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SURGICAL ENDOSCOPY
and Other Interventional Techniques

Carbon dioxide pneumoperitoneum causes severe peritoneal acidosis, unaltered by heating, humidification, or bicarbonate in a porcine model

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Abstract

Background: Carbon dioxide (CO_2) is the most common gas used for insufflation in laparoscopy, but its effects on peritoneal physiology are poorly understood. This study looks at the changes in peritoneal and bowel serosal pH during CO_2 pneumoperitoneum, and whether heating and humidification with or without bicarbonate alters the outcomes.

Methods: Twenty-one pigs divided into four groups as follows: (1) standard (STD) laparoscopy ($n = 5$); (2) heated and humidified (HH) laparoscopy ($n = 6$); (3) heated and humidified with bicarbonate (HHBI) laparoscopy ($n = 5$); and (4) laparotomy ($n = 5$). Peritoneal pH, bowel serosal pH, and arterial blood gas (ABG) were obtained at 15-min intervals for 3 h.

Results: Severe peritoneal acidosis (pH range 6.59–6.74) was observed in all laparoscopy groups, and this was unaltered by heating and humidification or the addition of bicarbonate. Bowel serosal acidosis was observed in all laparoscopy groups with onset of pneumoperitoneum, but it recovered after 45 minutes. No significant changes in peritoneal or bowel serosal pH were observed in the laparotomy group.

Conclusion: CO_2 pneumoperitoneum resulted in severe peritoneal acidosis that was unaltered by heating and humidification with or without bicarbonate. Alteration in peritoneal pH may conceivably be responsible for providing an environment favorable for tumor-cell implantation during laparoscopy.

Key words: Laparoscopy — Carbon dioxide — Peritoneal pH — Heating and humidification — Bicarbonate

Laparoscopic surgery is increasingly used in general surgery to perform more and more complex procedures. There have been quite a lot of studies on cardiopulmonary physiology during laparoscopic surgery [3, 7, 10]; however, the effect of pneumoperitoneum on peritoneal physiology is poorly understood. Most studies focused on the effect of pneumoperitoneum on tumor growth [8, 11]. Pneumoperitoneum is also known to have an effect on the morphology [6, 16, 18] and physiology [4] of the peritoneum. Exactly how these morphological and physiological changes influence tumor growth on the peritoneum after laparoscopy is unknown. Intracellular and extracellular pH of the peritoneum have been showed to be affected by CO_2 insufflation [18], and it has been hypothesized that these important regulators of cell functions, such as ATP production, cell proliferation, and apoptosis, could influence tumor cell implantation and survival during laparoscopy. In this study, we investigated the effect of CO_2 pneumoperitoneum on bowel serosal and peritoneal pH. We also looked at whether these effects of CO_2 pneumoperitoneum can be altered by heating and humidifying the gas with and without bicarbonate.

Methods

Twenty-one pigs divided into four groups as follows: (1) standard (STD) laparoscopy ($n = 5$); (2) heated and humidified (HH) laparoscopy ($n = 6$); (3) heated and humidified with sodium bicarbonate (HHBI) laparoscopy ($n = 5$); (4) laparotomy ($n = 5$). In the laparotomy group, the pigs received a lower midline incision from the umbilicus to just above the pubis. Carbon dioxide was used as the insufflation gas for all laparoscopy. The gas was heated to 37°C by allowing it to bubble through sterile water and diluted sodium bicarbonate solution for the HH and HHBI group, respectively. Diluted sodium bicarbonate solution (1.5%) was made from 8.4% sodium bicarbonate diluted to 5 times its own volume with distilled water. Animals that underwent laparoscopy had three 11-mm trocars inserted (left upper quadrant, left lower quadrant and right lower quadrant). CO_2 was delivered to the peritoneal cavity by insulation tubing via the left upper quadrant trocar. The aim of insulation tubing was to min-

