Characteristics of time-dependent \( PCO_2 \) tonometry in the normal human stomach


Summary

Factors that affect \( PCO_2 \) measurement in balloon saline during gastrointestinal tonometry are unclear. They include carbon dioxide diffusion rate, correction factors for calculation of equilibrium \( PCO_2 \) from measurements at saline dwell times that are shorter than needed for full equilibration, role of blood-gas analyser bias during ex vivo \( PCO_2 \) measurements in saline, and normal values for intragastric \( PCO_2 \) (\( P_{\text{ICO}_2} \)) and intramucosal pH (\( pHi \)) at equilibrium, and their differences from blood values. In a laboratory study, normal \( PCO_2 \) changes in a saline-filled tonometer balloon placed in a saline bath at constant \( PCO_2 \) were described by a non-linear model, with a half-time of mean 4.4 min and 95% equilibration at mean 83 min. In a study in 20 healthy volunteers, \( P_{\text{ICO}_2} \) build up in a saline-filled tonometer balloon placed in the stomach, measured at dwell times of 10, 20, 30 and 60 min, was slightly \((P < 0.05)\) slower than in vitro, with a half-time of mean 5.8 min and 95% equilibration at mean 110 min. Correction factors to derive equilibrium \( P_{\text{ICO}_2} \) at short dwell times and independently from blood-gas analyser bias were calculated. The factors differed \((P < 0.05)\) from those currently provided by the manufacturer. Normal threshold values (mean) were: equilibrium \( P_{\text{ICO}_2} \leq 8.6 \) kPa, \( pHi \geq 7.33, P_{\text{ICO}_2} \) to blood \( PCO_2 \) difference \( \leq 1.1 \) kPa and pH difference \( \geq -0.06. P_{\text{ICO}_2} \) did not differ from, and was directly related to, blood \( PCO_2 \). These values provide a reference base for other studies and show that gastric mucosal \( PCO_2 \) depends on alveolar ventilation if blood flow is adequate. (Br J Anaesth. 1998; 81: 669–675)

Keywords: carbon dioxide, measurement; gastrointestinal tract, pH; measurement techniques, tonometry

An increased intragastric \( PCO_2 \) (\( P_{\text{ICO}_2} \)), as measured by tonometry, or its derivative, decreased intramucosal pH (\( pHi \)), suggests inadequate gastric mucosal blood flow.\(^1\) If blood flow is sufficient and acid secretion is prevented, generation of carbon dioxide from bicarbonate buffering of gastric acid, \( P_{\text{ICO}_2} \), approximates supplying blood \( PCO_2 \).\(^5\) \( P_{\text{ICO}_2} \), relative to blood \( PCO_2 \), during ischaemia stems from a reduced washout of metabolically produced carbon dioxide after hypoperfusion and from buffering of anaerobically produced lactic acid by bicarbonate.\(^8\) Even though intramucosal bicarbonate may not be the same as the supplying blood bicarbonate content,\(^9\) \( pHi \) calculated from \( P_{\text{ICO}_2} \) and blood bicarbonate content using the Henderson–Hasselbalch equation, is often used as a measure of the adequacy of gastric mucosal blood flow. Clinical studies in critically ill patients suggest that a low \( pHi \) is predictive of a poor prognosis\(^10\)–\(^14\) and that \( pHi \) can guide therapy and improve survival.\(^15\),\(^16\) Although tonometry is a promising tool for assessment of adequacy of regional blood flow in critically ill patients, it has not gained wide acceptance, partly because of methodological uncertainties.

