Primary research

Lack of agreement between tonometric and gastric juice partial carbon dioxide tension

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Statement of findings

Our goal was to compare measurement of tonometered saline and gastric juice partial carbon dioxide tension (P_{CO_2}). In this prospective observational study, 112 pairs of measurements were simultaneously obtained under various hemodynamic conditions, in 15 critical care patients. Linear regression analysis showed a significant correlation between the two methods of measuring P_{CO_2} ($r^2 = 0.43$; $P < 0.0001$). However, gastric juice P_{CO_2} was systematically higher (mean difference 51 mmHg). The 95% limits of agreement were 315 mmHg and the dispersion increased as the values of P_{CO_2} increased. Tonometric and gastric juice P_{CO_2} cannot be used interchangeably. Gastric juice P_{CO_2} measurement should be interpreted with caution.

Keywords: gastric tonometry, intramucosal partial carbon dioxide tension, intramucosal pH

Synopsis

Introduction: In recent years there has been growing interest in tonometric estimation of gastric intramucosal pH (pHi). More recently, attention has focused on the gradient between intraluminal and arterial P_{CO_2}. pHi appears to be a useful diagnostic and prognostic tool in critically ill patients, and may also be used as a therapeutic guide. However, intraluminal P_{CO_2} is the parameter measured to calculate pHi, and it is assumed as equivalent to the P_{CO_2} of the upper layers of the gastric mucosa.

Direct measurement of P_{CO_2} in gastric juice might offer advantages over tonometry. Tonometer costs could be saved, and equilibration time would no longer be necessary. Additionally, preanalytic factors that account for poor reproducibility, such as inadequate volume of saline in the tonometer, errors in the dwell time of the sample or in the technique used to aspirate saline, mixing of the sample with tonometer dead space and delay in analysis, could be prevented. Nevertheless, to our knowledge few experimental or clinical studies have examined P_{CO_2} in gastric juice. Moreover, no comparison with simultaneous tonometric samples has been performed. Our goal was to compare simultaneous measurement of P_{CO_2} in gastric juice and in saline samples from a tonometer. Data from the present study show that gastric juice P_{CO_2} is systematically higher. Furthermore, differences widen at high P_{CO_2} values, and data dispersion becomes even more striking. Therefore, tonometric P_{CO_2} and gastric juice P_{CO_2} are not interchangeable.

Patients and methods: The present study was approved by the local ethics committee, and informed consent was obtained from the next of kin of each patient.

We studied 15 consecutive mechanically ventilated patients from a medical/surgical intensive care unit, in whom tonometric monitoring was indicated by attending physicians. All patients were receiving 50 mg intravenous ranitidine every 8 h. Gastric tonometers were filled with saline, which was extracted after 90 min of equilibration time. At the same time, gastric juice was

P_{CO_2} = partial carbon dioxide tension; pHi = intramucosal pH.

Table 1

Clinical characteristics and first value of arterial, tonometer and gastric juice P_{CO_2}

Patient	Sex	Age (years)	Diagnosis	Inotropes (μg/kg per min)	Outcome	P_{CO_2} (mmHg)		
						Arterial	Tonometric	Gastric juice
1	Female	53	Stroke, ARDS	Dopamine 32	Survival	30	48	165
2	Female	73	Intestinal obstruction, septic shock	Dopamine 40	Death	26	44	92
3	Male	37	Multiple trauma		Survival	21	28	41
4	Male	56	Multiple trauma		Survival	39	42	49
5	Female	64	Acute pancreatitis, shock, ARDS	Dopamine 18	Death	30	34	80
6	Male	17	Multiple trauma		Survival	43	60	60
7	Female	18	Fat liver of pregnancy		Survival	30	40	44
8	Male	73	Necrotizing celulitis, septic shock, ARDS	Epinephrine 1.2	Death	28	33	31
9	Male	64	Multiple trauma, pneumonia, ARDS		Death	36	41	57
10	Male	65	Lung cancer postoperatively, ARDS		Death	35	51	242
11	Male	65	Lung cancer postoperatively, ARDS	Dopamine 20	Death	36	30	125
12	Female	22	Neutropenia, septic shock, ARDS	Epinephrine 0.8	Death	50	69	81
13	Male	83	Perioperative shock	Dopamine 25	Survival	23	28	34
14	Male	52	Ventilator-associated pneumonia		Survival	43	43	126
15	Male	56	Colangitis, septic shock	Dopamine 36	Survival	38	44	92

