ERYTHROMYCIN INFUSION OR GASTRIC LAVAGE FOR UPPER GASTROINTESTINAL BLEEDING: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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BACKGROUND

- Endoscopy
  - determine the cause of bleeding and for hemostasis
  - should be performed within 12 hours of the first clinical signs of bleeding.
- The reliability of the endoscopy depends on the good visualization of the gastrointestinal tract
  - Nasogastric tube(NG)
    - to monitor bleeding on repeated gastric lavage
    - to clear the gastrointestinal tract.
  - Erythromycin(ER)
    - motilin receptor agonist that accelerates gastric emptying by inducing antral contractions
    - To clear the GI tract

BACKGROUND

- Randomized controlled studies
  - ER associated with NG(NGER) was more effective than NG alone.
- How about ER vs NG or vs combination treatment ?

STUDY DESIGN

- Prospective, randomized, multicenter, clinical trial.
- The emergency departments of 6 hospitals participated in the study.
- Patients were randomized in 3 parallel groups.

PARTICIPANTS

- Inclusion :
  - > 18 y/o, sourse from 6 ER, October ~ December 2007
  - Acute UGI bleeding : hematemesis or melena either at or during the 12 hours before ER

PARTICIPANTS

- Exclusion :
  - ECG contraindication to erythromycin (QTc prolong)
  - GCS < 15
  - Shock :
    - persistent decrease in SBP < 90 mm Hg and PR > 110 beats/min, unresponsive to fluid replacement
  - Allergy to erythromycin
  - Drugs interaction with erythromycin (tegretol, ergonomine, theophylline)
  - Pregnancy
  - Previous gastrectomy

INTERVENTIONS
RANDOMIZED PATIENTS INTO ONE OF 3 GROUPS

- **erythromycin iv** (250 mg during 20 minutes) and underwent endoscopy 30 minutes after the end of the infusion
- **NG replacement with gastric lavage**
  - 500 ml of water at room temperature and repeated every hour until the aspirated gastric fluid was clear, and endoscopy was performed 15 minutes after the last irrigation
- **Combined group**

END POINT

- Primary end-point:
  - the quality of gastrointestinal tract visualization,
    - Scoring system by Frossard et al
    - 4 areas (fundus, corpus, antrum, and bulbus) from 0 to 2
      - 0: < 25% of the surface visible
      - 1: 25% ~ 75% visible
      - 2: > 75% visible
    - The total score was the sum of the 4 individual scores and ranged from 0 to 8.
    - A total score of 6 or more indicated a satisfactory stomach visualization and a score below 6 an unsatisfactory visualization
- Secondary end point
  - outcomes until day 30,
  - duration of the endoscopic procedure
  - number of endoscopic hemostasis procedures,
  - ability to identify the source of bleeding,
  - adverse effects related to erythromycin infusion or nasogastric tube placement
  - number of transfused blood units
  - rebleeding, and death

