Haemodynamic, acid–base and blood volume changes during prolonged low pressure pneumoperitoneum in rabbits


1Medizinische Hochschule Hannover, Zentrum Anaesthesiologie, OE 8050, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany. 2Klinik für Anaesthesiologie und Intensivtherapie, Klinikum der Friedrich-Schiller-Universität Jena, Erlanger Allee 101, D-07747 Jena, Germany. 3Medizinische Hochschule Hannover, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany. 4Medizinische Hochschule Hannover, Biometrie, OE 8410, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany. 5Medizinische Hochschule Hannover, Kinderchirurgie, OE 6760, Carl-Neuberg-Strasse 1, D-30625 Hannover, Germany

*Corresponding author. E-mail suempelmann.robert@mh-hannover.de

Background. The anaesthetic management of small infants during advanced laparoscopic surgery can be complicated by the major pathophysiological effects of increased intra-abdominal pressure. In this study haemodynamic, acid–base and blood volume changes were investigated during pneumoperitoneum in a small animal model.

Methods. Ten fasted, anaesthetized, mechanically ventilated and multi-catheterized New Zealand rabbits were randomized to carbon dioxide pneumoperitoneum (PP, duration 210 min, pressure 8 mm Hg) or control group. Cardiac index was determined using transcardiopulmonary thermodilution and total blood volume was measured by thermal-dye dilution with indocyanine green using a fibreoptic monitor system.

Results. In PP cardiac index (CI), central venous oxygen saturation (S\textsubscript{CO}_2), total blood volume (TBV) and base excess (BE) decreased significantly during the study whereas all variables remained constant in the control group. After release of PP the measured variables did not return to baseline within 30 min [PP, baseline vs study end: CI 108 (22) vs 85 (14) ml kg \textsuperscript{-1} min \textsuperscript{-1}, S\textsubscript{CO}_2 81.4 (8.9) vs 56.7 (9.8)%, TBV 318 (69) vs 181 (54) ml, BE –1.9 (2.7) vs –8.7 (1.8) mmol litre \textsuperscript{-1}; P<0.01].

Conclusion. Our animal model suggests that a decrease in CI, metabolic acidosis and hypovolaemia could occur after prolonged low pressure pneumoperitoneum in small infants, which is possibly not detectable by the standard monitor setting. Therefore, the routine use of an extended monitoring including measurement of central venous oxygen saturation and acid–base parameters should be considered during and soon after operation, when pneumoperitoneum will last longer than 2 h.

Br J Anaesth 2006; 96: 563–8

Keywords: blood, volume; complications, acidosis; heart, cardiac index; infants; pneumoperitoneum

Accepted for publication: January 6, 2006

In recent years prolonged surgery using laparoscopic techniques have been performed more frequently in neonates and small infants. \cite{1,2} It has been postulated that these techniques are associated with low morbidity, a shorter hospital stay, lower costs and clinical results similar to those achieved by open surgery. \cite{3} Anaesthetic management of these patients is complicated by the major pathophysiological effects of pneumoperitoneum and patient positioning (reviews in refs 4–6). Our own clinical experience has shown that a prolonged low pressure pneumoperitoneum in small infants can lead to significant metabolic acidosis and high volume requirements after operation. Studies investigating the cardiovascular effects of prolonged laparoscopic surgery in small infants are rare. Therefore the aim of this study was to investigate haemodynamic, acid–base and blood volume changes during prolonged low pressure pneumoperitoneum using an experimental setting, which mirrors the clinical situation as closely as possible.
Methods