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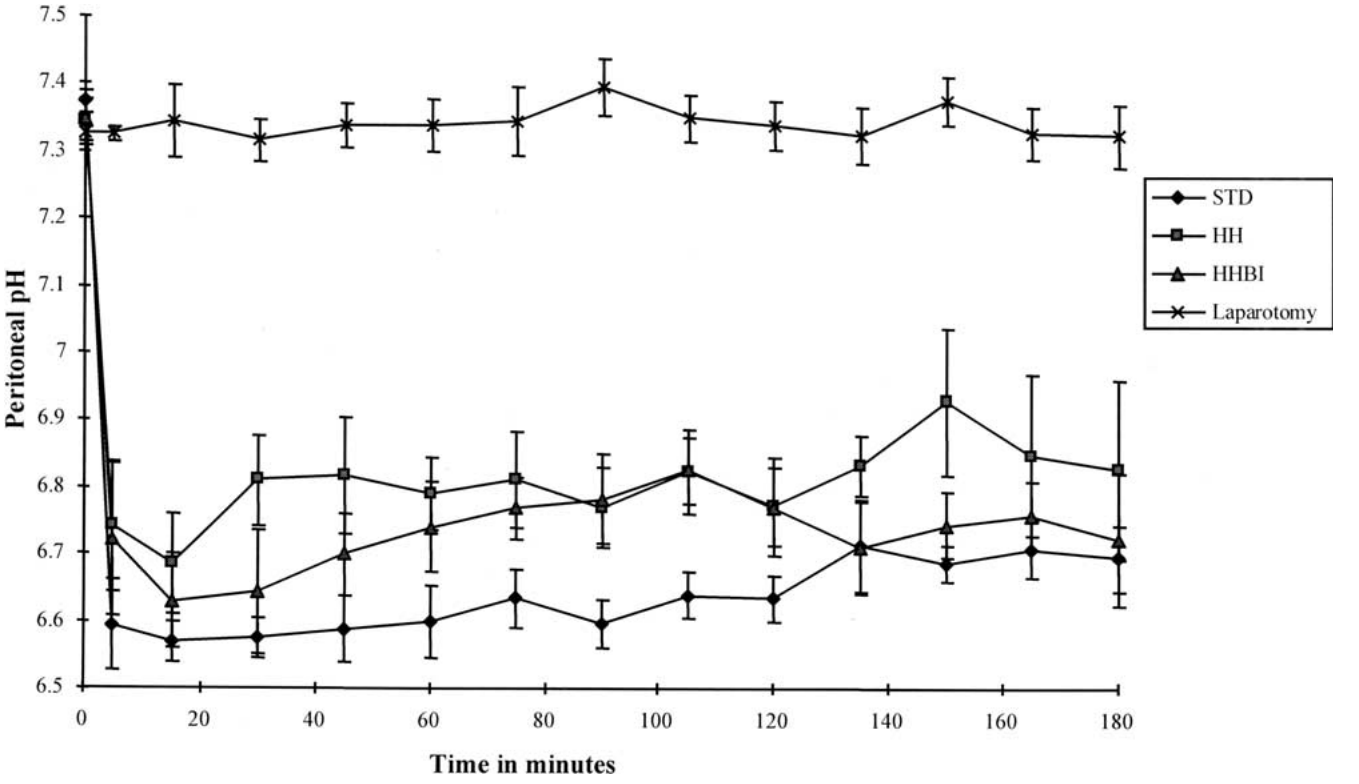

Fig. 1. Peritoneal pH vs time (mean ± SEM).

imize heat loss during passage of gas in the tubing. The right lower quadrant trocar was open to allow continuous egress of gas to maintain intraabdominal temperature at 37°C. The pH probe (Hanna Instrument HI 1413) was inserted via the left lower quadrant trocar to measure the peritoneal and bowel serosal pH. Pneumoperitoneum was maintained at 5 to 6 mmHg. All animals were ventilated at a fixed tidal volume of 120 ml/kg/min. Arterial blood gas (ABG) specimens were obtained from the right carotid artery. Peritoneal pH, bowel serosal pH, and ABG were obtained at the start of experiment (before insufflation) and 5 min and 15 min after insufflation. Thereafter the readings were measured at 15-min intervals for 3 h. Statistical analysis for comparison between two groups was carried out with unpaired two-tailed Student *t*-test.

