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Gastric pH and motility in a porcine model of acute lung injury using a wireless motility capsule

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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Summary

Background:

Evaluation of gastric pH and motility in a porcine model of acute lung injury using a novel, wireless motility capsule.

Material/Methods:

A motility capsule was applied into the stomach of 7 Pietrain pigs with acute lung injury induced by high volume saline lavage. Wireless transmission of pH, pressure and temperature data was performed by a recorder attached to the animal's abdomen. Gastric motility was evaluated using pH and pressure values, and capsule location was confirmed by autopsy.

Results:

Gastric pH values were statistically significantly different ($P < 0.003$) in the animals over time and ranged from 1.15 to 9.94 [5.73 ± 0.47 (mean \pm SD)] with an interquartile range of 0.11 to 2.07. The capsule pressure recordings ranged from 2 to 4 mmHg [2.6 ± 0.5 mmHg (mean \pm SD)]. There was no change in pressure patterns or sudden rise of pH > 3 pH units during 24 hours. All animals had a gastroparesis with the capsules located in the stomach as indicated by the pressure and pH data and confirmed by necropsy.

Conclusions:

The preliminary data show that Pietrain pigs with acute lung injury have a high variability in gastric pH and severely disturbed gastric motility.

key words:

motility capsule • gastric motility • animal model • gastrointestinal function

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BACKGROUND

Critically ill patients who are sedated and mechanically ventilated are likely to have gastrointestinal complications and motility disturbances [1–3]. Many methods used to determine gastric motility in the critical care setting are unreliable or impractical [4]. A newly developed motility capsule (Figure 1) for assessing gastric emptying in patients with suspected gastroparesis has been available since 2006 [5,6]. It is a wireless capsule that transmits pH, pressure, and temperature to a data recorder. This system detects gastric emptying by recording the abrupt rise of pH by more than 3 units that normally accompanies transition of the capsule into the duodenum with its pH of near 6.

Critically ill patients have a high variability in gastric pH, especially during enteral feeding [7–9], which could complicate detection of the capsule's arrival into the duodenum. The gastrointestinal physiology of the pig resembles that of humans in respect to gastric pH variability. In non-fasting pigs, the pH averages 4 to 5. We thus evaluated gastric pH and motility using a motility capsule in a swine model of acute lung injury over 24 hours. Specifically, we tested the hypothesis that motility capsules detect gastroparesis despite the variability in gastric pH associated with acute lung injury.

MATERIAL AND METHODS

This experimental study was approved by the Laboratory Animal Care and Use Committee of the District of Unterfranken, Germany and adheres to the NIH guidelines for ethical animal research.

The experiment was part of a study investigating different ventilation strategies in a large animal model of ARDS that has been validated and recently published [10]. Experiments were performed on 7 healthy female Pietrain pigs (53.7±3.9 kg) over a 24-hour period. Shortly after intramuscular premedication with ketamine (10 mg/kg), an intravenous line was obtained and the animals were anesthetized with continuous infusion of 5–10 mg/kg thiopental and 0.01 mg/kg/h fentanyl throughout the experiment. Neuromuscular block was achieved by continuous infusion of 0.1 mg/kg/h pancuronium. The trachea was intubated with a cuffed 8.5 mm ID endotracheal tube with an additional side lumen ending at the tip (Rueschelit®, Ruesch, Kernen, Germany). Severe ARDS was induced by bilateral pulmonary lavages with 30 mL/kg isotonic saline (38°C), repeated every 10 minutes until PaO₂ decreased to less than 60 mmHg and remained stable for 60 minutes with unchanged ventilator settings. On average, 7±2 lavages with approximately 12 L saline per animal were necessary for ARDS induction. The lungs were ventilated with high-frequency oscillation. A pH, pressure and temperature sensing capsule (SmartPill™, SmartPill Corp., Buffalo, NY) was positioned endoscopically with a capsule delivery device (AdvanCE™, US Endoscopy, Mentor, OH) into the stomach. The capsule data were transmitted to a recorder attached to the abdomen. MotiliGI software (MotiliGI 1.3.1, SmartPill, Inc.) was used to calculate gastric emptying of the capsule by measuring the time required for the pH to change from the acidic stomach to the alkaline duodenum, as well as a change in pressure patterns prior to emptying. Gastroparesis was defined by a gastric emptying time exceeding 5 hours [11]. Pressure



Figure 1. SmartPill® GI Monitoring Capsule.

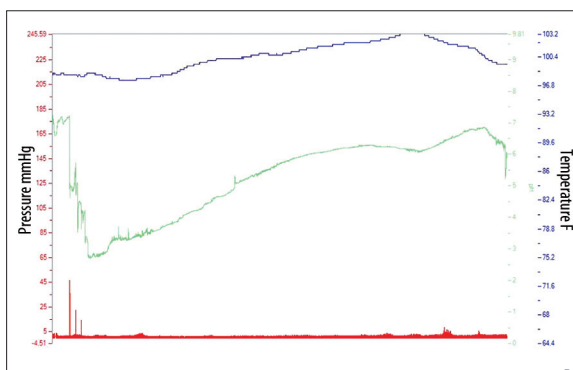


Figure 2. SmartPill pH, pressure and temperature tracing in one pig over 24 hours. The pH tracing is shown in green, the pressure tracing in red and the temperature in blue.

patterns are characterized as mean peak amplitude and mean contractions per minute. Mean peak amplitude is the quotient of the sum of amplitudes divided by the number of contractions. The location of the capsule was confirmed by autopsy after the animals were sacrificed after 24 hours.

