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Safety and Efficacy of Antipsychotics in Pregnancy and Lactation

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Abstract

The clinical profiles of antipsychotic medications have improved dramatically since the first generation was introduced in the 1950s. Second Generation Antipsychotic medications (SGAs), which became available in 1990, generate fewer side effects, including reduced incidence of extrapyramidal symptoms such as hyperprolactinemia. This improves the female patients' ability to become pregnant, a process which is compromised by first generation drugs. However, use of antipsychotic medications has become increasingly prevalent. The likelihood of females with depression, bipolar disorder, psychosis to have an unplanned pregnancy, and the incidence of foetal exposure to psychotropic drugs during the first trimester of pregnancy has also increased. The paucity of exposure and outcome data leaves the safety and effects of use of antipsychotic medications during pregnancy as a subject to controversy. The evidence is insufficient to provide adequate support for clinical practices, and also to the professionals in the related fields of psychiatry, obstetrics-gynecology, and primary care. There is often contradicting information given to patients due to the lack of current studies pertaining to this area. The studies of SGA's use during breastfeeding suggest that olanzapine, risperidone, and quetiapine may be safe at certain levels whereas medications like clozapine achieve relatively high concentrations in breast milk and may cause agranulocytosis and somnolence. Therefore, the purpose of this review is to report the most relevant and up-to-date findings of antipsychotic medication use during pregnancy and lactation in detail, so that physicians may have more insight regarding medications and provide female patients of childbearing potential with knowledge of the benefits and risks of antipsychotic drugs.

Keywords: Efficacy; Antipsychotics; Pregnancy; Lactation

Introduction

The prevalence of psychiatric disorders has increased over the years, with 50% of the population currently living with some form of psychological disorder [1,2]. This in turn has led to the direct increase of use of antipsychotic medications, which has experienced a great improvement over the years. The spectrum of use of antipsychotic medications has exponentially increased not only for schizophrenia and bipolar disorders, but they are also frequently prescribed for mood and anxiety disorders, self-harming behaviors, trauma-related conditions, and insomnia [3]. Thus, it is important that an adequate risk-benefit analysis be performed prior to any medication being prescribed. This is especially important in pregnancy, or in the case of a potential for pregnancy [4]. A large majority of psychiatric patients present symptoms between the ages of 14 and 24 years [5], coinciding with average age of onset of first pregnancy. In addition, there is an increase in fertility rate in women with psychiatric illnesses; this is partly due to improvements in drug formulation which confer reduced risk of hyperprolactinemia [6]. About 67% of women with mental disorders unexpectedly become pregnant, unplanned or unwanted [7]. Most of them lack or have no knowledge regarding family planning methods, and end up conceiving. These conceptions can also result from sexual abuse either from their counterparts or even people without psychiatric imbalances.

Pregnant women with psychiatric disorders are faced with treatment predicaments; the default clinical sanction over the years has been to discontinue antipsychotics, especially during the first trimester. Evidence has suggested that most psychotropic drugs are safe for use during pregnancy and failure to use them poses a great risk to both the mother's health and her ability to cater for the infant [8]. Studies conducted over a follow-up period of 2 years revealed that the rate of relapse can be increased after cessation of anti-psychotics, going as high as 50%, which compares to 15% in those who are on medication [9]. This calls for a meticulous risk evaluation, weighing the benefits and risks of anti-psychotic medication use during pregnancy.

Methodology

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology [1], a search for relevant published literature was performed using PubMed. The keywords and phrases used together with Boolean operators included: "antipsychotic medications," antipsychotic medications in pregnancy" [Mesh] AND OR "antipsychotic medications in lactation" [Mesh]. Other relevant

studies were found by a review of the primary studies obtained in the search as well as reference tracing of selected articles.

The inclusion and exclusion criteria were:

Any articles that reported the use of antipsychotic medications during pregnancy and lactation and their outcomes in mother and foetus.

Only peer-reviewed research studies which were published in English language from the years 2007-2017 were included.

Specific case studies, case letters, and grey literature as well as studies not published in English were excluded.

By the end of the literature search, 184 articles met the inclusion criteria, excluding duplicates. Out of these 184 articles, only 106 pertained to the topic. Relevance was based on the individual article and abstract review conducted by an independent researcher. From these 106 articles, 47 were pertinent with main aims of the study and were used to extract qualitative data and summarize the findings.

