Original Investigation

Erythromycin for Gastric Emptying in Patients Undergoing General Anesthesia for Emergency Surgery A Randomized Clinical Trial

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IMPORTANCE Patients undergoing emergency procedures under general anesthesia have impaired gastric emptying and are at high risk for aspiration of gastric contents. Erythromycin has strong gastric prokinetic properties.

OBJECTIVE To evaluate the efficacy of erythromycin lactobionate in gastric emptying in patients undergoing emergency surgery.

DESIGN, SETTING, AND PARTICIPANTS The Erythro-Emerge trial was a single-center, randomized, double-blinded, placebo-controlled clinical trial in patients undergoing emergency surgery under general anesthesia at Geneva University Hospitals. We included 132 patients from March 25, 2009, through April 10, 2013, and all patients completed the study. Randomization was stratified for trauma and nontrauma procedures. The randomization code was opened on April 23, 2013, and analyses were performed through July 26, 2013. We performed an intention-to-treat analysis.

INTERVENTIONS Patients were randomized to intravenous erythromycin lactobionate, <u>3 mg/kg</u>, or placebo <u>15 minutes before</u> tracheal intubation. Patients were followed up for 24 hours.

MAIN OUTCOMES AND MEASURES The primary outcome was a clear stomach, defined as less than 40 mL of liquids and no solids and identified through endoscopy immediately after intubation. The secondary outcome was the pH level of residual gastric content.

RESULTS A clear stomach was diagnosed in 42 of 66 patients (64%) receiving placebo compared with 53 of 66 patients (80%) receiving erythromycin (risk ratio, 1.26 [95% CI, 1.01-1.57]). In the population undergoing surgery for nontrauma, the association between receipt of erythromycin and having a clear stomach (adjusted odds ratio [95% CI]) was statistically significant (13.4 [1.49-120]; P = .02); in the population undergoing surgery for trauma, it was not (1.81 [0.64-5.16]; P = .26). Median (interquartile range) pH of the residual gastric liquid was 2 (1-4) in 36 patients receiving placebo and 6 (3-7) in 16 receiving erythromycin (P = .002). Patients receiving erythromycin had nausea (20 [30%] vs 4 [6%]) and stomach cramps (15 [23%] vs 2 [3%]) more often than those receiving placebo. One patient receiving erythromycin vomited before induction of anesthesia.

CONCLUSIONS AND RELEVANCE In patients undergoing general anesthesia for emergency procedures, erythromycin administration increased the proportion with a clear stomach and decreased the acidity of residual gastric liquid. Erythromycin was particularly efficacious in the nontrauma population. Adverse effects were minor. Further large-scale studies are warranted to confirm the potential of erythromycin to reduce the incidence of bronchoaspiration in patients undergoing emergency surgery.

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n the United States, approximately 40 million patients undergo general anesthesia each year,¹ and approximately 12 000 experience bronchoaspiration.² Bronchoaspiration of gastric juice may lead to acute respiratory distress syndrome,³ which carries a 40% mortality rate.⁴ The risk is increased 10-fold in patients undergoing emergency surgery.⁵ Patients admitted for trauma may have ingested food before their accident or may have swallowed blood from oral or nasal injuries. Also, gastric emptying is delayed owing to head injury, stress, pain, and opioid medication.⁶⁻⁹ Patients admitted for nontrauma may have delayed gastric emptying owing to paralytic ileus, critical illness, or cytokine release, leading to significant residual stomach content even after long fasting periods.^{10,11}

