

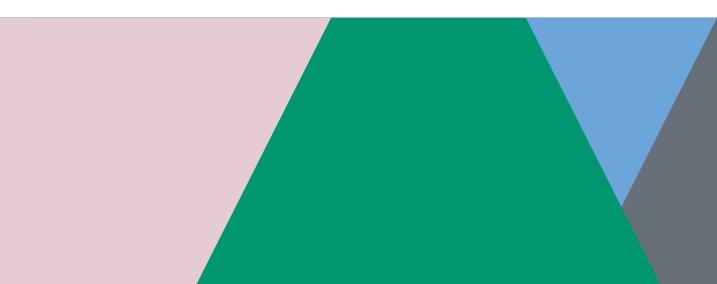
Journal presentation

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EFFECT OF INTRAVENOUS OMEPRAZOLE ON RECURRENT BLEEDING AFTER ENDOSCOPIC TREATMENT OF BLEEDING PEPTIC ULCERS

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Background

- Peptic ulcer bleeding recurs in 15 20 % of patients after endoscopic treatment
- Inhibition of gastric acid -> neutral/higher intragastric pH -> facilitation of platelet aggregation -> stabilizing clots -> prevention of recurrent bleeding
- Role of acid suppression in the management of bleeding peptic ulcers, particularly after endoscopic treatment, remains unclear
- Evidence of the effectiveness of histamine H2-receptor antagonists is conflicting
 - High-dose PPI is theoretically better than H2-receptor antagonist



Objective / Aim

- Evaluate the efficacy of continous intravenous PPI treatment after peptic ulcer bleeding
- Primary end point: Recurrent bleeding within 30 days after endoscopy

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Methods: Study design

- Randomized, double-blind, placebo-controlled study
- Enrolment between May 1998 July 1999
- Eligibility:
 - > 16 years
 - Admitted to Prince of Wales Hospital (Hong Kong)
 - Endoscopic treatment of actively bleeding ulcers or ulcers with nonbleeding visible vessels had been successful
 - No inclusion:
 - Unsuccessfull endoscopic treatment -> immediate surgery
 - Ulcers with clean bases or flat pigments



Methods: Study Treatment

- Random assignment
 - Intravenous infusion of placebo vs. omeprazole:
 - 80-mg bolus injection followed by continuous infusion of 8 mg/h for a period of 72 hours
- Enrollment of 240 patients, 120 in each group



Methods: Follow-up

- Monitored in a surgical ward for signs of further bleeding
- Blood pressure and pulse rate were recorded hourly during the first 24
 hours after infusion and 4 hourly thereafter until the patients were discharged
- Bleeding was considered to have recurred:
 - vomiting of fresh blood
 - shock (systolic blood pressure of <= 90 mmHg, pulse rate of >= 110 bpm)
 with melena
 - drop in hemoglobin > 2 g/dl within 24 hours after transfusion to a level of 10 g/dl



Methods: Follow-up

- Recurrent bleeding -> urgent gastroscopy
- Confirmation of recurrent bleeding:
 - active bleeding (spurting or oozing hemorrhage)
 - Coffeeground material or fresh blood in the stomach near a vessel
 - repeated endoscopic treatment (epinephrine injection or thermocoagulation)
- End of the omeprazole or placebo infusion (72 h) -> omeprazole 20 mg/d p.o. for 8 weeks



Methods: Statistical analysis

- Kaplan–Meier method to assess primary end point (recurrent bleeding within 30 days after endoscopy)
- Comparison of patients' baseline characteristics and outcome measures:
 - Student's t-test for parametric data
 - Mann–Whitney U test for nonparametric data
 - Pearson's chi-square / Fisher's exact test for proportions



Results

TABLE 2. OUTCOMES AFTER ENDOSCOPIC THERAPY.