Results

Peritoneal pH

All groups had a mean peritoneal pH between 7.33 to 7.37 at the start of experiments. Severe peritoneal acidosis was observed immediately after induction of pneumoperitoneum in all laparoscopy groups. STD group (mean pH 7.37 to 6.59), HHBI group (pH 7.35 to 6.72) and HH group (pH 7.34 to 6.74). These degrees of peritoneal acidosis persisted during the experiment (Fig. 1). The laparotomy group did not experience significant change in peritoneal pH at any point during the experiment. Peritoneal pH was significantly lower for all laparoscopy groups (STD, HH, and HHBI) compared to laparotomy ($p < 0.01$). The STD group had the lowest peritoneal pH of all laparoscopy groups. This did not reach statistical significance when compared to the HHBI group. However, when comparison was made with the HH group, the STD group had a significantly more acidotic peritoneal pH ($p < 0.05$) (Fig. 1). There was no significant difference in peritoneal pH between HHBI and HH group.

Bowel serosal pH

All laparoscopy groups experienced transient bowel serosal acidosis with induction of pneumoperitoneum. This effect lasted for ~45 min; thereafter bowel serosal acidosis gradually recovered (Fig. 2). This transient acidosis was not observed in the laparotomy group. The mean baseline bowel serosal pH ranged from 7.24 to 7.29. With induction of pneumoperitoneum transient bowel serosal pH changes were as follows: (1) STD—pH 7.29 ? 7.06; (2) HH—pH 7.28 ? 7.08; (3) HHBI—pH 7.28 ? 7.08; (4) laparotomy—pH 7.24 ? 7.24. There was no significant difference in bowel serosal pH between any groups at any point in time during the experiments.

Arterial blood gas changes

A significant rise in $PaCO_2$ was observed in all laparoscopy groups compared to laparotomy ($p < 0.01$). The rise in $PaCO_2$ (Fig. 3) was most marked in the HHBI group (32.8 ? 45.9), followed by the HH group (32.7 ? 41.3) and STD group (27.5 ? 38.0). HHBI and HH groups had significantly higher $PaCO_2$ compared to the STD group (HHBI vs STD—$p < 0.01$ and HH vs STD—$p < 0.05$). There was no significant difference in

