Augmented Arterial to End-Tidal $P_{CO_2}$ Difference during Laparoscopic CO$_2$ Insufflation in Man

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Abstract Acid-base status of the blood and tissue fluids and pulmonary gas exchange were continuously observed during intra-abdominal CO$_2$ insufflation for 2 h in 8 paralyzed and artificially ventilated patients who underwent laparoscopic cholecystectomy or resection of the sigmoid colon. Carbon dioxide pressure in the arterial and mixed venous blood as well as in end-tidal air started to increase already at 5 min CO$_2$ insufflation. On the other hand, appreciable elevation in $\dot{V}_{CO_2}$ and tissue $P_{CO_2}$ ($P_{T_{CO_2}}$) was noted only after 15 min. In vivo buffer value ($\beta$) was well within the normal physiological range at 5 min and gradually declined up to 2 h. These observations indicated that chemical buffering to CO$_2$ and redistribution of buffer base among the blood and tissue fluids were slowly developed during entire period of observation. In reflecting these experimental findings, arterial to end-tidal $P_{CO_2}$ difference (a-$AD_{CO_2}$) and respiratory gas exchange ratio ($R$) were promptly and significantly increased at 5 min and maintained slow increment up to 2 h. We conclude that these profiles of a-$AD_{CO_2}$ and $R$ can be explained by initially rapid and subsequently slow augmentation in ventilation-perfusion ratio ($\dot{V}_{A}/\dot{Q}$) during the specific type of respiratory acidosis elicited in this study.

Key words: a-$AD_{CO_2}$, laparoscopy, CO$_2$ insufflation, acid-base balance, gas exchange.

In recent years, insufflation of 100% CO$_2$ in the abdominal cavity during laparoscopy has become increasingly popular because the surgical procedure, examination, or treatment can be facilitated by this maneuver with minor invasion to the patients [14]. To secure a good visual space, the abdominal cavity is expanded by CO$_2$ and the patients are hyperventilated to prevent excessive CO$_2$ accumulation.

From the physiological point of view, this particular situation of the patients provides a unique opportunity to elucidate the control mechanisms in the respiratory acidosis because the conventional methods hitherto used to induce CO$_2$ exposure

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have been limited to the methods in alteration of pulmonary gas exchange system [5–9].

We have found an appreciable amount of arterial to end-tidal \( P_{CO_2} \) difference (a-\( AD_{CO_2} \)) from the beginning of \( CO_2 \) insufflation and this magnitude gradually increased with time. These findings are in contrast to a common recognition that a-\( AD_{CO_2} \) is negligible in amount [10]. We assumed that this substantial a-\( AD_{CO_2} \) was ascribed to markedly augmented ventilation-perfusion ratio (\( V_A/Q \)) during the specific feature of respiratory acidosis induced in the present study.

METHODS

Eight patients (3 males and 5 females) aged 51 ± 0.1 years (mean ± SD) and weighing 58.9 ± 9.2 kg were studied with consent. They underwent laparoscopic cholecystectomy (4 patients) or colonic extirpation (4 patients) during \( CO_2 \) insufflation. They were anesthetized with intravenous midazolam 0.1 mg/kg, paralyzed by pancuronium bromide 0.1 mg/kg, and artificially ventilated with tidal volume (\( VT \)) 10 ml/kg, respiratory frequency (\( f \)) 12 times/min, and inspiratory (\( T_i \)) to expiratory time (\( T_e \)) ratio being 1:2 by a pressure-limited ventilator throughout entire period of study. They were maintained by inhaling 35–40% \( O_2 \) gas mixture with 1% enflurane. After the control observation, which was lasted for about 30 min to achieve a steady state condition by observing end-tidal \( P_{O_2} \) and \( P_{CO_2} \), \( CO_2 \) was administered through a laparoscopic tubing for 2 h. Intra-abdominal pressure during \( CO_2 \) insufflation was maintained at approximately 12 mmHg.

