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# RISK CLASSIFICATIONS OF MEDICINAL PRODUCTS PRESCRIPTED TO INTERNAL LACTANTS IN THE MATERNITY OF A UNIVERSITY HOSPITAL

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**Abstract:** The use of medication by women during breastfeeding is a very common and growing practice in all stages of lactation and is among the factors most associated with early and abrupt weaning. This article presents a comparative analysis of risk classifications on medications used during lactation, identifying the most prescribed medications for breastfeeding women in a university hospital. For this, an observational, cross-sectional and descriptive study of the prescriptions of medications from the maternity hospital felt to the pharmacy sector during the months of September and October 2019 was carried out. Of the 507 prescriptions analyzed, 81 different types of medication were identified, with an average of 7, 24 medications / prescription. The prevalent prevalence of the therapeutic class was 16.28% of analgesics and 15.21% of antiemetics and antinauseants. According to the classification presented by the Ministry of Health, among the different types of medication observed in the study, 72.84% (n = 59) were classified as "compatible", 27.16% (n = 33) as "judicious" and no drug was identified as "contraindicated", if used during lactation. However, according to the international classification consulted, only 29.63% (n = 24) of these were categorized as "compatible". This divergence of results between the consulted databases indicates the importance of constantly updating the literature used by health professionals and the need to standardize the information provided to the patient, with a view to promoting safety during the use of medications and the breastfeeding process.

**Keywords:** Breastfeeding, Pharmacology, Lactation, Patient safety, Pharmaceuticals preparations.

## INTRODUCTION

Breastfeeding is universally recommended by the World Health Organization (WHO) due

to proven knowledge of all its benefits. Among the advantages provided by breastfeeding are the availability of nutrients and antibodies for the infant, promoting the strengthening of the affective bond between mother and child, stimulating the child's cognitive and psychomotor development and reducing the incidence of diseases in women (Caminha et al, 2015, Santos et al, 2017).

During the lactation period, it is common for women to use medication, especially in the first hours after childbirth. Studies show that the use of drugs during this period is among the factors most associated with early and abrupt weaning (Chaves; Lamounier; César, 2007). Although significant concentrations of the drug in breast milk are not frequently detected, many nursing mothers are advised to stop breastfeeding due to the use of some medication (Brasil, 2014).

Among the justifications for weaning in this condition are the excessive precaution regarding the risk of adverse and toxic effects for the baby, the lack of knowledge about the pharmacokinetics of drugs, the lack of in-depth information in the drug inserts, the lack of scientific studies in the literature on the safety of drugs in lactation and the fear of nursing mothers to use medication during this period (Costa et al, 2012 Sociedade Brasileira de Pediatria, 2017).

It is known that the lack of information about drug safety in lactation is a complicating factor in decision-making during prescription or guidance by the health professional (Fragoso; Silva; Mota, 2014). In this context, the present work presents a comparative analysis between the risk classifications, on drugs used in the lactation period, brought by the national bibliographic base of the Ministry of Health and the international base: *Medications and Mothers' Milk*, regarding the most commonly prescribed standardized medications in the maternity hospital of a university hospital.

## METHODS

An observational, cross-sectional and descriptive study was carried out in the Pharmacy Sector of the Hospital das Clínicas of the Federal University of Pernambuco, in which maternity prescriptions were evaluated. For this, the daily medical prescriptions of patients hospitalized for at least 24 hours in the maternity ward, from September to October 2019, which contained at least 1 medication, were used.

In the first stage, an analysis of the prescriptions was carried out to identify the most frequently prescribed drugs and then they were classified according to lactation safety, according to two chosen bibliographic references. The bibliographic databases selected for classification were: the 2nd edition of the 2010 Ministry of Health's "Breastfeeding and Use of Medicines and Other Substances Manual" and the "Medications and Mothers' Milk" by Hale & Rowe, version 2019, available on an online platform.

In the first classification system, drugs are separated into 3 categories: "Compatible" (their use is potentially safe during lactation), "Judicious" (their use during lactation depends on the risk/benefit assessment) and "Contrained" ( understands drugs that require interruption of breastfeeding) (Brasil, 2014).

The second uses 5 levels grouped into 4 categories according to the degree of evidence of potential harm to the infant: "Compatible - L1 level" (drugs with no reported adverse effects on the infant or drugs with negligible oral bioavailability), "Probably Compatible - L2 and L3 levels" (drugs without controlled studies in nursing mothers, but with the possibility of adverse effects for infants or controlled studies show only minimal and non-threatening adverse effects), "Possibly Dangerous - L4 level" (there is evidence of risk for the infant or for milk production) and "Dangerous - L5 level" (studies in nursing

mothers have shown that there is a significant and documented risk for infants or the drug has a high risk of causing significant harm to infants, therefore requiring the discontinuation of breastfeeding ) (Chaves; Lamounier; César, 2007, Fragoso; Silva; Mota, 2014).

