

Letters to the Editors

Z. ZELINKOVA*,
I. P. DE BOER†,
M. J. VAN DIJKE‡,
E. J. KUIPERS* &
C. J. VAN DER WOUDE*

*Department of Gastroenterology & Hepatology, Erasmus MC, Rotterdam, The Netherlands; †Department of Pediatrics, Diaconessenhuis, Utrecht, The Netherlands; ‡General Practitioner, Utrecht, The Netherlands.
E-mail: z.zelinkova@erasmusmc.nl

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Azathioprine treatment during lactation

SIRS, We read with interest the article by Christensen *et al.*¹ demonstrating a low penetration of mercaptopurine in maternal milk of eight inflammatory bowel disease (IBD) patients on azathioprine. On the basis of this reported low exposure of children to azathioprine (<1% of the maternal dose), breastfeeding during azathioprine therapy seems safe.

This study is of great importance as little is known about breastfeeding by IBD patients on azathioprine. However, considerable inter-individual variability in the absorption and metabolism of azathioprine^{2,3} makes it difficult to predict whether this very low dose in maternal milk would not eventually result in a clinically relevant cumulative dose in the individual child. Therefore, we proposed to monitor the azathioprine metabolites levels in the breastfed child as studied earlier.⁴ We wanted to demonstrate the feasibility of this approach in the case of a child born to a 31-year old mother with Crohn's disease. The child was fed maternal milk during the 3 months while the mother was treated with azathioprine, 100 mg a day (1.4 mg/kg). At day 8 of the breastfeeding, the peripheral blood levels of 6-methylmercaptopurine (6-MMP) and 6-thioguaninenucleotides (6-TGN) were assessed in the child; both appeared undetectable. At month 3, when the feeding with maternal milk was tapered to zero, the levels of 6-MMP and 6-TGN were again undetectable in the child, while the mother had therapeutic levels (6-MMP 410 pmol/10⁸ red blood cells, 6-TGN 470 pmol/10⁸ red blood cells). During the 6 months of the follow-up, the child thrived and did not suffer from any infections.

Thus, breastfeeding by IBD patients on azathioprine is probably safe. However, until more experience is gained, we advocate the monitoring of azathioprine metabolites as a method to safeguard the minimal exposure of a breastfed child.

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AP&T correspondence columns are restricted to letters discussing papers that have been published in the journal. A letter must have a maximum of 300 words, may contain one table or figure, and should have no more than 10 references. It should be submitted electronically to the Editors via <http://mc.manuscriptcentral.com/apt>.

REFERENCES

- 1 Christensen LA, Dahlerup JF, Nielsen MJ, Fallingborg JF, Schmiegelow K. Azathioprine treatment during lactation. *Aliment Pharmacol Ther* 2008; 28: 1209–13.
- 2 Schwab M, Klotz U. Pharmacokinetic considerations in the treatment of inflammatory bowel diseases. *Clin Pharmacokinetic* 2001; 40: 723–51.
- 3 Lennard L. TPMT in the treatment of Crohn's disease with azathioprine. *Gut* 2002; 51: 143–6.
- 4 Gardiner SJ, Gearry RB, Roberts RL, Zhang M, Barclay ML, Begg EJ. Exposure to thiopurine drugs through breast milk is low based on metabolite concentrations in mother-infant pairs. *Br J Clin Pharmacol* 2006; 62: 453–6.

L. A. CHRISTENSEN*,
J. F. DAHLERUP*,
M. J. NIELSEN*,
J. F. FALLINGBORG† &
K. SCHMIEGELOW‡

*Department of Medicine, Århus University Hospital, Århus, Denmark; †Department of Medicine, Aalborg University Hospital, Aalborg, Denmark; ‡Pediatric Clinic, Rigshospitalet, Copenhagen, Denmark.
E-mail: lisbchte@rm.dk

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Azathioprine treatment during lactation: authors' reply

SIRS, We thank Zelinkova *et al.* for the comments concerning our study of Lactating women on azathioprine.¹

We performed the study² because of the lack of knowledge about the exposition of azathioprine in maternal milk to the infant. The results of our study show a very low exposure, even if the highest measured concentration of the metabolite in the milk samples was used in the estimation.

As Zelinkova *et al.* correctly point out, no previous study has been able to demonstrate a detectable concentration of the azathioprine metabolites in infants of lactating mothers on azathioprine, even when very sensible methods have been used. Their findings in a single infant are in accordance with this. When we combine these findings, we cannot recommend blood tests of the child as general practice, as these will add no further information but will only be of discomfort to the infant.

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REFERENCES

- 1 Zelinkova Z, de Boer IP, van Dijke MJ, Kuipers EJ, van der Woude CJ. Monitoring Lactation Safety during Azathioprine Treatment. *Aliment Pharmacol Ther* 2009; 30: 90–1.
- 2 Christensen LA, Dahlerup JF, Nielsen MJ, Fallingborg JF, Schmiegelow K. Azathioprine treatment during lactation. *Aliment Pharmacol Ther* 2008; 28: 1209–13.

P. MATTHEWS

St Hugh's College, University of Oxford, Oxford, UK.

E-mail: paul.matthews@st-hughs.ox.ac.uk

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Glucocorticoids can help in acute severe alcoholic hepatitis

SIRS, Recently Rambaldi *et al.*¹ conducted a comprehensive meta-analysis on all trials of glucocorticoids in acute alcoholic hepatitis and found no overall effect on mortality or other complications and an increased rate of adverse events. However, they did find a beneficial effect on mortality (RR 0.37; 95% CI: 0.16–0.86) for objectively severe disease (Maddrey DF \geq 32 and/or encephalopathy) from a relatively small sample size of 249 patients.