SHORT REPORTS

Somatostatin and ranitidine in the control of iatrogenic haemorrhage of the upper gastrointestinal tract

Upper gastrointestinal haemorrhages often occur during treatment with steroidal and non-steroidal anti-inflammatory drugs. Until a few years ago the therapeutic policy for upper gastrointestinal hemorrhage was bed rest and sedation, blood transfusion, and occasional lavage

follow up continued until surgery (table). The haemorrhage stopped in 19 of the 20 patients treated with somatostatin, 13 of the 20 treated with ranitidine, and nine of the 20 treated with placebo. In the patients treated with somatostatin haemorrhage stopped eight to 12 hours after the beginning of treatment; in those treated with ranitidine 20 to 60 hours after; and in the patients treated with placebo 36 to 53 hours after. Statistical analysis of the bleeding time with the log rank test showed a highly significant difference between somatostatin and the other treatments ($\chi^2=48.13$, $df=1$, $p<0.0001$). No significant difference was found between ranitidine and placebo ($\chi^2=1.32$, $df=1$, $p\approx0.25$). Moreover, no patient treated with somatostatin rebled, while rebleeding occurred in three of the 13 patients treated with ranitidine whose haemorrhage had stopped (18, 24, and 33 hours after the interruption

Comparison of somatostatin with ranitidine and placebo in the control of iatrogenic haemorrhage of the upper gastrointestinal tract

Somatostatin				Ranitidine				Placebo			
Case No	Source of bleeding	Time till haemorrhage stopped	Follow up time	Case No	Source of bleeding	Time till haemorrhage stopped	Follow up time	Case No	Source of bleeding	Time till haemorrhage stopped	Follow up time
1	AHG	8 h		21	Duodenal ulcer	60 h		41	AHG	48 h	
2	Duodenal ulcer	8 h 30 min		22	Gastric ulcer	48 h		42	Duodenal ulcer		72 h*
3	AHG	8 h 30 min		23	AHG		62 h*	43	Gastric ulcer		72 h*
4	AHG	8 h 45 min		24	AHG	36 h		44	AHG	49 h	
5	Gastric ulcer	9 h 30 min		25†	AHG	20 h	44 h*	45	Duodenal ulcer		71 h*
6	Duodenal ulcer	10 h		26	Duodenal ulcer	51 h		46	Duodenal ulcer		68 h*
7	AHG	9 h		27	AHG	50 h		47	AHG		65 h*
8	Gastric ulcer	8 h 30 min		28	AHG		71 h*	48	Gastric ulcer	47 h	
9	AHG	11 h		29	Gastric ulcer		50 h*	49	AHG	50 h	
10	Gastric ulcer		48 h*	30	Duodenal ulcer	35 h		50	AHG		70 h
11	AHG	8 h 30 min		31†	Duodenal ulcer	30 h	48 h*	51	Gastric ulcer	51 h	
12	AHG	9 h		32	AHG		53 h*	52	AHG	49 h	
13	Duodenal ulcer	10 h		33	Gastric ulcer	48 h		53	AHG		80 h*
14	Gastric ulcer	12 h		34	AHG	50 h		54	Gastric ulcer		45 h*
15	AHG	9 h 30 min		35	AHG		74 h*	55	Gastric ulcer		64 h*
16	AHG	9 h		36	Duodenal ulcer	49 h		56	AHG	53 h	
17	Duodenal ulcer	10 h		37	AHG	45 h		57	Gastric ulcer		72 h*
18	Gastric ulcer	8 h		38	AHG		70 h*	58†	AHG	40 h	52 h*
19	AHG	11 h		39†	Gastric ulcer	40 h	73 h*	59	Duodenal ulcer	60 h	
20	AHG	9 h 30 min		40	Duodenal ulcer		56 h*	60†	AHG	36 h	58 h*

AHG = Acute haemorrhagic gastropathy.

*Surgical intervention.