Strategies have been proposed to decrease the risk for bronchoaspiration. The efficacy and the safety of digital pressure on the cricoid cartilage to occlude the upper esophagus during tracheal intubation¹² have been challenged.¹³ Because nonacidic gastric liquid is considered less deleterious,^{14,15} premedication with antacids, histamine, receptor antagonists, or proton pump inhibitors has been advocated.^{15,16} Another approach would be to facilitate gastric emptying or drainage. Clearly, a patient with an entirely empty stomach cannot regurgitate and aspirate through the trachea. Stomach drainage with a gastric tube¹⁷ does not guarantee complete emptying. Also, preoperative insertion of a gastric tube in a nonsedated patient is not without hazards18 and is only recommended in patients with bowel obstruction. An alternative would be to administer a prokinetic drug before induction of anesthesia.¹⁹ Erythromycin, a macrolide antibiotic and motilin receptor agonist, induces antral contractions²⁰⁻²² and increases the lower esophageal sphincter tone,²³⁻²⁶ which is an important barrier against gastroesophageal reflux.²⁷ Although the gastric emptying properties of erythromycin have been confirmed in various settings,²⁸⁻³⁶ the efficacy of erythromycin in patients undergoing emergency surgery has never been investigated, to our knowledge. We aimed to investigate whether erythromycin clears the stomach of patients undergoing general anesthesia for emergency surgery.

Methods

Study Design

The Erythro-Emerge trial was a single-center, randomized, placebo-controlled, double-blinded clinical trial. Participants were stratified into those undergoing trauma-related surgery (trauma population) and surgery for medical reasons (eg, acute abdomen) (nontrauma population). The protocol was approved by the commission central d'éthique de la recherché sur l'être humain, le comité départemental d'éthique (protocol NAC 06-225) and the Swiss Agency for Therapeutic Products (Swissmedic reference 2008 DR 2321), inspected by Swissmedic, and monitored by the Clinical Trials Centre of Geneva University Hospitals. A copy of the study protocol is found in Supplement 1. Written informed consent was obtained from all patients.

Patients

Adult patients who required general anesthesia for emergency surgery were eligible. Exclusion criteria were American Society of Anesthesiology physical status³⁷ of greater than 3; allergy to erythromycin; concomitant use of drugs interfering with erythromycin metabolism (eg, terfenadine); intermittent porphyria; severe liver or renal disease; severe asthma, exacerbated chronic obstructive lung disease, or acute pulmonary infection; acute coronary heart disease, decompensated cardiac insufficiency, or aortic aneurysm; esophageal and pharyngeal disease; status after gastric surgery; the need for an immediate surgical intervention; Glasgow Coma Scale score less than 13; inability to understand the study protocol; obstructive ileus; presence of a gastric tube; and pregnancy or breastfeeding among women.

Randomization and Masking

The Geneva Universities Hospitals Pharmacy performed randomization (ratio, 1:1) and prepared study medications in numbered 10-mL syringes of erythromycin lactobionate, 3%, and matching placebo (physiological saline). The content of a syringe was added to 90 mL of physiological saline. Of this solution, 1 mL/kg body weight was administered intravenously for 5 minutes (corresponding to a 3-mg/kg dose of erythromycin).³⁶ The allocation sequence was concealed until the study end.

Procedures

We randomized patients who had not received premedication to the study drugs on arrival in the operating room. Fifteen minutes after administration of the study drug, patients underwent preoxygenation for 3 minutes. General anesthesia was induced with a classic rapid-sequence procedure^{38,39} and maintained at the discretion of the attending anesthetist. Immediately after intubation, 1 of 3 senior gastroenterologists (J.-L.F., E.G., or L.S.) performed an endoscopy (GIF; Olympus) for qualitative and quantitative assessment of gastric content. The working channel of the endoscope (inner diameter, 9 mm) was used to aspirate gastric liquid. The volume of the aspirate was quantified using a milliliter-graded recipient, and when gastric content (ie, solid food, mixture of liquid and food) could not be aspirated, it was visually estimated (the opened forceps of the endoscope measures 7 mm in diameter; the volume of solid food was estimated as a multiple of this diameter).

