Paediatric and Perinatal Drug Therapy **Volume 8, Issue 2, 2007**

Contents

Paediatric and Perinatal Drug Therapy, 2007; 8 (2)

Mesalazine induced drug toxicity may mimic symptoms in Crohn's disease

Richard Siviter, Jonathan Lancashire, Imti Choonara

Academic Division of Child Health, Derbyshire Children's Hospital, University of Nottingham, Derby, UK

Corresponding author

Professor Imti Choonara, Academic Division of Child Health, University of Nottingham, The Medical School, Derbyshire Children's Hospital, Uttoxeter Road, Derby, UK. Email: imti.choonara@nottingham.ac.uk

Mesalazine is an aminosalicylate and is used to maintain remission in Crohn's disease. Adverse drug reactions to mesalazine include arthralgia, abdominal pain, diarrhoea and lethargy. These symptoms may all also be associated with Crohn's disease. A case of mesalazine causing arthritis, diarrhoea and tiredness is described. Clinicians need to be aware that mesalazine toxicity can mimic the symptoms in Crohn's disease.

Paed Perinat Drug Ther 2007; 8: 48–50

Keywords: mesalazine – Crohn's disease – toxicity

Introduction

Crohn's disease is an inflammatory bowel disease of unknown aetiology. The clinical features of Crohn's disease include gastrointestinal symptoms such as abdominal pain, diarrhoea with or without blood and weight loss. Other symptoms include anaemia, pyrexia, arthralgia, arthritis, perianal disease as well as oral ulceration. The incidence of Crohn's disease in children is increasing in developed countries[1]. First line treatment to induce remission consists of either corticosteroids or an elemental diet[2].

Aminosalicylates are used to maintain remission, although their value has been questioned[3]. Sulfasalazine was the first aminosalicylate to be used. It does, however, have a relatively high incidence of side effects and several new aminosalicylates have been developed. The main side effects of aminosalicylates are diarrhoea, nausea, vomiting, abdominal pain, exacerbation of symptoms of inflammatory bowel disease, headache and hypersensitivity reactions[4]. Generic mesalazine is available in several different preparations which undergo release in different parts of the gastrointestinal tract. Mesalazine toxicity is thought to be less of a problem than that of sulfasalazine[5]. We describe a case where mesalazine toxicity resembled the symptoms of Crohn's disease.

Case report

A 13 year old boy presented with a six month history of diarrhoea, abdominal pain and weight loss. He had been opening his bowels 3–4 times each day and had dark red blood in his motions on at least three occasions. His past medical history included asthma for which he was receiving salbutamol 100–200 micrograms prn and beclomethasone 200 micrograms twice daily.

On examination he was pale and had mild finger clubbing. Blood tests revealed a raised ESR (48 mm/h), low Hb (11.9 g/dl) and a raised platelet count (620 x 10^9/l). Colonoscopy showed ulceration in the terminal ileum and the sigmoid colon. The child and the mother were reluctant to receive an elemental diet and he was therefore commenced on oral budesonide 9 mg daily and oral mesalazine (Pentasa) 1 g three times daily.

He initially responded to this and gained 1.1 kg over a period of four weeks. He was opening his bowels once a day and his stools were formed. His budesonide was therefore reduced to 6 mg daily but after two weeks his symptoms returned with abdominal pain, diarrhoea and blood in his motions. His dose of budesonide was therefore increased again to 9 mg. This time he did not show a dramatic response to the budesonide in that his weight remained static. He was tired and had diarrhoea (bowels opened 1–2 times daily). He was therefore commenced on an elemental diet and weaned off the budesonide over a period of four weeks. He responded initially to the elemental diet and was successfully weaned off the budesonide.

He unfortunately developed diarrhoea (bowels opened between 3 and 5 times daily), weight loss of 2.2 kg over a period of three weeks and lethargy. He was also complaining of bilateral joint pain and swelling in his middle three toes on both feet. The child also had a needle phobia and therefore further blood tests were not possible. A clinical decision was made that this was likely to be mesalazine toxicity and this was therefore discontinued. The possibility of his symptoms being secondary to Crohn's disease was also considered. If he had not responded to the withdrawal of mesalazine, this possibility would have been explored further. Within two weeks of stopping the mesalazine he had gained 0.7 kg and was only opening his bowels twice a day. He felt better in himself and had no further joint pains. It was decided not to re-challenge with mesalazine or another aminosalicylate.

