefit to the mother need to be assessed[5]. The oral bioavailability of drugs in the gastrointestinal tract of infants also needs to be considered, since many drugs are not absorbed by their gastrointestinal system. Greater amounts of medications can be transferred to mother's milk in the colostral phase, but only minimal quantities are transferred to the infant, due to the limited volume of colostrum. On the other hand, with mature milk, there is a larger volume, but less drugs are transferred to breast milk because of the tight junctions between cells[7]. Characteristics related to the drug, such as molecular weight, liposolubility, binding to plasma proteins and half-life, are also very important to determine the amount that reaches maternal milk[3].

It is known that the use of medications by mothers can influence the success of breastfeeding. Studies suggest that more than 50% of women in the postpartum period need to use at least one medication [8]. Taking into account the fact that these women may interrupt breastfeeding or not adhere to treatment for fear of exposing the baby to the drug through breast milk[9], it is believed very important to understand the risks of medications for the mother and the baby, and knowing the existing risk classifications as well.

The main risk classifications of drugs in breastfeeding, and also the most cited, are those established by the Ministry of Health of Brazil (MS)[10], American Academy of Pediatrics (AAP)[11], WHO[12] and Newton and Hale[13]. They include information on drugs and breastfeeding, guiding health professionals on the use of medicines in this phase of a woman's life[14]; however, these publications must be constantly updated to afford health care professionals with greater assurance in providing care for breastfeeding mothers, as new medications appear every day on the market and since information is controversial in some situations.

The objective of the present study was to classify the risks of medications used during hospitalization for delivery by breastfeeding women participating in the 2015 Pelotas Birth Cohort. Different sources of information were used, and disagreements between the sources were determined; the possible interferences with breastfeeding or baby health were described.

METHODS

We conducted a cross-sectional study from June to October 2015, which was included in the perinatal follow-up of the 2015 Pelotas Birth Cohort. More details on the 2015 cohort can be found in the methodological article[15].

Daily, trained interviewers collected data through the mothers' medical records, after hospital discharge, regarding prescription and use of medications during the entire hospitalization period for delivery. The following information was also collected: hospitalization; type of anesthesia (spinal anesthesia; epidural; topical; general; none); and type of delivery (vaginal or cesarean).

The mothers' sociodemographic data were obtained in an interview shortly after delivery, still in the hospital, by trained interviewers. The variables analyzed were: age (categorized as: 13–19, 20–30 and 31–45 years old), economic classification, according to the Brazilian Market Research Association of Research[16] (A, B, C and D/E), self-reported skin color (white, black and brown) and education (categorized as: 0–4, 5–8, 9–11 and 12 or more years of study).

Medications used by mothers were classified according to the risk in breastfeeding by the MS manual[10], WHO[12], Newton and Hale's classification[13] and AAP[11]. These classifications place drugs in risk categories for use while breastfeeding, due to unwanted effects on the infant or milk production.

Newton and Hale's classification has the following categories:

- level 1 (L1): compatible;
- level 2 (L2): probably compatible;
- level 3 (L3): possibly compatible;
- level 4 (L4): possibly dangerous;
- level 5 (L5): contraindicated [13].

The MS manual uses the colors green, red and yellow for the classification of drugs, which indicate, respectively, compatible use with breastfeeding, contraindicated use and do not have reliable information about its use during breastfeeding (judicious use)[10]. The AAP classifies medicines into the following groups:

- Group A: compatible;
- Group B: judicious use;
- Group C: contraindicated;
- Group D: effects unknown in infants, but require care [11].

WHO classifies drugs as compatible use, judicious use and to be avoided during breastfeeding [17].

Taking into account that each source uses different criteria to classify drugs, we considered them to be concordant so that the classifications could be compared:

- compatible with breastfeeding: L1 and L2 (Newton and Hale), A (AAP), compatible (WHO and MS);
- judicious use: L3 (Newton and Hale), B and D (AAP), judicious use (WHO and MS);
- contraindicated: L4 and L5 (Newton and Hale), C (AAP), to be avoided in breastfeeding (WHO), contraindicated (MS).

