Monitoring Gastric Mucosal Carbon Dioxide Pressure Using Gas Tonometry

In Vitro and in Vivo Validation Studies

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Background: Saline gastric tonometry of carbon dioxide has been proposed as a means to assess the adequacy of splanchnic perfusion. However, this technique has several disadvantages, including the long time interval needed for gases to reach equilibrium in saline milieu. Thus the authors evaluated a system that uses a gas-filled instead of a saline-filled gastric balloon.

Methods: In vitro, we simultaneously placed two tonometry catheters in an equilibration water bath maintained at a predetermined constant pressure of carbon dioxide (P_{CO2}). The first catheter’s balloon was filled with air and the second with saline. The performance of gas tonometry was tested by comparing the P_{CO2}, measurements of the bath obtained via gas tonometry (P_{gas}) to the P_{CO2}, measurements of direct bath samples (P_{bat},). These results were also compared with the P_{bat}, measurements obtained simultaneously by saline tonometry (P_{sal}). The response time of gas versus saline tonometry was also studied. In vivo, the performance of gas tonometry was tested comparing the measurements of gastric intramucosal P_{CO2}, obtained by gas tonometry (P_{gas}) at different equilibration times with those obtained by saline tonometry (P_{sal}) using an equilibration time of 30 min. Two nasogastric tonometry catheters were placed simultaneously in seven stable patients in the intensive care unit. The first balloon was filled with air and the second with saline.

Results: In vitro, there was a close correlation between P_{bat} and P_{gas} for each level of P_{bat}, and for each different gas equilibration time. For an equilibration time of 10 min at a P_{bat}, level of approximately 40 mmHg, the bias of the gas device defined as the mean of the differences between P_{bat} and P_{gas}, and its precision defined as the standard deviation of the bias, were -0.3 mmHg and 0.7 mmHg, respectively. Using the same definitions, the bias and precision of saline tonometry were 11.2 mmHg and 1.4 mmHg, respectively. If the equilibration time-dependent correction factor provided by the catheter manufacturer for saline tonometry was applied, the bias and precision were -6.9 mmHg and 2.9 mmHg, respectively. In vivo, using an equilibration time of 10 min for gas and 30 min for saline tonometry, there was a close correlation between the two techniques (r^2 = 0.986). A Bland and Altman analysis revealed a bias (± 2 SD) of 0.1 ± 6.8 mmHg. The correlation between the two methods was not improved if we prolonged the equilibration time of the gas tonometer.

Conclusions: Gas tonometry is comparable to saline tonometry for measuring gastric intramucosal P_{CO2}. Because gas tonometry is easier to automate, it may offer advantages over saline tonometry. (Key words: Gastric intramucosal carbon dioxide pressure, Monitoring, splanchnic; gastric tonometry; gas tonometry; saline tonometry. Oxygen delivery. Splanchnic ischemia.)

MONITORING: gastric mucosal pressure of carbon dioxide (P_{CO2}) by gastric tonometry has been proposed to assess the adequacy of splanchnic perfusion. The technique first described by Fiddian-Green et al.¹ and by Grum et al.² included a saline-filled gas-permeable balloon placed in the gastric lumen. After a given time interval (typically 30 min or longer), allowing equilibration of the saline solution with the gut intraluminal P_{CO2}, the sample is aspirated for P_{CO2} determination using a conventional blood gas analyzer. Several problems have been associated with this procedure, including an important variability in the determination of saline P_{CO2}, depending on the type of blood gas analyzer used, the long time interval needed for gas to reach equilibrium in saline milieu, and errors introduced by saline solution manipulations.

Assuming free and rapid carbon dioxide diffusion between the gastric mucosa and the lumen, the equilibration time could be shorter if the catheter balloon is filled with air rather than saline. These theoretical considerations regarding gas diffusion suggest that a gas-filled balloon may offer advantages over a fluid-filled...
one. A recent study by Guzman and Kruse\textsuperscript{5} compared a capnometric recirculating gas tonometry system to saline tonometry in vitro using an equilibration chamber and in vivo in anesthetized dogs. The data indicated that continuous monitoring of gastric intramucosal $P_{co2}$ by gas tonometry was feasible and had a short equilibration time.

