



## Osteoporosis prophylaxis during corticosteroid treatment

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## LETTERS

### Osteoporosis prophylaxis during corticosteroid treatment

We congratulate Hart and Green for flagging up a worrying concern—failure to provide appropriate osteoporosis prophylaxis during planned long term corticosteroid treatment.<sup>1</sup> We would like to complement their views by sharing the results of a similar study undertaken in our district general hospital between May and July 2001.

On analysing case notes and prescription records of 308 consecutive medical inpatients, 60 patients (mean age 68.7 years, range 37–89 years; 62% females) on long term steroid treatment were identified who would have qualified for osteoporosis prophylaxis. Of these only 26 patients (43%) were on effective prophylactic treatment (24 on bisphosphonates, two on hormone replacement therapy). Structured interview of these 60 patients revealed that 73% were not advised on appropriate lifestyle changes (namely cessation of smoking, avoidance of alcohol consumption, weight bearing exercises if appropriate, adequate dietary calcium intake, and measures to avoid falls). Thirty five per cent of the patients were unaware of the side effects of long term steroid consumption, including the risk of osteoporosis.

Thus, apart from failing to appropriately screen and provide osteoporosis prophylaxis to patients on long term steroids, we are also inadequately educating patients on lifestyle measures and the risks associated with long term steroid usage as per guidelines.<sup>2</sup> Hospital physicians and general practitioners should make proactive attempts to improve this sub-standard practice. At least for hospital inpatients, we should not miss the opportunity to identify those on long term steroids and ensure that they are appropriately advised and commenced on osteoporosis prophylaxis.

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### 6-Mercaptopurine teratogenicity

We read with interest the review article on inflammatory bowel disease (IBD) in pregnancy.<sup>1</sup> The author mentions that there has never been any demonstration of teratogenicity of 6-mercaptopurine (or azathioprine) in humans. We would like to report a

case, which we encountered, of an infant with multiple congenital abnormalities whose mother received 6-mercaptopurine throughout her pregnancy, for whom no other explanation could be found.

A baby boy was born via induced vaginal delivery at 38 weeks' gestation to a 32 year old woman treated with 6-mercaptopurine (Purinethol, GlaxoSmithKline), 1 mg/kg/day, for Crohn's disease throughout, and for 10 years before, her pregnancy. Dental work was performed during the pregnancy, at weeks 8 and 12, requiring local lignocaine (lidocaine) injections. An amniocentesis was performed after increased nuchal translucency (7.4 mm) was seen on early first trimester ultrasound, revealing a normal male karyotype, 46,XY,inv(9)(p11q23), with no abnormalities on subsequent level 2 ultrasound at 20 weeks. Birth weight and head circumference were at the 25th percentile, and birth length was below the 5th percentile.

The baby had congenital hypotonia, a submucous cleft palate, a bifid uvula, dysmorphic facial features (hypertelorism, epicanthal folds, central hair whorl, and proximally placed third toes), and a meatal baffle (requiring surgical correction). Magnetic resonance imaging of the brain and electroencephalography were normal. FISH analysis for Wolf-Hirschhorn, Cri-du-chat, DiGeorge, and Prader-Willi syndromes revealed no deletions. Methylation analysis for Prader-Willi syndrome was normal. Parental karyotypes were normal (maternal karyotype with the same normal chromosome 9 variant inversion). Subtelomeric FISH was normal. Metabolic studies (lactate, ammonia, plasma amino acids, and urine organic acids) were unremarkable. Osseous survey revealed no evidence of axial skeletal abnormality and an echocardiogram was normal.

Family history showed the mother and maternal grandmother to have Crohn's disease. The father is in good health. They are both of Ashkenazi Jewish descent. There was no consanguinity. They have one other child, a 3 year old son, who has a notched uvula and auditory processing deficits, and was also exposed to 6-mercaptopurine throughout pregnancy. There are no other similarly affected family members.

6-Mercaptopurine is rated category D during pregnancy (Physicians' Desk Reference, 2002). Although studies have reported that this medication is relatively safe to take during pregnancy, well controlled data of adequate sample size have not been accumulated. The article cited, which directly explored the safety of 6-mercaptopurine in child bearing patients with IBD, followed up just eight patients treated with 6-mercaptopurine throughout pregnancy.<sup>2</sup> 6-Mercaptopurine has been associated with the production of a variety of embryonic malformations (cleft lip, jaw, and palate, limb reduction defects, syndactyly, and micrognathia) after single maternal exposure during embryogenesis in multiple species of experimental animals (chick, rat, mouse, hamster, and frog).<sup>3,4</sup> In

addition, reports have called into question the safety of 6-mercaptopurine treatment in males with IBD within three months of conception.<sup>5</sup>

Although we cannot state definitively that this association, between 6-mercaptopurine and our patient's constellation of congenital abnormalities, was causal or chance, its similarity to known teratogenic effects of 6-mercaptopurine in other animal species warrants careful consideration.

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#### Author's reply

I was interested to read the report from Tegay *et al* of an infant with multiple congenital abnormalities, born to a mother who took 6-mercaptopurine during her pregnancy. I agree with them that there are only a small number of reports of the outcome of pregnancy in women who have taken 6-mercaptopurine for IBD during pregnancy and it is very reasonable to suggest that further evidence is needed.

I would like to make two points. Thousands of women who have taken azathioprine in pregnancy after transplantation and for rheumatological disorders have, however, been followed up without evidence of significant occurrence of similar abnormalities. If the abnormalities reported in this child and his sibling are similar, surely it would have to suggest a genetic cause despite the exclusion of the known, common genetic abnormalities.

I think the author's conclusion that they cannot definitively state that these abnormalities are due to 6-mercaptopurine is correct. Further studies are certainly warranted in this area in which there are very little data.