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Review

Toxicity of Recreational Drugs and Medications During Lactation: A Systematic Review

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Abstract

Breastfeeding is recommended because of its benefits for the woman and the newborn, but during lactation, pre-existing or lactation-related health conditions that require medication can expose the minor to the risk of acute or chronic intoxication. While drug safety during pregnancy is a well-discussed topic, there is scarce evidence about the safety of common licit and illicit substances during breastfeeding. Hence, we performed a systematic review on the toxicity of licit and illicit substances during lactation. Applying PRISMA criteria for systematic reviews, we found 26 eligible papers published in the last ten years. Our review showed that human milk should be considered a specific (and dynamic) matrix for toxicological analysis, and relatively little is known about the actual levels of common substances in this matrix. Current recommendations on drug safety are mainly based on a benefit–risk ratio based on the little available information. Experimental research in this field should be promoted, which is also because of the relatively high frequency of sudden infant deaths that is currently unexplained.

Keywords: toxicology; forensic toxicology; lactation; breastfeeding; drugs

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1. Introduction

Breastfeeding for at least 1–2 years is usually recommended because of its short-term and long-term benefits, being associated with better cognitive development and lower risk of obesity, diabetes, hypertension, hyperlipidemia, cardiovascular disorders, and different oncological diseases [1]. There also are protective effects for the mother against postpartum depression, breast and ovarian cancer, hypertension, and type-2 diabetes [2]. Despite being generally recommended, lactation cannot be indicated when it can expose the newborn to health hazards, namely to drug intoxication. Indeed, in the perinatal period, the use of medications is common, both because during lactation some specific disorders can occur (e.g., postpartum depression and dermatological disorders in the nipple area) and because the abuse of recreational drugs is common (in particular, of alcohol, marijuana, and cocaine) [3]. In this context, recreational drugs are understood as drugs used non-medically for personal enjoyment, pleasure, stimulation, etc., often associated with a specific setting, as defined by EUDA [4]. However, while the safety of licit and illicit drugs

during pregnancy is a well-known and largely discussed issue, relatively little is known about the same issue during lactation [5]. This poor knowledge can represent a limitation not only for clinical toxicology, but also for forensic toxicology: in the first year of life, sudden death is fairly frequent (estimated incidence: 4.9/10,000 births) and is normally associated with negative (inconclusive) autopsies that may (also) be explained by fatal intoxications (that normally do not cause distinctive autopsy findings) [6,7].

For these reasons, we performed a systematic review on the toxicity of these drugs during breastfeeding.

2. Methods

We performed a systematic literature search according to the current Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) criteria (Figure 1). We searched the PubMed database for papers published between 1 January 2014 and 31 December 2024. We used a search string (restricted to the terms in the paper titles and abstracts) in which, using the Boolean operator "AND," we combined the terms ("drugs of abuse or drug therapy or psychoactive substances or new psychoactive substances or drugs or alcohol or medications") with the terms ("breastfeeding or breast feeding or breastfeed or breastfed or lactation"). Two researchers conducted independent searches. Our preliminary research identified 1394 papers. A total of 1050 papers were removed from the pool of eligible papers because they were books and documents, experimental studies in animal models, and articles that were not published in English. Of the 344 screened by title and abstract, 277 papers were excluded as they did not meet the inclusion criteria based on topic. Of the 67 articles remaining, 27 were excluded due to the lack of focus on breastfeeding, 2 were already published data, and 14 were excluded for other reasons. A total of 26 eligible publications were included in our review and were critically reviewed by four investigators who extracted data relevant to the purpose of the present study. All authors agreed on the final data included in our study. A flow diagram of the articles selected for this review is summarized in Figure 1.