Benefits versus Risks of Using Antipsychotics during Pregnancy

It is clear that all antipsychotic drugs are lipophilic and cross the placental barrier. The use of some anti-psychotic medications particularly the first-generation ones, have been associated with pregnancy complications like gestational diabetes and a number of potential adverse effects to the fetus, varying from low birth weight to serious neurodevelopmental issues have been attributed to their continued use [10].

Taking the two major groups of psychiatric disorders for instance, schizophrenia and bipolar disorder, both of these conditions are associated with an increased risk of complications in pregnancy such as pre-eclampsia, ante-partum hemorrhage, fetal distress, as well as the potential for adverse neurodevelopmental milestones, excluding any additional risk that may follow drug use [11]. A study concluded that the risks for low birth weight and small for gestational age neonates, among women with schizophrenia, did not differ irrespective of the exposure to antipsychotics. This suggests that little or nothing benefits from the discontinuation of medications during pregnancy [12]. Currently, the most commonly used antipsychotic medications during pregnancy are olanzapine, risperidone, and quetiapine; there is no specific evidence that they cause fetal malformations [13].

During lactation

The use of antipsychotic medication use during breastfeeding has been well documented. No association has been noticed between normal development of an infant and exposure to the antipsychotic drug during breastfeeding. Several studies [14-16] have exonerated risperidone, quetiapine, and olanzapine and their successful use has been recorded. However, caution should be taken before administration of antipsychotic medication to a lactating mother.

Generally, the choice of drug depends on the balance between safety and efficiency profile of the drug. Before a decision is made to give a particular antipsychotic medication during pregnancy and perinatal period, an adequate evaluation of its risks and benefits should be weighed, to ensure optimum care for the mother and child. An assessment of the patient's other medical conditions should also be taken into consideration, to dictate the most appropriate management strategy.

Antipsychotic Drugs during Pregnancy: Metabolism, Safety, and Adverse Effects

Metabolism

The period between conception and the end of puerperium (6 weeks post-partum), is a critical phase for a woman, as she experiences physiological, psychological, and social changes differing from her usual pre-gravid state. This period of transition can be challenging and a high-end care of the woman is crucial for both the mother, and the developing baby.

The 5th to the 8th week of gestation is the period of 'organogenesis', during which development of body organs takes place [17]. Caution must be taken in this period, before administration of drugs to avoid developmental anomalies as maximal effect of drug exposure is exerted during this phase. Every maternal organ adapts to pregnancy, there is expansion of vascular volume, increased cardiac output and decreased albumin level. All of these contribute to a reduced serum level of drugs, with a consequential increase in hepatic metabolism and renal clearance. The foetus, on the other hand, has immature hepatic and renal system, relatively permeable blood brain barrier, difficulties in transporting drug metabolites back to maternal circulation, and higher blood concentration of drugs about maternal level. Hence, the puzzle surfaces, when an adequate level of drugs is desired in the mother, and at the same time, it has to be less in the foetal circulation. It is a fact that the foetal hepatic and renal systems are immature. To circumvent this, the placenta functions to remove by products of metabolism from foetal circulation through P-glycoprotein, which transports products of metabolism back to maternal circulation. Drugs that are substrates of P-glycoprotein, like risperidone and quetiapine, have less tendency to reach a high concentration in foetal circulation, while poor substrates of P-glycoprotein will not be affected by this physiological mechanism, rather they reach levels dependent on their degree of lipid solubility, gestational age, and dose taken by the mother.

SafetyIn a study done on placental passage ratio of antipsychotics, the highest percentage was for olanzapine (mean=72.1%, SD=42.0%) followed by haloperidol (mean=65.5%, SD=40.3%), risperidone (mean=49.2%, SD=33.9%) and least for quetiapine (mean=23.8%, SD=11.0%) [18]. A 2009 literature review by Einarson and Boskovic showed no association of any teratogenic complication with the use of first-generation (typical) antipsychotics [13]. However, they clearly stated that flawed methodologies limit their ability to accept the findings without question, as the research standards were said to be less rigorous. The same review examined all available data regarding exposure of fetus to second-generation (atypical) antipsychotic medications, and no clear association with any specific malformation was observed. Although, it is known that all psychotropic medications cross the placenta, there is uncertainty regarding the teratogenic effects of their use on pregnancy.

