Psychiatr. Pol. 2022; 56(3): 493–508
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: https://doi.org/ 10.12740/PP/134254

Use of psychotropic medications during lactation – practical guidelines for psychiatrists

Aleksandra Kamińska-Sobczak[1], Oliwia Gawlik-Kotelnicka[2], Dominik Strzelecki[2]

[1] Department of Nutrition and Epidemiology, Medical University of Lodz
[2] Department of Affective and Psychotic Disorders, Medical University of Lodz

Summary

Breastfeeding is the best way of feeding infants. It is recommended by national, European and worldwide scientific associations. The advantages of breastfeeding for both the child and the mother have been proven by research. It is widely known that most Polish women start to breastfeed immediately after delivery; however, with each month, the percentage of infants given breast milk exclusively is decreasing. One of the frequent causes of breastfeeding cessation reported by women is the necessity of pharmacotherapy. There are many controversies over the use of psychotropic medications in particular. Nowadays, based on relevant current data, medications pharmacokinetics and applicable pharmacopeia, it is possible to find a therapy that may be both efficient for the mother and safe for the child. In this review, we examine available sources of data on the use of psychotropic medications during lactation. Different groups of psychiatric medications are discussed and rated in terms of their safety during breastfeeding. The Polish Psychiatric Association recommends a course of treatment to support lactation. Both termination of therapy by the mother and interruption of breastfeeding have negative consequences for both the mother and her child. The decision to let the mother continue breastfeeding may be difficult for a psychiatrist. The problem needs to be discussed thoroughly with the patient and should be carefully documented. Cooperation with other specialists such as a pediatrician and/or a lactation consultant is also highly recommended.

Key words: psychotropic medications, lactation, breastfeeding

Introduction

Breastfeeding is an optimal method of feeding newborns and infants. The World Health Organization (WHO) recommends that infants should be exclusively breastfed for the first six months of life, and that breastfeeding should be continued up to the age of at least two years. The American Academy of Pediatrics (AAP) and the

American College of Obstetricians and Gynecologists (ACOG) recommend exclusive breastfeeding for the first six months of life and advise continuation of breastfeeding in the following months when complementary foods are added, at least up to the first year of life. Similar recommendations are given by European scientific organizations, i.e., the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), as well as the Polish Society for Pediatric Gastroenterology, Hepatology and Nutrition [1]. The benefits of breastfeeding, both for the infant and mother, are proved by scientific research. Breastfeeding decreases mortality among infants and lowers the risk of occurrence of sudden infant death syndrome (SIDS) [2]. Additionally, it has been observed that the risk of development of lifestyle diseases such as obesity, diabetes mellitus or asthma in the future in breastfed children is lower [3–5]. Children fed with formula more often suffer from infections of the gastrointestinal tract, inner ear and the respiratory system [6]. The benefits of breastfeeding for the mother cannot be ignored either. Breastfeeding stimulates oxytocin secretion which accelerates shrinking of the uterus after childbirth and decreases the risk of bleeding. Breastfeeding women regain their pre-pregnancy body weight sooner. Breastfeeding lowers the risk of breast cancer, ovarian cancer, cardiovascular diseases and osteoporosis [7–12]. Moreover, what should not be forgotten in this context are economic and environmental benefits for the whole society. Breastfeeding is less expensive, and according to statistical data, breastfed infants fall ill or require hospitalization less frequently. It also reduces the amount of produced waste (bottles, formula boxes) related to the use of breast milk substitutes [8].

Polish mothers show high awareness of the advantages brought by breastfeeding and a vast majority (over 90%) of them begin breastfeeding immediately after birth. However, with each month, the number of women who continue breastfeeding decreases. One of the frequent reasons for breastfeeding cessation by mothers is a necessity of taking medications. The common knowledge on the safety of using drugs during lactation is not sufficient and in too many cases prescribing a medication leads to a recommendation of breastfeeding cessation. The status refers to, among others, medications applied in psychiatry. However, the situation has been changing gradually. In 2017, 97% of subjects participating in a survey conducted by the Lactation Center reported that their gynecologists searched for drugs that could be taken during lactation.

The decision on choosing an optimal medication, which is both effective and safe for the mother and the breastfed infant, as well as the decision on continuation or cessation of breastfeeding is often very difficult for a doctor. It should be emphasized that due to, among others, ethical reasons, there are no randomized trials on the use of drugs during lactation. The available information is based on simple observational research and analyses of cases or series of cases. It should be remembered that the results of studies on animals may not be directly extrapolated to the human population. Similarly, not every drug that is contraindicated or permitted for pregnant women will

have the same effect on a breastfed infant as it may have on the fetus in the mother's womb. A doctor should not treat a leaflet enclosed to a drug as a source of knowledge on pharmacotherapy in lactation. The information contained in it is often incomplete since manufacturers, when preparing such a leaflet, do not focus on current research and the details contained in it are overly conservative. Similar information and recommendations to stop breastfeeding may unfortunately also be found in the Summary of Product Characteristics (SmPC) [13].