\( P_{\text{ICO}_2} \) is measured ex vivo in saline aspirated from the intragastric tonometer balloon, after a given dwell time. To calculate the equilibrium \( P_{\text{ICO}_2} \) from dwell times shorter than the time needed for full equilibration, which exceeds 60 min, measured \( P_{\text{ICO}_2} \) is multiplied by dwell time-dependent correction factors. These factors are provided by the manufacturer of the tonometer.\(^17\),\(^18\) However, the normal rate of \( P_{\text{ICO}_2} \) change in the tonometer balloon in vitro and in the normal human stomach, and thereby the validity of the correction factors, taking into account the recently described catheter deadspace effect and \( PCO_2 \) measurement bias in saline by most blood-gas analysers,\(^19\)–\(^24\) are virtually unknown. Consequently, the normal ranges of equilibrium \( P_{\text{ICO}_2} \) and \( pHi \) and their differences from blood values are unclear. The lower limit of normal \( pHi \), for example, may vary between 7.31 and 7.35.\(^13\)\(^7\)\(^10\)\(^11\)\(^13\)\(^15\)\(^25\)–\(^27\) Finally, the premise that long dwell times yield more accurate \( P_{\text{ICO}_2} \) assessments than shorter ones is unproved.\(^24\)

In this study, we assessed normal \( P_{\text{ICO}_2} \) build-up in the tonometer balloon in vitro and in the stomach of healthy volunteers. We intended to provide a reference base for manual saline tonometry and thereby widen its clinical use, particularly if semicontinuous automated air tonometry (a technique that circumvents some of the methodological problems associated with saline tonometry) is not yet available.\(^22\)\(^28\)–\(^30\)

Subjects and methods

The in vitro study was performed at the Department of General and Large Animal Surgery, University of
Utrecht. The volunteer study was performed at the Free University Hospital, Amsterdam. The study was approved by the Local Ethics Committee.

For the in vitro study, a steady state $P_{CO_2}$ in a 5-litre, temperature-controlled (mean 37.0 (SD 0.2)°C) 0.9% saline-filled glass tank was achieved by bubbling carbon dioxide calibration gases (4.98% and 9.98% in nitrogen, accuracy 1%; NTG, Tilburg, The Netherlands) at a flow rate of 5 litre min$^{-1}$ via a microporous device placed on the bottom of the tank. There was a small hole in the rubber cover of the tank for gas insufflation and one for gas venting. Bath $P_{CO_2}$ was assumed to have reached steady-state after approximately 3 h when five consecutive determinations at 5-min intervals differed by less than 5%. Bias (mean difference from expected $P_{CO_2}$) and precision (SD of the bias) of $P_{CO_2}$ measured in saline with the blood-gas analyser (ABL 505, Radiometer, Copenhagen, Denmark) was determined by comparison of the measured bath $P_{CO_2}$ at steady state with the expected bath $P_{CO_2}$. The latter was calculated from the carbon dioxide content of the calibration gas, bath temperature and barometric pressure ($P$ bar), according to the gas law expressed in the equation $P_{CO_2}= (P$ bar – 47) $\times 100 \times $% $CO_2$ content, where 47 mm Hg represents water vapour pressure. With the blood-gas analyser used in this experiment, bias was −6.8% and precision 3.0%, in agreement with the literature. Thus for the in vitro experiment, all $P_{CO_2}$ measurements in saline were multiplied by a factor of 1.07 (= 100/93.2). Using this factor, measured bath $P_{CO_2}$ was mean 4.8 (SD 0.2) kPa and 9.4 (0.2) kPa, at an expected bath $P_{CO_2}$ of 4.8 kPa and 9.5 kPa, respectively. $P_{CO_2}$ at the start and end of the experiment was 4.8 (0.2) kPa and 34.7 (0.2) kPa, respectively, at low bath $P_{CO_2}$ and 9.4 (0.2) kPa and 9.4 (0.1) kPa, respectively, at high bath $P_{CO_2}$, indicating steady state during the experiment.