Adverse Effects

Second generation antipsychotic medications

Second generation antipsychotic medications are widely prescribed to women during pregnancy. There is no sufficient evidence showing the association between uses of atypical antipsychotics causing teratogenic effects on neonates [19]. Most commonly maternal hyperglycemia and weight gain are found to occur in pregnant women using atypical antipsychotic medications. Large for gestational age [20] is noticed in infants who were exposed to these medications in utero.

However, low birth weight infants with second generation antipsychotics were less common when compared to use of the first generation antipsychotics [12].

Olanzapine: Olanzapine is the most commonly used antipsychotic medication in pregnancy [21] with 72% placental passage. It is mainly used in treatment of schizophrenia and bipolar disorders. Increased risk of neural tube defects was observed with use of olanzapine [22]. However, there is no evidence supporting it. It is also associated with gestational diabetes [23] ectopic pregnancy, and spontaneous abortion in mothers. Increased birth weight, prematurity in infants.

Quetiapine: It is an antipsychotic with the placental passage of 23.8% [18]. Quetiapine has been associated with atrial septal defects, cleft lip/palate, pulmonary atresia, and hydrocephalus in new born. Concomitant use of quetiapine with zuclopenthixol has also been associated with atrial septal defects [24]. Spontaneous abortions were also reported in very few cases [25].

Risperidone: Risperidone is also one of the commonly used atypical antipsychotics. It has been associated with perinatal complications ranging from withdrawal syndrome to seizures [26]. Risperidone exposure was found to cause fetal malformations including Ivemark syndrome, Pierre-Robin syndrome, cardiomyopathy, cleft lip and palate, ear abnormalities, gastroschisis, gestational diabetes, and Turners' Syndrome [27].

Clozapine: Very few cases of spontaneous abortion in the mother, a case of the ectopic anus, and one lumbar myelomeningocele was found to occur due to use of clozapine.

There is very limited data available regarding use of newer atypical antipsychotics like aripiprazole, sertindole, and ziprasidone. Animal studies have demonstrated ventricular septal defects and renal malformations with doses similar to the therapeutic doses commonly used with these medications [28].

First generation antipsychotic medications

First generation or typical antipsychotics are less commonly used than second generation antipsychotic medications because they have a higher likelihood of causing extra-pyramidal side effects; like tone abnormalities, spasticity, and feeding difficulties. These side effects are found to occur due to their strong affinity for D2 receptors and they are often prescribed with anticholinergic agents to reduce these problems. Lesser reported complications in neonates of mothers who were using these agents are intestinal obstruction, neonatal jaundice, preterm birth, low birth weight, and posterior nasal disorders.

Haloperidol: It is a butyrophenone with a placental passage of 65.5% secondary to olanzapine [18]. First trimester exposure to haloperidol has been reported to cause limb defects [29] while cardiac anomalies are evidenced in the third trimester [30]. Other malformations that can occur with the use of haloperidol are micropthalmia, gastroschisis, trisomy 13 and 18, and renal dysplasia [27]. However, none of these are found to be significant when compared to general population.

Chlorpromazine: This medication has increased risk of non-specific teratogenic effects, withdrawal and extrapyramidal side effects following first trimester exposure. Fetal hypotonia may occur following a very high-dose intake of chlorpromazine in pregnancy [31]. An increased risk of neonatal jaundice in preterm infants has also been suggested with the use chlorpromazine during pregnancy [32].

Other side effects that are associated with typical antipsychotic medications include upper limb defects and foot deformities in infants whose mothers were exposed to penfluridol in the first trimester [30]. Congenital cataract, congenital heart block, tracheomalacia, hypospdiasis, VSD, undescended testis, pyloric stenosis, and ureter stenosis were reported with the use of zuclopenthixol in first trimester. Patent Ductus Arteriosus (PDA), situs inversus, cerebral cyst, VSD, cleft palate, accessory thumb, unstable hip, undescended testes, and gestational diabetes mellitus were reported with use of flupenthixol in first trimester [27]. However, more studies pertaining to zuclopenthixol and flupenthixol are needed before a conclusion can be made as regards to their safety for use in pregnancy.

Anti-psychotic Medications during Lactation

Use of antipsychotic medication during puerperium and lactation is not uncommon, particularly in women with severe psychiatric illness who relapse during the third trimester, or immediately post-partum.