What should be considered then when we want to provide our patient with reliable information?

What should be considered is that most of the drugs transfer into breast milk and that each substance has its individual pharmacokinetics. Usually, the best choice is monotherapy, administration of the lowest dose of a drug effective for the mother and implementation of medications that have been on the market for a long time and that have been more thoroughly tested than new drugs [13]. Throughout the whole pharmacotherapy period, the doctor treating the underlying disease should ensure that the infant remains under the constant care of a pediatrician. If possible, the level of medication in infant serum should be monitored.

To determine the safety of a drug, it is important to obtain details on the pharmacokinetics of its active substance. The amount of drug transferred into breast milk depends on many factors: route of administration, degree of absorption, molecular mass, pH value, distribution volume, its plasma bioavailability, half-life, protein binding, lipid and water solubility, ionization, and the ratio of its concentration in milk and plasma (milk/plasma ratio, M/P). It is believed that if the M/P ratio is <1, the drug is safe. Substances soluble in lipids, with a low molecular mass, low distribution volume and low serum protein binding penetrate into milk more easily [14].

It is useful to establish the most important parameter, the relative infant dose (RID), when evaluating the safety of a drug in breastfeeding. This parameter was developed by WHO and it defines the ratio of the active substance the infant receives with the mother's milk as compared to the dose the mother takes per kilogram body weight. As there are no specific guidelines regarding RID, medication is generally assumed to be safe if RID is <10% and recommended for breastfeeding patients when RID is <5%. There are, however, a few exceptions: medications with adverse properties regardless of RID (anticancer or immunomodulatory agents), and medications with a very long half-life (risk of accumulation) [14, 15].

The above-mentioned pharmacokinetic parameters are often not available in a traditional formulary or SmPC and practicing doctors do not have access to them. Therefore, to assess whether a drug may be taken by a breastfeeding patient, doctors may refer to lactation databases. The most recognized one is Medications & Mother's Milk created by Prof. Thomas Hale and updated every two years [16]. The manual contains categories created by the author that are helpful when assessing the safety

of a drug (Table 1). If a description of a searched drug is not included in the manual, one may ask Prof. Hale for assistance by contacting the Infant Risk Center founded by him via e-mail or phone (www.infantrisk.com).

Table 1. **Dr. Hale's Lactation Risk Categories**

Category	Description
L1	**Safest** Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. The product is not orally bioavailable in infants.
L2	**Safer** Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3	**Moderately safe** There are no controlled studies in breastfeeding women for a drug with possible adverse effects OR studies have shown evidence for mild non-threatening adverse effects. Drugs should be given only if the potential benefit justifies the potential risk. New medications that have no published data are categorized in this category, regardless of how safe they may be.
L4	**Possibly hazardous** Studies have shown evidence for risk to a nursing infant or to breastmilk production, but in some circumstances the drug may be used during breastfeeding when the benefits from use outweigh the risks (e.g., life-threatening situation in mother, lack of other alternatives).
L5	**Contraindicated** Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

The electronic database LactMed, practical in use and recommended by AAP, contains the description of a drug, lactation risk category according to Hale and scientific literature [17]. LactMed is also available in a free version as a mobile phone application. In December 2019, along with the whole TOXNET database, it was transferred to the NCBI platform, to the Bookshelf section.

The online base E-lactancia is very handy and easy to use. It is available free of charge, both in English and Spanish, and it includes four safety categories (Table 2) [18].

Table 2. **e-lactancia safety categories**

Very low risk	Safe. Compatible. Minimal risk for breastfeeding and infant.
Low risk	Moderately safe. Probably compatible. Mild risk possible. Follow up recommended. Read the Comment.

table continued on the next page

High risk	Poorly safe. Evaluate carefully. Use safer alternative or interrupt breastfeeding 3 to 7 T ½ (elimination half-lives). Read the Comment.
Very high risk	Very unsafe. Contraindicated. Use of an alternative or cessation of breastfeeding. Read the Comment.

In everyday practice, "Pharmacy Notebooks. Drugs and Breastfeeding", published in Poland may also be used. Each substance is described with reference to Hale's lactation risk categories, SmPC information and basic pharmacokinetic parameters.

Comparison of information included in SmPC with data contained in lactation formularies often raises doubts as to what we should be driven by when choosing a drug. What may be useful in this case is art. 4 of the Act on the Profession of a Doctor and Dentist which stipulates that in their practice, doctors should use current knowledge. A procedure aimed at protection of lactation is recommended by the Polish Psychiatric Association (PPA) [19, 20].