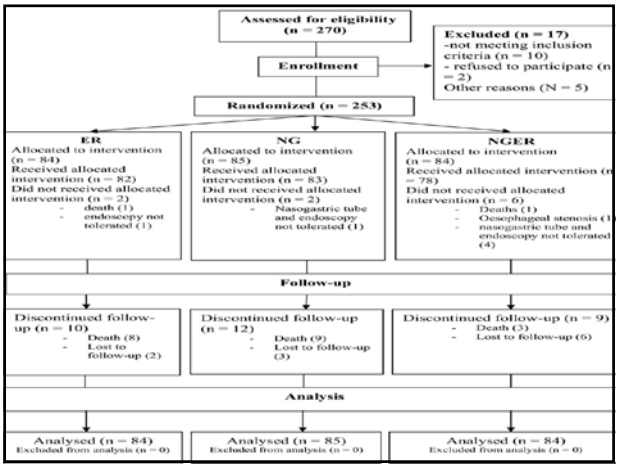

Table 2. Endoscopic features and treatment in each group.*

Endoscopic Features and Treatment	No. (%) or Median (IQR)			Difference (95% CI)		
	ER (N=84)	NG (N=85)	NGER (N=84)	ER vs NG	ER vs NGER	NG vs NGER
Endoscopic score	8 (8, 8)	8 (7, 8)	8 (7, 8)	0	0	0
Interval between onset of bleeding and endoscopy, h	5.3 (3, 12.5)	6.4 (2.8, 13.3)	5. 1 (3.2, 11.2)	−1.1 (−4.2 to 2.2)	0.2 (−2.1 to 2.4)	1.3 (−1.8 to 4.3)
Endoscopic findings						
Esophageal varices	25 (30)	30 (36)	31 (39)	−5.7 (−20.0 to 8.7)	−9.3 (−24.0 to 5.5)	−3.6 (−18.6 to 11.4)
Ulcer	36 (22)	24 (14)	31 (20)	7.5 (−0.8 to 15.8)	2.1 (−6.8 to 11.0)	−5.4 (−13.7 to 2.8)
Gastritis	8 (10)	20 (24)	19 (24)	−14.3 (−25.6 to −3.1)	−14.6 (−26.1 to −3.1)	0.3 (−13.0 to 13.5)
Mallory-Weiss syndrome	4 (5)	3(4)	3 (4)	1.3 (−4.9 to 7.4)	1.0 (−5.3 to 7.4)	0.2 (−5.6 to 6.1)
Other	11 (13)	9 (11)	8 (10)	2.6 (−7.4 to 12.5)	3.2 (−6.8 to 13.2)	0.6 (−8.9 to 10.1)
Empty stomach	69 (84)	68 (82)	69 (89)	2.2 (−9.2 to 13.7)	−4.3 (−14.9 to 6.3)	−6.5 (−17.4 to 4.4)
Hemostatic treatment	31 (38)	28 (34)	34 (44)	4.5 (−10.1 to 19.2)	−5.3 (−20.6 to 10)	−9.9 (−24.8 to 5.1)
Ability to identify the source of bleeding	64 (78)	65 (78)	66 (85)	0.3 (−12.3 to 12.9)	−6.6 (−18.6 to 5.5)	−6.3 (−18.3 to 5.6)
Duration of endoscopy (min)	10 (7, 16)	12 (7, 15)	14 (10, 20)	−2 (−5 to 4)	−4 (−5 to 3)	−2 (−5 to 5)
Need for a second endoscopy	14 (20)	20 (26)	17 (23)	−6.3 (−19.7 to 7.2)	−3.6 (−17.0 to 9.8)	2.7 (−11.1 to 16.5)

IQR, Interquartile range.
*There were no significant differences between groups for any variable.

Table 3. Patients with a clean gastrointestinal tract in subgroup analyses.

Patients	No. (%)			Difference (95% CI)		
	ER (N=84)	NG (N=85)	NGER (N=84)	ER vs NG	ER vs NGER	NG vs NGER
With cirrhosis	23 (85.2)	20 (71.4)	22 (95.7)	13.8 (−7.7 to 35.2)	−10.5 (−26.3 to 5.3)	−24.2 (−42.9 to −5.5)
Transfused	47 (82.5)	46 (76.7)*	52 (92.9)*	5.8 (−8.8 to 20.4)	−10.4 (−22.4 to 1.6)	−16.2 (−28.8 to −3.5)
Admitted to ICU	38 (84.4)	39 (78)	39 (88.6)	6.4 (−9.2 to 22.1)	−4.2 (−18.3 to 10.0)	−10.6 (−26.5 to 4.2)

*The percentage of transfused patients with a clean gastrointestinal tract was significantly higher in the NGER group than the NG group (93% versus 77%, P=.021; Breslow-Day test, P=.021).

Table 4. Outcomes.