The information was entered into a tablet and transferred to the computer, and the data were analyzed in the Stata statistical package version 12.0 (StataCorp., College Station, TX, USA). Descriptive analysis was performed. First, the prevalence of drugs in each risk class (compatible, judicious use, contraindicated) was detailed, and the absolute and relative frequencies of each medication used were then calculated. For continuous variables, we used the mean and standard deviation (SD) or median and interquartile range (IQR) when the distribution was not normal. For categorical variables, we determined the proportion of each category of the variable. The proportion of drugs with concordant classification in each risk category and the total proportion with their 95% confidence intervals were also calculated for the concordant and discordant medications.

The study was approved by the Research Ethics Committee of the School of Medicine, Federal University of Pelotas, under Certificate of Presentation for CAAE the No. 26746414.5.0000.5313.

RESULTS

The study included 1,409 women, with an average age of 27 ± 7 (13 to 45) years. Of these, 70.3% were white, 15.4% black and 14.3% brown. The majority (48.7%) belonged to economic class C, and 33.9% had 9 to 11 years of schooling.

Cesarean was the most frequent delivery form, as was spinal anesthesia, both at a rate of 67%. A detailed description of the sociodemographic and hospitalization characteristics of the sub-sample studied can be found in a previous study[18]. After analysis (not shown in the results, since it was only done for comparative purposes), it was shown that the mothers participating in this sub-study were similar to the others in the cohort with regard to sociodemographic characteristics.

The median number of medications used by mothers was 6 (IQR_{25-75} 3 – 9), with 14,673 being the total number of drugs. The number of different drugs used was 143. Table 1 shows the percentages of drugs used there were considered compatible, judicious use or contraindicated in each of the classifications used. The number of possible medications to be classified was different between the sources, since the sources did not contain all the drugs used. Through the MS manual it was possible to classify 112 (78.3%) medications, while 38 (26.6%) according to the Newton and Hale classification, 49 (34.3%) by AAP, and 65 (45.5%) by WHO. Among the drugs used, 71 (49.7%; 95%CI 41.2 – 58.1) were considered compatible regardless of the classification source. Only two (1.4%) were seen as contraindicated according to MS and Newton and Hale. The WHO classification included the

Table 1. Number and percentage of medications classified as compatible, judicious use and contraindicated in each of the classifications*: n = 143 different types of medications.

	Medications not classified n (%)	Compatible** n (%) (95%CI)	Judicious use** n (%) (95%CI)	Contraindicated** n (%) (95%CI)
Ministry of Health Manual	31 (21.7)	75 (52.4) (43.9 – 60.9)	35 (24.5) (17.7 – 32.4)	2 (1.4) (0.17 – 5.0)
Newton and Hale	105 (73.4)	28 (19.6) (13.4 – 27.0)	8 (5.6) (2.4 – 10.7)	2 (1.4) (0.2 – 5.0)
AAP	94 (65.7)	38 (26.6) (19.5 – 34.6)	11 (7.7) (3.9 – 13.3)	0 (0)
WHO	78 (54.5)	53 (37.1) (29.1 – 45.5)	3 (2.1) (0.4 – 6.0)	9 (6.3) (2.9 – 11.6)

*Collected from June to October 2015; **total medications classified in each risk category considering concordance between each other. 95%CI: 95% confidence interval. MS Manual: compatible; judicious use; contraindicated; Newton and Hale: L1 compatible; L2, probably compatible); L3, possibly compatible; L4, possibly dangerous; L5: contraindicated; AAP: American Academy of Pediatrics: group A (compatible); group B (judicious use); group C (contraindicated); group D (effects unknown in infants, care must be taken); WHO: World Health Organization: compatible; judicious use; to be avoided during breastfeeding.

most studied drugs in the category to be avoided during breastfeeding, which we identified as contraindicated (n = 9, 6.3%).

