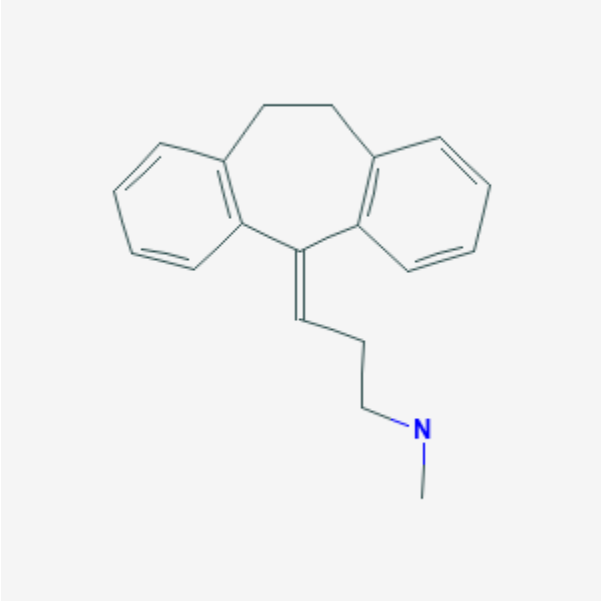
U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006-. Nortriptyline. [Updated 2018 Oct 31].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Nortriptyline

Revised: October 31, 2018.

CASRN: 72-69-5



Drug Levels and Effects

Summary of Use during Lactation

Because of the low levels of nortriptyline in breastmilk, amounts ingested by the infant are small and usually not been detected in the serum of the infant, although the less active metabolites are often detectable in low levels in infant serum. Immediate side effects have not been reported and a limited amount of follow-up has found no adverse effects on infant growth and development. Most authoritative reviewers consider nortriptyline one of the preferred antidepressants during breastfeeding.[1][2][3]

Drug Levels

Nortriptyline is metabolized to E-10-hydroxynortriptyline and Z-10-hydroxynortriptyline, the antidepressant activity of each considered to be 50% of nortriptyline's.[2]

Maternal Levels. Nortriptyline, a metabolite of amitriptyline, was measured in breastmilk in a mother who was taking amitriptyline 75 mg daily. Her milk levels were 75 and 63 mcg/L at 2 and 10 weeks, respectively, after starting treatment (time after dose not specified). After 19 weeks of therapy, an amitriptyline dose of 25 mg daily produced milk nortriptyline levels that were not detectable (<30 mcg/L).[4]

A mother began taking nortriptyline 125 mg daily immediately postpartum and exclusively breastfed her infant. Milk samples were taken 9 times over 36 hours on days 6 and 7 postpartum. Peak milk nortriptyline levels of about 220 mcg/L occurred 8 hours after the dose, and the average of the 9 milk levels was 180 mcg/L. Milk levels measured on days 20 and 48 postpartum while the mother was taking 125 mg and 75 mg daily, respectively, were similar to the levels on days 6 and 7. Milk levels taken after feeding were much higher than those taken before feeding, probably because of higher concentrations in the more fat-rich hindmilk. The authors estimated that an exclusively breastfed infant would receive 27 mcg/kg daily or 1.3% of the maternal weight-adjusted dosage.[5]

Another mother who was taking amitriptyline 175 mg daily had nortriptyline milk levels of 17 and 20 mcg/L on the morning and evening of the fist day of therapy and 87 mcg/L on day 26 of therapy. E-10-hydroxynortriptyline was found in milk in levels averaging 89 mcg/L over this time period.[6]

Infant Levels. In a pooled analysis of 32 mother-infant pairs from published and unpublished cases, the authors found that infants had an average of 10% (range 0 to 24%) of the nortriptyline plasma levels of the mothers'; 1 of the 32 infants had a plasma level greater than 10% of the mothers', which was defined by the authors as being elevated.[2] In mothers taking 75 to 150 mg/day of nortriptyline, E-10-hydroxynortriptyline was found in levels ranging from barely detectable (<4 mcg/L) to 16 mcg/L in the serum of 5 of 9 breastfed infants and Z-10-hydroxynortriptyline has been detected in levels ranging from barely detectable (<4 mcg/L) to 17 mcg/L in the serum of 5 of 9 breastfed infants.[7][8]

Effects in Breastfed Infants

At least 44 infants have been reported to have been exposed to nortriptyline in breastmilk with no reports of adverse reactions with maternal dosages from 25 to 175 mg daily.[4][5][7][9][10][11][12] The time of initial exposure ranged from the immediate newborn period to 3.5 months. The follow-up ranged from observation of the infants to full developmental testing.

Twenty-seven of the above infants were tested formally between 15 to 71 months and found to have normal growth and development.[10][12] Two small controlled studies found that other tricyclic antidepressants in breastmilk also had no adverse effect on infant development.[13][14]

Effects on Lactation and Breastmilk

Nortriptlyine usually increases serum prolactin only slightly, but has caused galactorrhea in nonpregnant, nonnursing patients rarely.[15][16]

An observational study looked at outcomes of 2859 women who took an antidepressant during the 2 years prior to pregnancy. Compared to women who did not take an antidepressant during pregnancy, mothers who took an antidepressant during all 3 trimesters of pregnancy were 37% less likely to be breastfeeding upon hospital discharge. Mothers who took an antidepressant only during the third trimester were 75% less likely to be breastfeeding at discharge. Those who took an antidepressant only during the first and second trimesters did not have a reduced likelihood of breastfeeding at discharge.[17] The antidepressants used by the mothers were not specified.