This study validated gas tonometry in vitro and in vivo and compared its performance to measurements using saline tonometry.

**Methods**

*In Vitro Studies*

We used a metal container filled with 150 ml distilled water as an equilibration chamber to perform in vitro tonometry. The gas source was provided by a mixture of nitrogen and carbon dioxide, introduced into the chamber at a nominal flow rate of 5 l/min. We adjusted the gas mixture to maintain the $P_{co2}$ of the bath (Pbath$_{co2}$) at approximately 40 mmHg or 80 mmHg, as desired. The container was placed in a larger water bath maintained at a constant temperature of 37°C.

A standard tonometry nasogastric tube equipped with a semipermeable Silastic balloon (TRIP, NGS catheter; Tonometrics, Helsinki, Finland) was placed in the bath and connected to an automated gas analyzer (Tonocap; Datex, Helsinki, Finland). This system pumps room air into the balloon and aspirates the sample after a predefined equilibration time of 10, 15, 30, or 60 min. The $P_{co2}$ in the aspirated air is measured by an infrared sensor. With each measurement cycle, 8 ml air is inflated into the balloon and aspirated after a set time. The first 2 ml of the sample is discarded, because this corresponds to the dead space of the system (including catheter, connecting tube, and tube in the Tonocap analyzer). The $P_{co2}$ is measured in the final 6 ml of aspirate. Thirty seconds later the balloon is reinflated with the same 8-ml sample and a new measurement is obtained. The entire sequence of inflation, aspiration, $P_{co2}$ measurement and reinflation is fully automated.

A second standard tonometry nasogastric tube was plunged into the bath, but this time it was filled with saline. It was prepared according to the manufacturer's instructions and filled with 2.5 ml saline solution. After a predetermined equilibration time, 1 ml of dead space volume was aspirated from the catheter and discarded. The remaining saline solution was then aspirated and analyzed for $P_{co2}$ (ABL 500; Radiometer, Copenhagen, Denmark).

We first studied the effect of changes in equilibration times on the $P_{co2}$ measurements obtained by the saline and the gas techniques. We stabilized the Pbath$_{co2}$ at about 40 mmHg and altered the equilibration times as follows: for each measurement technique, three gas $P_{co2}$ measures were obtained with an equilibration time of 10 min, followed by six measures with an equilibration time of 15 min, two with an equilibration time of 30 min, and two with an equilibration time of 60 min. The equilibration times were then progressively decreased in a similar manner: two measures with an equilibration time of 30 min, six with an equilibration time of 15 min, and three with an equilibration time of 10 min. The entire procedure lasted 8 h. The next day the process was repeated for a Pbath$_{co2}$ of 80 mmHg using the same tonometry catheters. The gas measurements were fully automated, with the operator needing to alter only the equilibration time of the gas device. The saline tonometry measurements were performed with the tonometry catheter in place, with only emptying and re-filling the balloon with saline solution. Thus 24 measures for each level of Pbath$_{co2}$ and for each measurement technique were recorded. Every 30 min, the Pbath$_{co2}$ was checked by analysis of a sample of bath water (Radiometer ABL 500 gas analyzer), and this value was used as the reference for the saline and gas $P_{co2}$ measurements obtained during the preceding 30 min. These in vitro manipulations were performed five times using a new pair of catheters for each manipulation.

The biases of the automated gas analyzer and the saline tonometer were defined as the mean of the differences between Pbath$_{co2}$ and $P_{co2}$, and between Pbath$_{co2}$ and $P_{co2}$, respectively. The precision is the standard deviation of the bias. Data are expressed as mean ± SD.