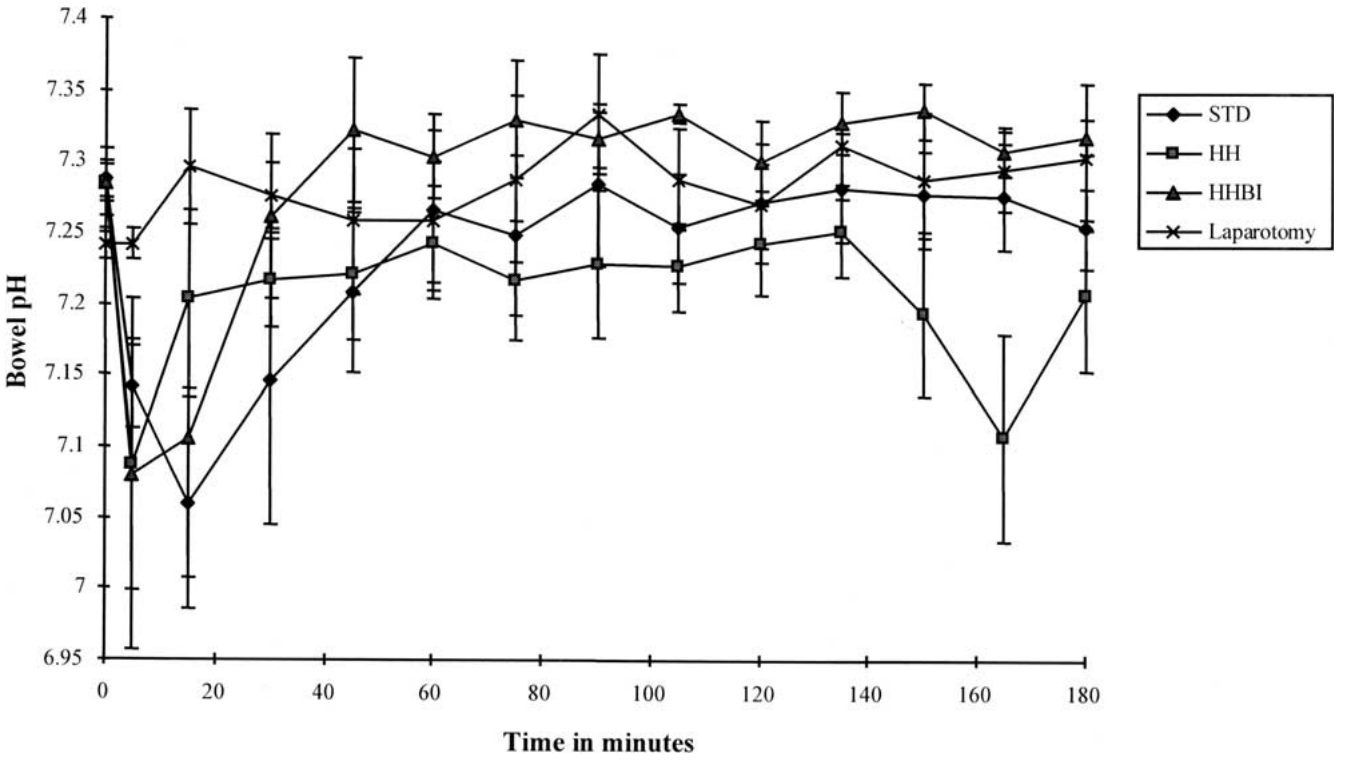

Fig. 2. Bowel pH vs time (mean ± SEM).

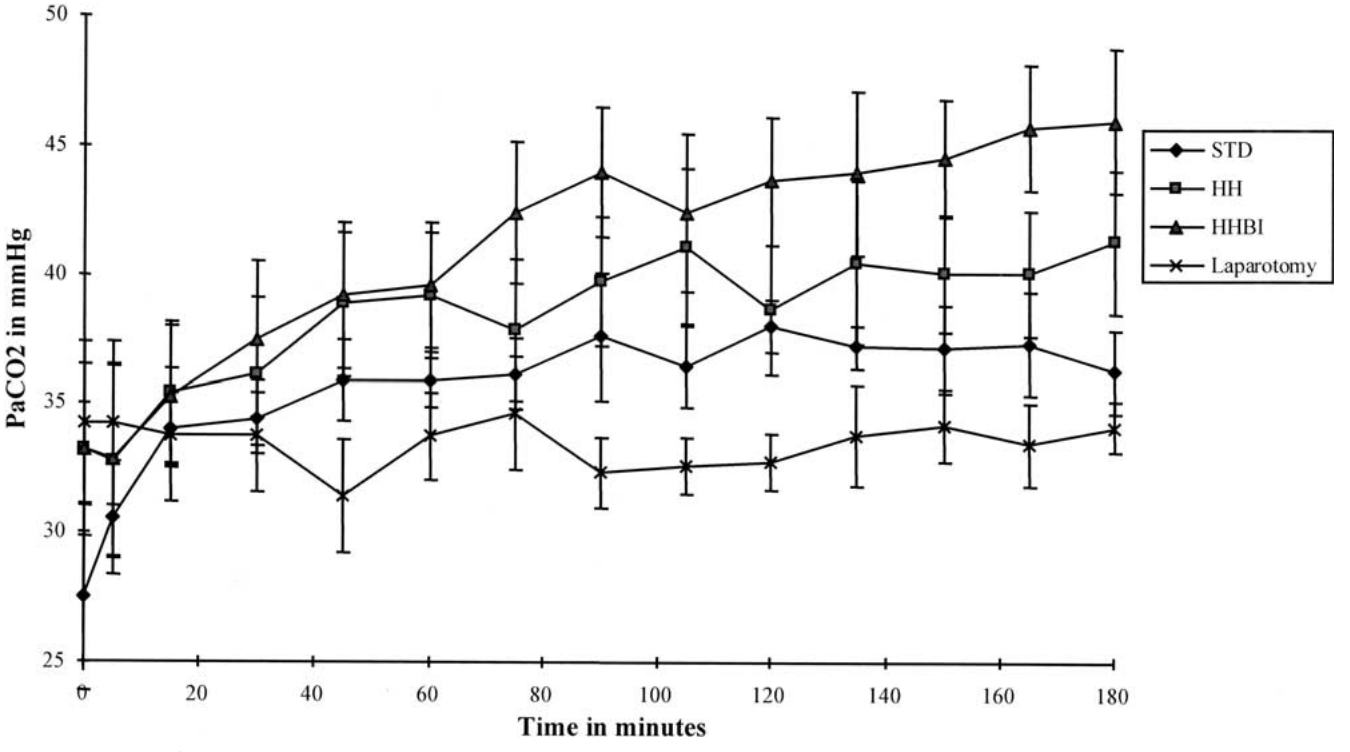

Fig. 3. $PaCO_2$ vs time (mean ± SEM).