In addition to the above, we should take into account the age of a child, potential prematurity, the amount of feeding sessions and estimated volume of ingested milk [14]. Additionally, it should be borne in mind that temporary weaning may generate numerous problems, both for the mother and the infant. It may involve suppression of milk secretion (galactoschesis) or even lead to mastitis; it may also have an adverse effect on the amount of produced milk. When making this decision, one should always remember about the benefits of breastfeeding.

Recommendations regarding the treatment of psychiatric disorders in women of childbearing age published by the PPA define general rules of pharmacotherapy in breastfeeding women: prescribing the lowest possible effective doses of medications, and caution in the case of deficiency of mechanisms of binding, metabolism or excretion of drugs in newborns or infants, as well as in children up to ten weeks of age and with neurological problems [19, 20]. There are still controversies regarding the recommendation to adjust the time of the feeding session to the time of medication ingestion, as this may be a source of additional difficulties in lactation maintenance [21, 22].

All psychotropic medications pass into breast milk, the majority of them in small amounts. A general rule regarding their prescription in the perinatal period is not changing the medication after delivery for breastfeeding if a mother has taken it during pregnancy. The exceptions are: the current treatment lost its efficacy, the current medication may pose a risk of serious adverse effects for the child (e.g., clozapine), and the infant suffers from side effects originating from a medication present in the milk. A common side effect of many psychotropic drugs is sedation, so an infant should be monitored for excessive sleepiness and feeding problems [23]. Sometimes it may be difficult to differentiate between side effects and normal developmental behavior of an infant and in these kinds of situations cooperation with parents is particularly important.

Antidepressants

If a woman was successfully treated with an antidepressant during pregnancy, the same medication should be used after delivery to avoid withdrawal symptoms and child exposure to different xenobiotics. There are no reasons to discontinue antidepressant treatment because of breastfeeding, especially in the case of severe mood disorders as it may substantially increase suicidal risk [19, 22, 24]. In the case of postpartum depression, usually the drugs of choice are selective serotonin reuptake inhibitors (SSRIs). Sertraline and paroxetine are characterized by the best safety profile. However, taking into account the more numerous side effects of paroxetine and withdrawal symptoms associated with discontinuation of treatment with this medication, the most often used drug representing this group is sertraline. Usually, only trace amounts (1.6-10 ng/ml) of the substance may be detected in the plasma of breastfed infants. More caution should be exercised when administering fluoxetine which due to a longer T½ (2-3 days) may show a higher concentration in the infant's plasma. In the case of citalopram, sleeping disorders have been observed occasionally; however, they subsided when the dose taken by the mother was decreased. Fewer side effects are reported in the case of escitalopram. However, if the above-mentioned medications were successfully administered during pregnancy, they may be prescribed during lactation while monitoring the infant for side effects. Fluvoxamine, because of scarce data, is not recommended in breastfeeding women [15, 17, 24–29].

A selective serotonin and noradrenaline reuptake inhibitor (SNRI) which has been quite well described in the context of breastfeeding is venlafaxine. No significant side effects in breastfed children have been identified. However, this drug is not recommended as a first choice because of RID of 7-8%. Duloxetine has a similar safety profile but a RID value of 1% and should be the drug of choice if the clinical situation requires an SNRI [15, 17, 26–28].

The concentration of tricyclic antidepressants (TCAs) in infants breastfed by mothers who take the drugs is usually 1-3% of the mother's dose. Side effects occurring in relation to the use of amitriptyline and clomipramine (e.g., excessive sedation, breastfeeding difficulties in the form of diminished volume of ingested milk, ineffective sucking) have been reported only occasionally, which makes these medications compatible with breastfeeding. The medication that breastfeeding women should avoid is doxepin since cases of serious side effects (respiratory depression, vomiting and sedation) have been observed. Due to limited data on safety, it is difficult to draw a clear conclusion based on a small number of cases and therefore, it is suggested that a drug other than doxepin should be chosen [15, 17, 25–30].

Data on the safety of mianserin and mirtazapine are limited. Thus, despite their low milk passage they are not recommended during lactation. If there is a clinical indication for a hypnotic antidepressant, trazodone is a good option for a breastfeeding woman. In the available literature, no significant side effects in breastfed infants of mothers taking this drug have been reported [15, 17, 23, 24, 26, 27, 29].

Extreme caution should be exercised in the case of women receiving bupropion due to single episodes of seizures in their breastfed infants [16–18, 31].

Monoamine oxidase inhibitors (available in Poland moclobemide) should not be prescribed to breastfeeding women because of the lack of data and known severe interactions; these medications are treated as possibly hazardous [16, 17, 25].

There are no clinical data available on the safety of newer antidepressants: agomelatine and vortioxetine. Literature search shows that only one case of agomelatine use in lactation has been published so far (there were no adverse events in the newborn) [32, 33].