Using an identical in vitro system, we compared the response times of gas and saline tonometry during acute changes in Pbath$_{co2}$. After ensuring that the Pbath$_{co2}$ was stable at about 40 mmHg, we abruptly increased Pbath$_{co2}$ to approximately 80 mmHg by altering the gas mixture. During the next 5 min, the Pbath$_{co2}$ was determined every minute by analyzing a direct sample of bath water (Radiometer ABL 500 gas analyzer). We used the shortest equilibration time of the gas analyzer that was provided by the manufacturer (10 min) and the same equilibration time for the saline tonometer. We repeated these measurements after an abrupt decrease
of the Phath$_{CO_2}$ from 80 to 40 mmHg. We did the entire procedure five times. The response time was defined as the time needed to reach 95% of the change in P$_{CO_2}$ for an abrupt change in Phath$_{CO_2}$.

For this in vitro part of the study, we first used uncorrected raw P$_{CO_2}$ measures obtained by the saline tonometry. Then we corrected these P$_{CO_2}$ measures by multiplying the raw P$_{CO_2}$ values by the correction factors provided by the catheter manufacturer, which depend on the length of time the saline solution remains in the tonometer balloon (correction factor 1.62 for equilibration time of 10 min; 1.44 for 15 min, 1.24 for 30 min; 1.13 for 60 min). We also calculated our own in vitro saline tonometer correction factors for each equilibration time by dividing the mean Phath$_{CO_2}$ value by the corresponding mean P$_{CO_2}$ value obtained at the corresponding equilibration time. We finally compared our correction factors to the manufacturer’s values.

In Vivo Studies

After obtaining approval of the ethics committee of Erasme University Hospital, two nasogastric tonometry catheters (Tonometrics) were inserted together in seven sedated, mechanically ventilated, and hemodynamically stable critically ill patients during a study period of 6 h. Three patients had septic shock due to cerebral abscess (n = 1) or bronchopneumonia (n = 2), two patients had acute respiratory distress syndrome due to peritonitis (n = 1) and pulmonary graft rejection (n = 1), and two patients had intracerebral bleeding. There were five men and two women aged 42-80 yr (mean, 62 ± 13 yr). All patients were mechanically ventilated, sedated (with midazolam and morphine), and paralyzed with pancuronium. All patients were invasively monitored with a pulmonary artery catheter (Swan Ganz catheter 93A-131-7F; Baxter Healthcare, Irvine, CA) and an arterial catheter. Every 30 min throughout the study, thermodilution cardiac output was measured (computer 9520 A, Baxter Healthcare) by successive injections of at least five boluses of 10 ml cold (< 8°C) 5% dextrose in water, via a closed system (CO-set system, Baxter Healthcare). Each patient had been treated with H$_2$ receptor blockers (150 mg ranitidine given intravenously each day), with no enteral feeding for at least the previous 6 h. In each patient, the position of the two nasogastric catheters was checked radiographically.

The first catheter, dedicated to saline tonometry, was prepared according to the manufacturer’s instructions and filled with 2.5 ml saline solution. After an equilibration time of 30 min, 1 ml dead space volume was aspirated from the catheter and discarded. The remaining saline solution was aspirated and analyzed for P$_{CO_2}$ (Radiometer ABL 500 gas analyzer). The adjusted saline P$_{CO_2}$ (P$_{CO_2}$) was obtained by multiplying the measured P$_{CO_2}$ by the correction factor obtained in our in vitro study for an equilibration time of 30 min.

The second catheter, dedicated to gas tonometry, was connected to an automated gas analyzer (Tonocap, Datex). After balloon filling with air in a closed circuit (see previous), the gas P$_{CO_2}$ (P$_{g CO_2}$) was automatically measured by infrared spectroscopy after pre-established equilibration times of 10, 15, or 30 min.

