Time Course of Acid-Base Regulation Following Intraperitoneal CO₂ Administration in Man

Akira AOKI

Department of Anesthesiology, Hyogo College of Medicine, Nishinomiya, 663 Japan

Abstract Chronological changes in acid-base status during laparoscopic CO₂ insufflation were studied for 2h in 10 patients who underwent laparoscopic cholecystectomy. Carbon dioxide pressure in alveolar air as well as arterial blood promptly and significantly increased within 5 min whereas amount of pulmonary CO₂ elimination significantly increased after 15 min. Pulmonary gas exchange ratio (R) exceeded the level of unity at 10 min and progressively increased toward the end of 2 h observation. These results indicated that CO₂ equilibrium process between different body compartments with different time constant took place and apparent equilibrium was not completed during observation. In vivo buffer value of the arterial blood started to decrease after 5 min and decreased to about one-third the in vitro buffer value until the end of observation. This indicated that CO₂ equilibrium between blood and interstitial fluids took place slowly during entire period of study and no significant contribution of cellular buffering was developed. We conclude that slower development of acid-base regulation in the present study than those reported in the previous studies may have been derived from small diffusion area and blood perfusion for CO₂.

Key words: hypercapnia, acid-base regulation, laparoscopic CO₂ insufflation, CO₂ stores, in vivo buffer value.

Chronological changes in acid-base balance in response to hypercapnic exposure has hitherto been extensively investigated by alteration in pulmonary gas exchange, i.e., diminished alveolar ventilation [1] or inhalation of CO₂ gas mixture [2-5]. In recent years, insufflation of 100% CO₂ into the abdominal cavity to secure an expanded and good visual space during laparoscopy became increasingly frequent [6, 7]. This procedure is indispensable during laparoscopic examination, treatment or surgery for the abdominal organs with less surgical invasion.

From the physiological point of view, intraperitoneal CO₂ administration gives a good chance to investigate acid-base regulation in another aspect of studies. The
conventional method elicits CO₂ accumulation from the gas exchange system in the lung whereas the procedure at issue induces hypercapnia from the abdominal space. The present study was conducted to clarify the time course of acid-base balance during CO₂ administration in the abdominal cavity and compared it with the results reported by the conventional studies.

METHODS

Ten patients (5 males and 5 females) aged 49±9.8 years (mean±SD) and weighing 59.9±9.8 kg, who underwent laparoscopic cholecystectomy under CO₂ insufflation, were studied with consent. They were anesthetized with intravenous midazolam 0.1 mg/kg, paralyzed by pancuronium bromide 0.1 mg/kg and artificially ventilated with VT 10 ml/kg, respiratory frequency (f) 12 times/min and inspiratory (T₁) and expiratory time (T₂) ratio being 1:2 by a pressure-limited ventilator. The patients were maintained by inhaling 35-40% O₂ gas mixture with 1% enflurane throughout entire period of study. The intra-abdominal pressure during CO₂ insufflation was maintained at approximately 12 mmHg.

Breath by breath measurement of respiratory flow by a respirometer (RM 300, Minato Med. Co.) and respiratory gas concentration by a mass spectrometer (Perkin Elmer Co.) was conducted. The end-tidal $P_{CO₂}$ ($P_{ETCO₂}$) and $VT$ were continuously monitored. As illustrated in Fig. 1, the profile of respiratory flow and CO₂ concentration during each breath cycle is quite different: the former is high in

![Graph showing respiratory flow and expired air CO₂ fraction ($FECO₂$) in each respiratory cycle. These signals were fed into a microcomputer and averaged $FECO₂$ in each expiration was obtained. For details, see text.](Japanese Journal of Physiology)
the beginning of expiration whereas the latter exhibits the peak at the end of expiratory phase. These signals were fed into a microcomputer installed in the respirometer and breath by breath \( V_{\text{CO}_2} \) output (\( V_{\text{CO}_2} \)) and \( \dot{V}_{\text{O}_2} \) consumption (\( \dot{V}_{\text{O}_2} \)) were continuously calculated from averaged expired \( \text{CO}_2 \) and \( \text{O}_2 \) concentrations times respiratory frequency. The average value of \( \text{CO}_2 \) elimination (\( \dot{V}_{\text{CO}_2} \)), \( P_{\text{ETCO}_2} \), \( V_T \) and gas exchange ratio (\( R \)) during control period and first 1 min of \( \text{CO}_2 \) insufflation were measured. The same measurement was also carried out for the last 1 min during 2–5, 6–10, 11–15, 31–60 and 61–120 min period, respectively. Arterial blood from the radial artery was withdrawn at 5, 10, 15, 30, 60 and 120 min during \( \text{CO}_2 \) insufflation. Blood gas measurement was performed within 2 min after blood sampling. Chronological changes in \( P_{\text{ACO}_2} \), pH and \textit{in vivo} buffer value calculated by \( -\Delta \text{HCO}_3^-/\Delta \text{pH} \) were also observed.

