Clinical Nutrition xxx (2015) 1–4

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Gastric feeding intolerance is not caused by mucosal ischemia measured by intragastric air tonometry in the critically ill

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ARTICLE INFO

Article history:
Received 13 January 2015
Accepted 22 May 2015

Keywords:
Intragastric tonometry
PCO_2 gap
Enteral nutrition intolerance
Gastric residuals
Gastric ischemia
Critically ill

SUMMARY

Background: Gastric mucosal ischemia may be a risk factor for gastrointestinal intolerance to early feeding in the critically ill.
Aims: To study intragastric PCO_2 air tonometry and gastric residual volumes (GRV) before and after the start of gastric feeding.
Methods: This is a two-center study in intensive care units of a university and teaching hospital. Twenty-nine critically ill, consecutive and consenting patients scheduled to start gastric feeding were studied after insertion of a gastric tonometry catheter and prior to and after start of gastric feeding (500 ml over 1 h), when clinically indicated.
Results: Blood gasometry and intragastric tonometry were performed prior to and 2 h after gastric feeding. The intragastric to arterial PCO_2 gap (normal <8 mm Hg) was elevated in 41% of patients prior to feeding and measured (mean ± standard deviation) 13 ± 20 and 16 ± 23 mm Hg in patients with normal (<100 ml, 42 ± 34 ml, $n = 19$) and elevated GRV (250 ± 141 ml, $n = 10$, $P = 0.75$), respectively. After feeding, the gradient did not increase and measured 27 ± 25 and 23 ± 34 mm Hg, respectively ($P = 0.80$).
Conclusion: Gastric mucosal ischemia is not a major risk factor for intolerance to early gastric feeding in the critically ill.

1. Introduction

It is generally recommended to start enteral nutrition (EN) as early as possible in the critically ill. Nevertheless, the intolerance to early gastric feeding may exceed 50% of patients, as manifested by large residues (usually defined as >100 ml) in the stomach after start of feeding, thereby hampering its efficiency. The risk factors for intolerance to enteral feeding, which are only partly preventable, are high-dose vasopressor therapy in the treatment of shock, use of deep sedation and opioids during mechanical ventilation, post abdominal surgery, and others [1–3]. In addition, gastrointestinal hypoperfusion, ischemia and acid–base disturbances have been suggested to impair gastrointestinal motility and thereby to induce intolerance of enteral feeding, but there is no objective evidence for this hypothesis and enteral feeding may even increase gut blood flow and oxygen balance as judged from intragastric luminal PCO_2 tonometry [1–6]. The latter is a minimally invasive and well documented method to measure the intragastric to arterial PCO_2 difference as an index of gastrointestinal mucosal hypoperfusion (normal values are <8 mm Hg and higher values denote hypoperfusion) [5,7–9]. It has mainly been used to monitor and guide treatment of shock [9]. Usually tonometry is done in the empty stomach after suppression of acid secretion [7,10]. Gastric feeding has a variable effect on intragastric tonometric variables, even when the stomach has emptied [4,6,7,10].

The current study was designed to test the hypothesis that gastric ischemia plays a role in the pathophysiology of intolerance to gastric feeding in the critically ill patient. We therefore performed intragastric tonometry before and after scheduled start of gastric feeding, on clinical grounds, in 30 patients in the intensive care unit (ICU).

2. Patients and methods

The protocol has been approved of by the medical ethical committee of the VU University Medical Centre (VUmc), Amsterdam, The Netherlands. It was performed in the general six-bed ICU

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http://dx.doi.org/10.1016/j.clnu.2015.05.015

of the Bronovo Ziekenhuis, a teaching hospital in The Hague, The Netherlands, by the principal investigator after leaving the VUmc having started the study in the general 30-bed ICU of this university hospital. Patients' next of kin gave informed consent prior to the study. Inclusion criteria were the clinical need to start EN and age above 18 years. Pregnancy and preterminal illness were exclusion criteria. Thirty consecutive patients were included. When the clinical need for start of gastric feeding (Nutrison standard, Nutricia/Danone, Zoetermeer, Netherlands) was determined, patients received esomeprazole 40 mg intravenously to suppress gastric acid secretion [7,9]. A specially constructed gastric tonometer was inserted via the nose into the stomach. Correct position was verified by aspiration of gastric contents. Patient demographics, disease severity scores, ventilatory settings, continuously infused sedative, analgetic, inotropic and vasopressor drugs were recorded. The Tonocap® (Datex Inc., Helsinki, Finland) was used for continuous air tonometry of intragastric PCO_2. We took blood samples in heparinized syringes from a routinely placed arterial catheter for blood gas analysis at the patient's body temperature (Radiometer Inc., Copenhagen, Denmark). After baseline measurements, gastric feeding was started a rate of 500 ml in 1 h and discontinued after the first hour. Two hours later, gastric residual volumes (GRV) were determined by aspiration, blood samples for gasometry were again taken and intragastric tonometry was repeated. A bolus infusion of EN, although not common practice in intensive care medicine, can be used as a feeding challenge [11]. The hypothesis that gastric ischemia is related to gastric feeding intolerance can only be demonstrated if the bolus is substantial. Potentially large GRVs evoked were considered safe as demonstrated before [13]. In this protocol the stomach was emptied before each tonometric evaluation, to ensure close contact between the gastric mucosa and the tonometer balloon [12]. Ventilatory settings and doses of continuously infused drugs were unchanged during these measurements.