Statistical analysis

Demographic results are expressed as means ±SDs or counts. Mean peak amplitudes and mean contractions per minute are expressed as median and interquartile ranges. Gastric pH values are summarized as median, interquartile range, minimum and maximum. The Wilcoxon test was used to compare the pH values between each animal over time. The level of significance was adjusted to P<0.003 due to multiple testing. Analysis was conducted with SAS 9.1.3 (The SAS Institute, Cary, NC).

RESULTS

Gastric pH of each animal was statistically significantly different (P<0.003) and ranged from 1.15 to 9.94 [5.73±0.47 (mean ±SD)], with an interquartile range of 0.11 to 2.07. Gastric pH values of each animal are summarized in Table 1. The capsule pressure recordings ranged from 2 to 4 mmHg [2.6±0.5 mmHg (mean ±SD)]. Mean peak amplitude was 1.66 mmHg (IQR=1.65–2.06) and mean contractions per minute was 2.32 (IQR=2.02–3.91). There was no significant (p<0.05) change in pressure patterns and sudden (within minutes) rise of pH >3 pH units within 24 hours. All animals

Table 1. Gastric pH values in pigs. Data are expressed as median (interquartile range), minimum and maximum.

Pig	pH	
	Median (IQR)	Min/max
1	5.71 (4.15–6.22)	2.69/7.34
2	6.75 (6.71–6.82)	6.54/7.11
3	2.84 (2.67–3.52)	2.24/3.94
4	6.65 (5.39–6.94)	4.73/7.09
5	7.28 (6.99–7.35)	1.15/9.94
6	5.59 (4.46–6.35)	4.37/9.58
7	6.65 (5.94–7.27)	1.29/8.65

had a gastroparesis with bloated stomach. All capsules were located in the stomach as indicated by the contraction and pH data and confirmed by necropsy. There were no complications associated with the placement of the capsules and subsequent data collection.

DISCUSSION

Delayed gastric emptying is a well-known problem in critically ill patients [12–16], and is associated with increased gastric residual volumes and inadequate nutritional status. Evaluating gastrointestinal function in critically ill ventilated patients is challenging. Many tests that are used under standardized, controlled conditions do not work in the critical care setting [11,17]. We compared the porcine model with humans because the GI system is similar in size and physiology. Pigs are known to be susceptible to gastroparesis with acute severe gastric dilatation as a cause of sudden death. Our animals were non-fasting and the pH exclusively reflects stomach secretion. The animals were sedated, intubated and ventilated, mimicking most critical care situation with a high probability of gastroparesis and variability in gastric pH. In the present study using the SmartPill motility capsule, the mean pH was 5.73 ± 0.47 , ranging from 1.15 to 9.94. Gastric pH values greater than 7 were measured at the end of the study period. In 1 pig, the pH was initially low (1.15) but after 24 hours drifted to a maximum of 9.94. There was also great variability in pH between each animal (interquartile range of 0.11 vs. 2.07). Previously reported values of stomach pH are similar and have ranged from 1.2 to 8.6 [18]. The same phenomenon occurs in critically ill patients that receive enteral nutrition. The actual effect of enteral nutrition on intragastric pH is variable. In 1 study, enteral nutrition was more effective in raising the pH than were H-2 blockers [19]. Two studies, however, showed no change in gastric pH during enteral feeding [7,8], and 1 study showed a decrease in the pH [9]. Apart from the pH data, the detection of gastric emptying relies on high amplitude pressure contractions and frequency. Gastric intraluminal pressure recordings ranged from 2 to 4 mmHg. There was no increase in contraction amplitude and frequency, suggesting that the capsule had passed through the pyloric sphincter. Gastrointestinal motility is characterized by cyclical patterns in contractions, called the migrating motor complex (MMC), in humans, dogs and pigs. The mechanism

of gastric emptying of a large non-digestible capsule correlates well with the phase III MMC, but also can be unrelated [5,20,21]. Phase III migrating motor complex is characterized by high pressure phasic contractions arising in the stomach and propagating distally into the duodenum. A study with young adult white Yorkshire pigs has shown that the mechanism of gastric emptying of large objects did not correlate with the presumed phasic activity [22]. One study in humans reported gastric emptying of non-digestible solids with no relation to antral phase III motor activity [23]. Despite this unrelated effect, none of the capsules in our study emptied from the stomach. Gastric motility is influenced by many factors, including analgesic requirements, duration of sedation and intestinal blood flow. The adverse effects of analgesia and sedation on gastric emptying are consistent with the inhibition of the motor response by morphine [24–27]. These and other factors were relatively well-controlled among the pigs.

This study is limited by the fact that this is not an established animal model for evaluating gastric motility. We also excluded the influence of enteral nutrition on stomach pH by not feeding the animals during the entire 24 hours. Another limitation seems to be that there never was any detection of transition of the capsule into the duodenum. The capsules did not empty from the stomach during the entire study period. Finally, gastrointestinal motility was measured for only 24 hours; we therefore cannot make any statements about intestinal function later in the critical care course.

CONCLUSIONS

Our findings in this large animal model show that Pietrain pigs with acute lung injury have a high variability in gastric pH and severely disturbed gastric motility within 24 hours, detected by motility capsule technology. Further studies are needed to evaluate the usefulness of motility capsules in the critical care setting.

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