$P_{CO_2}$ increase was determined in six sigmoid-type tonometers (TRIP, Tonometries Inc., Bethesda, ML, USA), consisting of a silastic nasogastric tube impermeable to carbon dioxide with a volume of approximately 1.0 ml, and a silicone carbon dioxide permeable balloon with a volume of 2.5 ml. These were placed in the saline bath at steady state $P_{CO_2}$ after saline bath dwell times of 10, 20, 30, 45, 60, 90 and 120 min. Measurements were performed for each tonometer at both expected bath $P_{CO_2}$ concentrations of 4.8 and 9.5 kPa. For each dwell time, saline 2.5 ml was introduced into the tonometer balloon. After a given dwell times, saline was aspirated and the first 1.0 ml was considered to represent the deadspace. Between dwell times, the tonometer was rinsed four times with 2.5 ml of fresh saline to remove all saline in the deadspace compartment, to avoid contamination of reintroduced saline by the fluid remaining in the deadspace after prior aspiration.

For the in vivo study, we studied 20 healthy volunteers, aged 21–26 (mean 23) yr, after obtaining informed consent. Volunteers did not eat or smoke for 10 h before the study, and did not drink for 2 h before or during the study. Volunteers were seated during the study. A glass electrode for continuous gastric juice pH measurement with integral Ag/AgCl reference electrode near its tip (Ingold 440, Ingold Messtechnik, Urdorf, Switzerland) was introduced via the nose into the stomach. Using direct pH measurement, the electrode was placed 10 cm beyond the gastro-oesophageal junction, which was recognized by an abrupt pH decrease. The pH electrode was connected to a recorder which stored mean pH every 8 s using a hospital-developed microcomputer system for pH analysis. A tonometer (TRIP, Tonometries Inc., Bethesda, ML, USA), sigmoid type, was repeatedly filled and emptied using saline to remove all air. We used the sigmoid-type catheter as it is better tolerated by healthy volunteers than the gastric type. The tonometer was placed via the nose, the same distance as the pH electrode. In each subject, 2 h after tonometry was started, gastric acid secretion was suppressed by an i.v. bolus dose of ranitidine 100 mg, followed by continuous infusion of 25 mg h$^{-1}$ via an infusion pump (Limed P55-330, Limed, Amsterdam, The Netherlands). Gastric acid secretion was suppressed to prevent buffering of gastric acid by bicarbonate, thereby increasing $P_{CO_2}$ independently from mucosal $P_{CO_2}$. We aimed to have a constant gastric juice pH > 4.0. In fact, 2 h after the start of drug infusion and before tonometry, gastric juice pH was 5.6 (1.5) and > 4.0 in each volunteer. pH remained > 4.0 for 92(3)% of the study time, indicating sufficient inhibition of gastric acid secretion for tonometry. We used saline for gastric tonometry as saline is commonly used and allows for relatively rapid balloon $P_{CO_2}$ build-up and for accurate measurements provided that an adequately anaerobic technique is used and blood-gas analyser bias is known. In each volunteer, $P_{CO_2}$ was measured after sequential saline dwell times in the tonometer balloon of 10, 20, 30 and 60 min. At the start of each measurement, 2.5 ml of fresh saline was introduced into the tonometer balloon. After a given dwell time, saline was aspirated and the first 1.0 ml, containing the deadspace volume of the catheter, was discarded. The next 1.5 ml was aspirated into a 2.5-ml polypropylene syringe (Monoject, Sherwood Medical, Ballymoney, Northern Ireland) which was closed with a plastic cap (Capillary caps, Ciba-Corning, Sudbury, UK). In this sample, $P_{CO_2}$ was measured within 15 min, using a blood-gas analyser (Corning 278, Ciba-Corning, Houten, The Netherlands). Bias and precision for $P_{CO_2}$ measurements in saline with this blood-gas analyser were determined, as described above. Bias was −15% and precision 3%, in agreement with the literature. Thus all measured $P_{CO_2}$ values in saline in the volunteer study were multiplied by 1.18 (= 100/85). When we did this volunteer study we were unaware of the catheter deadspace effect as a source of measurement error at short dwell times. Fresh saline was introduced for the 10-min dwell times. Overestimation of $P_{CO_2}$ in the next measurement with the 20-min dwell time caused by the deadspace effect amounts to 6%. Hence, the 20-min $P_{CO_2}$ data were corrected accordingly. The index finger of each subject was warmed in water for 3 min and two arterialized blood samples were obtained, one at the start and one at the end of the study. From these capillary samples, pH (pH), bicarbonate content (cBic, mmol litre$^{-1}$) and $P_{CO_2}$ ($P_{CO_2}$, kPa) were determined using a Corning 278 blood-gas analyser. Values in carefully drawn capillary blood approximate those in arterial blood.
CALCULATIONS AND STATISTICAL ANALYSIS