2.1. Statistical analysis

We estimated 15 patients per group were required to detect an increase in PCO_2 gradient from 10 (standard deviation 7) to 20 (14) mmHg, assuming that GRVs were >100 ml in 50% of patients, with 80% power at the $\alpha = 0.05$ level. Patients were arbitrarily divided into those with high (>100 ml) and low GRV and we compared categorical data with help of Fisher's exact test and continuous data with help of the Student's t test, since most data were distributed normally (Kolmogorov–Smirnov test $P > 0.05$). Pearson correlation coefficients were used. The data are summarized as mean (standard deviation, SD) and exact P values unless <0.001 are reported.

Table 1
Patient characteristics.

	Low GRV	High GRV	P
	n = 19	n = 10	
Age, year	65 ± 17	64 ± 10	0.82
Gender, male	12 (63)	8 (80)	0.43
Co-morbidity			
Cardiac	6 (32)	3 (30)	1.0
Pulmonary	4 (21)	2 (20)	1.0
Gastrointestinal	3 (16)	2 (20)	1.0
Renal	3 (16)	1 (10)	1.0
Neurological	2 (10)	1 (10)	0.53
Principal reason of admission			0.79
Cardiac	6 (32)	3 (30)	
Pulmonary	6 (32)	2 (20)	
Sepsis	2 (10)	2 (20)	
Trauma	2 (10)	1 (10)	
Postoperative	1 (5)	2 (20)	
Neurological	1 (5)	0	
Metabolic	1 (5)	0	
APACHE II	26.5 ± 8.0	25.1 ± 10.1	0.69
Vasopressor use	14 (74)	9 (90)	0.63
Opiates	14 (74)	10 (100)	0.13
Benzodiazepines	7 (37)	3 (30)	1.0
Propofol	10 (53)	5 (50)	1.0
Days after admission ICU	4 (5)	2 (2)	0.17

Mean (SD) or number (percentage), where appropriate. APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit.

3. Results

3.1. Patients

Clinical characteristics are shown in Table 1. Thirty patients were included; in one patient the study was discontinued for technical reasons. In all patients the 500-ml feed was given in 1 h and tolerated well without complications. Groups with and without increased GRVs (34% of patients showed intolerance) were comparable. All patients were mechanically ventilated, severely ill (high acute physiology and chronic health evaluation, APACHE), and most were in need for vasopressor therapy.

3.2. Blood gasometry and intragastric tonometry

Table 2 shows the blood gas and tonometric variables. Baseline intragastric-arterial blood PCO_2 gradients were elevated (>8 mm Hg) in 12 of 29 (41%) patients. The gradient prior to and 2 h after feeding correlated ($r = 0.65$, $P = 0.001$), but otherwise did not significantly differ.

3.3. Risk factors for high PCO_2 gradient and GRV

In univariate analysis, use of opiates was associated with an increased PCO_2 gradient ($P = 0.02$). There was no correlation between any gasometric variable and GRV (Fig. 1), except for pH which was higher from respiratory origin when GRV was relatively high.

4. Discussion

Our study suggests that gastric mucosal ischemia assessed by gastric air tonometry is not a risk factor for gastric feeding intolerance in the critically ill.

Our proof-of-principle study refutes the hypothesis that gastric mucosal ischemia is a major factor in early gastric feeding intolerance when commenced within a few days after admission into the ICU, as recommended by guidelines [14], since the intragastric-arterial PCO_2 gradient did not differ among patients with low or high GRV prior to and after feeding. Nevertheless, in six patients gastric feeding was started later than 2 days after admission, on clinical grounds. Intragastric feeding did not increase the PCO_2 gradient in our patients, and thus did not provoke ischemia either, which supports that early gastric nutrition is safe in this respect. In many patients, however, the intragastric to arterial PCO_2 gradient was elevated above the upper limit of normal of about 8 mmHg [7,9] and the use of opiates was the single demonstrable risk factor in our study. However, we cannot speculate on the cause and effect relationship nor on the implications of these observations, including prognosis that may be worse with elevated gradients [8,9]. Our study does not reveal any other risk factors for impaired gastric motility, apart perhaps from respiratory alkalosis [1], but confirms that the phenomenon may occur in a substantial number of critically ill patients and may impair the efficiency of enteral feeding unless prokinetic drugs are given or the duodenal route is used [1–3]. Of note, post-feeding intragastric PCO_2 is accurate when measured at least 2 h after feeding on an empty stomach

Please cite this article in press as: Streefkerk JO, et al., Gastric feeding intolerance is not caused by mucosal ischemia measured by intragastric air tonometry in the critically ill, Clinical Nutrition (2015), http://dx.doi.org/10.1016/j.clnu.2015.05.015