ARDS, acute respiratory distress syndrome.

anaerobically extracted from the aspiration port of the tonometer. The initial 20 ml was discarded. P_{CO_2} in both samples was measured using a blood gas analyzer (AVL 945; AVL List GMBH, Gratz, Austria). These measurements were taken at various time points in each patient, and under various haemodynamic and oxygen transport conditions, All measurements were performed with the patient fasted. Correlation between the two measurements was examined using the Bland–Altman technique.

We also performed an *in vitro* study to quantify the precision and bias for the AVL 945. For this purpose, a stable P_{CO_2} in saline solution was achieved by bubbling 5% carbon dioxide calibration gas.

Results: We performed 112 pairs of measurements in 15 patients. Table 1 shows clinical data and the first values of arterial, tonometered and gastric juice P_{CO_2} for each patient. Regression analysis demonstrated a significant correlation between both methods of measuring P_{CO_2} ($r^2 = 0.43$; gastric juice $P_{CO_2} = -28.79 + [2.55 \times \text{tonometric } P_{CO_2}]$; $P < 0.0001$; Fig. 1). However, the bias calculated as the mean difference of gastric juice and tonometric P_{CO_2} was 51 mmHg. The 95% limits of agreement were 315 mmHg (Fig. 2). For mean P_{CO_2} values lesser than 100 mmHg, the bias and the 95% limits of agreement were 19 and 102 mmHg, respectively. As mean P_{CO_2} increased, the scattering of differences widened ($r^2 = 0.71$; $P < 0.0001$).

In an effort to prevent the bias related to multiple measurements per patient, we performed Bland–Altman analysis with the first measurement of each patient. After this the results remained similar (bias 55 mmHg, 95% limits of agreement 216 mmHg).

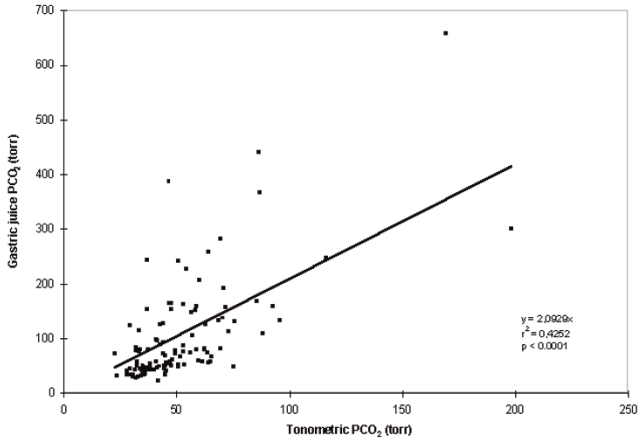
The AVL 945 blood gas analyzer showed a negative bias of 0.97 mmHg and a precision of 2.13 mmHg. This bias was considered negligible, so no further correction was made to saline tonometric values.

Discussion: The results of the present study show that tonometric P_{CO_2} and gastric juice P_{CO_2} are not interchangeable. Gastric juice P_{CO_2} is systematically higher. At high P_{CO_2} values the differences widen, and data dispersion becomes even more marked.

There is no clear cause for these observations. A possible explanation might be that tonometric P_{CO_2} is generated over a time interval, whereas gastric juice P_{CO_2} might reflect rapid changes in mucosal metabolism. Different equilibrium time could also account for data dispersion, but not for the positive bias for gastric juice. Rapid changes should occur in both directions.

