

Q&amp;A 263.4

## Chloramphenicol: is it safe in breastfeeding?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals  
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### Background

Chloramphenicol is a broad spectrum antibiotic, which also possesses activity against rickettsia, chlamydia, mycoplasma and spirochetes. It is available in the UK in several formulations—oral capsules, IV injection/infusion, ear drops, and eye drops and ointment [1]. However, as it is associated with serious haematological side-effects when administered systemically it is now recommended that systemic use should be reserved for the treatment of life-threatening infections, particularly those caused by *Haemophilus influenzae*, and also for typhoid fever [1].

The most common use of chloramphenicol is for superficial eye infections, for which it is considered to be the drug of choice [1]. Chloramphenicol ophthalmic products are frequently prescribed for eye infections, and are also available as over-the-counter medicines for the treatment of acute bacterial conjunctivitis in adults and children aged 2 years and over for a maximum of 5 days treatment [1].

Oral or parenteral chloramphenicol is normally considered to be incompatible with breastfeeding [2, 3] due to its potential toxicity, especially aplastic anaemia. However, the low systemic absorption of chloramphenicol from ophthalmic formulations frequently raises questions on the safety of using ophthalmic chloramphenicol in mothers who are breastfeeding their infants.

### Answer

#### Systemic chloramphenicol and breastfeeding

Variable but relatively high milk levels have been found in breast milk of mothers taking oral chloramphenicol after single doses or multiple doses [4–7]. In a study of 50 breastfed infants whose mothers were given oral chloramphenicol 1 g (n=20), 2 g (n=20), or 3 g (n=10) daily, several side effects were noted in the infants—poor sucking (100%), somnolence (50-60%), vomiting (10–90% depending on dose), and excessive abdominal gas and abdominal distension (100%) [8]. No other studies have reported infant side effects after ingesting chloramphenicol through breast milk. In the light of this evidence systemic (oral or intravenous) chloramphenicol is normally contra-indicated in lactating mothers due to reported side effects in their infants [8] and due to the risk, albeit theoretical, of small amounts of chloramphenicol in breast milk precipitating aplastic anaemia in the infant.

#### Toxicity of ophthalmic chloramphenicol

Systemic use of chloramphenicol has been associated with a 13-fold increase in the risk of aplastic anaemia (compared to idiopathic aplastic anaemia) and this effect is considered not to be dose-related [9]. There is, therefore, a theoretical risk that low amounts of chloramphenicol absorbed from ophthalmic formulations could precipitate aplastic anaemia. The evidence to support this is conflicting.

Chloramphenicol eye drops administered to children produced no detectable urine levels [10]. A review has identified 23 anecdotal case reports, including 10 deaths, which suggest a possible association between ophthalmic use of chloramphenicol and blood dyscrasias [11]. Analysis of these reports, supported by another analytical review [12], concludes that there is, however, only a theoretical risk of ophthalmic chloramphenicol-induced idiosyncratic aplastic anaemia. Retrospective studies have supported this conclusion.

In a 4-year retrospective study in the Netherlands, it was found that there was no excess risk of developing aplastic anaemia after use of ophthalmic chloramphenicol [13]. Another study in Scotland concluded that the epidemiology of acquired aplastic anaemia failed to make an association with topical chloramphenicol use [14].

A further analysis of the expected incidence of chloramphenicol-induced aplastic anaemia in the UK, based on the volume of prescribing relative to that in the USA, concludes that there is no increase in the incidence of aplastic anaemia when ophthalmic chloramphenicol is prescribed [15].

Overall, the balance of evidence suggests that the risk of blood dyscrasias with ophthalmic chloramphenicol has not been established. UK guidance also states that chloramphenicol eye drops are well tolerated and the recommendation that chloramphenicol eye drops should be avoided because of an increased risk of aplastic anaemia is not well founded [1].

### **Ophthalmic chloramphenicol and breastfeeding**

No evidence has been published relating to the levels of chloramphenicol in breast milk after administration of chloramphenicol eye drops or eye ointment to a lactating mother. Also, there have been no reported side effects in breastfed infants whose mothers have been treated with ophthalmic chloramphenicol.