As seen by the agreement between at least two classifications, of the total number of drugs used (n = 143), 49.7% (71; 95%CI 41.2 – 58.1), were classified as compatible and could be taken during breastfeeding. On the other hand, 11.9% (17; 95%CI 7.1 – 18.4) were classified as judicious use, and 1.4% (2; 95%CI 0.7 – 5.0) contraindicated. Disagreements were found for 28 (19.6%; 95%CI 13.4 – 27.0) medications, and for 25 (17.5%; 95%CI 11.6 - 24.7), there was no information.

Chart 1 lists the medications most used during hospitalization for delivery (at a rate more than 10%) that did not show disagreements between the study classifications. Included are oxytocin (n = 1,372, 97.4%), which is compatible with breastfeeding when used for a

Chart 1. Classification of risk to infant health for medications used during hospitalization for delivery that did not show disagreement between classifications and frequency of use between mothers: subsample* of 2015 Pelotas (RS) Birth Cohort (n = 1,409).

Medication	Ministry of Health Manual	Newton and Hale	AAP	WHO	Absolute frequency	%**
Ocytocin	Compatible	---	---	Compatible	1,372	97.4
Lidocaíne	Compatible	---	A	Compatible	1,058	75.1
Ketoprofen	Compatible	---	---	---	974	69.1
Cephalothin	Compatible	---	---	---	924	65.6
Diclofenac	Compatible	---	---	---	921	65.4
Paracetamol	Compatible	L1	A	Compatible	767	54.4
Ferrous sulfate	Compatible	---	---	---	759	53.9
Dipyrone	Compatible	L2	A	---	730	51.8
Simethicone	---	---	---	---	644	45.7
Metaraminol	---	---	---	---	558	39.6
Ondansetron	Compatible	L2	---	---	512	36.3
Bupivacaine	Compatible	---	---	Compatible	374	26.5
Scopolamine+dipirona	---	---	---	---	243	17.2
Fentanyl	Compatible	---	A	---	156	11.1
Droperidol	Judicious use	---	---	---	147	10.4

*Collected from June to October 2015; **relative frequency (shown are only those with a frequency greater than 10%); ---: No classification; AAP: Ministry of Health Manual: compatible; judicious use; contraindicated; Newton and Hale: L1: compatible; L2: probably compatible; L3: possibly compatible; L4: possibly dangerous; L5: contraindicated; AAP: American Academy of Pediatrics: group A (compatible); group B (judicious use); group C (contraindicated); group D (effects unknown in infants, care must be taken); WHO: World Health Organization: compatible; judicious use; avoid during breastfeeding.

short time. Its prolonged use should be avoided, as it can cause maternal dependence[17]. Next in order are lidocaine (n = 1,058; 75%), paracetamol (n = 767; 54.4%), dipyrone (n = 730; 51.8%), ondansetron (n = 512; 36.3%), bupivacaine (n = 374; 26.5%) and fentanyl (n = 156; 11.1%).

On the other hand, the most widely used drugs that showed disagreements between the classifications were: morphine (n = 905), which was classified by MS as for judicious use, by Newton and Hale as possibly compatible (L3) and by AAP and WHO as compatible; hyoscine (n = 324), classified by MS as judicious use and by AAP as compatible; and metoclopramide (n = 256), considered by MS as compatible and AAP as of unknown effects and which the WHO recommends being avoided during breastfeeding. Metronidazole and haloperidol are considered compatible with breastfeeding according to MS, and WHO recommends avoiding them, but they were respectively used by 1.6 and 0.1% of the mothers in this study. Ciprofloxacin was classified as compatible by AAP, as possibly compatible by Newton and Hale, as for judicious use by MS and as should be avoided by WHO with regard to breastfeeding (Chart 2).

DISCUSSION

The aim of this study was to classify the medications used during hospitalization for delivery regarding the risks of breastfeeding, by using four sources and determining the agreement between them. Of the total number of medications used, almost half were considered compatible with breastfeeding, while 6% were contraindicated. For one-fifth of the drugs, we found disagreements between the classifications.