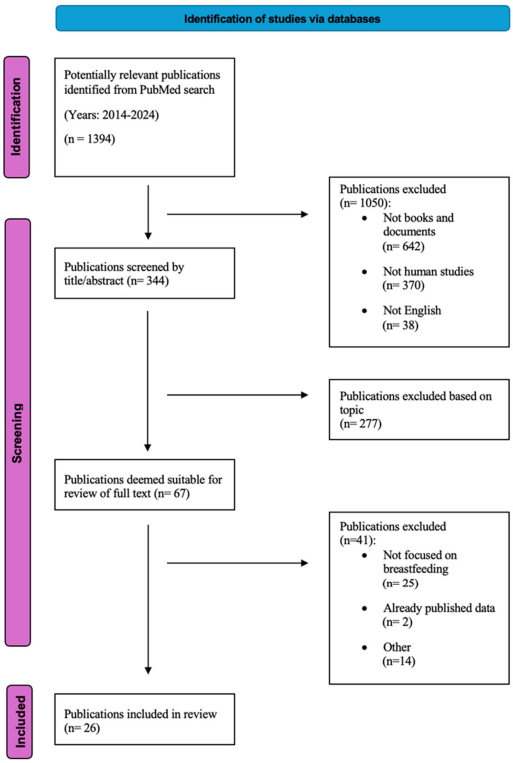

Figure 1. PRISMA flow diagram followed in this review.

3. Results

The studies included in this review can be grouped into major pharmacological categories: opioids (e.g., methadone and codeine), antidepressants and antipsychotics (e.g., SSRIs and clozapine), cannabinoids (e.g., THC), stimulants (e.g., methamphetamine), sedatives (e.g., benzodiazepines), alcohol, and immunomodulatory or dermatological drugs. These drugs were administered to women with psychiatric disorders, pain conditions, substance use disorders, or chronic autoimmune or dermatologic diseases. Observed neonatal effects included sedation, central nervous system (CNS) depression, feeding difficulties, delayed development, and, in rare cases, death. The evidence base consisted mainly of case reports, case series, observational studies, and pharmacological reviews. Where relevant, data on drug concentrations in breast milk and neonatal plasma were also specified.

3.1. Opioids

Madadi et al. described two cases of neonatal methadone intoxication during breastfeeding. The first case involved a 3-week-old infant found lifeless, with postmortem methadone levels of 79 mcg/L and genetic variants in CYP2B6*6 and ABCB1. The second case was an 18-day-old infant who died after hospital discharge, with postmortem methadone levels of 26–33 mcg/L and heterozygosity for three ABCB1 SNPs [8].

Soussan et al. analyzed adverse drug reactions (ADRs) in breastfed infants based on data from the French Pharmacovigilance Database (1985–2011). One of the drugs most frequently implicated in ADRs in breastfed infants was the opioid analgesic dextropropoxyphene, used alone or in combination with paracetamol. This opioid accounted for 11 reports (8.3%) of all adverse drug reactions in breastfed infants included in the study. Of these 11 reports, 9 (81.82%) were considered serious due to the presence of hypotonia, apnea, respiratory distress, and bradycardia. Following this pharmacovigilance report, dextropropoxyphene was withdrawn from the French market in 2011 [9].

Cheuk et al. noted that opioids, particularly codeine, led to CNS depression in 17 of 72 infants, with severe reactions in two cases linked to maternal genetic variations [10].

Verstegen et al. mentioned that morphine, codeine, oxycodone, tramadol, and fentanyl required caution and limited use [11].

3.2. Antidepressants and Antipsychotics

Newton and Hale in a 2015 article review drug categories and breastfeeding. SSRIs like sertraline are generally safe. Antipsychotics may cause sedation, poor feeding, extrapyramidal symptoms, irritability, and weight gain [12].

Payne examined psychotropic drug use in pregnancy and lactation. Antidepressants (except doxepin) were generally safe, while antipsychotics showed low breast milk levels but lacked long-term safety data. Clozapine and lithium were contraindicated [13].

Eleftheriou et al. reported that many antidepressants (including SSRIs and tricyclics) and benzodiazepines had relative infant doses below 10%. Clozapine and lithium remained risky [14].

Sprague et al. reviewed the safety of SSRIs, antiepileptics, mood stabilizers, and atypical antipsychotics during breastfeeding [15].

Babu et al. emphasized drug transfer mechanisms and the importance of monitoring in neonates [16].

A 2017 review on clozapine in lactation reported risks of agranulocytosis and bone marrow suppression in infants [17].

3.3. Cannabinoids

A 2018 study examined cannabinoids in breast milk from 50 mothers, detecting Δ9-THC in 63% of cases up to 6 days after use [18].

Williams et al. evaluated cannabis use during breastfeeding, noting limited data. THC remained in breast milk for up to 6 days and may have impaired infant motor development [19].