Placeb Placeb By day 7 By day 30 Recurrent bleeding within 30 days — no. of patients/total no. Actively bleeding ulcers Ulcers with nonbleeding visible vessels Endoscopic retreatment successful — no. of patients Burgery — no. of patients Median hospital stay <5 days — no. of patients (%) Duration of hospitalization — days Patients admitted for bleeding peptic ulcers Patients in whom bleeding developed in the hospital Placeb Placeb Rela Repe Units of blood transfused Refer endoscopic therapy After endoscopic therapy Death within 30 days — no. of patients Pound (0.000 to 1.000 to	Recurrence		Ourroom	OMEPRAZOLE GROUP	PLACEBO GROUP	RELATIVE RISK	P
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Place Plac	•	Omepr	Recurrent bleeding — no. of patients				
Placeb By day 30 Recurrent bleeding within 30 days — no. of patients / total no. 8† 27† 3.38 (1.60-7.13) <0.001		• p .	7 1 7	5		_ \	< 0.001
Recurrent bleeding within 30 days — no. of patients/total no. Actively bleeding ulcers 3/64 10/58 4.24 (1.10-16.3) 0.04			7 1 7	7		\	
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Endoscopic retreatment successful — no. of patients Surgery — no. of patients Surgery — no. of patients 3 9 3.00 (0.83-10.8) 0.14				3/64	10/58	4.24 (1.10-16.3)	0.04
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Median hospital stay < 5 days - no. of patients (%) 56 (46.7) 38 (31.7) 0.02		Hazi	Endoscopic retreatment successful — no. of patients	6	23	3.83 (1.62-9.08)	< 0.001
Duration of hospitalization — days Patients admitted for bleeding peptic ulcers	Recurrence		Surgery — no. of patients	3	9	3.00 (0.83-10.8)	0.14
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2.22 (2.22 (2.22)		• Reis	After endoscopic therapy	1.7 ± 1.9	2.4 ± 3.2		0.03
Ulcar basing at 9 wis no of patients /total no assessed 72 /95 77 /92 110 /0.00 1.20\ 0.14			Death within 30 days - no. of patients	5	12	$2.40 \ (0.87 - 6.60)$	0.13
endoscopically			Ulcer healing at 8 wk — no. of patients/total no. assessed endoscopically	72/85	77/83	1.10 (0.98-1.22)	0.14

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Results

- Need for surgery after bleeding:
 - Omeprazole group: 3 patients (4.2 percent)
 - Placebo group: 9 (20 percent)
 - Relative risk, 4.80
- Death within 30 days after endoscopy:
 - Omeprazole group: 5 patients (4.2 percent)
 - Placebo group: 12 (10 percent)
 - Relative risk, 2.40



Discussion

TABLE 2. OUTCOMES AFTER ENDOSCOPIC THERAPY.

- Ulcer healing
 - Omeprazo
 - · Placebo gr

Оитсоме	OMEPRAZOLE GROUP (N = 120)	PLACEBO GROUP (N = 120)	RELATIVE RISK (95% CI)*	P Value
Recurrent bleeding — no. of patients				
By day 3	5	24	4.80 (1.89-12.2)	< 0.001
By day 7	7	26	3.71 (1.68-8.23)	< 0.001
By day 30	8†	27†	3.38 (1.60-7.13)	< 0.001
Recurrent bleeding within 30 days - no. of patients/total no.				
Actively bleeding ulcers	3/64	10/58	4.24 (1.10-16.3)	0.04
Ulcers with nonbleeding visible vessels	5/56	17/62	3.85 (1.31-11.3)	0.02
Endoscopic retreatment successful — no. of patients	6	23	3.83 (1.62-9.08)	< 0.001
Surgery — no. of patients	3	9	3.00 (0.83-10.8)	0.14
Median hospital stay <5 days — no. of patients (%)	56 (46.7)	38 (31.7)		0.02
Duration of hospitalization — days Patients admitted for bleeding peptic ulcers				
Median	4	5		0.006
Range	3-65	3-64		
Patients in whom bleeding developed in the hospital				
Median	13	9		0.33
Range	3-40	4-46		
Units of blood transfused‡	2.7 ± 2.5	3.5 ± 3.8		0.04
Before endoscopic therapy	1.0 ± 1.3	1.1 ± 1.5		0.46
After endoscopic therapy	1.7 ± 1.9	2.4 ± 3.2		0.03
Death within 30 days — no. of patients	5	12	2.40 (0.87-6.60)	0.13
Ulcer healing at 8 wk — no. of patients/total no. assessed endoscopically	72/85	77/83	1.10 (0.98-1.22)	0.14





Strengths

- RCT / Double blinded
- Comparability (adjustment for confounding covariates) between groups



Limitations

- Single centre (Prince of Wales Hospital)
- Only asian population (smaller parietal-cell mass)
- No measurement of intragastric pH



Outlook / Take home

- After endoscopic treatment of bleeding peptic ulcers, high-dose infusion of omeprazole substantially:
 - Reduces risk of recurrent bleeding
 - Decreases need for endoscopic retreatment and blood transfusions
 - Shortens the length of hospitalization
- No significant difference after 8 weeks of oral PPI

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Thank you for your attention!