Outcomes

Because we had no consistent definition of what should be considered gastric emptying or clear stomach in patients undergoing surgery,⁴⁰ we defined clear stomach as a residual volume of less than 40 mL and the absence of solid food. We performed a sensitivity analysis using clear stomach definition 2 as no liquid and no solid as an alternative, more stringent definition of clear stomach. The secondary end point was the acidity (measured using pH indicator strips 0-14; Merck) of residual stomach contents. Additional end points were the volume and composition of residual gastric content (ie, liquid only, solid only, mixture of liquid and solid), delay from

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the last oral intake to the time of endoscopy, and preoperative opioid and antacid medication. In the trauma population, we computed an Injury Severity Score.⁴¹ In the nontrauma population, the diagnosis was recorded. Because patients undergoing emergency procedures are likely to have stress-induced hyperglycemia, which may reduce erythromycin-induced acceleration of gastric emptying,⁴² we measured blood glucose levels (Contour blood glucose meter; Bayer).

Safety end points included arrhythmia,⁴³ stomach cramps, and nausea or vomiting before induction of anesthesia. Patients were visited 24 hours after administration of the study drug and monitored for any adverse effects that could have occurred in relation to the study.

Sample Size

Based on a trial that evaluated the efficacy of erythromycin in patients with gastrointestinal tract bleeding,³⁶ we assumed a baseline incidence of 30% clear stomach with placebo and expected that erythromycin would increase this proportion to 80% (absolute risk difference, 50%). A sample of 20 patients per group was required (90% power; 2-sided test; type I error of .05). To allow for dropouts and enable subgroup analyses (trauma vs nontrauma populations), we intended to randomize 100 patients (25 for each stratum).

After randomization of 100 patients, an estimation of the baseline incidence of clear stomach in our study population (without opening the randomization code) showed that 76% of patients had clear stomach. Therefore, if erythromycin was 100% efficacious, the incidence of clear stomach with placebo could not have been less than 52% (76 - 50 = 26; 26/ 50 = 0.52), which was greater than we expected.³⁶ In addition, seeking an absolute increase of 50% in the incidence of clear stomach with erythromycin had become illusory. We consequently revised the initial power calculation to assume a baseline incidence of clear stomach of 50% but still to maintain the aim of increasing that incidence to 80% with erythromycin. We randomized an additional 32 patients (16 per group) to reach 90% power to detect this smaller absolute risk difference (2-sided test; type I error of .05). The protocol was amended accordingly and approved by the institutional ethics committee and Swissmedic.

Statistical Analysis

The data sets were held securely in a linked, deidentified form and analyzed at the Division of Anesthesiology, Geneva University Hospitals. The crude association between exposure to the study treatment and the primary end point was analyzed and reported using odds ratios (ORs) or risk ratios with 95% CIs. We analyzed crude associations between all potential confounding variables and the primary end point in the placebo group separately. Each variable that was associated with the primary end point in the placebo group was entered into a bivariate logistic regression model, including study treatment and primary end point. We compared crude and adjusted estimates to assess the degree of potential confounding. When the crude and adjusted estimates differed by more than 10%, the variable was included in a final multivariate model, including all potential confounders. We tested the effect of each variable on the fit of the model using a likelihood ratio test. If the *P* value of the test was less than .10, the potential confounder was kept in the model; otherwise it was excluded. Interaction between populations (trauma vs nontrauma) and study treatment was tested by introducing an interaction term into the model; if the fit of the model to the data was increased by the interaction term, the results were presented separately for the 2 strata. Sensitivity analyses using clear stomach definition 2 were performed in a similar manner. Continuous secondary end points were compared using a nonparametric test of equality of distributions. We compared adverse effects using univariate analysis and reported the results as ORs with 95% CI. Analyses were performed with commercially available statistical software (STATA, Release 11; StataCorp LP).

Results

Patients

From March 25, 2009, through April 10, 2013, we randomized 66 patients admitted for trauma and 66 patients admitted for nontrauma to receive erythromycin or placebo (**Figure 1**). All patients received the assigned study treatment, and all underwent endoscopy and evaluation of the primary end point. All analyses were based on intention to treat. The 2 groups were balanced regarding baseline characteristics (**Table 1**).