After approval by the animal protection authorities (Protocol No. 509C-42502-02/549) 10 New Zealand rabbits were randomized and divided into two groups of five rabbits each [pneumoperitoneum (PP) and control]. After i.m. premedication with 25 mg s\(^{-1}\) ketamine, 5 mg midazolam and 0.15 mg buprenorphine the rabbits were anaesthetized with i.v. propofol, orotracheally intubated and mechanically ventilated with 1.5–2\% isoflurane in oxygen (ventilatory frequency 30 min\(^{-1}\), Servo 900 B, Siemens Elema, Stockholm, Sweden). Tidal volume was adjusted to maintain an arterial $P_{CO_2}$ of 35–45 mm Hg. All animals received 10 $\mu$g kg\(^{-1}\) fentanyl and 0.5 mg kg\(^{-1}\) rocuronium before surgical catheter placement. Using standard cut down techniques the following catheters were introduced: a 22 G central venous catheter (Arrow, Reading, USA; insertion length 3.5 cm) over a jugular vein, a 1.3 F arterial thermistor-tipped catheter (Picco PV 2011, Pulsion, Munich, Germany) for thermodilution over a femoral artery and a 4 F thermal-dye dilution catheter (Pulsiocath PV 2024, Pulsion, Munich, Germany) over a contralateral femoral artery. For the thermodilution catheters an inline injectate sensor was connected to the central venous line. In both groups a 3.5 mm trocar (30117 H4, Storz, Tuttinglen, Germany) was introduced intraperitoneally. In the PP-group carbon dioxide was insufflated using an electronic endoflator (26430530, Storz, Tuttlingen, Germany). Insufflation was limited to an intraabdominal pressure (IAP) of 8 mm Hg. All animals received 10 ml kg\(^{-1}\) single bolus infusion before catheter placement and thereafter 4 ml kg\(^{-1}\) h\(^{-1}\) of a buffered isotonic electrolyte solution i.v. (Plasmalyte A, Baxter, Irvine, USA). Monitoring during the study included direct measurement of arterial and central venous pressure (CVP), ECG, capnography and measurement of rectal body temperature. All animals were warmed with an infrared lamp and a circulating-water mattress.

Haemodynamic measurements and blood samples

Measurements were performed at baseline and after insufflation at 30, 60, 120, 180 and 210 min. A final measurement was made 30 min after abdominal decompression (240 min). At each time point mean arterial pressure (MAP) and CVP were recorded from calibrated pressure transducers. Cardiac output (CO) was determined by trans-cardiopulmonary thermodilution (Picco plus, Pulsion, Munich, Germany) after central venous injection of 5 ml ice-cold isotonic saline (mean of three measurements). Total blood volume was measured by the thermal-dye dilution catheter connected to an integrated fiberoptic monitor system (COLD Z-021, Pulsion, Munich, Germany) after injection of 0.5 mg kg\(^{-1}\) indocyanine green solution (concentration 1 mg ml\(^{-1}\)) at baseline, 120 and 240 min. Central venous and arterial blood samples were collected in heparinized syringes and pH, $P_{O_2}$, $P_{CO_2}$, base excess (BE), actual bicarbonate (HCO\(_3\)) and oxygen saturation were measured using a standard bloodgas oximetry system (ABL 735, Radiometer, Copenhagen, Denmark).

Statistical analysis

Statistical evaluation was based on comparisons of the means between both treatment arms at each time point of measurement. Thus, as multiple tests were conducted, appropriate procedures had to be used in order to control the experimentwise error rate $\alpha=0.05$ for each parameter. As the basic assumption of a possible effect was that of a monotone time-dependent relationship until study end, the principle of ‘closed test procedures’ could be applied in connection with hierarchically ordered hypotheses: the sequence of hypotheses was ordered by time point of measurement. Beginning with the last value (240 min), each comparison with the control group was performed by conducting a two-sided $t$-test (in the modified Welsh version, if necessary) at the local significance level $\alpha=0.05$. The procedure stopped as the first non-significant result occurred. Therefore, $P$-values <0.05 for any comparison after the stop of the procedure may not be interpreted as significant. Thus, compared with the Bonferroni procedure, the local significance level does not need to be corrected, resulting in a higher power in the situation of ordered alternatives. The closed test procedure was applied in the same way to the comparison of each measurement with the baseline value within each treatment arm using the two-sided paired $t$-test. Evaluation of the first measurement after baseline and the last measurement after abdominal decompression was regarded as a separate secondary analysis and was not included in the multiple test procedure. The assumption of normal distributions was checked for all parameters before the analysis by applying the Kolmogorov–Smirnov test. Data were analysed using SPSS 12.0 and presented as mean (SD).