In each patient, 24 P$_{g CO_2}$ measures were performed successively, in the following order: six measures with an equilibration time of 10 min, four measures with an equilibration time of 15 min, four with an equilibration time of 30 min, four with an equilibration time of 15 min, and six with an equilibration time of 10 min. The P$_{g CO_2}$ values obtained during a period of 30 min were compared with the simultaneous P$_{CO_2}$ value obtained after the same 30 min of equilibration.

The effects of acute changes in P$_{a CO_2}$ on P$_{g CO_2}$ were also studied in one sedated, paralyzed, and mechanically ventilated patient with acute respiratory failure as part of the study of respiratory mechanics under a P$_{i}$ of 100%. The gastric mucosal P$_{CO_2}$ was measured by saline tonometry (P$_{s CO_2}$) with an equilibration time of 30 min and by gas tonometry (P$_{g CO_2}$) with an equilibration time of 10 min, and the arterial pressure of carbon dioxide (P$_{a CO_2}$) was measured every 10 min using a blood gas analyzer (Radiometer ABL 500).

Statistical evaluation included linear regression and a Bland and Altman analysis.

Results

In Vitro Studies

The Phath$_{CO_2}$ remained stable during all the studies at 40.2 ± 0.7 mmHg (lower level) and 76.4 ± 0.8 mmHg (higher level), respectively. There was a close correlation between Phath$_{CO_2}$ and P$_{g CO_2}$ values for each level of Phath$_{CO_2}$ and for each gas equilibration time. For the lower level of Phath$_{CO_2}$, and for an equilibration time of 10 min, the bias and the precision of the gas tonometer were −0.3 mmHg and 0.7 mmHg, respectively. Table 1 shows the bias and precision for the two Phath$_{CO_2}$ levels and different equilibration times. Increasing the equilibration time of the gas analyzer did not improve the precision or decrease the bias of the P$_{g CO_2}$ measurements.
In Vivo Studies

All patients were hemodynamically stable and had no cardiac output changes greater than 5% during the study. There was a close correlation between $P_{c,\text{CO}_2}$ and $P_{s,\text{CO}_2}$ for each gas equilibration time, with the following regression coefficients: equilibration time of 10 min, $r^2 = 0.986$ (fig. 1); 15 min, $r^2 = 0.967$; 30 min, $r^2 = 0.946$. A Bland and Altman analysis was performed for each gas tonometry equilibration time. The bias (±2 SD) was $0.1 ± 6.8$ mmHg for an equilibration time of 10 min (fig. 2), $-2.1 ± 11.4$ mmHg for an equilibration time of 15 min, and $-5.1 ± 11.4$ mmHg for an equilibration time of 30 min.

When each patient was included only once, analyzing only the $P_{s,\text{CO}_2}$ value obtained at the end of the equilibration time for the $P_{s,\text{CO}_2}$, the correlation coefficients were similar ($r^2 = 0.992$, data not shown).

In the patient in whom hypercapnia developed acutely, there was a close correlation between $P_{a,\text{CO}_2}$, $P_{c,\text{CO}_2}$, and $P_{s,\text{CO}_2}$ (fig. 3).

Discussion

First our study demonstrates first that in vitro $P_{c,\text{CO}_2}$ measurements obtained by gas tonometry are reliable. Second, due to the rapid carbon dioxide diffusion in gas, these measurements do not require an equilibration time of more than 10 min. In fact, the accuracy of gas tonometry was not greater with prolonged equilibration times. The great bias between the in vitro $P_{a,\text{CO}_2}$ value and the saline tonometry $P_{c,\text{CO}_2}$ measurements, especially for short equilibration times (10 and 15 min), is due to the incomplete equilibration of saline solution with environmental $P_{c,\text{CO}_2}$ after these short equilibration times. Factors have been developed in in vitro and in vivo studies to correct for this incomplete equilibration if the measurement time, as applied in many studies, is.
much shorter (+30 min) than the complete equilibration time. In vitro saline tonometry biases remained greater than those of gas tonometry, even after correction of raw saline $P_{CO_2}$ values by the manufacturer’s correction factors. This difference may be due to the correction factor recommended by the manufacturer. This measurement bias for short equilibration times may be clinically compromising if we consider that a normal $P_{CO_2}$ gap value, as defined by the difference between gastric mucosal $P_{CO_2}$ and arterial $P_{CO_2}$, is less than 6 mmHg. We derived our own scale of correction factors from the in vitro study and obtained values that were different from those of the manufacturer, especially for short equilibration times. The differences between our correction factors and the manufacturer’s values could be due to use of different blood gas analyzers. Therefore, use of such a correction factor can amplify the $P_{CO_2}$ measurement error. Equilibration times of less than 30 min, which need the greatest correction factors, therefore cannot be recommended for saline tonometry. The in vitro study shows that $P_{CO_2}$ measurements by gas tonometry correlate well with those obtained by saline tonometry and again do not require an equilibration.

