PostScript

LETTERS

Cyclosporin A treatment of steroid-refractory ulcerative colitis during pregnancy: report of two cases

Treatment of fulminant, steroid-resistant ulcerative colitis during pregnancy is extremely challenging. Calcineurin antagonists like cyclosporin A (CyA) have been used in the past in fulminant colitis; yet, the experience using CyA during pregnancy is limited, as are the data on the long-term course after the initial treatment phase.

Case reports

The first patient is a 31-year-old woman with a 7-year history of ulcerative colitis. During her first pregnancy, she developed an acute flare of ulcerative colitis confirmed using endoscopy. Despite taking intravenous steroids, disease activity remained high, necessitating the transfusion of packed red blood cells. Within 7 days after initiating intravenous CyA the blood loss and abdominal pain subsided, and the frequency of bowel movements was reduced to 5 per day. The patient was discharged home on oral CyA. As a side effect, she developed hirsutism, which subsided after CyA was discontinued. The patient refused treatment with azathioprine, so we began oral mesalazine for maintenance of remission. In the 36th week of her pregnancy, she gave spontaneous birth to a healthy child. During the 7-year follow-up period, the child developed normally, the patient had four more flares of colitis, yet only one was severe enough to warrant inpatient treatment. She is now in remission using mesalazine.

The second patient is a 34-year-old woman with a 13-year history of ulcerative colitis presenting with an acute flare of ulcerative colitis in the 13th week of her first pregnancy. She failed to respond to conventional treatment with mesalazine, oral and intravenous steroids. After confirming the diagnosis by sigmoidoscopy, we began treatment with intravenous CyA. Within 1 week, the patient improved significantly. After 21 days of treatment with intravenous CyA, the treatment was changed to oral CyA for five more weeks. During CyA treatment, the patient had one self-limiting episode of second-degree arteriovenous block and developed hypertrichosis. In the 25+5 week of pregnancy, she underwent an emergency caesarean section for suspected placental insufficiency. The child suffered a femur fracture, a third-degree intracerebral haemorrhage and respiratory distress syndrome of the neonate. Yet, follow-up after discharge showed normal intellectual development and no impairment of motor skills. In the following 10 years, the patient herself had two more flares of ulcerative colitis, which were treated with oral and intravenous steroids, respectively. She is now in remission under mesalazine treatment.

Conclusions

The main goal of CyA treatment in pregnant patients with ulcerative colitis is to avoid

emergency colectomy, because of its high risk for the mother and for the unborn child, with a mortality of 22% and 49%, respectively.¹ CyA has been proven to induce remission in patients with fulminant ulcerative colitis rapidly and effectively² in patients who did not respond to 7 days of intravenous steroids. Our results once again show that CyA is highly potent (fig 1) in inducing remission in patients with ulcerative colitis, and seems to be safe when used at lower dosage, aiming for blood levels of 200 ng/ml. In addition, our follow-up data also suggest that the long-term prognosis in pregnant patients might be different from the prognosis in non-pregnant patients with severe or fulminant ulcerative colitis, regarding the need for later colectomy. Yet recent encouraging results in the treatment of fulminant colitis using infliximab,³ and the fact that infliximab is rated risk category B during pregnancy by the Food and Drug Administration whereas CyA is rated as category C, indicate that the question as to what drug to recommend is not yet solved.

Wolfgang Reindl, Roland M Schmid, Wolfgang Huber

Department of Internal Medicine II, Klinikum Rechts der Isar, Technical University of Munich, Munich, Germany

Correspondence to: Dr W Reindl II, Medizinische Klinik, Klinikum rechts der Isar, Ismaninger Str 22, Munich D-81675, Germany; Wolfgang.Reindl@lrz.tum.de

Informed consent has been obtained from the patients for publication of their details in this letter.

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Proton pump inhibitors and gastric neoplasia

We read the leading article by Kuipers (*Gut* 2006;**55**:1217–21) with great interest. The conclusion that proton pump inhibitor (PPI) treatment does not increase the risk of gastric neoplasia is reassuring. The overview by Kuipers, however, lacks a few important points:

1. *Hypergastrinaemia.* The maximal trophic effect of gastrin is reached at concentrations lower than that realised by most clinicians, both in rats and in humans.¹ A concentration of 400 ng/ml or 200 pM induces nearly maximal effect.
2. *Hypergastrinaemia and gastric carcinoids.* Kuipers claims that prolonged hypergastrinaemia leads to enterochromaffin-like (ECL) cell carcinoids only in rats.² This is not correct. Mice also develop gastric carcinoids when treated with insurmountable histamine 2 antagonists.³ PPIs have low potency in this species, which is the cause of the widespread misunderstanding that hypergastrinaemia in mice does not induce ECL cell carcinoids. Moreover, long term treatment of dogs with PPI was reported not to induce any changes in the gastric mucosa.⁴ Unfortunately, the dose used was not sufficient to induce hypoauidity and accompanying hypergastrinaemia. Even in humans gastric endocrine tumours have been described after PPI treatment,¹ although, surprisingly, a more detailed report on these patients does not

Figure 1 Rachmilewitz Index at admission to the intensive care unit (ICU) and after 7 days of treatment with intravenous cyclosporin A (CyA).