One limitation of this study we can point out is the difficulty of reconciling, in the same risk category, drugs classified by different sources, as they resort to different nomenclatures to establish the risks, which led us to carry out a reclassification, to try to find concordances and divergences referring to the risk of the medication during breastfeeding. This lack of standardization and the disagreement between the classifications can result in uncertainty among health care professionals, often causing doubt about whether a medication is compatible or not with breastfeeding, which can lead to the discontinuation of breastfeeding or the medication that could be necessary.

The main factors that can explain these disagreements are:

- the use of different risk criteria and classifications between the sources;
- the type of evidence used by the sources to support their recommendations;
- updating each source (review).

In a study by Long and Montouris[19] based on the responses to questionnaires given to 202 professionals who participated in the annual meeting of the American College of Physicians in 2003, of which 92% were physicians, it was reported that more than 50% did not know that most anticonvulsants are safe when taken during breastfeeding. Therefore, constant

Chart 2. Classification of risk to infant health for medications used during hospitalization for delivery that showed disagreement between classifications and frequency of use between mothers: subsample* of 2015 Pelotas (RS) Birth Cohort (n = 1,409).

Medication	Ministry of Health Manual	Newton and Hale	AAP	WHO	Absolute frequency	%**
Morphine	Judicious use	L3	A	Compatible	905	64.2
Hyoscine	Judicious use	---	A	---	324	23.0
Metoclopramide	Compatible	---	D	To be avoid ed during breastfeeding	256	18.2
Promethazine	Compatible	L3	---	Compatible	189	13.4
Povidone-iodine	Judicious use	---	A	To be avoid ed during breastfeeding	153	10.9
Atropine	Judicious use		A	Compatible	129	9.2
Ephedrine	Judicious use	---	---	Compatible	103	7.3
Methylergometrine	Judicious use	---	---	Compatible	89	6.3
Diazepam	Judicious use	---	D	Compatible	35	2.5
Metronidazole	Compatible	L2	D	To be avoid ed during breastfeeding	23	1.6
Cabergoline	Contraindicated	---	---	Judicious use	8	0.6
Chlorpromazine	Judicious use	L3	D	To be avoid ed during breastfeeding	6	0.4
Acetylsalicylic acid	Judicious use		B	Compatible	2	0.1
Ciprofloxacin	Judicious use	L3	A	To be avoid ed during breastfeeding	2	0.1
Furosemide	Judicious use	L3	---	To be avoid ed during breastfeeding	2	0.1
Codeine	Judicious use	L4	A	Compatible	1	0.1
Fluoxetine	Compatible	L2	D	---	1	0.1
Haloperidol	Compatible	L3	D	To be avoid ed during breastfeeding	1	0.1
Rifampicin + isoniazid + pyrazinamide + ethambutol	Judicious use	---	A	Compatible	1	0.1
Atenolol	Judicious use	---	B	To be avoid ed during breastfeeding	1	0.1

*Collected from June to October 2015; **relative frequency (shown are only those with a frequency greater than 10%); ---: No classification; AAP: Ministry of Health Manual: compatible; judicious use; contraindicated; Newton and Hale: L1: compatible; L2: probably compatible; L3: possibly compatible; L4: possibly dangerous; L5: contraindicated; AAP: American Academy of Pediatrics: group A (compatible); group B (judicious use); group C (contraindicated); group D (effects unknown in infants, care must be taken); WHO: World Health Organization: compatible; judicious use; avoid during breastfeeding.

update on medication safety is essential to avoid interruption of breastfeeding. Doctors should choose to prescribe medications already studied for their safety in breastfeeding[1].

With regard to the choice of sources used, the use of the WHO classification was due to the fact that it is known worldwide and that of the Ministry of Health because the study was carried out in this country. The other two were the most cited in scientific articles; we found AAP to be the most cited. The Food and Drug Administration (FDA) classification was not mentioned here, since a new FDA classification came into effect in June 2015, Pregnancy and Lactation Labeling Rule, for use of drugs during pregnancy and lactation. Therefore, considering that it was being incorporated recently and that it did not allow us to compare it with the other classifications that were already being analyzed in the study, we chose not to use it, since it does not place drugs in risk categories, but rather exposes the risks to the infant or to milk production.