The information was submitted to a comparative analysis between the aforementioned literatures. The drug (listed by therapeutic class), the most up-to-date national/international classification and the guidelines for use when necessary were correlated, respectively. In this work, the requirements regarding confidentiality and secrecy of the information obtained were respected, in accordance with the determinations of Resolution 466/1214 and the Declaration of Helsinki. The study was approved by the Research Ethics Committee of the Hospital das Clínicas of the Universidade Federal de Pernambuco on December 6, 2018 (CAAE 01206918.3.000.8807).

## RESULTS

A total of 507 medical prescriptions were analyzed and 81 types of medication were identified among the 3668 records. The average number of prescription drugs issued was 7.24. Among the most prescribed drugs, ferrous sulfate, simethicone, ondansetron and dipyrone stood out, as seen in Table 1.

Regarding the therapeutic classification, the classification system was used: *Anatomical Therapeutic Chemical* (ATC), level II, systematization provided by the WHO. In this classification, drugs are divided into different groups, distributed into five different levels, according to the organ or system in which they act and their chemical, pharmacological and therapeutic properties (World Health Organization, 2018).

According to the ATC classification, the prevalence of prescription drugs was: N02 – Analgesics, 16.28% (n=597); A04 - Antiemetics and Antinauseants, 15.21% (n=558); B03 - Antianemic Preparations, 14.75% (n=541); A03 - Medicines for Functional Gastrointestinal Disorders, 14.45% (n=530); C09 - Agents that act on the Renin-Angiotensin System, 9.84% (n=361); C02 - Antihypertensives, 7.66% (n=281); M01 - Anti-inflammatory and anti-rheumatic products, 7.55% (n=277); J01 - Antibacterials for Systemic Use, 3.46% (n=127); A10 - Drugs used in Diabetes, 1.61% (n=59); C08 - Calcium Channel Blockers, 1.34% (n=39); and Others, 7.85% (n=288). This result can be seen in the figure 1.

As for the presentation and pharmaceutical form, of the total prescribed drugs, 43.85% were oral solids (tablets and capsules); 41.80% injectable solutions; 14.05% oral solutions; 0.27% sprays; and 0.03% creams/ointments. In the comparative analysis of the risk classifications of medications regarding breastfeeding, it was observed that, according to the classification presented by the Ministry of Health, of the 81 different types of medication observed in the study, 72.84% (n=59) were classified as "compatible", 27.16% (n=33) as "judicious" and no drug was identified as "contraindicated", if used during lactation. According to the classification made by Hale & Rowe (2018), 29.63% (n=24) of the identified drugs were categorized as "compatible", 62.96% (n=51) as "probably compatible", 6.17% (n=5) as "possibly dangerous" and 3.70% (n=3) were not found in this international classification (Figure 2).

According to the international reference:*Medications and Mothers' Milk*, 59,32% of the drugs considered "compatible" by the national database of the Ministry of Health, demonstrate some potential for harm to the infant by scientific evidence or by the absence of studies proving otherwise, with recommendations for monitoring during

| Drug | Frequency (n) | % |
|---|---|---|
| Ferrous sulphate | 507 | 13,82 |
| Simethicone | 496 | 13,52 |
| Ondansetron | 484 | 13,20 |
| Dipyrone | 450 | 12,27 |
| Captopril | 335 | 9,13 |
| Ketoprofen | 277 | 7,55 |
| Hydralazine | 222 | 6,05 |
| Tramadol | 122 | 3,33 |
| Scopolamine | 54 | 1,47 |
| Nifedipine | 49 | 1,34 |
| Ceftriaxone | 38 | 1,04 |
| Metoclopramide | 34 | 0,93 |
| Regular Insulin | 31 | 0,85 |
| Insulin NPH | 27 | 0,74 |
| Methyldopa | 26 | 0,71 |
| Acetaminophen | 25 | 0,68 |
| Hydrochlorothiazide | 24 | 0,65 |
| Scopolamine + Dipyrone | 20 | 0,55 |
| Ferripolimaltose | 20 | 0,55 |
| Clonidine | 18 | 0,49 |

Table 1: Prevalence of the most prescribed drugs for patients hospitalized at the HC/UFPE maternity hospital.