For the in vitro experiments, the kinetics and equilibrium of \( \text{PCO}_2 \) build-up were assessed by the least squares technique and non-linear regression analysis according to models 1 and 2. For model 1: \( \text{PCO}_2(t) = \text{PCO}_2 \) at equilibrium \( \times (1 - e^{-kt}) \); for model 2: \( \text{PCO}_2(t) = \text{PCO}_2 \) at equilibrium \( \times T_1/t \). \( \text{PCO}_2(t) \) is \( \text{PCO}_2 \) measured after \( t \) min, \( k \) is a constant, \( T_1 \) is the halftime of \( \text{PCO}_2 \) increase and \( t \) is time in minutes. The goodness of fit of the models was evaluated by the coefficient of determination \( (r^2) \) and the ability of estimated equilibrium \( \text{PCO}_2 \) to predict bath \( \text{PCO}_2 \). For the in vivo study, a curve according to model 2 that best represented the in vitro data, was used to describe the course of measured values. Time-dependent correction factors were calculated according to: correction factor \( (t) = \text{PCO}_2 \) at equilibrium \( \times T_1/t \). The means of the dwell time-dependent correction factors were used to estimate the equilibrium \( \text{PCO}_2 \) from \( \text{PCO}_2 \) at each dwell time. The coefficient of variation \( (\text{CV} = \text{sd/mean}) \) was used as an index of reproducibility of equilibrium \( \text{PCO}_2 \) assessments at each dwell time. pH was calculated according to the (Henderson–Hasselbalch equation from \( \text{pH} = 6.1 + \log \left( \frac{\text{Bic}}{0.03 \times \text{PCO}_2 \text{ at equilibrium}} \right) \)). Linear regression analysis was used to correlate equilibrium \( \text{PCO}_2 \), with \( \text{PCO}_2 \). We calculated normal values for the tonomeric variables at each dwell time, using individually measured values multiplied by the mean dwell time-dependent in vitro correction factor, and for the values estimated at equilibrium in each patient. The threshold values were defined as mean \( \pm 2 \) sd where appropriate. Data are expressed as mean (sd) or range, where appropriate. \( P<0.05 \) was considered statistically significant.

Results

IN VITRO STUDY

\( \text{PCO}_2 \) increase in the tonometers at each bath \( \text{PCO}_2 \), calculated according to models 1 and 2, is shown in figure 1. Both types of curves fitted well: mean \( r^2 \) was 0.96 for model 1 and 0.98 for model 2. However, \( \text{PCO}_2 \) at equilibrium calculated with model 1 was lower than measured bath \( \text{PCO}_2; 8.8 \) (0.2) kPa vs 9.4 (0.2) kPa (\( P<0.001 \)) and 4.5 (0.1) kPa vs 4.8 (0.2) kPa (\( P<0.001 \)) for high and low bath \( \text{PCO}_2 \), respectively.

\( \text{PCO}_2 \) at equilibrium, calculated using model 2, did not differ from measured bath values: 9.5 (0.1) vs 9.4 (0.2) and 4.8 (0.1) vs 4.8 (0.2) kPa. Therefore, model 2 was used for the subsequent evaluation of \( \text{PCO}_2 \) build-up in volunteers. According to model 2, in vitro \( T_1 \) was 4.4 (0.5) min and mean time to reach 95% equilibration was 83 min. The dwell time-dependent correction factors in vitro are given in table 1. They differed from those provided by the manufacturer.