![Equilibration time: 10 min](image1)

**Fig. 1.** Linear correlation between gastric mucosal $P_{CO_2}$ measurements obtained by saline tonometry ($P_{CO_2}$, equilibration time: 30 min) and gas tonometry ($P_{CO_2}$, equilibration time: 10 min) in the seven patients ($n = 84$ measurements) studied.

![Equilibration time: 10 min](image2)

**Fig. 2.** Bland and Altman analysis of gastric mucosal measurements obtained by saline tonometry ($P_{CO_2}$, equilibration time: 30 min) and gas tonometry ($P_{CO_2}$, equilibration time: 10 min) in the seven patients ($n = 84$ measurements) studied.

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**Table 4. Changes in $P_{CO_2}$ (mmHg) and $P_{CO_2}$ (%) Measured by the Automated Gas Analyzer and Saline Tonometry (Raw Uncorrected Data) with Time (Equilibration Time = 10 min) Following Acute Changes in $P_{CO_2}$ at T Zero min**

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<td>$P_{CO_2}$ (mmHg)</td>
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<td>$P_{CO_2}$ decrease from ±40 to ±80 mmHg</td>
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<td>Saline tonometry</td>
<td>30.7 ± 2.1</td>
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<td>Gas tonometry</td>
<td>40.8 ± 0.5</td>
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<td>$P_{CO_2}$ decrease from ±80 to ±40 mmHg</td>
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<tr>
<td>Saline tonometry</td>
<td>55.6 ± 2.3</td>
<td>39.6 ± 2.4</td>
<td>31.1 ± 2.2</td>
<td>30.7 ± 2.4</td>
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<td>Gas tonometry</td>
<td>80.6 ± 0.9</td>
<td>47.2 ± 0.5</td>
<td>40.6 ± 0.6</td>
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<td>Change in $P_{CO_2}$ (%)</td>
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<td>$P_{CO_2}$ increase from 40 to 80 mmHg</td>
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<td>Saline tonometry</td>
<td>0.0 ± 6.8</td>
<td>71.4 ± 10.9</td>
<td>96.3 ± 5.2</td>
<td>96.6 ± 5.2</td>
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<td>Gas tonometry</td>
<td>0.0 ± 1.2</td>
<td>87.8 ± 2.3</td>
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<td>$P_{CO_2}$ increase from 80 to 40 mmHg</td>
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<tr>
<td>Saline tonometry</td>
<td>100.0 ± 4.1</td>
<td>-66.8 ± 6.4</td>
<td>-95.3 ± 3.3</td>
<td>-98.4 ± 1.8</td>
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<td>Gas tonometry</td>
<td>100.0 ± 1.1</td>
<td>-85.5 ± 3.2</td>
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tion time of more than 10 min. In a recent study in pigs, Knichwitz et al. described a fiberoptic $P_{\text{CO}_2}$ sensor that can determine intramucosal gut $P_{\text{CO}_2}$ in a precise and reliable manner. Their in vitro study indicated that the response time of their $P_{\text{CO}_2}$ sensor was identical to our gas device.