	No. (%) or Median (IQR)			Difference (95% CI)		
	ER (N=84)	NG (N=87)	NGER (N=84)	ER vs NG	ER vs NGER	NG vs NGER
Number of blood units transfused						
First 24 h	2 (0, 3)	2 (0, 3)	2 (0, 3)	0 (−2 to 2)	0 (−2 to 1)	0 (−2 to 0.5)
First week	2 (0, 4)	2 (0, 4)	2.5 (0, 4.5)	0 (−1.0 to 0.5)	−0.5 (−1.5 to 0)	−0.5 (−1.5 to 1)
First month	2 (0, 4)	2 (0, 4)	3 (0, 5)	0 (−1 to 1)	−1.0 (−2.0 to 0.5)	−1 (−2 to 1)
Rebleeding						
First 24 h	6 (7)	8 (10)	8 (10)	−2.4 (−10.9 to 6.0)	−2.9 (−11.6 to 5.8)	0.5 (−8.7 to 9.7)
First week	13 (16)	17 (20)	19 (23)	−4.5 (−16.0 to 7.0)	−7.1 (−19.0 to 4.7)	−2.6 (−15.0 to 9.7)
First month	19 (23)	18 (21)	19 (23)	1.4 (−11.0 to 13.9)	0 (−12.7 to 12.7)	−1.4 (−13.9 to 11.0)
Deaths						
First 24 h	3 (4)	2 (2)	3 (4)	1.2 (−3.9 to 6.3)	0 (−5.6 to 5.6)	−1.2 (−6.3 to 3.9)
First week	7 (9)	5 (6)	3 (4)	3.1 (−5.4 to 11.5)	5.5 (−2.3 to 13.4)	2.5 (−4.3 to 9.2)
First month	9 (12)	9 (12)	3 (4)	0.3 (−10.0 to 10.6)	8.1 (−0.4 to 16.6)	7.8 (−0.6 to 16.2)
Orientation from the ED						
ICU	46 (55)	52 (61)	48 (58)	−6.4 (−21.3 to 8.4)	−2.4 (−17.4 to 12.6)	−4.0 (−18.8 to 10.8)
ED	22 (26)	23 (27)	18 (21)	−0.9 (−14.2 to 12.5)	4.8 (−8.1 to 17.6)	5.6 (−7.3 to 18.5)
Medical department	14 (17)	10 (12)	17 (20)	4.9 (−5.6 to 15.4)	−3.6 (−15.3 to 8.2)	−8.5 (−19.5 to 2.5)
Return home	2 (2)	0	0	2.4 (−0.9 to 5.6)	2.4 (−0.9 to 5.6)	0

DISCUSSION

- Gastrointestinal visualization by endoscopy in patients with acute upper gastrointestinal bleeding is **not** influenced by the method of patient preparation : ER, NG, ERNG
- **Outcomes in the month** after endoscopy did **not differ** significantly
- **NG** provided **no** additional clinical benefit over **ER** with acute gastrointestinal bleeding

DISCUSSION--2

- The seminal randomized study by Frossard et al
  - A high occurrence of good gastrointestinal tract preparation by **ER** before endoscopy has already been observed in patients with UGI bleeding with placebo
- Carbonell N, Pauwels A, Serfaty L, et al
  - **NGER** also led to an **increase and improved** the quality of endoscopy over **NG alone**
  - Our study did not detect any significant difference in satisfactory stomach visualization frequency with ER and NGER

DISCUSSION--3

- In **transfused/ Cirrhosis** cases: **NGER better than NG**
- Rebleeding and mortality rate: similar in 3 groups

CONCLUSION

Erythromycin infusion might be a good substitute for gastric lavage, avoiding nasogastric tube placement before endoscopy, in ED patients with acute UGI bleeding

YOUNG PATIENTS WITH CHEST PAIN: 1-YEAR OUTCOMES

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BACKGROUND

- Prior studies
  - young adult chest pain patients are at low risk (<1%) for ACS and 30-day follow
    - No known cardiac disease
    - No cardiac risk factors
    - Normal EKG
- Vancouver Rule:
  - patient who can be discharged without additional cardiac testing
    - < 40 y/o
    - Normal ECG
    - No history of myocardial infarction, angina, or nitrate
      - Christenson J, Innes G, McKnight D, et al Ann Emerg Med 2006;47:1-10

BACKGROUND--2

- Hypothesis: patients **younger than 40 years without past cardiac history** and a **normal ECG** are at less than 1% risk for **1-year adverse cardiovascular events**

STUDY DESIGN

- Prospective observational study
- Evaluating ED patients
  - < 40 y/o
  - with ECG for evaluation of potential ACS
    - **for 1-year actual adverse cardiovascular events** (death, AMI, PCI)