Table 3. **Antidepressants**

Name	Hale's category	RID
Agomelatine	-	-
Amitriptyline	L2	1.08-2.8
Bupropion	L3	0.11-1.99
Citalopram	L2	3.56-5.37
Clomipramine	L2	2.8
Doxepin	L5	0.32-3
Duloxetine	L3	0.1-1.1
Escitalopram	L2	5.2-7.9
Fluoxetine	L2	1.6-14.6
Fluvoxamine	L2	0.3-1.4
Mianserin	-	1.4
Mirtazapine	L3	1.6-6.3
Moclobemide	L4	3.4
Paroxetine	L2	1.2-2.8
Sertraline	L2	0.4-2.2
Trazodone	L2	2.8
Venlafaxine	L2	6.8-8.1
Vortioxetine	L3	-

To sum up, antidepressants as a class of psychotropic medications are safe during lactation, their levels in breastfed children are low or undetectable, and side effects are rare. Sertraline is the antidepressant of choice, followed by paroxetine, duloxetine or trazodone. The only contraindicated drug during lactation from this group is doxepin.

A practical tip regarding the choice of an antidepressant for a pregnant woman is taking into account the intention of breastfeeding, which may help avoid deliberations about changing the drug during the early postnatal period [21].

Anxiolytic and hypnotic drugs

Hydroxyzine is described as a drug that may be used during lactation and no adverse effects in breastfed infants have been observed [17].

Benzodiazepines (BZD) reach low plasma concentrations in infants breastfed by mothers who take these drugs. Side effects are rarely reported; however, despite this fact BZD with a short and moderate half-life (lorazepam, alprazolam, oxazepam, midazolam) are rather recommended. Due to the risk of respiratory depression and abstinence syndrome in breastfed infants, they should be used for as short as possible, and long half-life BZD, such as diazepam, only occasionally [15, 17, 19, 25, 26, 28].

Table 4. **Benzodiazepines**

Name	Hale's category	RID
Alprazolam	L3	8.5
Diazepam	L3	0.88-7.14
Lorazepam	L3	2.6-2.9
Midazolam	L2	0.63
Oxazepam	L2	0.28-1

There is limited data on the effects of zopiclone, zolpidem and zaleplon on infants breastfed by mothers taking these drugs. Due to their low penetration into breast milk and rapidly decreasing level after a single dose they seem to be safe for lactating women [16, 17, 21, 28].

Table 5. **Hypnotics**

Name	Hale's category	RID
Zaleplon	L2	1.5
Zolpidem	L3	0.02-0.18
Zopiclone	L2	1.5

Pregabalin, due to lack of data, should not be used during lactation [15-17].

It is worth mentioning that apart from penetration into milk and direct effect on a child, the issue of taking care of an infant and young child by a mother who is under the influence of sedatives should be mentioned.

Normothymic drugs

Lithium, one of the most effective mood stabilizers, is at the same time the most troublesome in the context of breastfeeding. Due to its relatively high milk and plasma concentration in infants (RID 12-30%, plasma level in children 24-40% of mothers' plasma levels), lithium was generally regarded as contraindicated during lactation.

Occasionally, serious adverse effects in infants of mothers taking lithium while breastfeeding were reported such as cyanosis, hypotonia, heart murmurs, lethargy, thyroid function abnormalities (hypothyroidism may be harmful to the development of the central nervous system of a young child). Recent research shows, however, that the lithium plasma concentration in a breastfed infant is up to 0.25 mEq/l, and the occurring side effects mainly concern abnormalities in laboratory tests such as increased concentrations of urea, creatinine and thyroid-stimulating syndrome (TSH) and abnormal electrocardiogram (ECG) readings. If the medication shows high efficacy and tolerance in the patient, continuation of the treatment applied so far may be considered, while monitoring the drug concentration in the infant serum and the above-mentioned laboratory parameters. It should be remembered that dehydration, more often seen in infants than adults, may lead to toxic lithium levels [14, 15, 20, 21, 23–25, 34, 35].

Despite single cases of side effects caused by valproic acid (one case of thrombocytopenia and anemia in an infant) and carbamazepine (cases of transient hepatotoxicity, sedation, impaired sucking in infants), because of low RID and a large amount of data on the safety of these medications, including the influence on neurodevelopment of a child, they are allowed to be used during lactation. Valproic acid use does not involve any laboratory tests in children. Liver function tests and the level of the drug concentration in infants whose mothers take carbamazepine are ordered. Lamotrigine is not recommended routinely due to high RID (up to 18%), reported cases of central nervous system depression and the risk of developing skin lesions in breastfed infants (so far, no cases of Stevens-Johnson syndrome have been reported). However, safe use of lamotrigine during lactation is possible in doses up to 200 mg/day. A study published in 2020 and conducted on a large group of children of mothers receiving antiepileptic drugs during the breastfeeding period shows that their blood concentrations in infants were significantly lower than in mothers [14, 15, 21, 23, 26, 34, 36–41].