$PaCO_2$ between the HHBI group and the HH group ($p = 0.08$). The rise in $PaCO_2$ was reflected by a proportionate lowering in arterial pH (Fig. 4). There were also significant reductions in arterial pH for all laparoscopy groups (STD, HH, and HHBI) compared to laparotomy ($p < 0.01$). In addition, the HHBI and HH groups also had significantly lower arterial pH than the STD group (Fig. 5). No significant difference in arterial pH was observed between the HHBI group and the HH group.

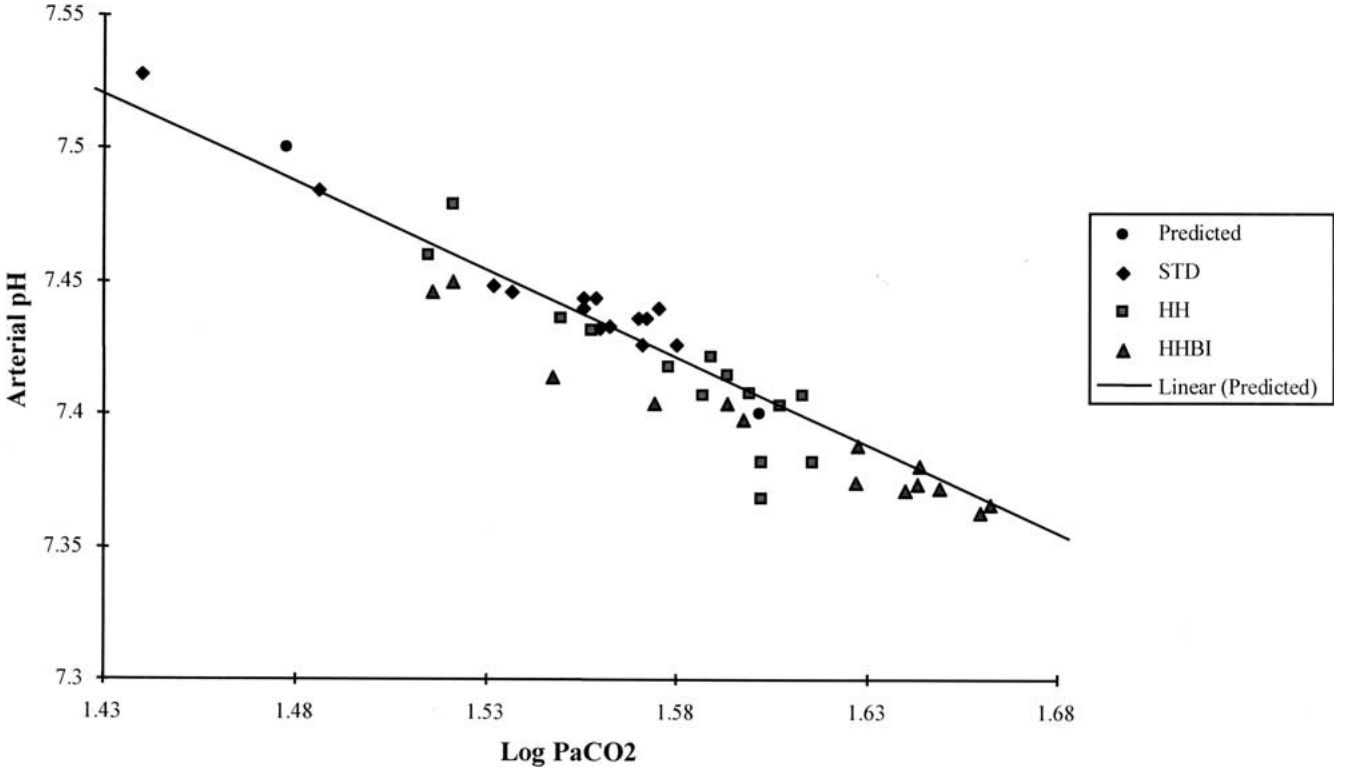

Fig. 4. Arterial pH vs log $PaCO_2$ (mean ± SEM).