Estimated \( \text{PCO}_2 \) at equilibrium, using mean correction factors for multiplication with measured \( \text{PCO}_2 \) were, at an expected bath \( \text{PCO}_2 \) of 4.8 kPa, 5.0 (0.1) kPa (CV 1.8%) at the 10-min dwell time, 4.7 (0.2) kPa (CV 3.5%) at the 20-min dwell time, 4.7 (0.1) kPa (CV 2.0%) at the 30-min and 4.9 (0.1) kPa (CV 1.5%) at the 60-min dwell time. At an expected bath \( \text{PCO}_2 \) of 9.5 kPa, estimated \( \text{PCO}_2 \) at equilibrium was at the 10-min dwell time 9.7 (0.2) kPa (CV 1.6%), at the 20-min dwell time 9.4 (0.2) kPa (CV 2.3%), at the 30-min dwell time 9.5 (0.2) kPa (CV 2.0%) and at the 60-min dwell time 9.7 (0.2) kPa (CV 1.5%). Hence, estimation of expected \( \text{PCO}_2 \) was accurate, independent of dwell time.

IN VIVO STUDY

\( \text{PCO}_2 \) build-up in vivo

The rate of \( \text{PCO}_2 \) increase in vivo was slower than in vitro (\( T_1 \) of 5.8 (1.9) min, \( P<0.05 \) vs in vitro) (Fig. 2). Mean \( r^2 \) was 0.95. Calculated \( \text{PCO}_2 \) at equilibrium was 5.7 (0.5) kPa, while 95% equilibration was reached at mean 110 min (\( P<0.05 \) vs in vitro). The in vitro correction factors differed from those supplied by the manufacturer. The in vivo and in vitro correction factors differed at the 10-min dwell time only (table 1). Note that the in vitro correction factors were independent of blood-gas analyser bias. The CV values of the \( \text{PCO}_2 \) measurements were 12%, 11%, 9% and 10%, at 10-, 20-, 30- and 60-min dwell times, respectively (table 2), which were higher than those in vitro but independent of dwell time, so that short dwell times should allow for accurate estimation of equilibrium \( \text{PCO}_2 \). Table 2 also shows pH vs and differences between tonomeric and blood variables at each dwell time.

Capillary blood

For capillary blood samples, there were no differences between initial and final values. Mean \( \text{pH} \) was

<table>
<thead>
<tr>
<th>Dwell time (min)</th>
<th>Manufacturer</th>
<th>In vitro</th>
<th>In vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>1.57</td>
<td>1.44 (0.05)†††</td>
<td>1.58 (0.17)†</td>
</tr>
<tr>
<td>20</td>
<td>1.39</td>
<td>1.22 (0.02)†††</td>
<td>1.29 (0.09)†††</td>
</tr>
<tr>
<td>30</td>
<td>1.29</td>
<td>1.15 (0.02)†††</td>
<td>1.19 (0.06)†††</td>
</tr>
<tr>
<td>45</td>
<td>1.19</td>
<td>1.10 (0.01)†††</td>
<td>1.13 (0.04)†††</td>
</tr>
<tr>
<td>60</td>
<td>1.17</td>
<td>1.07 (0.01)†††</td>
<td>1.10 (0.03)†††</td>
</tr>
<tr>
<td>120</td>
<td>1.17</td>
<td>1.04 (0.01)†††</td>
<td>1.05 (0.02)†††</td>
</tr>
</tbody>
</table>

\( \text{PCO}_2 \) from measured \( \text{PCO}_2 \) corrected for blood-gas analyser bias (mean (sd)). ††† \( P<0.001 \) vs manufacturer’s correction factor; * \( P<0.05 \) vs in vitro.
7.39 (0.01), \( P_{\text{CO}_2} \) 5.5 (0.4) kPa and Bic 24.8 (0.9) mmol litre\(^{-1}\). \( P_{\text{CO}_2} \) and pH did not differ from \( P_{\text{in}} \) and pH, respectively.