PARTICIPENT

- All ED patient with chest pain
- Inclusion:
  - < 40 y/o
  - They had EKG performed
- Exclusion:
  - Cocaine(+)
  - CAD history (+)
  - Cancer (+) with life expectancy < 1 year

Table 1 Demographics and risk factors of study population

	n	%
Sex		
Male	258	42
Female	351	58
Age (y)		
Younger than 25	14	2
25-29	35	6
30-34	237	39
35-39	323	53
Race		
Asian	11	2
Black	423	69
Hispanic	14	2
White	156	26
Other	5	1
Cardiac risk factors		
Tobacco use	157	26
Hypertension	157	26
Family history of early CAD	62	10
Hypercholesterolemia	51	8
Diabetes mellitus	48	8
No. of cardiac risk factors		
None	288	47
1	211	35
2	75	12
>2	35	6

CAD indicates coronary artery disease.

Table 2 Chest pain characteristics

	n	%
Location of chest pain		
Mid chest	275	45
Left arm/left chest	220	36
Right chest	45	7
Epigastrium	13	2
Other/unknown	56	9
Quality		
Pressure/tightness/crushing	234	38
Stabbing	184	30
Aching	74	12
Burning	37	6
Tearing	5	1
Other/unknown	75	12
Radiation of pain		
Left arm	105	17
Neck	34	6
Back	61	10
Right arm	37	6
Other	19	3
Associated symptoms		
Shortness of breath	275	45
Diaphoresis	87	14
Nausea	110	18
Vomiting	48	8
Lightheadedness	97	16
Syncope	16	3
Palpitations	81	13

Table 3 Electrocardiogram interpretation for whole study population

	n	%
Interpretation for ischemia [a]		
Normal	427	70
Nonspecific	117	19
Early repolarization only	15	2
Abnormal but not diagnostic	28	5
Ischemia (known to be old)	3	<1
Ischemia (not known to be old)	14	2
Suggestive of AMI	4	<1
ST elevation		
None	580	95
1-2 mm	26	4
>2 mm	2	<1
ST depression		
None	592	97
0.5-1 mm	12	2
1-2 mm	4	<1
T-wave inversion		
None	521	86
Flattening	41	7
1-5 mm	45	7
>5 mm	1	<1
Hyperacute T waves >5 mm	6	1
Pathologic Q-waves	11	2
Right bundle-branch block	9	1
Left bundle-branch block	3	<1

[a] One was unavailable for review.

Table 4 One-year adverse cardiovascular event rates for the prespecified subgroups

	n	% (95% CI)
No cardiac history with a normal ECG (n = 560)		
All-cause mortality	2	0.4 (0.04-1.3)
AMI	3	0.5 (0.1-1.6)
Percutaneous intervention	2	0.4 (0.04-1.3)
Composite cardiovascular events	6	1.1 (0.4-2.3)
No cardiac history or cardiac risk factors (n = 288)		
All-cause mortality	0	0 (0-1.3)
AMI	1	0.3 (0.01-1.9)
Percutaneous intervention	1	0.3 (0.01-1.9)
Composite cardiovascular events	1	0.3 (0.01-1.9)
No cardiac history or cardiac risk factors, and a normal ECG (n = 269)		
All-cause mortality	0	0 (0-1.4)
AMI	1	0.4 (0.01-2.1)
Percutaneous intervention	1	0.4 (0.01-2.1)
Composite cardiovascular events	1	0.4 (0.01-2.1)
No cardiac history, cardiac risk factors, a normal ECG, and initially normal cardiac markers (n = 268)		
All-cause mortality	0	0 (0-1.4)
AMI	0	0 (0-1.4)
Percutaneous intervention	0	0 (0-1.4)
Composite cardiovascular events	0	0 (0-1.4)

CONCLUSION

- **We found that adults younger than 40 years with chest pain**
  - **No known cardiac history,**
  - **No classic cardiac risk factors**
  - **Normal ECG**

  had a less than 1% risk of 1-year adverse cardiovascular events.
- The addition of cardiac markers (-) at the time of ED arrival reduced the risk of 1-year cardiovascular outcomes even further.
- We believe that this decision rule, if validated, could be used to refer a cohort of young patients for outpatient evaluation of their chest pain, limiting unnecessary hospital admissions