Of the four classifications studied, the one with the highest number of medications was that of MS (n = 112), followed by the WHO classification (n = 65). The Newton and Hale and AAP classifications showed fewer drugs (38 and 49, respectively). Looking at the recommendation for use during breastfeeding, the WHO classification had the highest number of contraindicated drugs, appearing to be the most rigorous classification.

Regarding the nomenclature used by the classifications mentioned, all with the exception of Newton and Hale, are very clear and objective. In the case of Newton and Hale, it was difficult to see the difference between L2 (probably compatible) and L3 (possibly compatible). Therefore, to be able to compare the classifications and considering greater safety for the infant, we chose to group L2 and L1 (compatible). L3 was considered as judicious use like in the other classifications, and L4 (possibly dangerous), grouped with L5 (contraindicated).

In the discussion of the results, emphasis was placed on medications that showed disagreements in the study classifications and/or whose effects were considered important. The drugs whose disagreements were greater and that had a higher prevalence of use were morphine, hyoscine, metoclopramide, promethazine, povidone-iodine, atropine and ephedrine.

The narcotic pain reliever morphine (n = 905) is excreted in low concentrations in breast milk[20,21]. WHO and AAP consider its use compatible with breastfeeding [11,12,17]. MS[8] and Newton and Hale[13] consider it to be for judicious use. Although AAP classifies this drug as safe, it recommends that its serum level be measured in babies [11], a procedure that is difficult in clinical practice[21]. Morphine can cause significant effects on suckling, apnea, bradycardia and cyanosis[13,17] and sedation in infants[10]. Prolonged treatment, at high doses, can increase its plasma concentration, leading to greater levels in breast milk, so the risk-benefit of breastfeeding should be evaluated[13,17,22]. MS recommends that breastfeeding should be stopped when there is maternal dependence on opioids[10].

Hyoscine (n = 324) is classified as judicious use by MS[10] and compatible with breastfeeding by AAP[11]. Although babies are sensitive to anticholinergic effects[22], AAP considers hyoscine safe, perhaps due to the fact that it is excreted in breast milk in insignificant amounts, with no side effects reported in infants[10,21].

Metoclopramide (n = 256) is classified as compatible with breastfeeding according to MS[10] and contraindicated by WHO[12], while AAP[11] classifies it as judicious use. It is excreted in breast milk, accumulating after repeated doses. This drug stimulates the release of prolactin in women with reduced or inadequate milk production[10,17,23]. MS considers the drug compatible when used for a short period. When used for more than four weeks, agitation, sedation and extrapyramidal manifestations have been described in the nursing mother[10], and infants may experience problems in neural development[17] and symptoms of gastrointestinal discomfort[21]. Metoclopramide apparently does not pose a risk for the infant with the use of maternal doses of up to 45 mg per day[21].

Promethazine (n = 189) is considered by WHO[12] and MS[10] to be compatible with breastfeeding when taken in a single dose, but Newton and Hale[13] consider it as judicious use. When repetitive doses are used, some adverse effects should be monitored, such as drowsiness[10,17], dry mouth, extrapyramidal symptoms and risk of apnea[13] in infants. In lactating women, milk flow may be reduced[10].

As for povidone-iodine (n = 153), repetitive topical applications of the solution should be avoided, as it can be absorbed and concentrate in breast milk, reaching a toxic level in the infant. Therefore, its chronic use is not recommended and it is recommended to monitor the baby's thyroid function[10]. AAP[11] considers the substance to be compatible with breastfeeding and MS[10] for judicious use, while WHO[12] contraindicates its use. It is advisable to monitor infants for hypothyroidism[17], as it was observed that breastfed newborns of mothers who used this medication had a 25 to 30-fold increase in the rate of congenital hypothyroidism compared to bottle-fed babies[21]. MS reports that there may be an increase in iodine level in breast milk and, consequently, changes in the neonatal concentration of thyroid stimulating hormone[10,21]. This increase in iodine in breast milk causes a strong odor from the baby's skin[11,21].