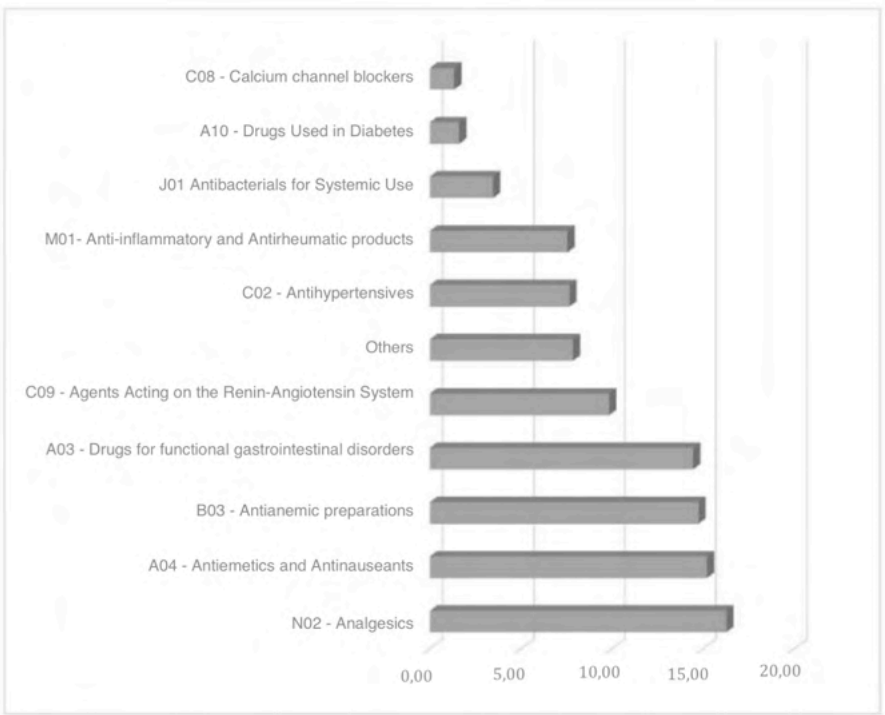


Figure 1: Prevalence of the most prescribed therapeutic classes (ATC) for patients admitted to the maternity hospital of HC UFPE.

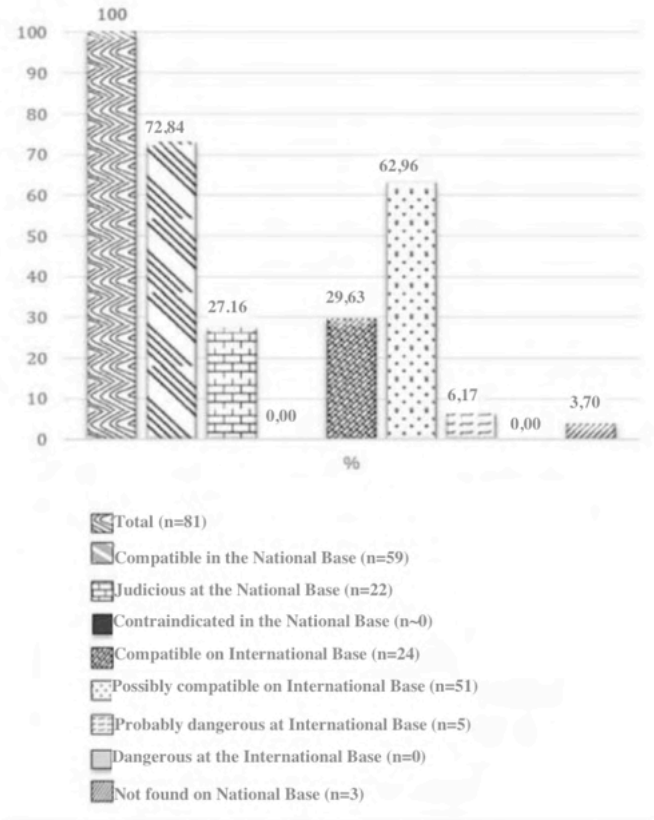


Figure 2: Prevalence of risk classifications during breastfeeding for drugs prescribed at the HC UFPE maternity hospital.