Outcomes

Clear stomach defined as less than 40 mL of liquid and no solid content was diagnosed in 42 of 66 patients receiving placebo (64%) and in 53 of 66 receiving erythromycin (80%) (risk ratio, 1.26 [95% CI, 1.01-1.57]) (**Figure 2**). Clear stomach defined as no liquid and no solid content was diagnosed in 24 of 66 patients (36%) receiving placebo and in 40 of 66 receiving erythromycin (61%) (risk ratio, 1.67 [95% CI, 1.15-2.42]) (Figure 2).

Multivariate Analyses

Variables associated with the primary end point in the placebo group were the study population (trauma vs nontrauma), age, body weight, blood glucose level, delay since the last oral intake, and preoperative opiate use (**Table 2**). In a bivariate logistic regression model, body weight and delay from the last oral intake to endoscopy changed the crude OR point estimate by more than 10%. When these variables were included in the multivariate model, the association between erythromycin and clear stomach increased (adjusted OR, 2.96 [95% CI, 1.28-6.83]). Introducing an interaction term between the population (trauma vs nontrauma) and study treatment significantly increased the fit of the model to the data; the impact of erythromycin was different according to the population studied.

Trauma vs Nontrauma Populations

In the trauma population, the median time since the last meal was about 7 hours and since the last liquid intake was about 9 hours (eTable 1 in Supplement 2); 83% had received opiates and 8% had received antacids. The median Injury Severity Score was 4 (interquartile range, 4-9). Of 41 trauma patients with re-

Figure 1. CONSORT Diagram of the Erythro-Emerge Trial



Details of the study treatments are given in the Randomization and Masking subsection of the Methods section.

sidual gastric content, 21 (51%) had liquid only and 20 (49%) had solid only or a mixture of liquid and solid (eTable 2 in Supplement 2). The association between erythromycin and clear stomach was not statistically significant (adjusted OR, 1.81 [95% CI, 0.64-5.16]; *P* = .26) (Table 2).

In the nontrauma population, the median time since the last meal was 20.3 hours; the median time since the last liquid intake ranged from 13.4 to 17.2 hours (eTable 1 in Supplement 2); 14 patients (21%) had received opiates and 31 (47%) had received antacids (eTable 1 in Supplement 2). In the nontrauma population, 54 patients (82%) underwent surgery for acute appendicitis or cholecystitis. Of the 27 nontrauma patients with residual gastric content, 24 (89%) had liquid only and 3 (11%) had solid only or a mixture of liquid and solid (eTable 2 in Supplement 2). The association between erythromycin and clear stomach was statistically significant (adjusted OR, 13.40 [95% CI, 1.49-120.00]; P = .02) (Table 2).

Sensitivity Analyses

Using clear stomach definition 2 (no liquid and no solid content), only the blood glucose level was associated with the primary end point in the placebo group. Including blood glucose level into a bivariate logistic regression model did not change the OR point estimate by more than 10% (Table 2).

Secondary End Point

The pH of stomach aspirates could be measured in 52 patients. The median (interquartile range) pH was 2 (1-4) in 36 patients receiving placebo and 6 (3-7) in 16 receiving erythromycin (P = .002). A pH of at least 2 was diagnosed in 20 of 36 patients receiving placebo (56%) compared with 1 of 16 receiving erythromycin (6%) (P = .001). Antacids were administered in 11 of 36 patients (31%) receiving placebo in whom gastric pH could be measured, compared with 1 of 16 patients (6%) receiving erythromycin (P = .06). In a logistic regression model describing the binary variable pH of 2 or less or greater than 2 and including antacid intake and study treatment, both vari-

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ables were found to be predictive of pH. The OR (95% CI) for antacid use was 5.71 (1.19-27.40); for erythromycin use, 30.20 (3.38-270.00).

Additional End Points

The median (interquartile range) volume of residual gastric content was 43.5 (15-100) mL in 42 patients receiving placebo and 27.5 (10-75) mL in 26 patients receiving erythromycin (P = .38) (eTable 2 in Supplement 2). Residual volumes tended to be larger in the trauma population (median, 70.0 mL in 23 patients receiving placebo and 50.0 mL in 18 patients receiving erythromycin) compared with the nontrauma population (median, 26.0 mL in 19 patients receiving placebo and 15.5 mL in 8 patients receiving erythromycin) (**Figure 3** and eTable 2 in Supplement 2).

