

# BREASTFEEDING AND THE USE OF ANTIDEPRESSANTS

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## ABSTRACT

The use of medications in lactating women presents a challenging clinical dilemma to clinicians who are faced with trying to effectively maintain maternal well-being while promoting breastfeeding. The maternal and infant health benefits of breastfeeding are well established although the presence of medication in mother's milk raises questions about safety for the child. In many cases, mothers may be able to continue breastfeeding while taking antidepressant and a summary of the information is presented here.

**Key Words:** *Breastfeeding, depression, antidepressants*

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While existing evidence suggests that most SSRIs and SNRIs are compatible with breastfeeding, we do not have any strong evidence to recommend one antidepressant over another and there is no particular rationale to switch from one SSRI to another to increase infant safety. One has to evaluate each mother infant pair individually, recognizing that the mother needs to be clinically well if she is going to be able to care for her child effectively.

This talk addresses an important issue when caring for a breastfeeding mother, namely how to appropriately treat a depressed mother who wishes to breastfeed her child. Our patients ask, will their medication make their babies sick? Will we be doing more harm by exposing the child not only *in utero*, but in the postnatal period? Breastfeeding is the biological feeding norm for mammals and it is the ideal feeding method under most circumstances, although it does require constant support and encouragement. It has significant maternal, child and societal benefits.<sup>1</sup> By and large, most women can successfully breast feed.

### Depression in Postpartum Women

Major depression can occur in both the prenatal and postnatal period. It is a psychiatric condition

defined by DSM-IV criteria. What is important to acknowledge is that depression is a serious illness that can have significant impacts on mother, child and the entire family. While the period after childbirth can be challenging and overwhelming for a new mother, it is critical that maternal symptoms are not simply dismissed. Clinical monitoring and investigation is warranted if a patient is having difficulty coping. Post-partum depression can affect up to 20% of women and it is distinct from 'baby blues', which can affect a higher proportion of new mothers. Depression symptoms may also overlap with anxiety and it is not uncommon to find both conditions in these patients. Moreover, stressful life events can be a trigger, just having had a baby, not having had adequate sleep for days will certainly be a trigger for a relapse or a new occurrence of major depression. Treatment for post partum depression can include psychotherapy, sleep hygiene therapy and pharmacotherapy with antidepressants.<sup>2</sup> Currently the SSRI's are the agents we are most commonly seeing used in this population. If a patient has chosen to breastfeed, knowing that we need to support her, what are the options?

This situation is complicated by the fact that there are now two patients to consider. You have the mother who needs treatment and you have a

baby who doesn't need drug treatment but needs a healthy mother. We must always consider inherent toxicities of the drug, we need to consider how much of a particular drug gets into the milk, the risks of untreated maternal illness, and the benefits of treatment for both mother and baby. We have heard already that there are significant risks of relapse after delivery if the mother discontinues treatment. The goal is to adequately treat maternal depression while still maintaining breastfeeding; keeping the patient euthymic, relieving her symptoms, restoring her function, and preventing recurrence.

### **Drug Excretion into Human Milk**

Essentially all drugs can be excreted into human milk. For the most part, excretion occurs by passive diffusion, though there is likely some active transport occurring. It is often cited that infant exposures of less than 10% of a weight adjusted dose is considered safe for a breast fed infant.<sup>3</sup> While this is somewhat of an arbitrary guideline, it is reasonable to believe that such small exposures would not likely cause significant adverse events in most infants. The possibility of idiosyncratic reactions, which not dose related, can never be ruled out however and should always be considered. The difficulty is that the literature on the effects of drugs in breastfeeding is sparse and is largely confined to case reports and small case series. This complicates the risk assessment for any particular mother-infant pair. It is also important to note that even though drug can get into milk it does not remain trapped there indefinitely. This is a dynamic process governed by both the physicochemical characteristics of the drug but also they maternal physiology and feeding pattern. Practically, it is not feasible to try to time an infant's feeding schedule around a dosing schedule and therefore its best to be informed about what literature exists on mother's who continued to breastfeed while receiving treatment.

To follow is a brief summary of the literature which discusses the use of the most commonly used antidepressants during lactation. As mentioned, the literature is limited to case reports and even a few small cohort studies that have followed mothers and infants after exposure.

### **Antidepressants in the Lactating Patient**

In general the evidence suggests that less than 10% of the maternal weight adjusted dose is excreted into human milk for most SSRI's and SNRI's.<sup>4</sup> For a patient who has previously responded to a particular agent there is no particular preference or priority for one agent over another. Because of its time on the market the largest number of cases exist in the literature for fluoxetine.<sup>4</sup> In cases where the infant's blood was measured for drug, it was largely undetectable, with few exceptions. This alone can be very reassuring to both the clinician and patient. However, there were sporadic adverse events reported in some infants. Adverse events such as uneasy sleep, colic, irritability, poor feeding and drowsiness have all been reported. Most of these were associated with fluoxetine, though this may be attributed, in part, to the fact that it was the first agent of its class on the market. Despite these adverse events, there has not been any clear or consistent pattern of adverse events across all the agents. The adverse events are generally transient and rarely verified by a clinician. Nevertheless, it is important that mothers be aware of the potential for infant exposure and both mother and her clinician should be observant for any changes in the child that are of concern.