The major advantage of gas tonometry is that balloon filling with air rather than saline allows a fully automated procedure that avoids saline manipulations, which are time consuming and potential sources of error. The proper interpretation of $P_{\text{CO}_2}$ requires the recognition of two important principles. First, $P_{\text{CO}_2}$ is directly influenced by $P_{\text{a,CO}_2}$ so that changes in ventilatory status can alter $P_{\text{a,CO}_2}$ in the absence of any change in regional blood flow. This observation was made in 1959 when a group of Hungarian physicians proposed the measurement of gastric $P_{\text{CO}_2}$ in lieu of arterial $P_{\text{a,CO}_2}$ during mechanical ventilation. Similar observations were reported more recently in animals. We had the opportunity to document an excellent correlation between $P_{\text{a,CO}_2}$ and $P_{\text{v,CO}_2}$ or $P_{\text{g,CO}_2}$ in one patient in whom transient hypercapnia developed (fig. 3). Thus one should always use the $P_{\text{CO}_2}$ gap (the $P_{\text{g,CO}_2} - P_{\text{a,CO}_2}$ difference) when assessing gastric oxygenation. This is not an additional constraint, because $p\text{Hi}$ measurement should be considered in relation to arterial $p\text{H}$ to avoid the influence of metabolic acidosis. The use of capnometry in patients with a stable dead space ratio may be very valuable, especially during anesthesia.

Second, an increase in $P_{\text{g,CO}_2}$ (like a reduction in $p\text{Hi}$) does not necessarily reflect gut hypoxia. According to the Fick equation, a reduction in blood flow is associated with an increase in the venoarterial gradient in carbon dioxide content and thus in $P_{\text{CO}_2}$. However, the decrease in oxygen delivery below a critical value is associated with a much greater increase in the venoarterial $P_{\text{CO}_2}$ gradient because the $P_{\text{CO}_2}$ generated by the acidic cells accumulates locally. Hence, an increased $P_{\text{g,CO}_2}$-$P_{\text{a,CO}_2}$ gradient should be interpreted as reduced splanchnic perfusion, which does not necessarily indicate splanchnic hypoxia.

The clinical importance of early identification of organ ischemia to prevent the development of multiple organ dysfunction and its associated high mortality rate has been well recognized. Monitoring systemic oxygen transport lacks the sensitivity to detect regional, or even global, tissue underperfusion. Gut monitoring has three attractive features. First, splanchnic blood flow is reduced early during even minor cardiovascular alterations in an attempt to preserve blood supply to more vital organs, namely the heart and the brain. Second, the tip of the gut villus may be particularly susceptible to a reduction in blood flow, given the local countercurrent mechanism supplying oxygen. Third, the gut is easily accessible to regional monitoring by inserting a nasogastric or rectal probe.

Our study did not evaluate the clinical utility of $P_{\text{g,CO}_2}$ monitoring. Several clinical studies have indicated that a low $p\text{Hi}$, and especially the persistence of a low $p\text{Hi}$, are associated with a greater incidence of organ dysfunction and increased mortality rates in critically ill patients. Whether gastric tonometry can influence the individual management of an acutely ill patient has not been fully determined. A multicenter study has suggested that $p\text{Hi}$-guided therapy may improve outcome, but this was true only in patients with normal $p\text{Hi}$ on admission, which emphasizes the importance of the early detection of splanchnic hypoperfusion. Another study indicated that gastric tonometry may help to identify failure to wean from mechanical ventilation. Nevertheless, several groups of investigators have stressed that the interpretation of these measurements in individual patients is sometimes difficult.

Gas tonometry thus represents an alternative reliable technique for bedside monitoring of gastric perfusion. Clinical studies can now evaluate the clinical utility of gas tonometry. We hope that improved monitoring of tissue perfusion will help to identify those patients who would benefit from increased oxygen delivery, facilitating a more tailored approach to therapy, rather than maintaining supranormal
References