Breath-by-breath measurement of respiratory flow by a respiromonitor (RM 300, Minato Med. Co.) and of respiratory gas concentration by a mass spectrometer (Perkin-Elmer Co.) was conducted. The end-tidal \( P_{CO_2} \) (\( PET_{CO_2} \)), \( VT \) were continuously monitored. Signals representing dynamic profile of respiratory flow and airway \( CO_2 \) concentration during each respiratory cycle were fed into a microcomputer installed in the respiromonitor and breath-by-breath \( CO_2 \) output (\( \dot{V}_{CO_2} \)) and \( O_2 \) consumption (\( \dot{V}_{O_2} \)) were continuously calculated on-line as reported previously [11]. To measure tissue fluid \( P_{CO_2} \) (\( P_{T_{CO_2}} \)), a catheter-type probe covered with a Teflon membrane was inserted into the subcutaneous space in the upper arm and the sampling gas was continuously introduced into a mass spectrometer (Medispect mass spectrometer) [12, 13]. During the last 1 min of the control period and 4–5, 9–10, 14–15, 29–30, 59–60, and 119–120 min in \( CO_2 \) insufflation period, the average value of \( \dot{V}_{CO_2} \), \( \dot{V}_{O_2} \), \( VT \), gas exchange ratio (\( R \)), \( PET_{CO_2} \), and \( P_{T_{CO_2}} \) were observed. Arterial and mixed venous blood were also withdrawn during the above observation periods from the radial artery and central vein, respectively. \( P_{O_2} \), \( P_{CO_2} \), and \( pH \) of these blood samples were measured within 5 min. In vivo arterial buffer values were calculated by the ratio of \( \Delta HCO_3^- \) to \( \Delta pH \), where \( \Delta \) signifies the difference between control and respective value measured during \( CO_2 \) period.

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RESULTS

Table 1 represents main results of the measured and calculated data. $P_{ETCO_2}$, $P_{ACO_2}$, $P_{ICO_2}$ as well as $R$ and a-AD$_{CO_2}$ increased promptly from the beginning of CO$_2$ insufflation and a gradual augmentation was followed until the end of 2 h observation. On the other hand, $P_{TCO_2}$ and $V_{CO_2}$ started to increase with less magnitude and slowly and progressively augmented toward the end of CO$_2$ administration. Figure 1 illustrates the consecutive drop from $P_{TCO_2}$, then $P_{ICO_2}$, $P_{ACO_2}$, and finally down to $P_{ETCO_2}$. This profile of pressure cascade is well maintained during entire period of observation and the slope of cascade appears to become steeper with time. A good linear relationship among these variables was verified as shown in Fig. 2.

Figure 3 depicts the changes in in vivo buffer slope during CO$_2$ ingestion. Its magnitude at 5 min is nearly 30 slyke, which is close to the normal in vitro value [6, 14, 15], and progressively decreased to about 10 slyke at 2 h.

Figure 4 compares the time course of changes in a-AD$_{CO_2}$ and $R$. The former increased promptly at 5 min then gradually increased with time whereas the latter progressively elevated during entire period of observation.

DISCUSSION

The present study demonstrated in the first place that carbon dioxide pressure in the arterial and mixed venous blood as well as in the alveolar air promptly increased in response to intra-abdominal CO$_2$ administration and these processes were followed by a gradual increase in tissue fluid $P_{CO_2}$ and $V_{CO_2}$. Secondly, these changes were understood to have reflected the chemical buffering to CO$_2$ and redistribution of buffer base among the blood and tissue fluids [7, 16] and complete equilibrium was not attained up to the end of 2 h observation. This interpretation was supported by the profile of time course in in vivo buffer value ($\beta$) shown in Fig. 3. Arterial $\beta$ is initially close to the in vitro value, 30 slyke, then progressively diminished with time, and approached down to 10 slyke. This must indicate that mixing high and low buffering capacity fluids, i.e. blood and tissue fluid, was slowly advancing. Since this $\beta$ curve did not level off until the end of 2 h, we considered that complete mixing was not achieved. Thirdly, as demonstrated in Fig. 4, in comparing with normal values during spontaneous breathing arterial to end-tidal $P_{CO_2}$ difference as well as gas exchange ratio are fairly high already at the control period, then these values kept increasing until the end of CO$_2$ period.

