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Letter to the editor

Colchicine is excreted at high concentrations in human breast milk

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Colchicine is a well-known lipophilic drug acting on microtubule growth. It can be used to prevent attacks of fever, arthritis and peritonitis in patients with familial Mediterranean fever (FMF). No human cytogenetic or teratogenic effects have been attributed to colchicine; in particular, the increased incidence of Down's syndrome initially reported appears to be coincidental and it is now considered that long-term prevention should not be interrupted during pregnancy [1,2]. Breast-feeding is contra-indicated because of the possible side-effects for the baby, but very limited data are available on colchicine concentrations in breast-milk [3].

A 21-year-old patient (para 1, gesta 1), received colchicine throughout pregnancy for FMF and was delivered of a healthy girl weighing 3300 g, at 39 weeks of gestation. She remained on 1 mg of colchicine once a day and decided to breast-feed, against our advice. The baby gained weight and the neonatal period was uneventful. Maternal and neonatal urine samples and breast milk were collected 5 and 15 days after birth. As colchicine is sensitive to light and difficult to assay, the validity of measurements is highly dependent upon the conditions of sampling and the analytical method. We used a fluorimetric method, with a sensitivity of 5 ng/ml [4].

In humans, colchicine absorption appears to be variable but the peak plasma concentrations occur within 60 min of administration. The drug is 50% protein-bound, rapidly distributed, metabolised by the liver and eliminated primarily in the bile (60–80%) and urine (10–20%) [4,5]. The maternal urine concentrations were similar to previously reported values in adults on the same dosage schedule [4]. Colchicine concentrations were high in the milk in the hours following maternal consumption, demonstrating that colchicine is rapidly and strongly excreted in the human milk. Based on 150 ml/kg of milk ingested by the baby per day and a mean colchicine concentration of 30 ng/ml in the milk in the 8 h following maternal drug ingestion, we calculated that the dose per kg ingested by the infant during the 8 h following maternal dosing was 10% of the dose per kg taken by the mother, assuming a bioavailabiblity of colchicine of 100% in the baby [6].

Colchicine has a low therapeutic index in adults. In neonates, liver metabolism and renal elimination are immature and colchicine may accumulate, with the risk of hematological and digestive toxicity. Our results, in contrast with previous data, demonstrate that colchicine is

Table 1
Colchicine concentrations

	Day 5	Day 15
Maternal 24-h urine (ng/24 h)	276 000	123 000
Infant 12-h urine (ng/12 h)	nd	nd
Milk[a] (ng/ml)		
0 h		nd
2 h	31	
4 h	24	27
7 h		10
11 h		nd
15 h	nd	
21 h	nd	

nd, not detectable.
[a]Time after colchicine.

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highly excreted in the human milk [3] and should be confirmed by further studies. In the meantime, if breastfeeding is chosen, a nightime consumption and breastfeeding 8 h later would be an option to minimize infant exposure, but the measurement of colchicine concentration in the milk would be needed to confirm the low concentration 8 h after maternal consumption.

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