**RESULTS**

Table 1 represents chronological changes in respiratory and acid-base status of the arterial blood during \( \text{CO}_2 \) insufflation in the abdominal cavity. During control period which lasted at least for 30 min, the patients were maintained at a relatively hyperpneic condition so that \( P_{\text{ETCO}_2} \) and \( P_{\text{ACO}_2} \) were less than 30 mmHg and arterial pH was higher than 7.5. After \( \text{CO}_2 \) administration, \( P_{\text{ETCO}_2} \) significantly increased already at 1 min and \( P_{\text{ETCO}_2} \) and \( P_{\text{ACO}_2} \) were progressively elevated with time up to 42 and 42 mmHg at 120 min, respectively. On the other hand, arterial pH progressively decreased with time down to 7.354 at 120 min. It was noted that \( V_T \) significantly depressed right after \( \text{CO}_2 \) ingestion, despite constant setting of artificial ventilation. This may have been derived from positive intra-abdominal pressure amounted to 12 mmHg, which mechanically restricted ventilatory movement. Gas exchange ratio (\( R \)) also progressively elevated with time and exceeded unity at 10 min.

Figure 2 compared the time course of \( P_{\text{ETCO}_2} \) and \( V_{\text{CO}_2} \) changes. Up to 5 min, we defined this period stage A where \( P_{\text{ETCO}_2} \) progressively and significantly increased but \( V_{\text{CO}_2} \) remained nearly at control level. In the period of 5 to 10 min defined as stage B, both \( P_{\text{ETCO}_2} \) and \( V_{\text{CO}_2} \) still progressively increased. During the period of 15 to 120 min defined as stage C, \( V_{\text{CO}_2} \) still progressively elevated but rate of \( P_{\text{ETCO}_2} \) increment became less pronounced. It was also noted that \( R \) exceeded unity from the late period of stage B.

Figure 3 represents the time course of averaged \textit{in vivo} buffer values (\( \beta \)) which were calculated from the parameters in Table 1. At 5 min, \( \beta \) was 30.4 sylke (mm/pH), which is approximately equivalent with \textit{in vitro} buffer value in normal humans \([8, 9]\). Then, \( \beta \) diminished to 12.4 sylke at 10 min and maintained at about 10 sylke until the end of entire period of \( \text{CO}_2 \) insufflation.
Table 1. Chronological changes in respiratory and acid-base parameters during intra-abdominal CO₂ insufflation.

<table>
<thead>
<tr>
<th>Measured variable</th>
<th>Control min</th>
<th>1 min</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>$\dot{V}_{\text{CO}_2}$ (ml/min)</td>
<td>189 ± 27</td>
<td>188 ± 30</td>
<td>208 ± 35*</td>
<td>228 ± 43**</td>
<td>228 ± 41**</td>
<td>245 ± 35**</td>
<td>260 ± 34**</td>
<td>284 ± 38**</td>
</tr>
<tr>
<td>$P_{\text{aCO}_2}$ (mmHg)</td>
<td>27 ± 2.6</td>
<td>35 ± 5.5**</td>
<td>36 ± 5.6**</td>
<td>37 ± 5.8**</td>
<td>38 ± 5.6**</td>
<td>40 ± 5.7**</td>
<td>42 ± 6.4**</td>
<td></td>
</tr>
<tr>
<td>$P_{\text{ETCO}_2}$ (mmHg)</td>
<td>26 ± 2</td>
<td>28 ± 2.4**</td>
<td>32 ± 4**</td>
<td>35 ± 5**</td>
<td>36 ± 6**</td>
<td>37 ± 5.1**</td>
<td>38 ± 5.3**</td>
<td>40 ± 6.3**</td>
</tr>
<tr>
<td>$VT$ (ml)</td>
<td>608 ± 95</td>
<td>569 ± 104**</td>
<td>565 ± 107**</td>
<td>562 ± 108**</td>
<td>552 ± 107**</td>
<td>568 ± 95*</td>
<td>574 ± 95</td>
<td>580 ± 91</td>
</tr>
<tr>
<td>$R$</td>
<td>0.92 ± 0.07</td>
<td>0.97 ± 0.06**</td>
<td>0.97 ± 0.06*</td>
<td>1.02 ± 0.07**</td>
<td>1.05 ± 0.08**</td>
<td>1.10 ± 0.07**</td>
<td>1.15 ± 0.09**</td>
<td>1.21 ± 0.10**</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.515 ± 0.03</td>
<td>7.446 ± 0.05**</td>
<td>7.418 ± 0.06**</td>
<td>7.40 ± 0.06**</td>
<td>7.383 ± 0.05**</td>
<td>7.372 ± 0.05**</td>
<td>7.354 ± 0.05**</td>
<td></td>
</tr>
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</table>