There is still insufficient data about the safety and adverse effects of the use of antipsychotic medications in a lactating mother, partly due to ethical considerations [33]. Current literature describes the effect of antipsychotic use in case reports and studies including prospective and retrospective data [34]. To state whether an antipsychotic agent is safe for lactation or not, it must be ascertained whether the possible developmental disorder in the infant is due to the direct pharmacological effect of the medication or as a sequalae to mother's psychiatric condition.

Certain parameters have been employed to estimate the risk of exposure to the medication, these include Absolute Infant Dose (AID), Therapeutic Infant Dose (TID) and Relative Infant Dose (RID). AID=Concentration of drug in milk × Volume of milk taken. By calculating the Absolute Infant dose, the infant dose per kilogram per day can be estimated; this is then compared with the therapeutic infant dose. The Relative Infant Dose (Lowest Paediatric Dose) can also be determined by dividing the AID by the maternal dose in milligram per kilogram per day. It is assumed that RID less than 10% is safe [35].

Second generation antipsychotic medications

Risperidone: It is an atypical antipsychotic which is a benzisixazole derivative. It was initially reported to be unsafe for use during breastfeeding [15]. However, recent research [36] has suggested contrary to that, stating that risperidone secreted in breast milk is in low amounts, and has not been shown to have any adverse effects [37].

Clozapine: It is an atypical antipsychotic, dibenzodiazepine derivative that is readily secreted in breast milk [38]. It can cause a range of adverse side effects such as sedation, irritability, decreased suckling, seizures and cardiovascular instability in breast-fed infants of users because of its secretion in the breast milk [39,40]. The association of clozapine use with agranulocytosis and neutropenia has brought the authors of Therapeutic guidelines (2003) to conclude that clozapine isn't a first line choice of antipsychotic to recommend during pregnancy and lactation.

Olanzapine: Though chemically and pharmacologically it is similar to clozapine, olanzapine achieves very low levels in infant plasma [41]. A study has shown that olanzapine and risperidone only reached small amounts in breast milk; this makes olanzapine relatively safe for use during lactation [27].

Quetiapine: Quetiapine is found in low concentrations in breast milk. No adverse effects have been reported in a lactating mother due to its use [42].

First generation antipsychotic medications

The typical antipsychotics are generally considered safe for breastfeeding infants of users. Studies have shown that use of typical antipsychotics have no adverse effects associated with their use in lactating mothers. They all have a milk/plasma ratio of less than 1, which is considered safe [43].

Chlorpromazine: This medication is excreted in very low concentrations in breast milk. Several studies have revealed that a breast-fed infant of a mother taking chlorpromazine is estimated to ingest 0.03-1.3% of the lowest pediatric dose, which is very low and can't precipitate harmful effects in the infant [44-47]. However, not much has been reported about the simultaneous use of chlorpromazine and other psychotropic agents in a lactating mother, but with evidence, it can be concluded that monotherapy with an optimal dose of chlorpromazine is safe for mother and infant during lactation.

Haloperidol: This potent butyrophenone is another very commonly used typical antipsychotic shown to be safe for use in breast-feeding mothers. It is secreted in very low concentration in breast milk that is not significant enough to pose a pharmacological detriment to the infant [47].

The atypical antipsychotics, on the other hand, have an inconclusive data as regards to their safety. Some of the atypical antipsychotics are suggested to be safe for use, as they have precipitated no known adverse effects in the breast-fed infants of mothers that used them either during puerperium or during lactation [15], while some are suggested to be unsafe (Table 1) [48].