Atropine (n = 129) is classified as compatible by WHO[12] and AAP[11] and as judicious use by MS[10]. It is excreted in breast milk in small amounts, with peak plasma concentration occurring at one hour[10]. When used at high doses, it can cause decreased lactation. Although neonates are susceptible to anticholinergic effects, AAP and WHO consider this drug to be safe[22].

Ephedrine (n = 103) is classified as compatible during lactation by WHO[12] and AAP[11] and as judicious use according to MS[10]. It is recommended that irritability and disturbed sleep in infants be monitored[10,17]; these effects resolve spontaneously 12 hours after discontinuation of breastfeeding[21]. In mothers, the decrease in milk production must be monitored[10].

Methylergometrine (n = 89) is classified as compatible with breastfeeding according to WHO[12] and as judicious use by MS[10]. It is excreted in breast milk, which can cause ergotism[24], vomiting, diarrhea and seizures in the baby[25], and lactation and prolactin inhibition in the mother[17,24]. During the use of this drug, the infant's growth must be closely monitored[3].

Benzodiazepine such as diazepam (n = 35) and their metabolites are excreted in breast milk[21], but WHO classifies them as compatible with breastfeeding if taken in a single

dose. In repeated doses, however, they should be avoided when possible[12]. MS[10] and AAP[11] consider the drug as judicious use. If a benzodiazepine is necessary, short-term ones should be preferred[10,17]. This medication, when used by lactating women, has adverse effects on babies, such as slowness, sedation[17], low suction[10], weight loss, apnea, irritability, minimal risk of central nervous system depression[26] and electrocardiogram consistent with the use of sedative drug[10]. These effects may be present if breastfeeding occurs less than eight hours after the use of the drug, as the peak concentration in maternal plasma occurs between one and two hours after administration[10] and when the infant is premature or is underweight[17,21].

The active metabolite (oxazepam) has been found in the newborn's urine, but not in the mother's plasma or milk, even though showing a long half-life ub the baby. It is known that doses greater than 30 mg per day of diazepam should be avoided during lactation, while doses of 10 mg or less do not produce significant adverse effects in infants. However, more recently, significant effects have been noted with doses between 6 and 10 mg[22].

In regard to metronidazole (n = 23), WHO[12] contraindicates its use, and AAP[11] considers it as judicious use, while MS[10] views it compatible with breastfeeding. There is little systemic absorption with topical use, when used in low doses, and in short-term therapy it does not interfere with breastfeeding[20]. However, if the exposure is prolonged, it presents a potential risk of toxicity[27]. This drug is excreted in breast milk and can cause some adverse effects in infants, such as diarrhea, lactose intolerance[21] and changes in the baby's intestinal flora[6], in addition to the fact that it imparts an unpleasant taste in the milk. Therefore, it is recommended to discontinue breastfeeding for 12-24 hours after use by the mother[11,20,27]. An alternative to not discontinuing breastfeeding in this case is to collect the breast milk and store it in the refrigerator, in order to breastfeed the baby during this period[12]. Australian studies show that a third of doctors and pharmacists are unaware that metronidazole is compatible with breastfeeding when used as recommended[6].

As future perspectives, it is important to carry out studies with the drugs used by puerperal women, analyzing their effects on milk production and on important outcomes in the baby in the short and long term, to confirm the compatibility of these substances with this period in a woman's life.

FINAL CONSIDERATIONS

It is important that the mother and health care providers know the risks of the medications taken during breastfeeding, so that it is not interrupted if the use of medications is truly necessary, or that the patient does not stop using any needed medication because of concern that it may cause some risk to the child, or that if the medication is not safe, breastfeeding must be halted or another safer therapeutic option must be sought.

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