Table 6. **Mood stabilizers**

Name	Hale's category	RID
Carbamazepine	L2	2.8
Lamotrigine	L2	3.4-7.8
Lithium	L4	0.87-30
Valproic acid	L4	0.99-5.6

To summarize, among mood stabilizers the highest levels of a drug passing into milk were shown in the case of lithium and lamotrigine, and the lowest in the case of valproic acid. In general, side effects related to the use of lithium and antiepileptic drugs in the clinical situation under discussion are minimal. No differences in the intellectual development level of 3 – and 6-year old children breastfed by mothers taking these medications and children fed artificially were found (both groups of children were exposed to antiepileptic drugs intrauterine). The mood stabilizer of choice for

breastfeeding women is valproic acid. Lithium should be prescribed only in the case of lack of efficacy of the other normothymics or in the case of high risk of suicide; the precautionary measures described above should be implemented [14, 20, 25]. Antipsychotics with mood stabilizing properties are described below.

Antipsychotic drugs

Many of the first-generation antipsychotics pass into breast milk in small amounts (RID < 10%). However, due to their unstable milk and serum levels and limited data on their safety, they are not recommended during lactation. In infants breastfed by mothers taking chlorpromazine, occasional occurrences of drowsiness and apathy have been reported. In the literature, one may find case reports of developmental delay in children aged 12 to 18 months whose mothers simultaneously took haloperidol and chlorpromazine. However, it should be noticed that the mother's primary disease was not taken into account. Additionally, there is no long-term observational data [16, 17, 21, 26, 28, 42].

There are no satisfying research data regarding the safety issues of other first-generation antipsychotics. It is believed that promazine used early in the lactation period may, by influencing the level of prolactin in the mother, lower the amount of produced milk. Thioxanthene derivatives (chlorprothixene, flupenthixol, zuclopenthixol) pass into breast milk in tiny amounts, there are no reports on any side effects in breastfed infants and these medications seem to be compatible with breastfeeding provided that a child is monitored carefully [16, 17, 43].

No adverse effects have been reported in infants of mothers receiving quetiapine therapy. The substance is transferred into breast milk in an extremely low amount (RID up to 0.43%) and therefore, it seems to be the first-choice and a safe medication during lactation as compared to the other drugs in this class of antipsychotics. There are dozens of analyzed cases, and one prospective study on the use of olanzapine in breastfeeding women. It seems that due to its low blood serum concentration in infants (RID < 4%) and a good safety profile, administration of the drug during lactation may be considered as an option. Risperidone, on the other hand, transfers into milk in a much larger amount (RID up to 9%); it should not be used in breastfeeding women as a medication of choice but rather after previously prescribed antipsychotics have proven ineffective. There is scarce data on the safety of aripiprazole, it passes into milk in very small amounts (RID < 1%) and is not detectable in the serum of breastfed children. Available data suggest that it may be administered during lactation. Amisulpride is not recommended for use in breastfeeding women because of high RID (up to 10.7%). However, these recommendations are based on only a few cases. Additionally, amisulpride substantially increases the level of prolactin in the serum which may lead to galactorrhea. Ziprasidone is rarely described in the context of breastfeeding, and the available data suggest that it may be used during lactation if no safer alternative

exists. However, the infant's condition has to be monitored carefully. There is no data on paliperidone or lurasidone. It is known that paliperidone leads to an increased prolactin level and thus to galactorrhea. Clozapine, despite the fact that it passes into breast milk in low amounts, is regarded as a potentially dangerous drug during breastfeeding. In the literature, one may find a case report of an infant exposed to clozapine (during both pregnancy and the breastfeeding period) in whom delayed speech development was diagnosed. Hematologic disorders such as agranulocytosis, seizures and apathy are listed as possible adverse effects occurring in breastfed infants. However, if a woman being treated with clozapine as a drug of choice decides to breastfeed, the child should be carefully monitored for signs of sedation and complete blood count laboratory tests should be regularly performed [14-17, 20, 21, 25, 26, 28, 42, 44–46].

Table 7. **Antipsychotics**

Name	Hale's category	RID
Amisulpride	-	-
Aripirazole	L3	0.7-6.44
Chlorpromazine	L3	0.3
Chlorprothixen	-	>1
Clozapine	L3	1.33-1.4
Flupentixol	L3	0.7-1.75
Haloperidol	L3	0.2-12
Lurasidone	L3	-
Olanzapine	L2	0.28-2.24
Paliperidone	L3	-
Promazine	-	-
Quetiapine	L2	0.02-0.1
Risperidone	L2	2.8-9.1
Ziprasidone	L2	0.07-1.2
Zuclopenthixol	L3	0.4-1.55

On the basis of current data, the antipsychotics of choice during lactation are consecutively quetiapine and olanzapine, and the only drug in this group that is contraindicated in breastfeeding women is clozapine.

