Abstract

**Question** My patient has a urinary tract infection and is currently breastfeeding. Her son is only 3 weeks old. Is nitrofurantoin a safe antibiotic for treatment?

**Answer** The use of nitrofurantoin in breastfeeding mothers is generally safe, as only small amounts transfer into the breast milk. Despite the lack of documented reports, there is a risk of hemolytic anemia in all newborns exposed to nitrofurantoin owing to their glutathione instability, especially in infants with glucose-6-phosphate dehydrogenase deficiency. Although some suggest that nitrofurantoin be avoided in infants younger than 1 month, studies have noted that glutathione stability might be established by the eighth day of life. In infants younger than 1 month, an alternative antibiotic might be preferred; however, if an alternative were not available, the use of nitrofurantoin would not be a reason to avoid breastfeeding. In any such case the suckling infant should be monitored by his or her physician.

Human studies in breast milk

Nitrofurantoin is actively transported into breast milk, likely through the BCRP (breast cancer resistance protein) transporter. Older studies suggest that nitrofurantoin concentrations in breast milk are low, although the reported values are inconsistent. Two studies reported undetectable levels in breast milk—one in which 20 women took 100-mg doses 4 times a day, another in which 5 women each took a single 100-mg dose. In the latter study, an additional 2 of 4 women also had undetectable levels in breast milk following a 200-mg dose. In a more recent prospective single-dose pharmacokinetic human study, 4 healthy lactating women 8 to 26 weeks postpartum were each...
administered a single 100-mg dose of nitrofurantoin. A mean milk concentration of 1.3 mg/L was reported. The authors suggest that the relative infant dose would be about 0.2 mg/kg, or 6% of the maternal dose per day. Hence, these studies all indicate that nitrofurantoin’s relative infant dose is less than 10% of the maternal dose and is therefore compatible with breastfeeding.

The only potential concern in the infant is diarrhea, which was reported by 2 of 6 nursing mothers following nitrofurantoin use in a prospective follow-up study conducted by Motherisk.9

### Hemolytic anemia

There is a theoretical risk of hemolytic anemia in all newborns with exposure to nitrofurantoin owing to glutathione instability as a result of their immature erythrocyte enzyme systems.2 Therefore, some have suggested that mothers exposed to nitrofurantoin should avoid breastfeeding infants younger than 1 month,10,11 especially those infants with hyperbilirubinemia.11 This might be a conservative recommendation, as studies have shown that this phenomenon might be transient.12-14 In a follow-up study of term infants, the glutathione instability had normalized by the eighth day of life.15 In a serial estimation of glutathione stability in preterm infants, such a finding was also observed.16 Nevertheless, a similar concern might also be valid among infants, regardless of age, with an absolute or relative glucose-6-phosphate dehydrogenase (G6PD) deficiency.17 Such deficiencies are commonly observed in eastern Mediterranean (eg, in those of Sardinian, Italian, Greek, or Jewish ethnicity), African, and Southeast Asian populations.18 However, there are no published case reports of hemolytic anemia in infants caused by exposure to nitrofurantoin in breast milk.

### Conclusion

Although nitrofurantoin might be actively excreted into breast milk, it is present in low amounts, with a maximum relative infant dose documented in the literature of 6%.9 Some have suggested a theoretical risk of hemolytic anemia in infants younger than 1 month owing to glutathione instability. However, this appears to be a conservative view, as studies have reported normalization of this phenomenon by the eighth day of life in both term and preterm infants. Those with G6PD deficiencies, on the other hand, might be at risk regardless of age. Nevertheless, there have been no reported cases of complications in either at-risk group. If this is a concern for the patient or clinician, an alternative antibiotic might be prescribed. However, if the infant is older than 8 days and is unlikely to have a G6PD deficiency, then the use of nitrofurantoin might not be a reason to avoid breastfeeding.

### Competing interests

None declared

### References