Navarrete et al. discussed cannabis use during pregnancy and breastfeeding, highlighting potential neuropsychiatric effects linked to THC exposure [20].

3.4. Stimulants

Chomchai et al. reported that there are no significant differences in the absolute infant dose of amphetamines transferred into breast milk and reaching the infant, regardless of whether the drug is taken orally or intravenously. Absolute infant doses reported in different studies range from 21.3 to 51.7 μg/kg/day. Infants exposed to methamphetamine may experience neonatal abstinence syndrome, with irritability, poor sucking, and presence of autonomic stress symptoms. The authors also investigated the pharmacokinetics of smoked crushed pills of methamphetamine in breast milk, noting measurable neonatal exposure and that elimination from breast milk can occur before maternal urine tests return negative results [21].

3.5. Alcohol

Anderson reported cases of ileus and abdominal distension in Chinese infants linked to maternal "chicken wine" (chicken cooked in Chinese rice wine) consumption. Alcohol ingestion during breastfeeding was related to short- and long-term effects on neonates [22].

May et al. found that maternal alcohol consumption during breastfeeding correlated with lower weight and verbal IQ in infants [23].

Haastrup et al. reviewed alcohol levels in breast milk and associated behavioral outcomes [24].

Ter Horst et al. argued no safe dose of alcohol exists for lactation [25].

Oei provided a narrative review of perinatal alcohol exposure [26].

3.6. Sedatives and Benzodiazepines

Cheuk et al. noted that benzodiazepines were generally compatible with breastfeeding [10]. In 98.4% of exposed infants there were no CNS symptoms [27].

3.7. Antiepileptics and Anticonvulsants

Shawahna et al. reviewed antiepileptic drug levels in breast milk and infant plasma, noting variable exposure [28].

Hope et al. cited NEAD and MONEAD studies on breastfeeding and antiseizure medications (ASMs) [29].

3.8. Immunomodulatory and Dermatologic Drugs

Siegel and Sammaritano discussed drugs for autoimmune disease. Some (e.g., IVIG, colchicine, hydroxychloroquine) are compatible; others (e.g., methotrexate, leflunomide) are not [30].

Yaghi et al. studied dermatological treatments and antihistamines, noting which are safe or contraindicated during breastfeeding [31].

3.9. Summary Tables and Figures

Toxicity, assessed through observed neonatal adverse effects (Table 1), represents a key component of drug safety [32–36]. Complementarily, Figure 2 provides a visual

synthesis of breastfeeding compatibility, categorized according to risk levels established by the e-lactancia database [32].

Table 1. Drug transmission in breast milk.

Drug	Characteristics and Milk Transmission	Effects on the Infant	Recommendations	References
Methadone	Lipophilic, higher in mature milk and hindmilk. Reduces NAS (neonatal abstinence syndrome).	Possible delayed motor development.	Infant monitoring required.	[8]
Antidepressants (Sertraline, Citalopram, Venlafaxine)	Higher concentrations in hindmilk. Sertraline has low penetration; citalopram and venlafaxine have moderate–high penetration with accumulation risks.	Irritability, lethargy, long-term neurological effects.	Infant monitoring; sertraline preferred.	[37]
Cocaine	Highly lipophilic, accumulates in foremilk and hindmilk. Transfers 13.8 µg/100 mL, with 8.3 µg absorbed.	Risk of seizures, hypertonia, tachycardia.	Contraindicated; avoid breastfeeding after use.	[38–40]
Alcohol	Not highly lipophilic, mirrors plasma levels, peaks at 60 min.	Irritability, reduced deep sleep, developmental delays.	Avoid breastfeeding for at least 2–3 h after intake.	[22,23,25,26,41]
Cannabinoids (THC, CBD, CBN)	THC is highly lipophilic, detected up to 6 days. CBD/CBN lower or undetectable.	Potential neurotoxic effects.	Avoid cannabis use while breastfeeding.	[18]
Benzodiazepines (Diazepam, Lorazepam)	Pass into breast milk via diffusion; long half-life compounds accumulate more.	Sedation, lethargy, reduced sucking reflex.	Prefer short-acting lorazepam when needed; monitor closely.	[10]
Opioids (Morphine, Codeine)	Codeine metabolized into morphine, risk of accumulation in hindmilk.	Respiratory depression, sedation.	Avoid codeine; morphine can be used with caution.	[42]
Antipsychotics (Clozapine, Olanzapine)	Clozapine penetrates significantly, olanzapine moderately.	Clozapine: sedation, hypotonia, neutropenia. Olanzapine: lower risk but requires monitoring.	Clozapine not recommended; olanzapine used with monitoring.	[17]
GHB	Milk levels 71–80% lower than blood, return to endogenous levels after 5 h.	Low risks if waiting period is followed.	Safe after 5 h post-dose.	[43]
Ketamine	Low oral bioavailability, minimal secretion into milk.	Minimal neonatal exposure.	Breastfeeding can resume after 12 h.	[44]
Other (Methotrexate, Acitretin)	May accumulate in neonatal tissues.	High toxicity.	Contraindicated.	[31]
Immunoglobulins	Transfer into milk but no adverse effects.	No known risks.	Safe for the infant.	[30]