**Normal tonometry values**

Table 3 shows normal values for the tonometric variables and their differences from blood values. There was a significant correlation between equilibrium \( P_{\text{in}} \) and \( P_{\text{CO}_2} \) (fig. 3), suggesting that \( P_{\text{in}} \) is partly determined by blood \( P_{\text{CO}_2} \) supplying the gastric mucosa.

**Error analysis: correction for incomplete equilibration and for blood-gas analyser bias**

Using the dwell time-dependent correction factors provided by the manufacturer without correcting for blood-gas analyser bias, the expected \( P_{\text{in}} \) calculated with the correction for blood-gas analyser bias and with the \textit{in vivo} correction factors of this study was underestimated, particularly at short dwell times (table 4). If the correction for blood-gas analyser bias is superimposed on the manufacturer’s dwell time-dependent correction factors, \( P_{\text{in}} \) is overestimated, particularly at long dwell times (table 4). The lower limit of normal pH would thus vary, whether or not correction for blood-gas analyser bias is superimposed on the manufacturer’s correction factors for calculation of equilibrium \( P_{\text{in}} \) and whether short or long dwell times are used, between 7.38 (at 16% underestimation of expected \( P_{\text{in}} \) of 6.6 kPa) and 7.26 (at 12% overestimation of \( P_{\text{in}} \), of 6.6 kPa), respectively, compared with 7.31 at an expected \( P_{\text{in}} \) of 6.6 kPa.

**Discussion**

In this study, we have provided normal values for variables derived from gastric tonometry. From \( P_{\text{in}} \), increase in the \textit{in vitro} experiments and in the human stomach, new correction factors, different from those supplied by the manufacturer, were calculated to allow for saline dwell times shorter than needed for full equilibration. With the use of validated correction factors and the known blood-gas analyser-dependent \( P_{\text{CO}_2} \) measurement bias, \(^{19,20,22} P_{\text{in}} \) can be assessed accurately.

Our results showed that \( P_{\text{in}} \) build-up in the tonometer in the human stomach was slower than \textit{in vitro}. Coverage of the tonometer balloon by mucus in the stomach may reduce the diffusion rate. The clinical effect of a slower \( P_{\text{in}} \) build-up is small and limited to short dwell times. The use of \textit{in vitro} correction factors would lead to 10% and 5% underestimations of the expected \( P_{\text{in}} \) at 10- and 20-min dwell times, respectively, so that, in contrast with common practice, the use of \textit{in vitro} correction factors for \textit{in vivo} measurements seems inappropriate. For a dwell time of 30 min in clinical studies, the \textit{in vitro} correction factor can be used, as it does not differ from that \textit{in vivo}. The \textit{in vitro} correction factors found previously largely corresponded to ours, although it is unclear how they were derived.\(^\text{23}\) The larger CV values of \( P_{\text{in}} \) \textit{in vivo} than in the \textit{in vitro} study may be explained by varying \( P_{\text{in}} \) between individuals rather than a higher measurement error \textit{in vivo}. In other respects, the variability of \textit{in vivo} \( P_{\text{in}} \) assessments was independent of dwell-time, and therefore reliable \( P_{\text{in}} \) assessments at short dwell times are practicable.\(^\text{24}\)

As our correction factors are independent of blood-gas analyser bias, the use of our factors by others during \( P_{\text{CO}_2} \) tonometry should be supplemented by correction for \( P_{\text{CO}_2} \) measurement specific for the type of blood-gas machine and the tonometer fluid used.\(^\text{19,22}\) The higher correction factors supplied by the manufacturer than our \textit{in vitro} factors may thus have included, contrary to common belief,\(^\text{7}\) blood-gas analyser bias for measurements in saline. We learned that the \textit{in vitro} experiments performed by the manufacturer to develop correction factors involved numerous simultaneous measurements of tonometric balloon and surrounding bath \( P_{\text{CO}_2} \) at various dwell times in a randomized order, while blood-gas analyser bias for \( P_{\text{CO}_2} \) measurements in saline had not been appreciated (J. Kent, [Image]
Figure 3 Equilibrium $P_{CO_2} vs P_{CO_2}$. Solid line = regression line.