Adverse Effects

Stomach cramps and nausea occurred in 20 (30%) and 15 (23%) patients receiving erythromycin, respectively, compared with 4 (6%) and 2 (3%) patients receiving placebo, respectively (P > .001). One patient in the erythromycin group vomited before induction of anesthesia (eTable 3 in Supplement 2). No episodes of arrhythmia, regurgitation of gastric contents, or bronchoaspiration and no major adverse events occurred.

Discussion

This study is the first, to our knowledge, to show that administration of erythromycin increases the proportion of clear stomach among patients undergoing general anesthesia for emergency surgery. Depending on the definition of clear stomach, the absolute risk reduction ranged from 17% to 24%, equivalent to a <u>number needed to treat</u> of <u>4 to 6</u> patients to produce 1 completely cleared stomach.

Erythromycin also <u>decreased</u> the <u>acidity</u> of stomach liquid. This decrease might be related to erythromycin's inhibitory effect on motilin receptor-mediated acid secretion.³⁴ Animal data indicate that a gastric pH of less than 2.4 increases the risk for lung damage.^{14,44} Also, when gastric fluid is buffered effectively, higher volumes of aspirates are tolerated.^{15,45} We may assume that in patients undergoing surgery, erythromycin will decrease the likelihood of significant lung tissue damage should bronchoaspiration occur, despite the premedication.

Through its prokinetic properties, erythromycin more effectively clears liquids than solids from stomachs.^{28,29} This property may explain why the clearing effect of erythromy-

Table 1. Demographics and Baseline Characteristics	
of All Randomized Patients	

	Treatment Group ^a				
Characteristic	Erythromycin Lactobionate (n = 66)	Placebo (n = 66)			
Age, y	40.5 (31-58)	45.0 (29-55)			
Female sex, No. (%)	22 (33)	21 (32)			
Body measurements					
Weight, kg	74.5 (65-80)	78.0 (70-85)			
Height, cm	172.5 (164-180)	172.5 (169-180)			
BMI	24.3 (22.0-27.7)	25.0 (23.1-27.7)			
Time since last solid meal, h	13.8 (8.0-20.7)	16.0 (7.0-24.5)			
Time since last liquid intake, h	8.5 (6.3-16.1)	8.8 (6.0-18.3)			
Pain score on visual analog scale ^{b,c}	40 (10-50)	25 (10-50)			
Patients with diabetes mellitus, No. (%)	2 (3)	3 (5)			
Blood glucose level, mg/dL $^{\rm b}$	102.7 (92-115)	104.5 (92-117)			
Received opiate preoperatively, No. (%)	34 (52)	35 (53)			
Received antacid preoperatively, No. (%)	16 (24)	20 (30)			

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range.

SI conversion factor: To convert glucose to millimoles per liter, multiply by 0.0555.

^a Unless otherwise indicated, data are expressed as median (interquartile range).

^b Measured at arrival in the operating room.

^c Ranges from 0 to 100. Higher scores indicate greater pain intensity.

Figure 2. Risk Ratio (RR) for the Primary Outcome

	No. (%) of Patients						
Patient Group	Placebo	Erythromycin Lactobionate	RR (95% CI)	P Value ^a	Favors Favors Placebo Erythromyci	Favors Erythromycin	
All (N=132)							
Clear stomach, definition 1	42 (64)	53 (<mark>80</mark>)	<mark>1.26</mark> (1.01-1.57)	.052	le-l		
Clear stomach, definition 2	24 (36)	40 (61)	1.67 (1.15-2.42)	.009	⊢●⊣		
Trauma (n=66)							
Clear stomach, definition 1	17 (52)	21 (64)	1.23 (0.81-1.88)	.46	⊢ ●–1		
Clear stomach, definition 2	10 (30)	15 (46)	1.50 (0.79-2.84)	.31	⊢ •−1		
Nontrauma (n = 66)							
Clear stomach, definition 1	25 (76)	32 (97)	1.28 (1.05-1.57)	.03	•		
Clear stomach, definition 2	14 (42)	25 (76)	1.79 (1.15-2.78)	.01	⊢⊷⊣		
					0.1 1 1 RR (95% CI)	0	