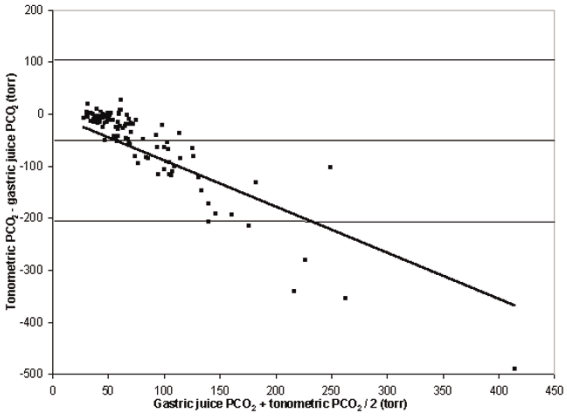
Another potential confounding factor is the ability of blood gas analyzers to measure P_{CO_2} in gastric juice. Measurement of P_{CO_2} in 0.9% saline is an important source of error in the estimation of pHi. Variation in P_{CO_2} values may occur with different P_{CO_2} equilibration solutions. For example, bias is −66.5% when the Nova Stat Profile 7 blood gas analyzer (Nova

Figure 1



Correlation between gastric juice and tonometric P_{CO_2}. We performed 112 pairs of measurements of gastric juice and tonometric P_{CO_2} in 15 critical care patients under different haemodynamic and oxygen transport conditions. The linear regression coefficient is significant. However, the slope value indicates systematic overestimation of gastric juice P_{CO_2} in relation to saline P_{CO_2}.

Figure 2



Bland–Altman analysis of the differences between gastric juice and tonometric P_{CO_2}. The bias calculated as the mean difference of gastric juice and tonometric P_{CO_2} was 51 mmHg. The 95% limits of agreement were 315 mmHg. The bias and the scattering of differences widened as P_{CO_2} increased.

Biomedical, Waltham, MA, USA) measures concentration of 1.95% of CO_2 equilibrated in normal saline. However, bias changes to +45.4% when 1.95% CO_2 is equilibrated in human albumin solution 4.5%.

It would not be surprising if gastric juice components such as proteins, mucopolisaccharides and others interfere with CO_2 solubility and its subsequent measurement by blood gas analyzers. In this way, intersubject and intrasubject variation in gastric juice composition could also account for data dispersion. Fiddian-Green *et al* [1] measured P_{CO_2} in gastric contents of anaesthetized dogs. They isolated the stomach from the oesophagus and the duodenum with ligatures, and washed it through a catheter with saline. Then, they instilled 250 ml 0.9% saline and took samples to measure P_{CO_2} and to estimate pHi. Simultaneously, mucosa pH was recorded with a microglass probe. They found a statistically significant correlation between both methods. However, data dispersion in the graph was considerable.

We were able to exclude analyzer underestimation of P_{CO_2} in saline as the cause for the present results. *In vitro* performance of the AVL 945 in blood was good. It showed a negative bias less than 1 mmHg and a precision of about 2 mmHg.

We cannot infer from the present data the technique that should be the gold standard for measuring P_{CO_2} in gastric mucosa. However, the studies that have established the normal values for pHi, prognostic changes and its uses as a therapeutic index have been performed with tonometry. Hence, more data are needed for the routine measurement of P_{CO_2} in gastric juice.

Full article

Introduction

In recent years there has been growing interest in tonometric estimation of gastric pHi. More recently attention has focused on the gradient between intraluminal and arterial P_{CO_2}. pHi appears to be a useful diagnostic and prognostic tool in critically ill patients, and may also be used as a therapeutic guide [2,3]. However, intraluminal P_{CO_2} is the parameter measured to calculate pHi, and it is assumed as equivalent to the P_{CO_2} of the upper layers of the gastric mucosa [4].

