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## **Wpływ stosowania farmakoterapii u matki w okresie laktacji na możliwość i bezpieczeństwo karmienia piersią**

### **Impact of maternal pharmacotherapy use during lactation on breastfeeding options and safety**

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**Abstract:**

Due to its unique composition, breast milk is the ideal food for the baby, as it contains all the necessary nutrients. Breastfeeding is recommended by numerous scientific societies and is associated with many immediate as well as long-term benefits for mother and child. The use of pharmacotherapy in mothers during lactation raises concerns about the adverse consequences of treatment and the health of the child due to the distribution of drugs into breast milk. The following paper aims to present the safety profile of selected drug products during breastfeeding.

**Key words: breastfeeding, lactation, drug safety during lactation, pharmacotherapy, pharmacokinetics**

**Aim:**

The role of this article is to present the health benefits of breastfeeding for mother and child and to discuss the impact of maternal pharmacotherapy on the possibility and safety of breastfeeding by analysing the available literature.

**Materials and methods:**

To highlight the safety of selected medicinal products during lactation, the databases of PubMed, Google Scholar, academic textbooks and government websites maintained by the National Institute of Public Health, among others, were analysed in March 2024 using the terms safety of medicines during lactation, distribution of medicines into breast milk, breastfeeding, pharmacotherapy.

**Introduction:**

Natural feeding ensures the child's proper development. Breast milk is an ideal source of protein, lipids, carbohydrates, cytokines, hormones, growth factors, immunoglobulins, digestive enzymes, minerals, vitamins and immune cells making it the best balanced diet for the baby. (1,2)

The World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF) recommend exclusive breastfeeding until the child is 6 months old and continuing breastfeeding until at least two years of age, while introducing appropriate complementary foods from 6 months of age. (4,5).

It is worth emphasising the benefits of breastfeeding, which benefit not only the baby but also the breastfeeding mother. This method of feeding strengthens the bond between mother and child, ensures a more favourable course of confinement and reduces the mother's risk of type 2 diabetes, hypertension, ischaemic heart disease, hyperlipidaemia, breast cancer, ovarian cancer and osteoporosis. Breastfeeding infants strengthens the child's immunity and reduces the risk of infections, including acute diarrhoea, bacterial meningitis, respiratory and middle ear infections and necrotising enterocolitis. Advantages also include reduced risk of allergic diseases and insulin-dependent diabetes, hypertension and obesity in later life. Sudden infant death syndrome is three times less common in naturally fed children. (1,3,9,10)

The benefits of breastfeeding outlined above are obvious, but the use of pharmacotherapy in lactating mothers raises concerns about adverse consequences of treatment and the health of the child due to the distribution of drugs into breast milk.

Most of the drugs used penetrate breast milk to some extent. The distribution of drugs into breast milk is influenced by factors such as the concentration of the drug in maternal plasma, the mother's ability to metabolise the drug, the extent to which the drug binds to plasma proteins, the molecular weight, lipophilicity and the half-life of the substance.

## Methods for assessing drug safety in lactation:

To assess the safety of the drug, we use parameters such as RID (relative infant dose), M/P (Milk/Plasma Ratio) and Professor Hale's classification of drugs used by breastfeeding women. The RID provides an estimate of the theoretical infant dose. The safe relative dose is calculated as the ratio of the dose received by the infant (per body weight) to the dose received by the mother (per body weight) or to the paediatric dose. Relative infant dose is expressed as a percentage. A value of <10% is considered a safe dose for the infant. The M/P parameter is the ratio of the concentration of the medicinal product in breast milk to its concentration in maternal serum. A drug is considered safe when the Milk/Plasma Ratio is less than 1. Professor Hale's classification of drugs used by breastfeeding women divides drugs into Lactation Risk Categories (LRC, lactation risk category). This classification includes 5 groups of drugs from L1 to L5: category L1 - safest drugs, L2 - safe drugs, L3 - probably safe drugs, L4 - probably harmful drugs, L5 - harmful drugs. (6,7,8,11,12)

Classification of drugs used by breastfeeding women according to Prof Hale and example drugs:

Category	Examples of drugs
L1	Amoxicillin, ampicillin, heparin, ibuprofen, insulin, nystatin, paracetamol, magnesium hydroxide, clotrimazole, folic acid, levothyroxine
L2	acyclovir, amitriptyline, diclofenac, cefuroxime, clindamycin, ranitidine, loperamide, tramadol, omeprazole, ketoconazole, prednisolone, metronidazole, terbutaline, lidocaine, hydrochlorothiazide

L3	Acetylsalicylic acid, metamizole, codeine, diazepam, bisoprolol, acarbose, morphine, montelukast, chlorpromazine, formoterol, clonazepam
L4	levodopa, nitroglycerin, clemastine, valproic acid, doxazosin, penicillamine, prazosin, thioridazine
L5	amiodarone, vincristine, iodine, danazol, doxepin, thalidomide, anastozol, chlorambucil, cyclophosphamide, cytaribine, melphalan, cannabis

#### Principles of safe medication taking:

In order to maximise the safety of breastfed children, maternal pharmacotherapy should take into account the age and weight of the child and use the lowest toxicity drugs (from categories L1-L2) at the lowest effective dose, for the shortest possible time, if possible acting locally, with low bioavailability, reaching low maximum serum concentrations, with a short half-life. Dosing should correlate with feeding, so that the administration of the drug falls after feeding, optimally before the longest feeding interval of the day. (11,13)

#### Absolutely contraindicated drugs during breastfeeding:

category	group/use	example of a drug
L5	anti-cancer	aminopterin, busulfan, chlorambucil, cisplatin, capecitabine, carboplatin, carmustine, cladribine, cyclophosphamide, dactinomycin, docetaxel, etoposide, imatinib, melphalan, mitomycin,

	pazopanib, tamoxifen, thalidomide, vinblastine, vincristine
anti-cough	carbetapentane
sympathomimetics	propylhexedrine
corticosteroids	clobetasol
immunosuppressants	everolimus, mitoxantrone
tricyclic antidepressants	doxepin
iron-chelating agent	deferasirox
isotopes	iodine I 123, iodine I 125, iodine I 131
antiretrovirals	delavirdine, didanosine, etravirine

Drugs that are absolutely contraindicated during breastfeeding include, in particular, anticancer drugs. Radioactive preparations and drugs causing addiction should not be given to breastfeeding women.

In the first 6 months of a child's life, some  $\beta$ -blockers should also be avoided - propranolol and labetalol are relatively safe and it is recommended to use ibuprofen or paracetamol instead of salicylic acid and its derivatives. Among analgesics, paracetamol is recommended for breastfeeding mothers. (7,11,15)

Classification of  $\beta$  -adrenolytics for use by breastfeeding women according to Prof Hale

category	example of a drug
L2	labetalol, propranolol, timolol

L3	acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, levobunolol, metoprolol, nebivolol, pindolol, sotalol
L4	nadolol

The preferred anticoagulant during lactation is heparin; warfarin may also be used.

The L1 category of safest drugs and the L2 category of safe drugs according to Professor Hale's classification include drugs used in lactating women such as: glucocorticosteroids: budesonide (inhaled), beclomethasone, prednisone; antidiabetic drugs: insulin, metformin.

Safe drugs for hypertension during lactation are: propranolol, labetalol, verapamil, nifedipine; however, sotalol and atenolol should be avoided, as well as angiotensin convertase inhibitors. Medications for hyperthyroidism and hypothyroidism are not a contraindication to breastfeeding. The anticonvulsant treatment of choice in breastfeeding mothers is valproic acid or gabapentin preparations. For antidepressants, sertraline and paroxetine from the selective serotonin reuptake inhibitor group are preferred. Most antibiotics can be used safely in breastfeeding women. However, fluoroquinolones and tetracyclines should be avoided. (7,11,14,15,16)

#### Summary:

Despite the undeniable benefits of breastfeeding for the child and the mother, many women using pharmacotherapy are abandoning this type of feeding in favour of artificial feeding because of concerns about adverse effects in the newborn due to their intake of medicinal products. The safety of medications taken during breastfeeding can be checked in updated databases such as lactation drug lexicons, among others. The pharmacological treatment used by the mother can often be adjusted so that the medicines she is taking



have properties that ensure that they do not pass into her milk or that they pass into her milk in the amount permitted by the relevant studies, which is why it is so important to contact the attending physician and other members of the medical staff and to provide appropriate care to lactating patients.