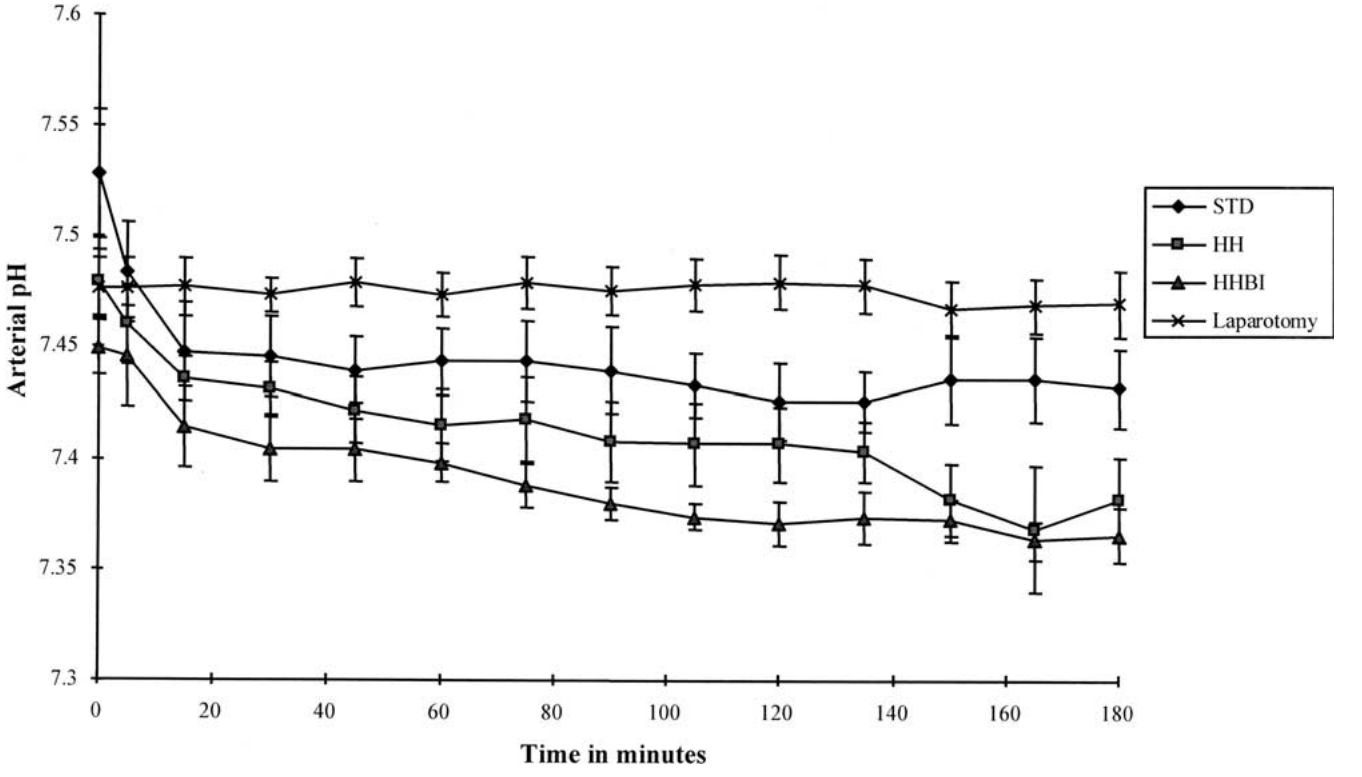

Fig. 5. Arterial pH vs time (mean ± SEM).

Discussion

Laparoscopic surgery has progressed tremendously since it was first introduced in general surgery for performing laparoscopic cholecystectomy. Nowadays most general surgical operations can be done laparoscopically, and in fact in many instances it is the preferred approach. Its cosmetic advantages and its faster recov-