THC: 9—tetrahydrocannabinol; CBD: Cannabidiol; CBN: Cannabinol; GHB: Gamma Hydroxybutyric

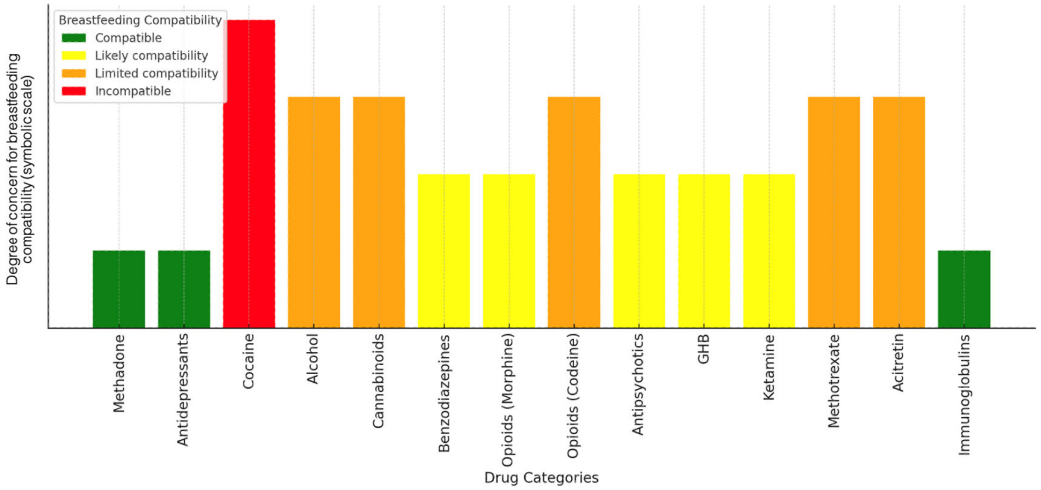

Figure 2. Breastfeeding compatibility of drug categories, based on e-lactancia database [32]. Bar height is symbolic and increases with the degree of concern from safe use to contraindicated.

4. Discussion

The safety of a drug used during lactation primarily depends on its capability of being transferred into milk. Passive diffusion is influenced by the drug's molecular weight, liposolubility, plasma protein binding capacity, and ionization, but also by other pharmacokinetic variables (e.g., route of administration, time since the assumption, half-life, and volume of distribution) [14]. Human milk is a very peculiar matrix from a chemical point of view, since its constituents vary highly over time, as shown in Table 2 [22,33–35].

Table 2. Aspects associated with changes in breast milk composition.

Categories	Aspects	Key Points	Notes
factors related to infants	Dynamic Nature	Changes in infant needs	Adapts nutritionally and immunologically
factors related to breastfeeding mothers	Maternal Diet	Affects fatty acid composition	Nutrition impacts milk
	Maternal Factors	Body weight, age, and ethnicity matter	Genetic influences
	Hormonal Control	Prolactin and oxytocin regulate milk flow	Key lactation hormones
	External Influences	Stress and medications alter milk	Emotional and medical factors
	Maternal Health	Infections and inflammation impact permeability	Health affects composition
factors related to breast milk	Colostrum	High in antibodies, proteins, and growth factors	Essential immune protection
	Transitional Milk	Increases in volume and fat	Intermediate stage
	Mature Milk	Balanced nutrients: macronutrients, vitamins, and minerals	Supports steady growth
	Foremilk	Watery and hydrates infant	Early feed
	Hindmilk	High in fat and energy-rich	Late feed
	Daily Variations	Fat peaks in the morning and drops at night	Diurnal changes

Table 2. *Cont.*

Categories	Aspects	Key Points	Notes
factors related to breastfeeding	Lactation Duration	Protein decreases and fat is stable	Long-term adaptation
miscellaneous	Influencing Factors	Lactation stage, feeding patterns, and maternal traits	Time, diet, health

An important aspect of safety is toxicity (Table 1).