The use of medications in the form of long-acting injectables (LAIs) is commonly recognized as contraindicated during lactation because of the lack of data on their safety. In the literature, however, there are single case studies of the use of olanzapine and aripiprazole in depot injections and no adverse events were seen in breastfed children [47, 48].

A retrospective study including a large clinical sample of 263 breastfeeding patients during several weeks directly after delivery shows that the most often used psychotropic medication in this group was paroxetine (43.3%), followed by sertraline (31.9%), olanzapine (12.2%) and quetiapine (6.1%). Only 41 women discontinued breastfeeding in the study period, the minority of them due to psychiatrists' recommendations or side effects of medications [49]. In the light of current data, breastfeeding during psychopharmacologic treatment becomes a standard mode of action.

Long-term side effects of chronic exposure to psychotropic medications

Along with the broadening of knowledge on the pharmacokinetics of medications and more frequent decisions on breastfeeding continuation by women receiving psychotropic drugs, there arise doubts concerning the impact they have on further child development and late side effects (e.g., extrapyramidal) in the course of antipsychotic treatment. In the literature there occasionally appear reports on the issue. Available data indicate that exposure to psychotropic medications during lactation does not exert any impact on growth, body mass, body mass index, motor development or the age of reaching specific milestones by children [43]. There is even less data on the effect the drugs may have on the future occurrence of behavior disorders. Available studies on animals may be useful; however, their results may not be transferred directly onto the human population [50]. Further studies are required for reliable assessment of the impact of antidepressants and other psychotropic medications. They should also include data on the level of their blood concentrations in infants [23].

Conclusions

A doctor should always offer a therapy that will be both effective for the patient and safe for her breastfed infant. Both discontinuation of treatment by the mother and breastfeeding cessation is unfavorable for the mother-child dyad. Knowledge of pharmacokinetics of a drug as well as the above recommended formularies will make the decision on choosing a proper medication much easier. First, medications from L1 and L2 categories according to Hale's breastfeeding safety ratings should be chosen, in their lowest effective dose, with a short half-life and a low relative infant dose (RID < 10%). In the case of prescribing a high risk medication, the infant's condition should be regularly monitored by his/her pediatrician and, if required, the drug plasma concentration in the infant should be marked. It is worth remembering that the older an infant and the lower the number of breastfeeds is, the safer the use of such medications. In the case of occurrence of adverse effects in the infant, breastfeeding should be immediately discontinued and a specialist in pediatrics should be consulted.

Aleksandra Kamińska-Sobczak and Oliwia Gawlik-Kotelnicka declare equal first-author contribution to this work.

References

1. WHO, UNICEF. *Global strategy for infant and young child feeding,* 2003. https://www.who.int/publications/i/item/9241562218 (retrieved: 14.02.2021).
2. Chen A, Rogan WJ. *Breastfeeding and the risk of postneonatal death in the United States.* Pediatrics 2004; 113(5): e435–9.
3. Oddy WH, Holt PG, Sly PD, Read AW, Landau LI, Stanley FJ et al. *Association between breast feeding and asthma in 6 year old children: Findings of a prospective birth cohort study.* BMJ 1999; 319(7213): 815–819.
4. Sadauskaite-Kuehne VV, Ludvigsson J, Padaiga Ž, Jašinskiene E, Samuelsson U. *Longer breastfeeding is an independent protective factor against development of type 1 diabetes mellitus in childhood.* Diabetes Metab. Res. Rev. 2004; 20(2): 150–157.
5. Armstrong J, Reilly JJ; Child Health Information Team. *Breastfeeding and lowering the risk of childhood obesity.* Lancet 2002; 359(9322): 2003–2004.
6. Howie PW, Forsyth JS, Ogston SA, Clark A, Du Florey VC. *Protective effect of breast feeding against infection.* BMJ 1990; 300(6716): 11–16.
7. Beral V, Bull D, Doll R, Peto R, Reeves G. *Breast cancer and breastfeeding: Collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50 302 women with breast cancer and 96 973 women without the disease.* Lancet 2002; 360(9328): 187–195.
8. Ball TM, Wright AL. *Health care costs of formula-feeding in the first year of life.* Pediatrics 1999; 103(4 Pt 2): 870–876.
9. Michaëlsson K, Baron JA, Farahmand BY, Ljunghall S. *Influence of parity and lactation on hip fracture risk.* Am. J. Epidemiol. 2001; 153(12): 1166–1172.
10. Chua S, Arulkumaran S, Lim I, Selamat N, Ratnam SS. *Influence of breastfeeding and nipple stimulation on postpartum uterine activity.* Br. J. Obstet. Gynaecol. 1994; 101(9): 804–805. doi:10.1111/j.1471-0528.1994.tb11950.x.
11. Dewey KG, Heinig MJ, Nommsen LA. *Maternal weight-loss patterns during prolonged lactation.* Am. J. Clin. Nutr. 1993; 58(2): 162–166. doi:10.1093/ajcn/58.2.162.
12. Schwarz EB, Ray RM, Stuebe AM, Allison MA, Ness RB, Freiberg MS et al. *Duration of lactation and risk factors for maternal cardiovascular disease.* Obstet. Gynecol. 2009; 113(5): 974–982. doi:10.1097/01.AOG.0000346884.67796.ca.
13. Hardy LT, Reichenbacker OL. *A practical guide to the use of psychotropic medications during pregnancy and lactation.* Arch. Psychiatr. Nurs. 2019; 33(3): 254–266. doi:10.1016/j.apnu.2019.04.001.
14. Pacchiarotti I, León-Caballero J, Murru A, Verdolini N, Furio MA, Pancheri C et al. *Mood stabilizers and antipsychotics during breastfeeding: Focus on bipolar disorder.* Eur. Neuropsychopharmacol. 2016; 26(10): 1562–1578.
15. Larsen ER, Damkier P, Pedersen LH, Fenger-Gron J, Mikkelsen RL, Nielsen RE et al.; Danish Psychiatric Society; Danish Society of Obstetrics and Gynecology; Danish Paediatric Society; Danish Society of Clinical Pharmacology. *Use of psychotropic drugs during pregnancy and breast-feeding.* Acta Psychiatr. Scand. Suppl. 2015; (445): 1–28. doi:10.1111/acps.12479.