Direct measurement of P_{CO_2} in gastric juice might offer additional advantages over tonometry. First, tonometer costs could be saved. Second, equilibration time would no longer be necessary. Finally, preanalytic factors that account for poor tonometric reproducibility, such as inadequate volume of saline in the tonometer, errors in timing the dwell time of the sample or in the technique used to aspirate the tonometered saline sample, mixing the sample with air from the tonometer dead space, and delays in specimen analysis, might be prevented [5].

Nevertheless, to our knowledge, very few studies, either experimental or clinical, have examined P_{CO_2} in gastric juice [1,6,7]. Moreover, no comparison with tonometric samples obtained at the same time has been done. Our goal was to compare P_{CO_2} obtained simultaneously in gastric juice and in saline samples from tonometers. The results of the present study show that gastric juice P_{CO_2} is systematically higher, and that for high P_{CO_2} values this difference widens and data dispersion is even more marked. Therefore, tonometric P_{CO_2} and gastric juice P_{CO_2} are not interchangeable.

Patients and methods

The present study was approved by the local ethics committee and informed consent was obtained from the next of kin of each patient.

We consecutively studied 15 mechanically ventilated patients from a medical/surgical intensive care unit, in whom tonometric monitoring was indicated by attending physicians. All patients were receiving 50 mg intravenous ranitidine every 8 h. Gastric tonometers were filled with saline and, after 90 min for equilibration, saline samples were collected, as has previously been described [2]. At the same time, gastric juice was anaerobically extracted from the aspiration port of the tonometer. Initial 20 ml were discarded. A blood gas analyzer (AVL 945) was used to measure P_{CO_2} in both samples. These measurements were taken at various time points in each patient, and under various haemodynamic and oxygen transport conditions. All measurements were performed with the patient fasted. Correlation between both of measurements was examined using the Bland–Altman technique [8].

We also performed an *in vitro* study to quantify the precision and bias of the AVL 945. For this purpose, a stable P_{CO_2} in saline solution was achieved by bubbling 5% carbon dioxide calibration gas. Bias (mean difference from expected P_{CO_2}) and precision (standard deviation of the bias) of P_{CO_2} measured in saline was determined by comparison of measured P_{CO_2} with expected P_{CO_2}. The latter was calculated from the carbon dioxide content of the calibration gas and from barometric pressure, according to gas laws. Measurements were repeated six times.

Results

We performed 112 pairs of measurements in 15 patients. Table 1 shows clinical data and the first values of arterial, tonometer and gastric juice P_{CO_2} taken in each patient. Regression analysis demonstrated a significant correlation between both methods of measuring P_{CO_2} ($r^2 = 0.43$; gastric juice $P_{CO_2} = -28.79 + [2.55 \times$ tonometric $P_{CO_2}]$; $P < 0.0001$; Fig. 1). However, bias, calculated as the mean difference between gastric juice and tonometric P_{CO_2}, was 51 mmHg. The 95% limits of agreement were 315 mmHg (Fig. 2). When mean P_{CO_2} values were less than 100 mmHg, bias and 95% limits of agreement were 19 and 102 mmHg, respectively. The scattering of differences widened as P_{CO_2} increased ($r^2 = 0.71$; $P < 0.0001$).

The two types of measurements are clearly correlated. However, they cannot be considered as interchangeable, because gastric juice P_{CO_2} was always higher and the 95% limits of agreement were clinically significant.

In an effort to prevent bias related to multiple measurements per patient we used another approach, taking into account the initial measurement of each patient. Despite this, results continued to be similar (bias 55 mmHg, 95% limits of agreement 216 mmHg).

The AVL 945 blood gas analyzer showed a negative bias of 0.97 mmHg and a precision of 2.13 mmHg. This was considered negligible, so no further correction was done to tonometric values.