Since it is commonly accepted that the magnitude of a-AD$_{CO_2}$ is negligible amount in most conditions, substantially large a-AD$_{CO_2}$ obtained in the present study merits discussion to consider the underlying physiologic mechanisms. As described in the METHODS section, the subjects were hyperventilated throughout the entire period of operation. This was reflected in less than 30 mmHg $P_{ETCO_2}$ in the control period, and may be the reason for relatively high $R$. The diagram for
Table 1. Results of measured and calculated data.

<table>
<thead>
<tr>
<th>Measured variable</th>
<th>Control</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{ETCO_2}$ (mmHg)</td>
<td>26 ± 2.6</td>
<td>29 ± 3.8</td>
<td>31 ± 4.6</td>
<td>32 ± 5.4</td>
<td>35 ± 6.5</td>
<td>35 ± 8.1</td>
<td>41 ± 10.0</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg)</td>
<td>30 ± 3.1</td>
<td>36 ± 5.2</td>
<td>37 ± 5.3</td>
<td>39 ± 6.6</td>
<td>42 ± 6.9</td>
<td>44 ± 8.7</td>
<td>50 ± 11.6</td>
</tr>
<tr>
<td>$P_{ICO_2}$ (mmHg)</td>
<td>33 ± 3.5</td>
<td>38 ± 3.9</td>
<td>40 ± 5.4</td>
<td>42 ± 5.4</td>
<td>45 ± 6.1</td>
<td>48 ± 7.5</td>
<td>54 ± 10.5</td>
</tr>
<tr>
<td>$P_{rCO_2}$ (mmHg)</td>
<td>39 ± 2.7</td>
<td>40 ± 6.0</td>
<td>42 ± 4.8</td>
<td>44 ± 5.0</td>
<td>49 ± 6.0</td>
<td>57 ± 8.5</td>
<td>65 ± 8.8</td>
</tr>
<tr>
<td>$V_{CO_2}$ (ml/min)</td>
<td>126 ± 23</td>
<td>134 ± 29</td>
<td>142 ± 35</td>
<td>148 ± 33</td>
<td>157 ± 36</td>
<td>173 ± 40</td>
<td>200 ± 57</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.5 ± 0.02</td>
<td>7.45 ± 0.03</td>
<td>7.42 ± 0.03</td>
<td>7.4 ± 0.04</td>
<td>7.38 ± 0.04</td>
<td>7.37 ± 0.05</td>
<td>7.32 ± 0.06</td>
</tr>
</tbody>
</table>

Values are mean±SD. * and ** indicate that the differences from the control value are significant at 5 and 1% level, respectively. * and *** indicate that the differences in values between adjacent two columns are significant at 5 and 1% level, respectively.
Fig. 1. Profile of consecutive drop in carbon dioxide pressure starting from the tissue fluid ($P_{TCO_2}$), then mixed venous blood ($P_{VCO_2}$), arterial blood ($P_{aCO_2}$), and finally to end-tidal air ($P_{ETCO_2}$). The feature of cascade profile is well maintained during entire period of the observation and the slope of cascade appears more pronounced toward the end of CO₂ insufflation period.