16. Hale's Medications & Mothers' Milk. https://www.halesmeds.com/ (retrieved: 14.02.2021).

17. Drugs and Lactation Database (LactMed) – NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK501922/ (retrieved: 11.02.2021).

18. e-lactancia. Is this compatible with breastfeeding? http://www.e-lactancia.org/ (retrieved: 13.02.2021).

19. Samochowiec J, Rybakowski J, Gałecki P, Szulc A, Rymaszewska J, Cubała JW, Dudek D. *Recommendations of the Polish Psychiatric Association for treatment of affective disorders in women of childbearing age. Part I: Treatment of depression.* Psychiatr. Pol. 2019; 53(2): 245–262. doi:10.12740/ PP/103385.

20. Rybakowski J, Cubała WJ, Gałecki P, Rymaszewska J, Samochowiec J, Szulc A, Dudek D. *Recommendations of the Polish Psychiatric Association regarding the treatment of affective disorders in women of childbearing age. Part II: Bipolar disorder.* Psychiatr. Pol. 2019; 53(2): 263–276. doi:10.12740/PP/103555.

21. Mcallister-Williams RH, Baldwin DS, Cantwell R, Easter A, Gilvarry E, Glover V et al.; British Association for Psychopharmacology. *British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017.* J. Psychopharmacol. 2017; 31(5): 519–552. doi:10.1177/0269881117699361.

22. Romaine E, McAllister-Williams RH. *Guidelines on prescribing psychotropic medication during the perinatal period.* Br. J. Hosp. Med. (Lond.) 2019; 80(1): 27–32. doi:10.12968/hmed.2019.80.1.27.

23. Payne JL. *Psychopharmacology in pregnancy and breastfeeding.* Med. Clin. North Am. 2019; 103(4): P629–650.

24. Meltzer-Brody S, Howard LM, Bergink V, Vigod S, Jones I, Munk-Olsen T et al. *Postpartum psychiatric disorders.* Nat. Rev. Dis. Primes. 2018; 4: 18022.

25. Shah AA, Aftab A. *Are psychotropic drugs safe to use during lactation?* Psychiatr. Ann. 2015; 45(2): 77–82. doi:10.3928/00485713-20150212-05.

26. Kronenfeld N, Berlin M, Shaniv D, Berkovitch M. *Review article use of psychotropic medications in breastfeeding women.* Birth Defects Res. 2017; 109(12): 957–997.

27. Schoretsanitis G, Augustin M, Saßmannshausen H, Franz C, Gründer G, Paulzen M. *Antidepressants in breast milk; comparative analysis of excretion ratios.* Arch. Womens Ment. Health 2019; 22(3): 383–390. doi:10.1007/s00737-018-0905-3.

28. Tripathi BM, Majumder P. *Lactating mother and psychotropic drugs*. Mens Sana Monogr. 2010; 8(1): 83–95. doi:10.4103/0973-1229.58821.

29. Fischer Fumeaux CJ, Morisod Harari M, Weisskopf E, Eap CB, Epiney M, Vial Y et al. *Risk-benefit balance assessment of SSRI antidepressant use during pregnancy and lactation based on best available evidence – An update.* Expert Opin. Drug Saf. 2019; 18(10): 949–963.

30. Matheson I, Pande H, Alertsen AR. *Respiratory depression caused by N-desmethyldoxepin in breast milk.* Lancet 1985; 326(9464): 1124.