†Rebleeding occurred after treatment stopped.

with ice water and emergency surgery. More recently, patients have been treated with H_2 receptor antagonists and somatostatin. Somatostatin is a tetradecapeptidic ubiquitous hormone that inhibits secretion of gastric acid and pepsin, and serum gastrin concentrations,¹ and reduces gastric motility and splanchnic blood flow.² On the basis of our results and the results of other authors we performed a study aimed at evaluating the efficacy of somatostatin compared with ranitidine and placebo in controlling iatrogenic upper gastrointestinal haemorrhage.^{3,4}

Patients, methods, and results

We studied 60 patients (men and women aged under 60) who presented with acute upper gastrointestinal haemorrhage (losing more than four units of blood/24 h); they were all undergoing short or long term treatment with non-steroidal anti-inflammatory drugs or corticosteroids for various co-existent diseases. The pathological lesions were acute haemorrhagic gastropathies (31 patients), gastric ulcers (15), and duodenal ulcers (14). The 29 patients with either gastric or duodenal ulcers had had their ulcers for from two to five years. All the patients underwent emergency endoscopy and insertion of a gastric tube. No antacids were administered.

Patients were randomly allocated to three groups of 20. The first group underwent somatostatin treatment (an intravenous bolus injection of 250 μ g for not less than five minutes followed by continuous infusion of 250 μ g/h with a peristaltic pump). The second group received ranitidine 50 mg intravenously every four hours. In the third group (placebo) treatment comprised only insertion of a gastric tube. Haemoglobin concentration and packed cell volume were measured every six hours, and serum glucose, urea, creatinine, and electrolyte concentrations every 12 hours. Each drug used in the study was continued for 12 hours after the first report of clear gastric juice. The haemorrhage was considered to have stopped when in the following 12 hours without any treatment the lavage juice remained clear. Endoscopy was then repeated. In patients in whom the haemorrhage had stopped the endoscopy showed that those with acute haemorrhagic gastropathies had hyperaemic mucosa with no erosions, while those with a gastric or duodenal ulcer had an ulcerative lesion covered by a blood clot that was noticeably adherent and not bleeding.

All patients whose haemorrhage had definitely stopped were examined for 120 hours after the interruption of treatment. In all patients in whom surgery was necessary because the haemorrhage did not stop or because of rebleeding,

of treatment) and in two of the nine patients treated with placebo whose haemorrhage had stopped (12 and 22 hours after the interruption of the treatment).

Comment

This comparative study shows that somatostatin is more effective than ranitidine and placebo in the control of iatrogenic gastro-duodenal haemorrhages due to acute haemorrhagic gastropathies and to gastric and duodenal ulcer. The cessation of bleeding induced by somatostatin is probably due to the hormone's capacity to reduce secretion of gastric acid and pepsin, serum gastrin concentrations, and splanchnic blood flow, and to its considerable gastric cytoprotective effect.⁵

¹ Konturek SJ, Tasler J, Cieszkowski M, Coy D, Schally AV. Effect of growth hormone release-inhibiting hormone on gastric secretion, mucosal blood flow and serum gastrin. *Gastroenterology* 1976;70:737-41.

² Sonnenberg GE, Keller U, Perruchoud A, Burckhardt D, Gyr K. Effect of somatostatin on splanchnic hemodynamics in patients with cirrhosis of the liver and in normal subjects. *Gastroenterology* 1981;80:526-32.

³ Coraggio F, Spina M, Scarpato P, et al. Studio comparativo sull'efficacia terapeutica della somatostatina e della ranitidina nelle emorragie del tratto gastroenterale superiore indotte da farmaci antiinfiammatori non steroidei. *Clin Ter* (in press).

⁴ Kayasheh L, Gyr K, Keller U, Stalder GA, Wall M. Somatostatin and cimetidine in peptic-ulcer haemorrhage. *Lancet* 1980;i:844-8.

⁵ Szabo S, Usadel KH. Cytoprotection-organoprotection by somatostatin: gastric and hepatic lesions. *Experientia* 1982;38:254-8.

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University of Naples, 80131 Naples, Italy

FRANCESCO CORAGGIO, MD, associated professor in emergency medicine, 1st faculty of medicine and surgery
PAOLO SCARPATO, MD, fellow in medicine
MARCELLO SPINA, MD, fellow in medicine
SERGIO LOMBARDI, MD, research fellow in emergency surgery, 2nd faculty of medicine and surgery

Correspondence to: Professor F Coraggio.