Despite the negligible serum levels that may be expected in a breastfed infant after maternal use of ophthalmic chloramphenicol, there is still a theoretical risk, not supported by clinical evidence, of dose-unrelated aplastic anaemia [6, 14].

The manufacturers of ophthalmic preparations of chloramphenicol marketed in the UK advise against or caution their use in lactation as safety has not been specifically established [16–19].

Because evidence of the safety of ophthalmic use of chloramphenicol in mothers breastfeeding their infants is lacking, expert opinion advises that the use of ophthalmic chloramphenicol should be avoided unless the clinical condition of the mother justifies the theoretical risk. It should not be used in mothers whose infants are premature or where there is a past or family history of blood dyscrasias [2, 14, 20]. Fusidic acid eye drops are preferred during breastfeeding if the organism is sensitive, to eliminate the theoretical concerns about topical chloramphenicol-induced blood dyscrasias [2].

If it is clinically essential to use chloramphenicol eye drops in lactation the mother can reduce potential systemic absorption further by naso-lachrymal occlusion (squeezing tear ducts in the corner of the eye for a few minutes after application) [21].

## **Summary**

- ◆ Systemic chloramphenicol is normally contra-indicated in breastfeeding mothers due to relatively high milk levels and reported adverse effects in breastfeeding infants, although the quality of this evidence is poor.
- ◆ Ophthalmic chloramphenicol products, eye drops and eye ointment, are routinely used, and considered to be the treatment of choice for superficial eye infections.
- ◆ There is conflicting evidence that ophthalmic chloramphenicol can precipitate blood dyscrasias, especially aplastic anaemia, due to systemic absorption, as this reaction is not dose-related. However, the balance of evidence suggests that the association of ophthalmic chloramphenicol and aplastic anaemia has not been established. This conclusion, therefore, also applies to the use of ophthalmic chloramphenicol in mothers who are breastfeeding their infants. It does, however, remain a theoretical risk.
- ◆ There is no direct evidence on the safety of ophthalmic chloramphenicol in breastfeeding infants after maternal use. Although risks of toxicity in the infant are theoretical, and not supported by direct clinical evidence, it is advised that mothers should avoid ophthalmic chloramphenicol if clinically justifiable, using an alternative preparation containing fusidic acid if microbiologically appropriate. Ophthalmic chloramphenicol should be avoided if the infant is premature or if there is a family history of blood dyscrasias.
- ◆ If chloramphenicol eye drops are considered appropriate during breastfeeding, systemic absorption can be minimised by naso-lachrymal occlusion immediately after administration.

### Limitations

- Evidence relating to excretion of chloramphenicol in breast milk is relatively poor and old, although it is not a drug in enough current common use to expect new evidence.
- The only evidence relating to chloramphenicol side effects in breastfeeding infants is old (1972) and from a foreign language source.
- There is no evidence relating to excretion of chloramphenicol into breast milk after ophthalmic administration.
- There is inconclusive evidence relating to the risks of non-dose related haematological toxicity of chloramphenicol, which may be relevant to levels that may be expected to be found in breast milk after ophthalmic administration to the mother.

The information above applies to an infant born at term and who is healthy. In more complex cases, such as infant prematurity or morbidity, or concurrent medication taken by the mother, further advice can be sought from the UK Drugs in Lactation Advisory Service provided jointly by the Trent Medicines Information Service and the West Midlands Medicines Information Service (Telephone: 0116 258 6491 or 0121 311 1974).

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### Search strategy

For chloramphenicol in breast milk:

- Embase and Medline (Standard Search Pattern)
- UKDILAS resources: [www.ukmi.nhs.uk/activities/specialistServices/default.asp?pageRef=2](http://www.ukmi.nhs.uk/activities/specialistServices/default.asp?pageRef=2)
- UKDILAS database: [www.ukmi.nhs.uk/ukdilas](http://www.ukmi.nhs.uk/ukdilas)
- Manufacturers (eMC)

For ophthalmic toxicity of chloramphenicol

- Embase
  1. Chloramphenicol /ae
  2. Chloramphenicol /io/tp
  3. 1 and 2