The heterocyclic antidepressants are not a class that we see as commonly anymore, but all of them are well below the 10% infant exposure threshold. In some cases, authors have reported infant outcomes, which are generally normal. Again, in most cases the infant drug levels were undetectable or extremely low. Most of the data available is for the tricyclic antidepressants, mostly nortriptyline, amitriptyline. The amount that was found in milk appears to be low.

In contrast, doxepine, is one drug that we have often advised to avoid if possible.<sup>5</sup> There are two relatively significant infant adverse events reported, one with a child admitted to hospital with poor suck and swallow and shallow breathing. The amounts of drug measured in milk were not high, only 2.5%, the infant did not have detectable levels, yet this baby clearly had symptoms which were serious and which resolved when the drug was removed. A second case in the literature was similar. It is difficult to know what this means or what the incidence of such adverse events are without knowing the prevalence of use

of doxepin. However, because there are so many other medications with a preferable side effect profile it would be prudent to consider alternate agents in a breastfeeding mother who requires pharmacotherapy for depression.

Monoamine Oxidase Inhibitors (MAOIs) are a class we see very rarely today in this population. This is largely because MAOIs have an unfavorable side effect profile, even in non-pregnant or non-lactating adults. However, in the few published cases we have, the amounts in milk again were low.

Some of the other medications that are used in this population, bupropion, nefazodone and trazodone are all sporadically reported in the literature, with small amounts of the drug found in milk. There are cases of drowsiness or lethargy reported and in particular, premature infants may be more prone to such side effects. This may relate to their immature drug elimination pathways and hence they may be more sensitive to small amounts of drug.<sup>5</sup>

### **Other Medications Commonly Used in this Population**

The benzodiazepines are important to mention, not because they are used to treat depression, but because anxiety is so frequently found in these patients. We often see mothers on polypharmacy with both an antidepressant and an anxiolytic. They may also be taking these agents due to difficulty sleeping. This is an even more challenging situation because for a patient who is trying to nurse, her sleep will certainly be interrupted regardless. It is a difficult balance between keeping the patient clinically well, allowing them to sleep, while still promoting and encouraging breastfeeding. In fact, these may be counterproductive and this can be problematic. However, these patients with risks of relapse of serious maternal disease truly can benefit from sleep and that may be assisted with the use of benzodiazepines. The literature on the excretion of these drugs is reassuring again, with approximately 1% of oxazepam and up to 8% of alprazolam found in milk. A recent prospective control study failed to show CNS depression with benzodiazepines.<sup>6</sup> Newborns have diminished capacity to eliminate drugs and drug can accumulate in their systemic circulation over time.

Using an agent with a shorter half-life may mitigate the concerns around accumulation.

### **Concluding Remarks**

Finally, I wish to take a moment to summarize and present a few 'take home' messages. We often need to reassure mothers and remind them that, when they have been taking a medication for the previous nine months of pregnancy their infant has already been exposed for some time. They can be comforted by the fact that the absolute infant exposure was greater in pregnancy than it is during lactation. Moreover, the exposure through breastmilk is much lower than a therapeutic exposure. At the same time it is important to reinforce the importance of breastfeeding and its benefits but not at all costs, we need to present a balanced view. This includes also stressing the importance of optimal treatment of her condition and this may mean treatment with medications.

We are often asked by both patients and clinicians, which antidepressant is best? The answer is not a single agent, the best medication is the one that's most likely to be effective. In general, this would mean to continue using what was used in pregnancy or resume with an agent that the patient has used and responded to in the past. All of these agents are likely going to be excreted into breast milk but we can manage this, and generally the literature does not suggest that serious adverse events are frequent. In the case of the premature infant, because of their ability to clear drugs is diminished compared to when they reach full term, some caution is warranted.

To reiterate, we do not have any strong evidence to recommend one antidepressant over another and there is no particular rationale to switch from one SSRI to another to increase infant safety. We have to evaluate each mother infant pair individually, recognizing that the mother needs to be clinically well if she's going to be able to care for her child effectively. In all cases, infants can and should be monitored by both the mother and by the child's healthcare provider. We do not have all the answers and can never rule out the possibility of a rare or even serious adverse event in the infant. However, with appropriate monitoring and management, a patient on antidepressants can successfully breastfeed.

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