Tonometry of $P_{CO_2}$

Tonometrics, personal communication). The idea that the factor of blood-gas analyser bias has been erroneously incorporated into the manufacturer’s correction factors is supported by a correction factor at 120 min of 1.17 for the sigmoid and 1.11 for the gastric tonometer, at a time when equilibration approaches 96% and should be associated with a correction factor of only 1.04.

If a correction for blood-gas analyser bias is superimposed on the manufacturer’s correction factors for measurements in saline, overestimation of $P_{CO_2}$ and underestimation of pH i results, particularly at long dwell times. This may explain a normal mean pH i of as low as 7.31, found in healthy volunteers by others, using both correction for blood-gas analyser bias and the manufacturer’s dwell time-dependent correction factors. Nevertheless, our normal variables largely agree with those found in healthy volunteers in a recent study, even though the latter study does not provide information on correction factors and measurement bias. Finally, a slightly negative tonometer balloon–blood $P_{CO_2}$ difference was found in a few subjects in our study, contrary to expectations based on normal physiology. A negative difference could be explained by a fall within the tonometer and blood $P_{CO_2}$ measurement error, that would be approximately 5% at maximum, if both the blood and tonomeric assessments, as judged from the CV values of the tonometer readings in vitro, carry an error of approximately 2.5%.

The catheter deadspace, serving as a reservoir for the $P_{CO_2}$ increase, may help to explain why model 2 fitted the measured data better than model 1. The deadspace reservoir effect depends on the volume and diffusion capacity of the balloon and the volume of the tonometer catheter lumen, so that the correction factors would become dependent on the catheter type used. For example, we have shown that a 50% increase in length increased the $T_2$ of the balloon $P_{CO_2}$ increase by 20% and resulted in higher correction factors at 10-and 20-min dwell times. As the gastric tonometer commonly used in critically ill patients is approximately 30% shorter than the sigmoid type, $P_{CO_2}$ increase will be 10% faster. From the data in our previous study, it can be estimated that the correction factor at the 10-min dwell time would be approximately 4% less for the gastric than for the sigmoid tonometers used in vivo (i.e. 1.56 instead of 1.58). Thus the correction factors for the common dwell times in clinical practice (20 min or more), as presented in this study for the sigmoid tonometer, are also applicable to the gastric tonometer. Further, carbon dioxide remaining in the deadspace saline after each aspiration can influence subsequent measurements by pushing, upon reintroduction of saline, some carbon dioxide-containing saline into the balloon and increasing starting $P_{CO_2}$, resulting in overestimation of $P_{CO_2}$ of 10% and 6% at dwell times of 10 and 20 min, respectively. Rinsing of the tonometer four times before each reintroduction of saline circumvents this effect. We took this phenomenon into account, thereby explaining a similar goodness of fit of model 2 for the in vivo as for the in vitro data.

There is large variation in calculated normal $P_{CO_2}$ and pH i between centres, and our study suggests that this may be from differences and errors in methodology (table 4). For example, in many studies, information on the blood-gas analyser, dwell time used, or both, was not provided. The saline method has been compared with the recently developed automated, semicontinuous air tonometry, an apparently simple and reliable technique that may circumvent many of the methodological problems associated with manual saline tonometry in vivo and in critically ill patients. In contrast with this method, $P_{CO_2}$ measured by saline tonometry and corrected for dwell time may overestimate surrounding $P_{CO_2}$, particularly at short dwell times. This overestimation may be from high correction factors for short dwell times provided by the manufacturer, erroneously incorporating bias of the blood-gas analyser. In comparing saline with air tonometry in vivo, however, fair agreement was observed, but since blood-gas analyser bias was not reported, it cannot be judged how the normal saline tonometric variables used as a gold standard were obtained. The correction factors and normal values for saline