For instance, mothers undergoing stable methadone therapy can breastfeed with appropriate monitoring of the infant. Due to its lipophilic nature, its concentration tends to be higher in mature milk and hindmilk, where fat content is greater. It can help reduce neonatal abstinence syndrome (NAS), but it may also be associated with delayed motor development [36].

Concentrations of antidepressants such as sertraline, citalopram, or venlafaxine tend to be higher in hindmilk, especially with prolonged use or high dosages [37]. Sertraline has a low milk-to-plasma ratio and minimal lipid binding, making it a preferred choice for postpartum depression treatment, with rare reports of infant irritability. In contrast, citalopram exhibits higher penetration and moderate lipid binding, potentially leading to irritability, lethargy, and long-term neurological effects. Venlafaxine has a moderate milk-to-plasma ratio and active metabolites that may accumulate. In all cases close monitoring of exposed infants is recommended [37].

Cocaine rapidly accumulates in both foremilk and hindmilk due to its high lipophilicity, posing severe risks of seizures, hypertonia, and tachycardia. A study estimated that a single 100 mL breast milk sample could contain up to 13.8 μg of cocaine, exposing the infant to potential toxic effects of this substance [36,38].

Alcohol is not highly soluble in lipids, mirroring plasma concentrations, with peak levels occurring 60 min after consumption in breast milk. Chronic exposure may lead to irritability, reduced deep sleep, and developmental delays. It is recommended to avoid breastfeeding for at least 2–3 h after alcohol intake [23].

Numerous studies have demonstrated a clear link between maternal alcohol consumption during lactation and reduced reasoning abilities in children aged 6 to 7 years compared to their peers. Additionally, smaller studies have identified potential associations between breastfeeding under these conditions and issues in infants, such as sleep disturbances, irritability, and difficulties with sucking [26].

Due to their high lipid solubility and alkaline pKa, cannabinoids accumulate particularly in hindmilk. THC concentrations may range from 1 to 323 ng/mL, with an average detectable presence up to 6 days after last cannabis use. CBD and CBN levels were lower or not detected. Given the persistence of THC in breast milk and its potential effects on infant neurodevelopment, mothers are advised to avoid cannabis use while breastfeeding [36,45].

Benzodiazepines, including diazepam and lorazepam, pass into breast milk through passive diffusion, with variability depending on the specific drug. They can cause sedation, lethargy, and diminished sucking reflexes in infants, with an increased risk of accumulation for long half-life compounds. Short-acting benzodiazepines, such as lorazepam, are preferred, when necessary, with close infant monitoring. Their lipophilic nature leads to greater accumulation in hindmilk [36].

Whether opioids transfer into breast milk depends on their lipophilicity. Codeine, in particular, is metabolized into morphine and can accumulate in the milk, increasing the risk of respiratory depression and sedation. Codeine use should be avoided, whereas morphine may be used cautiously under monitoring. These substances tend to have higher concentrations in the lipid-rich hindmilk [36].

Many antiseizure medications (ASMs), including carbamazepine, lamotrigine, topiramate, gabapentin, valproic acid, ethosuximide, levetiracetam, primidone, phenylethylmalonamide, and phenobarbital, can be found in the plasma and serum of infants at significant concentrations. This is attributed to their small molecular size and lipophilicity. However, none of the studies identified specific risks to the health or neurodevelopment of newborns. Notably, there have been no significant adverse effects reported in infants, such as growth retardation or reduced IQ development. The medications that raised concerns include phenobarbital, primidone, clobazam, clonazepam, lamotrigine, and felbamate. Infants exposed to phenobarbital, primidone, clobazam, or clonazepam showed an increased risk of lethargy, hypotonia, poor sucking reflexes, or apnea. Lamotrigine may require dosage adjustments post-delivery to ensure the safety of both mother and infant. Breastfeeding is generally not recommended for mothers taking felbamate due to insufficient safety data and known risks associated with this drug in adults, including acute liver failure and aplastic anemia. However, it remains unclear whether these effects stem from lactation exposure or intrauterine exposure. Consequently, close monitoring of infants whose mothers are on antiepileptic therapy is advised. If an infant exhibits excessive sedation or poor growth, medication intake should be limited or discontinued [15,28].