Discussion

The present data show that tonometric P_{CO_2} and gastric juice P_{CO_2} should not be considered interchangeable, because gastric juice P_{CO_2} was systematically higher. With high P_{CO_2} values, this difference widened, and data dispersion became even more marked.

There is no clear cause for these observations. It can be argued that tonometric P_{CO_2} is a value that is measured over a predetermined period, whereas gastric juice P_{CO_2} may generate data on minute-to-minute changes in mucosal metabolism. This different equilibrium time could account for data dispersion. However, the positive bias for gastric juice is harder to interpret, because such rapid changes should appear in both directions.

Another potential confounding factor is the ability of blood gas analyzers to measure P_{CO_2} in gastric juice. Measurement of P_{CO_2} in saline is an important source of error in the estimation of pHi. The error lies both in the kind of blood gas analyzer used and in the P_{CO_2} value itself [9,10]. Different solutions might modify P_{CO_2} measurement. For example, bias is −66.5% when the Nova Stat Profile 7 blood gas analyzer measures concentration of 1.95% of CO_2 equilibrated in normal saline. However, bias changes to +45.4% when 1.95% CO_2 is equilibrated in human albumin solution 4.5% [9].

It would not be surprising if different gastric juice buffers, such as proteins, mucopolisaccharides and others, interfere with CO_2 solubility and its subsequent measurement. In this way, intersubject and intrasubject variation of gastric juice composition could also account for data dispersion. Therefore, analytic issues related to the various constituents of gastric juice could have added to the observed differences.

Fiddian-Green *et al* [1] measured P_{CO_2} in gastric content of anaesthetised dogs. They isolated the stomach from the oesophagus and the duodenum with ligatures, and washed it through a catheter with saline. Then they instilled 250 ml saline and intermittently took samples to measure P_{CO_2} and estimate pHi, which was compared with simultaneous direct mucosa pHi measurement performed using a microglass probe. They found a statistically significant correlation between both methods, but there was considerable data dispersion in the graph. However, in that study, as well as in others in which P_{CO_2} was measured without a tonometer [6,7], some kind of saline lavage was used. On the other hand, we directly measured P_{CO_2} in gastric juice, which could produce marked differences in the results.

Differences between tonometric P_{CO_2} and gastric juice P_{CO_2} could be due to blood gas analyzers that are calibrated for blood gas analysis, and could systematically underestimate P_{CO_2} in saline [9,10]. Nevertheless, this explanation is not supported by the present *in vitro* results. The performance of the AVL 945 was fairly good. It showed a minor negative bias of less than 1 mmHg and a precision of approximately 2 mmHg. Thus, it appears to be a suitable device for saline tonometry.

We ascribe the high P_{CO_2} values obtained in the present study to shock and subsequent gut hypoperfusion, as can be deduced from the clinical characteristics of our patients. Also, in the presence of hydrochloric acid, duodenal or gastric bicarbonate buffering could produce important amounts of carbon dioxide [11]. Although we cannot exclude spurious generation of carbon dioxide, measurements were performed in the fasted state, the position of the tonometer was checked by X-ray, and ranitidine was administered in each patient. If P_{CO_2} in gastric juice and in the tonometer were interchangeable, their values would be similar, regardless of CO_2 source or absolute value. However, gastric juice P_{CO_2} and tonometric P_{CO_2} were quite different. We believe that this is the novel point in this study.

Gastric juice P_{CO_2} has been used in some clinical studies [6,7,12]. Mohsenifar *et al* [12] advocated its advantages over tonometry. However, the present results suggest that the two techniques are not interchangeable. From the present data we cannot infer which should be the gold standard technique for measurement of gastric mucosa P_{CO_2}. Nevertheless, knowledge regarding pHi has evolved from gastric tonometry; studies regarding normal values, prognostic changes and its uses as a therapeutic guide were performed using tonometry. Hence, until more and clearer data are reported, P_{CO_2} measurement in gastric juice should be considered with caution.

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