Table 4 Effects of tonometer type, manufacturer’s dwell time-dependent correction factors, and blood-gas analyser bias on expected $P_{CO_2}$

<table>
<thead>
<tr>
<th>Dwell time (min)</th>
<th>Sigmoid/Gastric type correction factor of the manufacturer</th>
<th>Without correction for blood-gas analyser bias of</th>
<th>With correction for blood gas analyser bias of</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% Difference from expected $P_{CO_2}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Without correction for blood-gas analyser bias</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>of $P_{CO_2}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$-15%$</td>
<td>$-7%$</td>
</tr>
<tr>
<td>10</td>
<td>1.57/1.62</td>
<td>$-16%/ -13%$</td>
<td>$-8%/ -5%$</td>
</tr>
<tr>
<td>20</td>
<td>1.39/1.36</td>
<td>$-9%/ -11%$</td>
<td>$0%/ -2%$</td>
</tr>
<tr>
<td>30</td>
<td>1.29/1.24</td>
<td>$-8%/ -12%$</td>
<td>$+1%/ -3%$</td>
</tr>
<tr>
<td>45</td>
<td>1.19/1.16</td>
<td>$-11%/ -13%$</td>
<td>$-2%/ -5%$</td>
</tr>
<tr>
<td>60</td>
<td>1.17/1.13</td>
<td>$-9%/ -13%$</td>
<td>$-1%/ -5%$</td>
</tr>
<tr>
<td>120</td>
<td>1.17/1.11</td>
<td>$-5%/ -10%$</td>
<td>$+4%/ -2%$</td>
</tr>
</tbody>
</table>
tonometry reported in this study may, in turn, form a reference base for future evaluation of other types of tonometry in vivo.

It may be questioned if \( P_{CO_2} \) increase in healthy volunteers applies to critically ill patients. Critically ill patients may have mucosal hyperperfusion, oedema and swelling, which may slow transmucosal \( P_{CO_2} \) diffusion and tonometer \( P_{CO_2} \) increase. Limitation of intramucosal diffusion may not adversely effect \( 2CO_i \)

ill patients may have mucosal hypoperfusion, oedema

volunteers applies to critically ill patients. Critically

rather than mucosal

the difference in

mucus

build-up in the tonometer balloon.

Any transmucosal diffusion is needed to offset \( 2CO_i \)

build-up in the tonometer balloon.

Finally, the idea that \( P_{CO_2} \) is partly dependent on \( P_{CO_2} \) in blood supplying the gastric mucosa, is supported by the relationship between the two variables in our study, even in the relatively narrow blood \( P_{CO_2} \) range in healthy subjects. Our results indicate that the normal gastric mucosal \( P_{CO_2} \) depends on alveolar ventilation, if blood flow is adequate. As changes in arterial \( P_{CO_2} \) may affect \( P_{CO_2} \) in a similar direction, the difference in \( P_{CO_2} \) between gastric lumen and arterial blood is more likely to constitute a sensitive and specific measure for the adequacy of mucosal blood flow than \( P_{CO_2} \) and pH per se, that do not incorporate blood \( P_{CO_2} \). Further, pH is confounded by arterial blood bicarbonate content, that may vary independently from mucosal bicarbonate content.

Therefore, we supplied normal values for \( P_{CO_2} \)–pH and blood \( P_{CO_2} \)–pH differences in addition to those for \( P_{CO_2} \) and pH alone.

In summary, we have provided, for the first time, valid and measurement bias-independent correction factors and normal values for variables obtained by manual saline tonometry in the human stomach. The study may improve comparability of results among centres and may widen the clinical acceptance of the technique.

Acknowledgements

The study was made possible by Glaxo Wellcome BV, The Netherlands. We thank L. Zwarenak, Department of Clinical Physics, for help with the in vitro studies. We also thank B. Holte and J. Kent, Tonometrics, for valuable comments.

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