ery in many instances are obvious. Cardiopulmonary physiology during laparoscopic surgery has been studied rather extensively in the past [3, 7, 10]. In the past few years, there has been interest in studying the effect of pneumoperitoneum on peritoneal defenses [3, 12, 19] in an attempt to understand its role in tumor growth after laparoscopic surgery. Studies on the morphology and physiology of the peritoneal environment, however, are still scanty. Tumor recurrence after laparoscopic surgery commonly occurs at the port site and peritoneal surface [8, 11, 19]. Previous studies had demonstrated that there are structural and microenvironmental changes of the mesothelial cells of the peritoneum [6, 16, 18]. Mesothelial cells were found to be swollen and the underlying basal lamina exposed on scanning electron microscopy after CO_2 pneumoperitoneum [6]. Intracellular and extracellular pH and calcium level are altered with CO_2 pneumoperitoneum [18]. pH and calcium are important regulators of cell functions such as ATP production, cell cycle, intracellular signaling and apoptosis [1, 14, 18]. It is likely that all these changes influence the favorability of tumor-cell implantation at the time of laparoscopic surgery. This study aims to characterize further the effect of CO_2 pneumoperitoneum on peritoneal pH and bowel serosal pH, and whether this can be reversed by heating and humidification or addition of bicarbonate to the gas.

Severe peritoneal acidosis is seen during CO_2 laparoscopy. Parietal peritoneal pH ranges from 6.59 to 6.74 (Fig. 1). This is likely to have resulted from absorption of carbon dioxide by the peritoneal surface. Similarly, this may explain the initial bowel serosal acidosis (Fig. 2). Peritoneal acidosis persisted for the duration of the experiment, whereas bowel serosal acidosis recovered (Figs. 1, 2). The visceral peritoneum covering the bowel has a larger circulatory bed compared to the parietal peritoneum, and the calibers of vessels present in the former are bigger. Larger vessels are less likely to collapse during pneumoperitoneum, and together with a larger circulatory bed, this enables the bowel serosa to clear its acid load more efficiently.

Heating and humidification seem to have a positive effect on peritoneal acidosis. The HHBI and HH groups had higher peritoneal pH than the STD group (Fig. 1). Heating [9] and humidification may cause dilatation of the circulatory bed in the peritoneum, resulting in more efficient removal of CO_2. This is supported in our study by a lower arterial pH and a higher $PaCO_2$ in the HHBI and HH groups.

Bicarbonate also seems to increase the acid load presented to the bowel and peritoneum. That the HHBI group had the highest $PaCO_2$ supported this. Addition of bicarbonate has been known to cause paradoxical acidosis [17].

We have not been able to demonstrate a metabolic contribution to the acidosis from pressure-induced tissue hypoxia. However, others have found increased serum lactate during pneumoperitoneum [15]. The arterial pH drop in our study had a proportionate increase in $PaCO_2$ with no metabolic component to the acidosis (Fig. 4). Nevertheless, we only used a pressure of 5 to 6 mmHg for our experiments. Pressures used in the other studies had been much higher [15]. It is likely that the contribution of pressure to metabolic acidosis varies with different species, intravascular volume status, positioning of the animal during the experiment, and length of exposure to increased intraabdominal pressure [4].

Carbon dioxide used to create pneumoperitoneum has been reported to be associated with increased tumor growth during laparoscopy in animal studies [8, 11]. The mechanism behind this phenomenon is unclear, and it has been proposed that the microenvironment of the peritoneum may be important in the regulation of cell growth and division [1, 14]. Griffiths et al. found that a low extracellular pH increased tumor expression of platelet-derived endothelial cell growth factor [5]. Endothelial cell growth factor is an angiogenic factor that is responsible for tumor cell growth and survival [13, 20]. CO_2 pneumoperitoneum was also found to damage the mesothelial layer of the peritoneum, thereby exposing the underlying basal lamina [6, 16]. Bared basal lamina could provide a good attachment site for spilled tumor cells at surgery [2]. Volz et al. had proposed that peritoneal acidosis was responsible for the damaging effect on peritoneum [16]. It is therefore not difficult to envisage that low peritoneal pH associated with carbon dioxide laparoscopy could potentially be implicated in providing a favorable environment for the growth of spilled tumor cells.

Carbon dioxide pneumoperitoneum resulted in severe peritoneal acidosis, and this was unchanged by heating and humidification or the addition of bicarbonate. Peritoneal acidosis may play a role in promoting tumor cell implantation during laparoscopic oncologic surgery. Understanding of the role of peritoneal microenvironment in tumor-cell growth is far from complete. Many more studies need to be done in the area to enable us to determine the safest approach to laparoscopic oncologic surgery.

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