Fig. 2. The relationships among the values of $P_{ETCO_2}$, $P_{aCO_2}$, $P_{VCO_2}$, and $P_{TCO_2}$. Simple regression lines and 95% confidence bands for the mean are shown. A good linearity is found between all pairs of two variables.
Fig. 3. In vivo buffer value during the period of CO₂ insufflation. Its magnitude is close to normal in vitro value, 30 slyke, at 5 min, then progressively decreases to about 10 slyke at 1 to 2 h. This feature signifies that chemical buffering to CO₂ and redistribution of buffer base among the blood and tissue fluids are slowly developing and do not attain the complete equilibrium by the end of observation. * and ** indicate that the differences from the 5 min value are significant at $p<0.05$ and $p<0.01$, respectively. # and ## indicate that the differences in values between adjacent two levels are significant at $p<0.05$ and $p<0.01$, respectively. Data are expressed as mean±SD.

ventilation-perfusion relationship ($\dot{V}_A/Q$) predicts that the higher the $R$, the higher the $\dot{V}_A/Q$ [17, 18]. Therefore, the presence of appreciable $a-AD_{CO_2}$ is conceivable. Following the start of CO₂ insufflation, the intra-abdominal pressure was elevated up to 12 mmHg. This magnitude is considered to be high enough to intervene in the venous return [1,3]. Accordingly, $\dot{V}_A/Q$ ratio may have increased more and induced further rise in $a-AD_{CO_2}$. Subsequently, gradual augmentation in CO₂ elimination continued during the rest of CO₂ period. This was assumed to be the reason for progressive rise in $R$ and $\dot{V}_A/Q$ as well as in $a-AD_{CO_2}$. Additionally, since the $\dot{V}_A/Q$ curve represents parabolic nature, elevated $P\dot{V}_{CO_2}$ toward the end of CO₂ period may have resulted in steeper slope of this curve [17, 18]. This will effect further increase in $a-AD_{CO_2}$. Our finding that $a-AD_{CO_2}$ increases with increasing $P_aCO_2$ is well in accord with the reports by Brampton and Watson [19] and Yusa et al. [20] who obtained a positive linear relationship between $a-AD_{CO_2}$ and $P_aCO_2$.

It must be noted, however, that Yusa et al. [20] reported the incidence of negative instead of positive $a-AD_{CO_2}$ found in this study. They claimed the possibility that diminished functional residual capacity (FRC) due to positive intra-abdominal pressure induces a gravity-dependent airway closure during late expiratory period. This will elicit temporarily diminished physiological dead space ($\dot{V}_D$), so that $PET_{CO_2}$ will increase. A few other investigators [21–23] also discussed the possibility for a reverse $a-AD_{CO_2}$ when FRC similarly reduced in pregnancy or
Fig. 4. Comparison of time course between a-$AD_{CO_2}$ (●) and $R$ (■) values at control and following intra-abdominal CO$_2$ period. The magnitudes of a-$AD_{CO_2}$ and $R$ are fairly high already at the control period, which may have reflected the relatively high ventilation induced by the ventilator. Following CO$_2$ insufflation a-$AD_{CO_2}$ is promptly elevated, then maintained gradual increment up to 120 min whereas $R$ is progressively augmented throughout the entire period of observation. These changes are considered to be ascribed to initially prompt decrement in venous return and subsequently gradual rise in CO$_2$ elimination. * and ** indicate that the differences from the control value are significant at $p < 0.05$ and $p < 0.01$, respectively. # and ## indicate that the differences in values between adjacent two levels are significant at $p < 0.05$ and $p < 0.01$, respectively. Data are expressed as mean±SD.

obesity. Gurtner and Traystman [24] also claimed the presence of the reverse a-$AD_{CO_2}$ during markedly elevated airway $P_{CO_2}$ and proposed the charged membrane hypothesis to explain their results. Nevertheless, in agreement with the data of Brampton and Watson [19], we did not experience the negative a-$AD_{CO_2}$ in our studies, although our patients may have had a diminished FRC and increased airway $P_{CO_2}$.

In summary, the dynamic and transient state in blood gas, acid-base as well as gas exchange status were observed during the intra-abdominal CO$_2$ insufflation. The specific feature of respiratory acidosis during this procedure induced a substantial augmentation in arterial to end-tidal $P_{CO_2}$ difference. Physiologically and
pathophysiologicallly, this is an important caution because arterial $P_{CO_2}$ level of the subject cannot reasonably be estimated from the non-invasive analysis of respired gas composition.

REFERENCES