He was successfully weaned off the elemental diet but unfortunately relapsed two months later with diarrhoea and weight loss. He did not want to receive an elemental diet again and was therefore treated with oral budesonide 9 mg daily to which he showed a good response. At this time he was also commenced on azathioprine 100 mg daily. He was successfully weaned off the budesonide and is currently well on oral azathoprine.

Discussion

Aminosalicylates are used to maintain remission both in ulcerative colitis and Crohn's disease in children and adults. Aminosalicylates have a direct effect on the gastrointestinal mucosa and hence the site of release is important in relation to efficacy. Their value is well established in the maintenance of remission in ulcerative colitis[2,3]. The benefit of aminosalicylates in maintaining remission in Crohn's disease, however, has not been confirmed[3]. They are, however, recommended as maintenance therapy in the British National Formulary for Children[4].

Several studies have suggested that mesalazine has less side effects than sulfasalazine in children with inflammatory bowel disease[5,6]. We feel it is likely that the diarrhoea, lethargy and arthritis experienced by this child were an adverse drug reaction to the mesalazine. His symptoms improved dramatically after withdrawal of the mesalazine. If his symptoms had been due to his Crohn's disease, one would not have expected such a dramatic improvement coinciding with the withdrawal of the mesalazine. A systematic review of the toxicity of mesalazine and other aminosalicylates suggests that the most frequent adverse drug reactions are arthralgia, headache, abdominal pain, nausea, vomiting, diarrhoea, lethargy, rash and pyrexia. The prevalence of these adverse drug reactions ranges from 1 to 30%[5].

In our case, it was the presence of arthritis that alerted clinicians to the possibility of this being an adverse drug reaction. The prevalence of arthralgia ranged from 2 to 24% of patients in a systematic review of mesalazine toxicity[5]. Arthritis, where the joint is both painful and swollen, has previously been reported in association with mesalazine therapy[7]. It is of interest that this child had been receiving mesalazine for three months prior to developing drug toxicity. Unfortunately there is little information about the time onset of drug toxicity with mesalazine. Previous studies describing drug toxicity describe the frequency of adverse drug reactions over a given time period rather than detailing the onset of the adverse drug reaction[5].

In a child with inflammatory bowel disease, symptoms such as abdominal pain and diarrhoea, as well as tiredness, are suggestive of a relapse of the underlying condition. Because of the similarity between drug toxicity and clinical features of the underlying disease, clinicians need to always consider the possibility of symptoms being secondary to an adverse drug reaction.

References

1. Ravikumara M, Sandhu BK. Epidemiology of inflammatory bowel diseases in childhood. Ind J Ped 2006;73:717-721.
2. Spray CH, Sandhu BK. Therapeutic aspects of inflammatory bowel disease in children. Paed Perinat Drug Ther 2005;6:157-165.
3. Bergman R, Parkes M. Systematic review: the use of mesalazine in inflammatory bowel disease. Aliment Pharmacol Ther 2006;23:841-855.

4. Loftus Jr EV, Kane SV, Bjorkman D. Systematic review: short-term adverse effects of 5-amino-salicylic acid agents in the treatment of ulcerative colitis. Aliment Pharmacol Ther 2004;19:179-189.
5. British National Formulary for Children 2006. pp. 66-75. BMJ, RPS and RCPCH Publications, London 2006.
6. Barden L, Lipson A, Pert P, Walker-Smith JA. Mesalazine in childhood inflammatory bowel disease. Aliment Pharmacol Ther 1989;3: 597-603.
7. Lin AG, Hine KR. Drug points: fever, vasculitic rash, arthritis, pericarditis, and pericardial effusion after mesalazine. BMJ 1994;308:113.

CrossRefs are available in the online published version of this paper:
http://www.librapharm.com
Paper PPDT-0182_4, *Accepted for publication:* 05 April 2007
Published Online: 18 June 2007
doi:10.1185/146300907X178923