Comment

Oral ketoconazole appreciably reduced the rate of isolation of the outbreak strain from both systemically infected and colonised patients. The outbreak strain did not reappear when ketoconazole was withdrawn. All cases of systemic candidiasis acquired in the unit before April 1984 were caused by the outbreak strain, whereas after May 1984 all cases were caused by other strains.

Control of an outbreak depends on its identification and the prevention of cross infection. Existing handwashing reagents can be replaced with fungicidal disinfectants such as Hibisol or Betadine, and antifungal prophylaxis can be given. Recent work in neutropenic patients in whom infection was probably due to an endogenous isolate showed that ketoconazole was as effective as amphotericin B, and prophylaxis with either agent failed.[5] In this study ketoconazole failed in six cases, perhaps because of poor absorption in the gut as five patients had undergone major gastrointestinal surgery. Treatment with ketoconazole resulted in the virtual elimination of the outbreak strain, the incidence of cases returning to its former value, with occasional cases caused by the patients' own yeast flora.

A much shorter course of prophylaxis might have been equally effective and could be considered in any unit where the incidence of candidal sepsis is unacceptably high and cross infection a problem.

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Department of Medical Microbiology, London Hospital, London E1
J P BURNIE, MB, MRCP, lecturer
W LEE, BSC, research assistant
J D WILLIAMS, MD, FRCPATH, professor of microbiology

Department of Medical Microbiology, St Bartholomew's Hospital, London
R C MATTHEWS, MB, MSC, lecturer

Department of Medical Microbiology, University of Leicester, Leicester
F C ODDS, PHD, MRCPATH, senior lecturer

Correspondence to: Dr Burnie.

Controlled trial of arbaprostil in bleeding peptic ulcer

In patients with acute upper gastrointestinal bleeding no convincing effect on the bleeding has been reported after treatment with antisecretory drugs such as histamine H_2 receptor antagonists,[1] antifibrinolytic agents such as tranexamic acid,[1] or somatostatin,[2] which reduces both splanchnic blood flow and acid secretion. "Cytoprotective" prostaglandin analogues may be an innovation in treatment[3] and were claimed to be beneficial in a single patient.[4] We have carried out a prospective double blind, placebo controlled trial of the efficacy of 15(*R*)-15-methylprostaglandin E_2 (arbaprostil[4]; 50 μg by mouth every six hours for seven days) in stopping acute bleeding from erosive or ulcerative lesions of the stomach and duodenum and preventing rebleeding.

Patients, methods, and results

During one year 237 consecutive patients admitted for haematemesis or melaena were considered for the study, which was approved by the ethical committee of Funen and Vejle Conties, Denmark. Criteria for entry were evidence of bright red or coffee ground gastric aspirate on lavage, gastritis or gastric or duodenal ulcer with active bleeding or fresh clot formation seen during the subsequent endoscopy, a transfusion requirement of 2 units or more and packed cell volume of 0·30 or less, or a postural change in diastolic blood pressure of 10 mm Hg or more. Of 87 patients aged over 18 who satisfied these criteria, four needed emergency surgery, one died before endoscopy, and in one case informed consent was not obtained. The remaining 81 patients were given at least four doses of trial medicine and were considered suitable for analysis (table). Arrest of bleeding was defined as stabilisation of the packed cell volume and vital signs, clearance of nasogastric aspirate, and a reduced requirement for or no further need of transfusion.

The 95% confidence interval for the observed difference[5] between arbaprostil and placebo in stopping bleeding within 48 hours ranged from 6% in favour of arbaprostil to 38% in favour of placebo. As regards the frequency of rebleeding the same interval ranged from 6% in favour of arbaprostil to 32% in favour of placebo. These estimates suggest that we had not overlooked any major therapeutic difference. Endoscopic assessment of 72 patients at completion of the trial disclosed no difference in the rate of ulcer healing. A statistically significant ($p < 0·05$) improvement in concomitant gastritis and duodenitis, however, was shown by means of a scoring system. Four patients aged 73-81 years died. Necropsy was done in three cases and showed concomitant acute leukaemia and ovarian and renal carcinoma, respectively.

Comparability of groups and outcome of treatment

	Arbaprostil (n = 40)	Placebo (n = 41)	Significance
Sex (M/F)	20/20	24/17	NS*
Mean age (years)	70·1	68·8	NS†
No (%) of smokers	16 (40)	21 (51)	NS*
No (%) taking aspirin like drugs	19 (48)	23 (56)	NS*
Mean systolic blood pressure (mm Hg)	131	132	NS†
Mean pulse rate/min	91	91	NS†
Mean serum urea (mmol/l)	14·9	13·1	NS†
Mean packed cell volume	0·26	0·25	NS†
No (%) with bleeding gastric ulcer	27 (68)	24 (59)	NS*
No (%) with bleeding duodenal ulcer	12 (30)	16 (39)	NS*
No (%) with haemorrhagic gastritis	1 (2·5)	1 (2·4)	NS*
No (%) with visible vessel	26 (65)	24 (59)	NS*
No (%) whose bleeding stopped after 24 h and did not recur	19 (48)	22 (54)	NS*
No (%) whose bleeding stopped after 48 h and did not recur	20 (50)	27 (66)	NS*
Mean transfusion requirements (units)	6·7	6·7	NS†
No (%) with rebleeding	12 (30)	7 (17)	NS*
No (%) operated	9 (23)	7 (17)	NS*
No (%) of deaths	2 (5)	2 (5)	NS*

*χ^2 test: $p > 0·05$.
†Student's t test: $p > 0·05$.
Conversion: SI to traditional units—Urea: 1 mmol/l ≈ 6 mg/100 ml.

Comment

These findings show that arbaprostil is unlikely to have a substantial effect on outcome in patients with acute bleeding from ulcerative lesions in the stomach or duodenum. Although our sample was too small to exclude a marginal beneficial effect on mortality, the results challenge the belief that "direct cytoprotection"[3] provides a major breakthrough in medical treatment of patients with upper gastrointestinal bleeding and for the prevention of rebleeding.

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Department of Medical Gastroenterology, Odense University Hospital, DK-5000 Odense C, Denmark
K LAURITSEN, MD, senior registrar
L S LAURSEN, MD, senior registrar
T HAVELUND, MD, senior registrar
P BYTZER, MD, senior registrar
J RASK-MADSEN, MD, consultant physician

Correspondence and requests for reprints to: Dr J Rask-Madsen, Department of Medicine B, Bispebjerg Hospital, University of Copenhagen, DK-2400 Copenhagen NV, Denmark.