In terms of the safety of commonly prescribed medications for depression and bipolar disorder, including SSRIs, antiepileptics, mood stabilizers, and atypical antipsychotics, breast milk contains negligible concentrations of these medications except for fluoxetine (an SSRI), lamotrigine (a mood stabilizer), and risperidone (an atypical antipsychotic), where concentrations may be clinically relevant. Importantly, no specific health risks were identified for infants exposed to these medications; however, monitoring for signs of lethargy, psychomotor slowing, or rare side effects like agranulocytosis is recommended. Given the heightened risk of suicide within the first year postpartum and the minimal health risks associated with therapeutic doses of these medications in infants, the authors do not recommend discontinuing treatment for individuals with mood disorders [46]. Antipsychotics such as clozapine and olanzapine differ in their safety profiles. Clozapine penetrates breast milk significantly, with risks of sedation, hypotonia, and neutropenia, making it generally unsuitable for breastfeeding. On the contrary, olanzapine has a moderate milk transfer rate and a lower risk profile, but infants should still be monitored for sedation. Both drugs exhibit higher concentrations in hindmilk [36].

GHB (Gamma hydroxybutyrate) is used as sodium oxybate for narcolepsy treatment. In a case study of a mother taking 4.5 g of sodium oxybate, GHB peaked in blood at 108.34 mg/L after 1 h and in breast milk at 23.19 mg/L. GHB levels in milk were 71–80% lower than in blood during the first 3 h but returned to endogenous levels after 5 h. Based on these findings, breastfeeding is considered safe at least 5 h after the last dose [43].

Limited data are available for ketamine. However, infant exposure is expected to be minimal due to the low oral bioavailability of this substance. These findings suggest that breastfeeding can be resumed as soon as the mother is alert and capable, typically within 12 h post-dose [44].

Indeed, there are substances, like intravenous immunoglobulins, that can be transferred into the milk but have no deleterious consequences for the newborn [31]. On the other end, even low doses of some transferred drugs (e.g., methotrexate, acitretin) may be toxic, because of the accumulation inside the tissues that is not balanced by the (immature) renal clearance [31].

That being said, as shown by our review, there is relatively scarce evidence about the concentration of drugs in human milk due to the few reports addressing this issue and to the variable reliability of the quantification methods (i.e., reliable quantification should always be achieved through gas/liquid chromatography–mass spectrometry) [14]. This

limitation is particularly strong with regard to recreative substances, due to the lack of substantial research on the matter.

In addition, the process by which drugs accumulate in breast milk and infant plasma, as well as the potential adverse effects, does not follow a straightforward or linear pattern. Researchers have proposed several mechanisms to explain these variations, taking into account factors such as the relative infant dose (RID), the milk-to-plasma drug concentration ratio (M/P ratio), and how efficiently the mother clears the drug from her system [46].

For instance, when drugs have a high RID (greater than 10%) and infant serum concentrations exceed 80%, as seen with medications like acebutolol, dapsone, lamotrigine, and phenobarbital, it is often due to significant drug transfer through breast milk. This is typically combined with either low clearance of active metabolites in infants or cases of maternal overdose. On the other hand, some drugs with a low RID (less than 10%) can still result in high infant serum concentrations (above 80%), as observed with atenolol, carbetapentane, doxepin, fluoxetine, lithium, aspirin, and iodine. In these cases, the primary issue seems to be the infant's limited ability to metabolize and eliminate the drug efficiently.

Finally, there are drugs with both a low RID (below 10%) and low infant serum concentrations (below 60%), such as citalopram, diazepam, doxepin, lithium, sulfasalazine, and valproic acid. For these medications, adverse effects are more likely linked to pharmacodynamic toxicities or idiosyncratic reactions rather than a direct result of drug dosage.