31. Chaudron LH, Schoenecker CJ. *Bupropion and breastfeeding: A case of a possible infant seizure.* J. Clin. Psychiatry 2004; 65(6): 881–882.

32. Schmidt FM, Lichtblau N, Uribe MM, Kirchherr H, Himmerich H. *Agomelatine in breast milk.* Int. J. Neuropsychopharmacol. 2013; 16: 497–499.

33. Montgomery SA, Nielsen RZ, Poulsen LH, Häggström L. *A randomised, double-blind study in adults with major depressive disorder with an inadequate response to a single course of selective serotonin reuptake inhibitor or serotonin-noradrenaline reuptake inhibitor treatment switched to vortioxetine or agomelatine.* Hum. Psychopharmacol. 2014; 29(5): 470–782. doi:10.1002/ hup.2424.

34. Drugs and Lactation Database (LactMed). 2006.

35. Galbally M, Bergink V, Vigod SN, Buist A, Boyce P, Chandra P et al. *Breastfeeding and lithium: Is breast always best?* Lancet Psychiatry 2018; 5(7): 534–536.

36. Ohman I, Vitols S, Tomson T. *Lamotrigine in pregnancy: Pharmacokinetics during delivery, in the neonate, and during lactation.* Epilepsia 2000; 41(6): 709–713.

37. Birnbaum AK, Meador KJ, Karanam A, Brown C, May RC, Gerard EE et al.; MONEAD Investigator Group. *Antiepileptic drug exposure in infants of breastfeeding mothers with epilepsy.* JAMA Neurol. 2020; 77(4): 441–450. doi:10.1001/jamaneurol.2019.4443.

38. Sharma S, Tripathi P. *Gut microbiome and type 2 diabetes: Where we are and where to go?* J. Nutr. Biochem. 2019; 63: 101–108.

39. Uguz F, Sharma V. *Mood stabilizers during breastfeeding: A systematic review of the recent literature.* Bipolar Disord. 2016; 18(4): 325–333.

40. Viguera AC, Newport DJ, Ritchie J, Stowe Z, Whitfield T, Mogielnicki J et al. *Lithium in breast milk and nursing infants: Clinical implications.* Am. J. Psychiatry 2007; 164(2): 342–345.

41. Stahl S, Neiderud J, Vinge E. *Thrombocytopenic purpura and anemia in a breast-fed infant whose mother was treated with valproic acid.* J. Pediatr. 1997; 130(6): 1001–1003.

42. Yoshida K, Smith B, Craggs M, Kumar R. *Neuroleptic drugs in breast-milk: A study of pharmacokinetics and of possible adverse effects in breast-fed infants.* Psychol. Med. 1998; 28(1): 81–91. doi:10.1017/S0033291797005965.

43. Kronenfeld N, Baran TZ, Berlin M, Karra N, Dinavitser N, Cohen R et al. *Chronic use of psychotropic medications in breastfeeding women: Is it safe?* PLoS One 2018; 13(5): e0197196. doi:10.1371/journal.pone.0197196.

44. Uguz F. *Second-generation antipsychotics during the lactation period: A comparative systematic review on infant safety.* J. Clin. Psychopharmacol. 2016; 36(3): 244–252.

45. Cuomo A, Goracci A, Fagiolini A. *Aripiprazole use during pregnancy, peripartum and lactation. A systematic literature search and review to inform clinical practice.* J. Affect. Disord. 2018; 228: 229–237.

46. Mendhekar DN. Possible delayed speech acquisition with clozapine therapy during pregnancy and lactation. J. Neuropsychiatry Clin. Neurosci. 2007; 19(2): 196–197.

47. Manouilenko I, Öhman I, Georgieva J. *Long-acting olanzapine injection during pregnancy and breastfeeding: A case report.* Arch. Womens Ment. Health 2018; 21(5): 587–589. doi:10.1007/ s00737-018-0840-3.

48. Ballester-Gracia I, Pérez-Almarcha M, Galvez-Llompart A, Hernandez-Viadel M. *Use of long acting injectable aripiprazole before and through pregnancy in bipolar disorder: A case report.* BMC Pharmacol. Toxicol. 2019; 20(1): 52. doi:10.1186/s40360-019-0330-x.

49. Uguz F, Kirkas A, Aksoy ZK, Yunden S. *Use of psychotropic medication during lactation in postpartum psychiatric patients: Results from an 8-year clinical sample.* Breastfeed. Med. 2020; 15(8): 535–537. doi:10.1089/bfm.2020.0111.

50. Zucker I. *Psychoactive drug exposure during breastfeeding: A critical need for preclinical behavioral testing.* Psychopharmacology (Berl) 2018; 235(5): 1335–1346.

Address: Oliwia Gawlik-Kotelnicka
Medical University of Lodz
Department of Affective and Psychotic Disorders
92-216 Łódź, Czechosłowacka Street 8/10
e-mail: oliwia.gawlik@umed.lodz.pl