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cin appeared to be particularly strong in the nontrauma population. In these patients, the delay from the last oral intake to induction of anesthesia was longer compared with that in the trauma population because the former group sometimes waited long periods with no oral intake until a diagnosis was confirmed and they were finally scheduled for surgery. In patients undergoing emergency surgery, liquid may accumulate in the stomach during fasting.

Our study has strengths and weaknesses. One strength of our study is the randomization, which ensures a balanced distribution of potential known and unknown confounding factors and may explain why we found only 2 variables (body weight and delay from the last oral intake to endoscopy) influencing the crude OR by more than 10%. Future studies may identify other factors associated with gastric content that may act as confounders, despite the randomization (eg, volume of the last meal, presence of gastroparesis). Another strength was the use of endoscopy to evaluate gastric content. Estimation of the volume of gastric content with aspiration through nasogastric tubes underestimates the volume of residual gastric liquid.^{46,47} Also, endoscopy allows for visual inspection of the gastric cavity and evaluation of solids.

Our study has several weaknesses. First, we did not include patients with mechanical ileus or patients needing immediate emergency surgery. Most patients in the nontrauma population had acute appendicitis or cholecystitis. Because appendectomy is the most common emergency general surgical procedure,⁴⁸ we may assume that our nontrauma cohort represented daily clinical practice in an emergency center and that our results are likely to be representative of this population. However, trauma patients had a low median Injury Severity Score, indicating mostly minor trauma. Second, we tested a single erythromycin regimen only. An erythromycin lactobionate dose of 1.5 mg/kg enhanced fasting gastric tone, but a dose of 3.0 mg/kg, as in our trial, reduced the duration of meal-induced relaxation.^{22,49,50} In a dose-finding study, 3.0 mg/kg was the most effective regimen to enhance gastric emptying in healthy individuals with a reasonable adverse effect profile. In patients undergoing surgery, no dose-finding study has been performed so far. Whether higher doses would further increase efficacy or whether smaller doses, which may have a better adverse effect profile, are still efficacious

> Definition 1 for clear stomach Indicates less than 40 mL of liquid content and no solid content; definition 2, no liquid or solid content.

^a Calculated as a 2-sided Fisher exact test.

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Table 2. Adjusted Outcomes

	Clear Stomach ^a								
	Definition 1, Placebo Group ^b			Definition 1			Definition 2		
Variable	No. of Patients	OR (95% CI)	P Value	No. of Patients	Adjusted OR (95% CI) ^c	P Value	No. of Patients	Adjusted OR (95% CI) ^c	P Value
Crude OR ^c	NA	NA	NA	132	2.33 (1.06-5.12)	.04	132	2.69 (1.33-5.44)	.006
Variable associated with clear stomach in placebo group									
Trauma, present or absent	66	0.34 (0.12-0.97)	.04	132	2.58 (1.12-5.96)	.03	132	2.84 (1.37-5.86)	.005
Age, y	66	0.96 (0.93-1.00)	.03	132	2.33 (1.05-5.21)	.04	NA	NA	NA
Body weight	66	1.04 (1.00-1.08)	.05	132	2.60 (1.16-5.85)	.02	NA	NA	NA
Blood glucose level	66	0.41 (0.23-0.73)	.003	132	2.31 (1.02-5.27)	.046	132	2.65 (1.30-5.39)	.007
Delay since last oral intake	66	1.05 (0.99-1.10)	.10	132	2.63 (1.17-5.94)	.02	NA	NA	NA
Preoperative opiate use, yes compared with no	66	0.41 (0.14-1.17)	.10	132	2.43 (1.07-5.50)	.03	NA	NA	NA
Adjusted OR ^d	NA	NA	NA	132	2.96 (1.28-6.83)	.01	NA	NA	NA
Trauma	NA	NA	NA	66	1.81 (0.64-5.16)	.26	NA	NA	NA
Nontrauma	NA	NA	NA	66	13.40 (1.49-120.00)	.02	NA	NA	NA

Abbreviations: NA, not applicable; OR, odds ratio.