These findings emphasize the need to carefully evaluate both the properties of drugs taken by breastfeeding mothers—such as their plasma levels and half-life—and the specific characteristics of infants, including their metabolic capacity. This dual consideration is essential for ensuring drug safety during breastfeeding.

Forensic toxicological analysis of breast milk still represents a main challenge. As mentioned above, breast milk has a high lipid and protein content, which makes the extraction and detection of drugs and metabolites challenging [47,48]. Additionally, the composition of breast milk varies over time, affecting drug partitioning and making standardization difficult. Matrix effects, which can lead to ion suppression or enhancement during mass spectrometry analysis, impacts sensitivity and quantification. Recovery rates for different substances vary significantly, ranging from 51.6% to 86.5%, and process efficiency can be as low as 46.8%. Ensuring method accuracy requires extensive validation, including testing for freeze–thaw stability, carryover, and degradation due to pasteurization [47,48]. Different drug classes pose specific analytical difficulties. Lipophilic substances, such as cannabinoids and methadone, tend to accumulate in milk due to their high fat content, whereas more polar substances (e.g., cocaine metabolites) show disproportionate distribution between blood and milk. The presence of endogenous interferences and varying drug protein-binding properties further complicates the analysis. To address these challenges, liquid chromatography tandem mass spectrometry (LC-MS/MS) is the preferred method due to its high sensitivity, specificity, and ability to analyze multiple substances simultaneously. Despite its effectiveness, issues such as low recovery rates for some drugs, variability in matrix effects, and differences in drug stability remain. These findings emphasize the need for continued optimization of analytical methods to ensure accurate detection and quantification of drugs in breast milk [47,48].

In conclusion, our review showed that many drugs used for common disorders are safe, despite some medications still requiring close monitoring of the child. For instance, while antifungal and antiviral drug use is used contraindicated during lactation, most antibiotics are safe for breastfeeding but monitoring of the minor is still needed because of the potential effects of these drugs on gut flora (with consequent gastro-enteric symptoms like diarrhea) [31]. When a potentially harmful drug is the best choice for a condition that cannot

be left untreated (e.g., postpartum depression), monotherapy with the lowest effective dose of the drug and close monitoring of the mother and of the child is generally recommended.

From a medico-legal perspective, exposure to unsafe medications and consequent child endangerment/intoxication can be a source of criminal/civil liability for the prescriber (if there was evidence contraindicating the drug) and/or the mother (if she used an unprescribed drug or an illicit substance) [49]. Accurate forensic toxicology routine should always be a priority in sudden infant deaths, because, even if there is scarce evidence of the relationship between exposure to drugs during lactation and sudden death, this issue is well-known as being critical with regard to both prenatal use of drugs and pediatric accidental intoxications [50,51]. In particular, in fatal cases, successful detection of drug concentrations in the breast milk (with known toxic and lethal thresholds to interpret these levels) is pivotal from a forensic point of view, since autopsy findings in sudden toxic deaths are highly nonspecific, especially in infancy, and are associated with a high prevalence of negative autopsies [6]. As also shown by our review, a specific topic is represented by the use of methadone and buprenorphine during breastfeeding: in cases of neonatal abstinence syndrome, the intake of these drugs—when prescribed—should be encouraged, because they help to mitigate the syndrome's symptoms concurring with psychological interventions like rooming-in, skin-to-skin contact, and swaddling [52].

Limitations

The first limitation is that even regarding frequently used drugs like ketamine, we were able to find little data, because few research papers investigate these aspects.

Regarding methodological aspects, heterogeneous analytical techniques were used to evaluate concentrations in human milk.

5. Conclusions

Breast milk is a highly peculiar matrix from a chemical point of view, also due to its highly variable and dynamic composition, representing a challenge for proper toxicological analysis. Little evidence on the actual concentrations of common drugs is reported with consequent poor knowledge about toxic and lethal levels in this matrix. This is a serious limitation for postmortem analysis in cases of suspected intoxications, due to the high prevalence of negative autopsies in infants' sudden deaths. From a clinical point of view, decision-making on a drug prescription during lactation should always represent a balance between current toxicological knowledge, the drug's capability to be transferred into milk, and the health needs of the woman. Education on proper drug management should be promoted to all stakeholders to avoid stigmatization of safe and needed drugs during lactation (e.g., antidepressants or methadone) and, on the other hand, to avoid the use of unnecessary substances that may/do endanger the infant.

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