Source of the Study	Sample Studied	Antipsychotic Medications Used	Results
Goldstein et al. [22]	34	Olanzapine	First trimester: 3 spontaneous abortions, 1 still birth, 1 downs syndrome were reported. All trimesters: Perinatal complications like jaundice, cardiomegaly, tachycardia, heart murmur, convulsions, Sudden Infant Death Syndrome (SIDS)
Biswas et al.	18	Clozapine	All trimesters: 2 spontaneous abortions, 1 pregnancy were terminated due to lumbar myelomeningocele in the fetus.
Lee et al. [42]	303	Atypical antipsychotics	First trimester: 3 major malformations occurred in infants including Atrial Septal Defect (ASD), Chiari malformations, small bowel atresia, and hypospadiasis
McKenna et al. [19]	60 36 49 6	Olanzapine Quetiapine Risperidone Clozapine	First trimester: cleft lip, encephalocele, and aqueductal stenosis None None None Overall 22 spontaneous abortions and 4 still births were reported in this study.
Diav-Citrin et al. [30]	188	Haloperidol	Third trimester: Ventricular Septal Defect (VSD), developmental delay, lung hypoplasia, severe bullous emphysema, limb deformity, congenital heart defects are noted
	27	Penfluridol	First Trimester: Upper limb reduction defect and foot deformity were noted in 1 infant.
Newport et al. [18]	14 21 13	Olanzapine Quetiapine Haloperidol	Second and third trimester: Cardiovascular and neonatal respiratory complications, hypotonia with Haloperidol and Olanzapine
	6	Risperidone	None
Twaites et al. [25]	6	Quetiapine	First trimester: 5 patients-1 spontaneous abortion. Second and third trimester: 1 patient- 1 spontaneous abortion
Coppola et al. [49]	201	Risperidone	All trimesters: 14 Major malformations and 3 minor malformations including Ivemark syndrome, Pierre –Robin syndrome, gastroschisis, cardiomyopathy, cleft lip and palate, ear abnormalities. 4 still birth, 31 induced abortion, 42 spontaneous abortion 45 other causes like perinatal syndromes, prematurity and, developmental syndromes
Reis and Källén [27]	4	Quetiapine	First Trimester: None
	18	Clozapine	First trimester: One case of ectopic anus

	44	Haloperidol	First trimester: Microphthalmia, gastroschisis, renal dysplasia, trisomy 13 and 18, unstable hip
	51	Risperidone	First trimester: 1 Anal atresia, lung malformation, Turners syndrome, 1 Gestational Diabetes Mellitus
	79	Olanzapine	First trimester: Craniosynostosis, VSD, hand/finger reduction, 3 cases of gestational diabetes mellitus were reported
	5	Chlorprotixene	First Trimester: None
	75	Zuclopenthixol	First trimester: Congenital cataract, congenital heart block, tracheomalacia, hypospdiasis, VSD, undescended testis, pylorostenosis, and ureter stenosis
	98	Flupentixol	First Trimester: Patent Ductus Arteriosus (PDA), situs inversus, cerebral cyst, VSD, cleft palate, accessory thumb, unstable hip, undescended testes, 1 case of gestational diabetes mellitus were reported
Newham et al. [20]	45	Typical antipsychotics	All trimesters: 1 infant with Large for gestational age (LGA)
	25	Atypical antipsychotics	All trimesters: 5 infants with LGA
Wichman [50]	2	Aripiprazole	All trimesters: Ventriculomegaly and hydrocephalus in an infant exposed to aripiprazole
	10 4 1	Quetiapine Risperidone Ziprasidone	Small for gestational age, prematurity, heart murmurs, and feeding difficulties are also noted in infants exposed to other antipsychotic medications
Babu et al. [51]	70	Olanzapine Other antipsychotics	All trimesters: Olanzapine was associated with higher birth weight in new-born compared to other antipsychotic medications
Lin et al. [12]	194	Typical antipsychotics	All trimesters: Infants exposed to typical antipsychotic medications are found to have more low birth weight (LBW), preterm birth, small for gestational age compared to infants exposed to atypical antipsychotic medications
	48	Atypical antipsychotics	
Bodén, et al. [52]	169	Olanzapine/clozapine	All trimesters: Increased risk for macrocephaly
	338	Other antipsychotic medications	Increased risk for Gestational Diabetes Mellitus with exposure to all antipsychotic medications
Johnson et al. [53]	22	Antipsychotic medications	All trimesters: Infants exposed to antipsychotic medications as fetus had lower neuromotor performance at 6 months of age compared to infants with exposure to antidepressant medications or no exposure to antipsychotic medications
(Brunner, et al.) [54]	610	Olanzapine	All trimesters: 57 spontaneous abortions, 3 ectopic pregnancy, 60 premature birth infants, 5 still births, 27 infants with congenital anomalies, 49 infants with perinatal condition, 3 with post perinatal condition
Habermann et al. [55]	287	Typical antipsychotics	All trimesters: Preterm birth, Low birth weight infants, post nasal disorders
	561	Atypical antipsychotics	All trimesters: More risk for congenital malformations, post nasal disorders
Peng et al. [56]	152	Atypical antipsychotic medications	From birth of infant till 12 months: At 2 months of age, short term developmental delays in cognition, motor, social, emotional, and adaptive behavior. However, at 12 months no significant difference compared to other infants
Kulkarni et al. [24]	11	Clozapine	All trimesters: 2 babies had malformations like craniosynostosis, horse shoe shaped kidney, gastroschisis, hypospadiasis, and hypertelorism
Huybrechts et al. [57]	1,341 ,715	Typical and atypical antipsychotic medications	All trimesters: More congenital malformations including cardiac malformations were noted with atypical antipsychotic medications

Table 1: Antipsychotic medications and their potential side effects during pregnancy.