A retrospective cohort study of hospital electronic medical records from 2001 to 2008 compared women who had been dispensed an antidepressant during late gestation (n = 575) to those who had a psychiatric illness but did not receive an antidepressant (n = 1552) and mothers who did not have a psychiatric diagnosis (n = 30,535). Women who received an antidepressant were 37% less likely to be breastfeeding at discharge than women

without a psychiatric diagnosis, but no less likely to be breastfeeding than untreated mothers with a psychiatric diagnosis.[18] None of the mothers were taking nortriptyline.

Alternate Drugs to Consider

Paroxetine, Sertraline

References

1. Berle JO, Steen VM, Aamo TO et al. Breastfeeding during maternal antidepressant treatment with serotonin reuptake inhibitors: infant exposure, clinical symptoms, and cytochrome P450 genotypes. J Clin Psychiatry. 2004;65:1228-34. PubMed PMID: 15367050.
2. Weissman AM, Levy BT, Hartz AJ et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. Am J Psychiatry. 2004;161:1066-78. PubMed PMID: 15169695.
3. Wisner KL, Parry BL, Piontek CM. Postpartum depression. N Engl J Med. 2002;347:194-9. PubMed PMID: 12124409.
4. Brixen-Rasmussen L, Halgrener J, Jorgensen A. Amitriptyline and nortriptyline excretion in human breast milk. Psychopharmacology. 1982;76:94-5. PubMed PMID: 6805016.
5. Matheson I, Skjaeraasen J. Milk concentrations of flupenthixol, nortriptyline and zuclopenthixol and between-breast differences in two patients. Eur J Clin Pharmacol. 1988;35:217-20. PubMed PMID: 3191943.
6. Breyer-Pfaff U, Nill K, Entenmann A et al. Secretion of amitriptyline and metabolites into breast milk. Am J Psychiatry. 1995;152:812-3. Letter. PubMed PMID: 7726331.
7. Wisner KL, Perel JM, Findling RL et al. Nortriptyline and its hydroxymetabolites in breastfeeding mothers and newborns. Psychopharmacol Bull. 1997;33:249-51. PubMed PMID: 9230638.
8. Mammen O, Perel JM, Wheeler S. Antidepressants and breast-feeding. Am J Psychiatry. 1997;154:1174-5. Letter. PubMed PMID: 9247422.
9. Wisner KL, Perel JM. Serum nortriptyline levels in nursing mothers and their infants. Am J Psychiatry. 1991;148:1234-6. PubMed PMID: 1883004.
10. Misri S, Sivertz K. Tricyclic drugs in pregnancy and lactation: a preliminary report. Int J Psychiatry Med. 1991;21:157-71. PubMed PMID: 1894455.
11. Altshuler LL, Burt VK, McMullen M et al. Breastfeeding and sertraline: a 24-hour analysis. J Clin Psychiatry. 1995;56:243-5. PubMed PMID: 7775366.
12. Nulman I, Rovet J, Stewart DE et al. Child development following exposure to tricyclic antidepressants or fluoxetine throughout fetal life: a prospective, controlled study. Am J Psychiatry. 2002;159:1889-95. PubMed PMID: 12411224.
13. Buist A, Janson H. Effect of exposure to dothiepin and northiaden in breast milk on child development. Br J Psychiatry. 1995;167:370-3. PubMed PMID: 7496646.
14. Yoshida K, Smith B, Kumar R. Psychotropic drugs in mothers' milk: a comprehensive review of assay methods, pharmacokinetics and safety of breast-feeding. J Psychopharmacol. 1999;13:64-80. PubMed PMID: 10221361.
15. Nielsen JL. Plasma prolactin during treatment with nortriptyline. Neuropsychobiology. 1980;6:52-5. PubMed PMID: 7366815.
16. Kukreti P, Ali W, Jiloha RC. Rising trend of use of antidepressants induced non-puerperal lactation: A case report. J Clin Diagn Res. 2016;10:VD01-VD02. PubMed PMID: 27504388.
17. Venkatesh KK, Castro VM, Perlis RH et al. Impact of antidepressant treatment during pregnancy on obstetric outcomes among women previously treated for depression: An observational cohort study. J Perinatol. 2017;37:1003-9. PubMed PMID: 28682318.
18. Leggett C, Costi L, Morrison JL et al. Antidepressant use in late gestation and breastfeeding rates at discharge from hospital. J Hum Lact. 2017;33:701-9. PubMed PMID: 28984528.

Substance Identification

Substance Name

Nortriptyline

CAS Registry Number

72-69-5

Drug Class

Breast Feeding

Lactation

Antidepressive Agents

Antidepressive Agents, Tricyclic