#### Author's contribution

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## References:

1 Pediatrics vol. 1 Wanda Kawalec, Ryszard Grenda, Marek Kulus Edition II  
Publisher: PZWL

2 Dorota Kowalska, Eliza Gruczyńska, Joanna Bryś Breast milk - the first food  
in human life Probi High Epidemiol 2015, 96(2): 387-398

3 Pediatrics Tom Lissauer, Will Carroll 5th Edition Publisher: Edra Urban &  
Partner

4 Breastfeeding - Ministry of Health - Gov.co.uk Portal [Internet]. Ministry of  
Health. [cited 2 March 2024]. Available from:  
<https://www.gov.pl/web/zdrowie/karmienie-piersia>

5 Breastfeeding - World Health Organization [Internet]. [cited 2 March 2024].  
Available from: [https://www.who.int/health-topics/breastfeeding#tab=tab\\_2](https://www.who.int/health-topics/breastfeeding#tab=tab_2)

6 Marta Młodawska, Jakub Młodawski, Grażyna Pazera, Wojciech Rokita  
Breast is the best - or what every gynaecologist should know about  
breastfeeding Gynaecology and Practical Perinatology 2019 vol 4, no 1, pages  
23-33 Copyright © 2019 Via Medica ISSN 2451-0122

7 Richard Lauterbach Drug use and breastfeeding [Internet]. [cited 2 March  
2024]. Available from:

<https://podyplomie.pl/publish/system/articles/pdfarticles/000/012/263/original/77-85.pdf?1473166563>

8. Paulina Opalska, Magdalena Elżbieta Hurkacz Safety of drugs used during pregnancy and breastfeeding as a result of changes in their pharmacokinetics *Pharmacja Polska*, ISSN 0014-8261 (print); ISSN 2544-8552 (online)

9 Behrman Richard E., Jenson Hal B., Kliegman Robert M., Marcandante Karen J. *Nelson Pediatrics Volume 1* Publisher: Urban & Partner

10 Breastfeeding: the health benefits for the child and mother and the social benefits of breastfeeding [Internet]. [cited 3 March 2024] Available at: <https://www.mp.pl/pacjent/pediatrica/karmienie-piersia/84219,karmienie-piersia-korzysci-zdrowotne-dla-dziecka-imatki-oraz-korzysci-spoeczne-karmienia-piersia>

11. Dominika Holowaty, Bronisława Pietrzak, Paweł Krajewski, Mirosław Wielgoś Breastfeeding during maternal immunosuppressive therapy *Gynaecology and Practical Perinatology* 2022; 7 (2): 75-80 vol. 6, no. 1, pages 7-12, Copyright © 2022 Via Medica ISSN 2544-4212

12 Hale TW, Rowe HE. *Medications and Mothers' Milk* 2017 Springer Publishing Company. New York 2017

13. Drug use guidelines [Internet] [cited 3 March 2024] Available at: <https://cnol.kobiety.med.pl/pl/leksykon-lekow/zasady-stosowania-lekow/>

14. *General and clinical pharmacology volume I* Katzung Bertram G., Masters Susan B., Trevor Anthony J. Publisher: Czelej

15. *Lactation Drug Lexicon - Centre for Lactation Science* [Internet] [cited 3 March 2024] Available at: <https://www.kobiety.med.pl/leki/search.php>

16. Breastfeeding and antidepressants through the eyes of a paediatrician and lactation counsellor [Internet] [cited 3 March 2024] Available at: <https://www.mp.pl/medycynarodzinna/ekspert/pytania-do->

eksperta/195673,karmienie-piersia-a-leki-przeciwdepresyjne-okiem-pediatry-  
i-doradcy-laktacyjnego