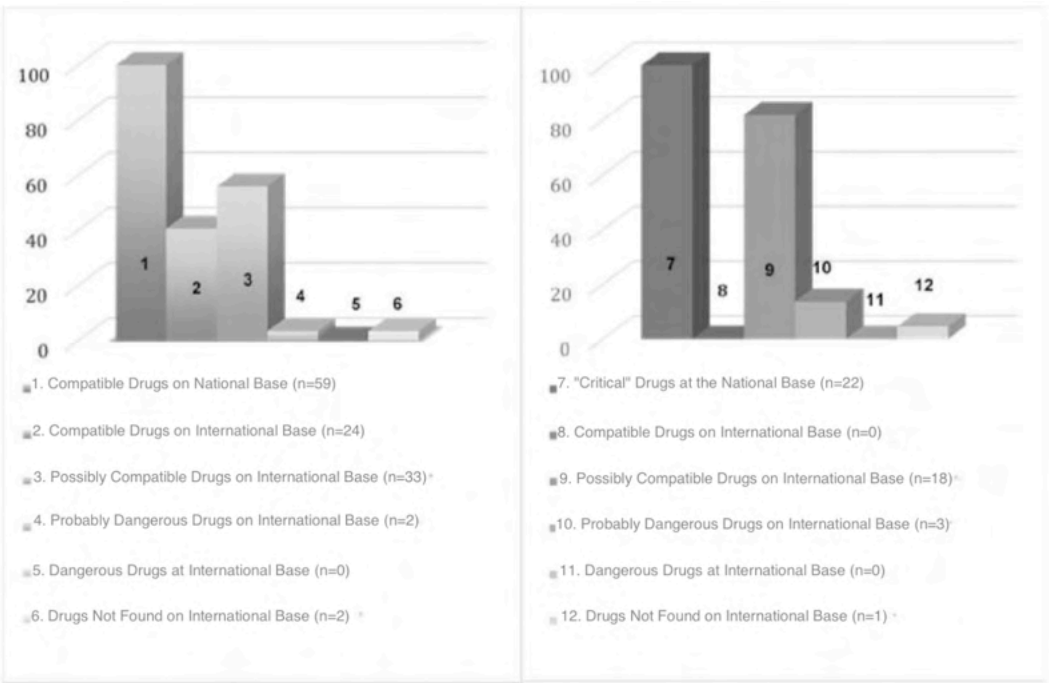


Figure 3: Comparative analysis between risk classifications during breastfeeding for drugs prescribed in the maternity ward of HC UFPE.

use. It was observed that 33 prescription drugs (55.93%) were considered "Probably Compatible" and 2 (3.39%) "Possibly Dangerous", as shown in the figure 3.

## DISCUSSION

The average number of medications prescribed at the HC-UFPE maternity hospital allowed us to observe a "polypharmacy" regimen in the evaluated prescriptions. It is important to know the quantity of medications the patient uses to develop strategies aimed at promoting the safe use of medications, as the quantity of medications is associated with increased risk and severity of adverse drug reactions, cumulative toxicity, errors medication and increased morbidity and mortality (Nascimento et al, 2017).

Regarding the comparative analysis between the classifications, some discrepancies were identified between the national and international references used in the study. The most relevant classification divergence found in the study was with the drug dipyrone, due to the frequency of its prescription in the ward, classified as "compatible" by the national literature and as "possibly dangerous" by the international database (Fragoso; Silva; Mota, 2014 ).

The classification of dipyrone as "possibly dangerous" by Hale and Rowe was due to two episodes reported in the literature of cyanosis in newborn infants after maternal use of the drug. It is interesting to note that Fragoso et al. (2014), considering the classification of the Ministry of Health, found that even the drugs being considered compatible with breastfeeding, 19.2% of the lactating women interviewed reported that their babies had unwanted symptoms after using them (Fragoso; Silva; Mota, 2014).

Another drug that had its divergent classification, "Compatible" (on the national basis) and "Possibly Dangerous" in the international reference studied, was valproic acid. Despite having a less expressive prescription than dipyrone due to its therapeutic, anticonvulsant purpose, the finding was equally important, given that the infants of nursing mothers who use it may present sedation or irritability, poor diet and weight gain (Veiby; Engelsen; Gilhus, 2013, Meador et al, 2014). Based on clinical symptoms, some infants may need liver enzyme or platelet monitoring (Hale; Rowe, 2018).

This discrepancy is probably due to the difference between the publication period of the bases of about a decade (National manual with more recent content in 2010 and reprinted in 2014 and international base with 2019 version, published in 2018) suggesting a likely gap of scientific studies and experiments carried out and published in the period between the publications of the bases that were not observed during the edition of the referred national source. The increasingly early appearance of new drugs and the publication of new studies or reports on the use of drugs in the lactation condition were determining factors for the differences found (Nikolova et al, 2013).

Constant updating of health professionals on the use of medications during lactation is essential to promote the rational use and safety of nursing mothers and infants. As shown in this study, it is necessary to periodically discuss the theoretical frameworks on the topic, identifying possible limitations, in order to build up-to-date protocols and keep them optimized to ensure not only maternal health, but also minimize exposures. the infant providing child monitoring when necessary. In this sense, the pharmacist, and his expertise in medicines, plays an important role as a health educator.

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