INSELGRUPPE

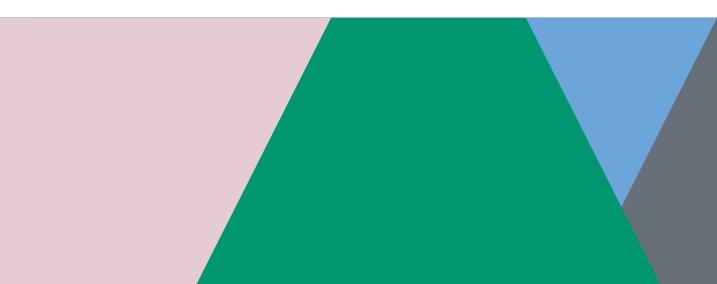# Journal presentation

21.08.2024, Roy Frei

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

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

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

- Recurren[...]

  - Omepr[...]

  - Placeb[...]

    - Haza[...]

- Recurren[...]

  - Omepr[...]

  - Placeb[...]

    - Rela[...]

TABLE 2. OUTCOMES AFTER ENDOSCOPIC THERAPY.

OUTCOME	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

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

- Ulcer healing

  - Omeprazol

  - Placebo gr

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Strengths

- RCT / Double blinded

- Comparabilty (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

Thank you for your attention!