DRUG INFORMATION
Jonathan Banks
Bob Buckham
Sharon Gardiner

Canterbury DHB
District Health Board
Te Poari Hauora o Waitaha

CLINICAL PHARMACOLOGY
Murray Barclay
Evan Begg
Chris Hutchinson
Petra Lowe
Jane Vella-Brincat
Mei Zhang

SAFETY OF INTRA-ARTICULAR TRIAMCINOLONE IN BREASTFEEDING

Question:
A woman is being considered for a single intra-articular knee joint injection of triamcinolone acetonide (assumed to be 40mg). What is the safety of this when she is breastfeeding a 5 month old infant?

Answer:
Drug safety during breastfeeding can be assessed by determining the magnitude of infant exposure ie. the dose ingested via milk and infant pharmacokinetics, and the drug's inherent toxicity. The infant's dose (mg/kg) can be expressed as a percentage of the maternal dose (mg/kg). For drugs with relatively low toxicity, an infant dose that is less than 10% of the maternal dose (weight-adjusted) is probably compatible with breastfeeding. However, for drugs with greater inherent toxicity (e.g. immunosuppressives), this cut-off is too high and even low drug exposure may be contraindicated. Higher exposure for a given dose may occur in premature infants and those with impaired renal or hepatic function due to reduced ability to eliminate drugs[1,2].

Triamcinolone acetonide
We are not aware of any information describing the transfer of triamcinolone into human breast milk[1,3-6]. However, we can use the limited pharmacokinetic data that are available on intra-articular administration of triamcinolone acetonide to predict the dose that the baby will ingest via milk.

Derendorf *et al.,*[7] described triamcinolone acetonide plasma concentrations following administration of 10 (n=4), 20 (n=4) and 40mg (n=9) into the knee joint of men and women. Triamcinolone acetonide was detected in plasma for more than two weeks, with 58 to 67% of the drug being released from the joint within the first three days. Concentrations of triamcinolone acetonide in plasma after a 40mg intra-articular dose peaked at 10mcg/L within one day of administration then declined to below 1mcg/L by the end of the week.

The milk concentration is the product of the concentration of drug in plasma and the milk to plasma (M/P) concentration ratio. For a worst-case scenario, the peak plasma concentration (10mcg/L) and an M/P ratio of 5.0* can be used and result in a peak milk concentration of 50mcg/L.
Infants are assumed to ingest 0.15L/kg/day of milk which gives an infant daily dose of 0.0075mg/kg/day (ie. 50mcg/L x 0.15L/kg/day). If we assume that the maternal dose is 0.667mg/kg/day, the infant's dose represents around 1% of the maternal dose, weight-adjusted**

*Most drugs studied thus far have a M/P ratio of less than or equal to 1.0 while 25% have a ratio of >1.0 and 15% have a ratio >2.0[8]. Therefore, using an M/P ratio of 5.0 is likely to overestimate the milk concentration considerably.
**The infant dose and the maternal dose have been overestimated and have not taken into account that the mother only receives a single dose of intra-articular steroid.

Conclusions:
The calculated infant dose of 1% is likely to over-estimate the degree of infant exposure and is well below the arbitrary cut-off of 10% which guides drug safety. Based on this estimate of infant dose,

we believe that a single intra-articular injection of a standard dose of triamcinolone (eg. 40mg) is likely to be compatible with breastfeeding. However, as always it would be prudent to monitor the infant for any evidence of adverse effects such as poor suckling or altered sleeping pattern.

References:

1. Bennett PN. Drugs and Human Lactation (2nd ed), 1996
2. Gardiner SJ, Begg EJ. Prescriber Update: May 2001 (www.medsafe.govt.nz).
3. Drugdex, Micromedex database
4. Briggs GG *et al.* Drugs in Pregnancy and Lactation (5th ed), 1998
5. Medline database 1966-2001
6. Embase database 1988-2001
7. Derendorf H *et al.* Clin Pharmacol Ther 1986; 39: 313-7.
8. Ito S, Koren G. Br J Clin Pharmac 1994; 38: 99-102.

Date prepared:
January 2002