Values are mean ± SD. * and ** signify that differences from the control values are significant at $p < 0.05$ and $p < 0.01$, respectively (paired $t$-test).
Fig. 2. Chronological changes in $P_{ETCO_2}$ and $V_{CO_2}$ during intraperitoneal CO$_2$ administration. Vertical lines indicate mean ± SD. Stage A is characterized by the findings that $P_{ETCO_2}$ significantly increases whereas $V_{CO_2}$ was maintained nearly unchanged from the control period. Stage B is the period where both $P_{ETCO_2}$ and $V_{CO_2}$ progressively increase. Stage C is the period where rate of $P_{ETCO_2}$ elevation diminishes whereas $V_{CO_2}$ still progressively increases with time.

DISCUSSION

The present study demonstrated that during intra-abdominal CO$_2$ insufflation respiratory as well as acid-base variables did not attain apparent steady state condition despite maintaining constant artificial ventilation for 2 h. Slow equilibrium in CO$_2$ stores between different compartments in the body fluids has well been established by a number of investigators [1, 3–5, 10–17]. For example, to characterize this specific feature, Nunn [17] proposed to define rapid, medium and slow compartments. We assume that our data at stages A and B may correspond to equilibrium in the rapid compartment which takes place among the well-perfused body fluids and organs. From stage C, the medium compartment, less-perfused body fractions, may be involved and this may have been still in process at the end of 2 h CO$_2$ exposure.

Another way to analyze the time course of CO$_2$ equilibrium in the body fluids can be obtained by observing in vivo buffer value during CO$_2$ exposure. Woodbury [4] stated that in vivo buffer value decreases to about two thirds at 2–4 min and
Fig. 3. Chronological changes in in vivo buffer value during CO$_2$ insufflation. $\beta$: buffer value. The magnitude of in vivo $\beta$ at 5 min is nearly identical with in vitro $\beta$. Between 10 to 15 min, in vivo $\beta$ approaches down to 10 slyke which signifies attainment of chemical buffering and redistribution between blood and interstitial fluids. Until the end of 2 h observation, in vivo $\beta$ was maintained nearly unchanged.

Further decreases to about one third the in vitro buffer value at 10 to 60 min which represents the chemical buffering and redistribution process between blood and interstitial fluids [12]. After CO$_2$ exposure for 2 h, in vivo buffer value restores to about one half of the in vitro buffer value which signifies involvement of cellular buffering contribution. Hata and Honda [1], however, found that cellular contribution took place by about 10% already at 30 min by the acid-base analysis of the thoracic duct lymph in the dog.

When time course of in vivo buffer value obtained in the present study (Fig. 3) was compared with those of previous investigations mentioned above, our data showed markedly slower changes than the previous ones. Our in vivo buffer value at 5 min still showed the equivalent magnitude with the in vitro value and attained the one third value after some 10 to 15 min. Thereafter, it was kept almost unchanged up to 2 h, indicating no cellular buffering contribution in our experiment. Two possible reasons to explain the different results between present and previous investigations were considered.

1) Differences in diffusion area. Conventional studies used the lung to expose the body compartments to CO$_2$ accumulation. The amount of alveolar as well as pulmonary capillary surface is known to be some 60 to 80 m$^2$ which is available for CO$_2$ diffusion. In the present study, available diffusion surface to CO$_2$ consists of parietal and visceral surface of the abdominal cavity: the former is 0.5 m$^2$ at the most and the latter about 0.33 m$^2$. Thus the total diffusion area for CO$_2$ in the previous studies is assumed to be 60 to 90 times the present one.
2) Difference in blood perfusion. Intra-abdominal pressure of the magnitude of 12 mmHg during CO₂ insufflation may be high enough to compress abdominal venous vessels and interfere with venous return [6]. This may have resulted in higher ventilation-perfusion ratio in the lung and thus elevated gas exchange ratio (R). This in fact was reflected in high R at 1 min after CO₂ ingestion. Furthermore, as described in the results section, VT was mechanically inhibited by augmented intra-abdominal pressure. These factors may have resulted in less blood perfusion of CO₂ in the present study.

The above considerations imply that equilibrium process of ingested CO₂ should be slower in our patients. From the clinical point of view, this is beneficial because impairment of acid-base homeostasis by abdominal CO₂ administration is maintained in moderate degree so that its recovery process after surgery may not need an extremely long time.

In summary, laparoscopic CO₂ insufflation induced slow impairment of CO₂ homeostasis which was effectively affected by less diffusion and perfusion for CO₂ equilibrium.

REFERENCES