^a Definition 1 for clear stomach indicates less than 40 mL of liquid content and no solid content; definition 2, no liquid or solid content.

^b Variables that were shown to be associated with the primary outcome in the

placebo group were entered into a bivariate logistic regression model that included study treatment and primary outcome.

^c The OR compares erythromycin lactobionate with placebo.

^d Adjusted for body weight and delay since last oral intake.



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remains unknown. Third, perhaps erythromycin should be given earlier. After administration of erythromycin, halftimes of gastric emptying after a solid meal reportedly ranged from 40 minutes²⁹ to 160 minutes.²⁸ Fourth, our choice of the primary end point may be debated. Clear stomach is a surrogate end point because only the prevention of bronchoaspiration is of clinical relevance. No episodes of regurgitation or bronchoaspiration occurred in our study population. However, our study was not powered to quantify these more severe, but much less frequent, events, and patients who have no liquid and no solid stomach content should not be able regurgitate and subsequently aspirate gastric content into their lungs. Fifth, stomach content at the end of surgery remained unknown. Gastric liquid may be secreted during surgery and result in bronchoaspiration at extubation. However, prokinetic properties of ervthromycin persist to 2 hours in the presence of gastric content.51,52 Whether pretreatment with erythromycin decreases the risk for perioperative bronchoaspiration, and thus for pulmonary complications, in nonfasting patients undergoing emergency surgery remains to be shown formally. Finally, we did not investigate the occurrence of postoperative infection. As with all macrolide antibiotics, induction of bacterial resistance remains a concern. We believe that this concern remained theoretical. We gave a single dose of erythromycin lactobionate, and the dose was low compared with a standard antibiotic treatment (1-4 g/d).

We observed stomach cramps and nausea, and 1 patient vomited during study drug perfusion. These drug-related adverse effects are unlikely to prevent clinicians from administering premedication with erythromycin in patients undergoing emergency surgery. A longer administration time is likely to reduce these risks because they correlate with plasma concentrations of erythromycin.⁵³ No allergic reactions or episodes of symptomatic cardiac arrhythmia occurred; postoperative electrocardiography was not performed systematically. These results are in accordance with the results of other singledose erythromycin studies.^{33,36,54} In elderly individuals, coprescription of erythromycin with a statin metabolized through cytochrome P450 isoenzyme 3A4 was shown to increase the toxic effect of statins.⁵⁵ Whether these data may be extrapolated to our study remains unclear.

The research agenda includes testing the efficacy of erythromycin in additional surgical populations, for instance, as in children, or as in women who are undergoing emergency cesarean section. Because erythromycin seemed more effective in producing a clear stomach in a nontrauma compared with a trauma population, performance of liquid- and solidphase gastric emptying studies in nontrauma populations would be of interest. These studies would help to confirm the differential effects on solid vs liquid gastric emptying. Endoscopy should be used to evaluate residual stomach content qualitatively and quantitatively. To confirm the potential of erythromycin to reduce the incidence of bronchoaspiration in patients undergoing emergency surgery, a large-scale study is warranted with perioperative regurgitation and bronchoaspiration and its consequences as main outcomes.

Conclusions

In patients undergoing general anesthesia for emergency procedures, erythromycin increased the proportion of clear stomach and decreased acidity of residual gastric liquid. Erythromycin was particularly efficacious in the nontrauma population. Adverse effects were minor. Further large-scale studies are warranted to confirm the potential of erythromycin to reduce the incidence of bronchoaspiration in patients undergoing emergency surgery.

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