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Effect of cimetidine on upper gastrointestinal bleeding after renal transplantation: a prospective study

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Abstract

In 97 consecutive patients undergoing renal transplantation the incidence of upper gastrointestinal bleeding was registered over 180 days after allocation to treatment with either cimetidine or placebo. Bleeding episodes occurred in 12 patients, 11 of whom were receiving placebo and only one cimetidine ($p < 0.01$). All bleeding episodes occurred during the first month after allotransplantation. Treatment with cimetidine did not lead to an increased incidence of rejection of the allograft.

It is concluded that cimetidine is effective and safe in protecting against upper gastrointestinal bleeding after renal transplantation.

Introduction

Peptic ulceration is common in chronic renal failure. After renal transplantation the risk of upper gastrointestinal bleeding increases considerably. The incidence is 5-12%,¹⁻⁵ and because mortality in patients in whom it develops is above 50% prophylactic gastric surgery has been considered.¹ The reason for the increase in bleeding episodes is uncertain. Chisholm *et al* found a significant increase in peak acid output in men after renal transplantation but not in women.⁴ The increase was not related to the steroid dose, the presence of hyperparathyroidism,

or the severity of the previous uraemia. They concluded that prophylactic surgery was not indicated. Conversely, Doherty suggested that upper gastrointestinal bleeding after renal transplantation could be prevented if steroids were used more sparingly, but he gave no information on the effect on secretion of acid.⁶

Histamine H₂ receptor antagonists are potent inhibitors of secretion of gastric acid and might prove useful in preventing upper gastrointestinal bleeding after renal transplantation. The aim of this prospective study was to assess the effects of cimetidine on upper gastrointestinal bleeding after renal transplantation and on allograft function and the incidence of rejection.

Patients and methods

Ninety seven patients consecutively admitted for renal transplantation (40 women, 57 men) entered the study after giving their informed consent. Ninety two of the patients were screened for gastric or duodenal ulcer before transplantation with radiological studies or gastroduodenoscopy or both: we excluded from the study patients aged under 16, patients with acute gastroduodenal ulcer, and patients with blood or liver diseases.

Treatment with placebo or cimetidine was started immediately after the transplantation. During the postoperative intestinal paralysis the drug was given intravenously. The dose of cimetidine or placebo was adjusted to renal function as follows: creatinine clearance below 15 ml/min, 200 mg twice daily; 15-40 ml/min, 200 mg thrice daily; and over 40 ml/min, 200 mg thrice daily and 400 mg at bedtime. The immunosuppressive regimen was azothioprine 3 mg/kg/day and prednisone 1 mg/kg/day reduced to 20 mg daily after four weeks. The trial was designed to be continued for 180 days.

Gastrointestinal bleeding was defined as the occurrence of haematemesis or melaena, or both, with a fall in haemoglobin concentration. If gastrointestinal haemorrhage occurred the patient was withdrawn from the trial and treated with emergency operation or cimetidine.

The χ^2 test was used for statistical analysis.

Results

Several patients dropped out before the end of the observation period, mostly because of removal of the graft, upper gastrointestinal bleeding, or death. None were withdrawn because of side effects of cimetidine. Sixty nine patients were observed for 30 days, 49 for 90

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days, and 44 for 180 days. Fifty patients received placebo and 47 cimetidine.

Severe upper gastrointestinal bleeding occurred in 12 patients (seven men, five women). None of them had a history of peptic ulcer, and the examinations of the upper gastrointestinal tract before transplantation had yielded normal results. During the acute bleeding episode six of these patients were examined either radiographically or endoscopically. Two had an acute gastric ulcer, and four had diffuse bleeding from gastric or duodenal erosions. Eleven patients had received placebo and one cimetidine. This difference was significant ($\chi^2=7.07$, $p<0.01$). All bleeding episodes occurred within the first 30 days after renal transplantation (median 12, range 1-30 days).

Ten patients given placebo and 12 given cimetidine had their renal graft removed after five to 145 (median 35) days because of rejection. This difference was not significant ($\chi^2=0.167$).

Discussion

Only a few, retrospective studies of the prophylactic use of cimetidine in renal transplant recipients have been reported. These have compared the incidence of upper gastrointestinal haemorrhage in patients treated with cimetidine with that in historic controls not receiving cimetidine. In such retrospective studies Jones *et al* and Roermund *et al* found a significant effect of cimetidine^{7,8} and Garvin *et al* reported some effect.⁹ In the only prospective study reported Schiessel *et al* found no significant effect of cimetidine after renal transplantation in 55 patients.¹⁰ Primack suggested that treatment with cimetidine might increase the incidence of allograft rejection.¹¹ Schiessel *et al* did not confirm this.¹⁰

Our study showed that in most patients cimetidine prevents upper gastrointestinal bleeding after renal transplantation. This

accords with the results of the previous retrospective studies. In the prospective study of Schiessel *et al* three patients given cimetidine and two given placebo had upper gastrointestinal bleeding.¹⁰ The apparent difference between these findings and those of our study may be explained by the different number of patients studied.

In conclusion, our study showed that cimetidine acts as effective and safe prophylaxis against upper gastrointestinal bleeding after renal transplantation. There was no indication that it influenced the incidence of rejection of the renal graft.

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Anaphylactic reaction to aprotinin despite negative ocular sensitivity tests

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Abstract

A man with a history of pancreatitis was given aprotinin intravenously just before endoscopic retrograde pancreatography. Despite negative sensitivity tests with aprotinin eye drops he developed a profound anaphylactic reaction on intravenous administration of the drug.

Ocular sensitivity tests may not predict severe anaphylactic reactions to intravenous aprotinin.

Introduction

Serious allergic reactions to aprotinin occur in less than 0.1% of patients receiving this drug.¹ We report on a man who,

despite negative ocular sensitivity tests, had a severe anaphylactic reaction after the intravenous administration of aprotinin.

Case report

A 44 year old man with a clinical history suggestive of chronic pancreatitis secondary to alcohol abuse was referred to this hospital for endoscopic retrograde pancreatography.

He gave a history of having been admitted several times to the referring hospital with upper abdominal pain, often associated with appreciable hyperamylasaemia. He was usually treated conservatively with intravenous fluids and analgesics and according to the records had twice received an infusion of aprotinin. In June 1982 he had undergone suction drainage of a ruptured pancreatic pseudocyst, after which he had further episodes of abdominal pain, often necessitating admission to hospital and treatment with narcotic analgesics.

Recent investigations had shown normal haematology and biochemistry. Ultrasound scanning of the pancreas showed some dense echoes in the head and body; the tail, however, could not be clearly defined. A Lundh test meal was indicative of early pancreatic insufficiency.

Our policy with patients undergoing endoscopic retrograde pancreatography who have a history of pancreatitis was to administer 500 000 Kallikrein inhibiting units (KIU) aprotinin intravenously,

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