Discussion

Psychiatric illnesses during pregnancy and puerperium are not uncommon. The affected women deserve optimum management whether they are planning the pregnancy, are currently pregnant or nursing a new-born, to avoid adverse obstetric and neonatal outcomes. A common concern for healthcare providers and pregnant women with mental disorders is the relapse of psychotic symptoms, following discontinuation of antipsychotic medications. This mandates the continual use of antipsychotic medications during this phase. Although, the general paucity of studies examining the safety of antipsychotic medications during pregnancy and breast feeding makes the decision to continue antipsychotic use a risk; health care providers should educate mothers about the advantage of accepting a possible, modest increase in teratogenic risk rather than a relapse, which in itself can distort normal growth and development of their offspring. For the clinicians, certain patient factors are to be considered before prescribing the most appropriate antipsychotic medication to pregnant women, and this indirectly translates to individualization of treatment. Cases become difficult when there are other associated medical conditions that must be attended to, but in the absence of that, monotherapy is best employed.

Given that randomized placebo-controlled designs are the gold standard and a preferred approach in making certain conclusions about safety of drugs, they can also be ethically challenging. So, the current available data from case reports and studies, including prospective and retrospective data, suggest that most antipsychotic medications are safe for use during pregnancy, with no definite pattern of malformations reported. But whenever possible, non-pharmacological approaches should be exercised. The antipsychotic drugs have also been reported safe for use during breast feeding, except clozapine, which is assumed to be unsafe due to its ability to reach significant concentrations in breast milk.

Vital issues to be bear in mind during management of patients include advice on the planning of pregnancies, folate supplementation in women of reproductive age. Other issues include documentation, discussion with patients and relatives about the available options of management and the limitation of research and current evidence regarding the safety of antipsychotic drugs in pregnancy. A functional liaison between all disciplines involved in perinatal care including the obstetrician, psychiatrist, ultra-sonographers, neonatologist, midwives and social workers, should be created. More studies are needed for clinicians to balance better maternal mental health, healthy pregnancies, and good infant health results.

Conclusion

Women with psychiatric illnesses, who are either planning a pregnancy, are pregnant, or breastfeeding require appropriate discussions with their health care providers in regards to whether to continue or discontinue antipsychotic medications. These decisions can go as far as defining the rest of the course of the life of the infant or even the mother. This paper has reviewed studies on the use of common antipsychotics in pregnancy and during lactation, in a bid to assist in quality decision making by clinicians and other health care workers. Although studies on some newer generation antipsychotics like aripiprazole, amisulpiride, ziprasidone are still sparse, both the most commonly used typical (chlorpromazine, haloperidol) and atypical groups (olanzapine, clozapine, quetiapine, risperidone) of antipsychotics have been studied, and the risks associated with their use in pregnancy and lactation have been identified.

The currently available data is not enough to conclude that any antipsychotic is entirely safe for use in pregnancy and lactation because the studies have not fulfilled the ethically challenging gold-standard which involves the use of randomized placebo-controlled trials. The concerns regarding the potential effects of the antipsychotic medications on the developing baby have been braced by the reports from studies that have associated varying congenital anomalies with the use of antipsychotic medications either in pregnancy or during lactation. However, the broad review of congenital malformations in the infants of women who received antipsychotics during pregnancy and lactation reveal the occurrence of only few cases of congenital defects, most of which are not higher than in the general population.

In the meantime, the benefits of the continued use of antipsychotic medications in pregnant and breastfeeding women with psychiatric illnesses and during breastfeeding must be weighed against the risks of antipsychotic exposure to the infant, untreated maternal illness, and potential for a relapse to reach a quality decision. On this basis, the use of antipsychotic drugs during pregnancy and lactation can be justified only if its benefit outweighs such potential risks, while conclusive elucidation still awaits well-controlled studies.

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