Results

There were no differences in weight [PP 3.57 (0.45); control 3.77 (0.14) kg] or height [PP 53.3 (1.48); control 54.67 (2.42) cm] between the groups. Minute ventilation (MV) and peak airway pressure (PAP) were not different at baseline and study end but significantly higher in PP during the pneumoperitoneum. Arterial carbon dioxide tension ($P_{CO_2}$) was comparable at baseline and during the pneumoperitoneum but significantly higher in control at the study end (Table 1 and Fig. 1).

Haemodynamics and blood volume

There were no differences in measured haemodynamic parameters at baseline. During the study, MAP remained within the normal range in both groups but was significantly lower in PP-group from 60 min to the study end. Heart rates were comparable at each time point. CVP was higher in PP during insufflation but there were no significant differences at
Prolonged low pressure changes in rabbits

Table 1 Comparison of haemodynamic changes at baseline and study end. [PP, pneumoperitoneum; mean (SD)]. *P<0.05, study end vs baseline; †P-value of baseline, PP vs control; ‡P-value of study end, PP vs control. †After 240 min, in PP 30 min after abdominal decompression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Control</th>
<th>P-value‡</th>
<th>Study end†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pressure (mm Hg)</td>
<td>65 (6)</td>
<td>69 (7.9)</td>
<td>n.s.</td>
<td>59 (9.4)</td>
</tr>
<tr>
<td>Heart rate (min⁻¹)</td>
<td>298 (22)</td>
<td>299 (24)</td>
<td>n.s.</td>
<td>274 (8)</td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>6.7 (1)</td>
<td>6 (2)</td>
<td>n.s.</td>
<td>4.7 (1.3)</td>
</tr>
<tr>
<td>Cardiac index (ml min⁻¹ kg⁻¹)</td>
<td>108 (22)</td>
<td>135 (23)</td>
<td>n.s.</td>
<td>85 (14)*</td>
</tr>
<tr>
<td>Total blood volume (ml)</td>
<td>318 (69)</td>
<td>243 (91)</td>
<td>n.s.</td>
<td>181 (54)*</td>
</tr>
<tr>
<td>Global end-diastolic volume (ml kg⁻¹)</td>
<td>13.9 (4)</td>
<td>13 (4.4)</td>
<td>n.s.</td>
<td>12.9 (5.5)</td>
</tr>
<tr>
<td>pH</td>
<td>7.34 (0.1)</td>
<td>7.37 (0.1)</td>
<td>n.s.</td>
<td>7.2 (0.1)*</td>
</tr>
<tr>
<td>$P_{O_2}$ (mm Hg)</td>
<td>499 (56)</td>
<td>451 (90)</td>
<td>n.s.</td>
<td>472 (52)</td>
</tr>
<tr>
<td>$P_{CO_2}$ (mm Hg)</td>
<td>36 (4.1)</td>
<td>39 (5.4)</td>
<td>n.s.</td>
<td>33 (2.8)</td>
</tr>
<tr>
<td>HCO₃ (mmol litre⁻¹)</td>
<td>23.1 (2.3)</td>
<td>23.2 (1.2)</td>
<td>n.s.</td>
<td>17.9 (1.3)*</td>
</tr>
<tr>
<td>Base excess (mmol litre⁻¹)</td>
<td>−1.9 (2.7)</td>
<td>−2.4 (2.4)</td>
<td>n.s.</td>
<td>−8.7 (1.8)*</td>
</tr>
<tr>
<td>Svo₂ (mm Hg)</td>
<td>81.4 (8.9)</td>
<td>83.4 (9.9)</td>
<td>n.s.</td>
<td>56.7 (9.8)*</td>
</tr>
</tbody>
</table>

Discussion

The main finding of this study was that a prolonged low pressure pneumoperitoneum can lead to decreased CI, metabolic acidosis and hypovolaemia in rabbits. The cardiovascular system, dimensions (weight and height) and anatomical proportions (small thorax and large abdomen) of rabbits are comparable with those of neonates and small infants. Rabbits have already been used in other studies as models for the investigation of infant cardiovascular physiology and abdominal hypertension. The measurement of CO using arterial thermodilution in small animals and the measurement of total blood volume with an integrated fibreoptic monitoring system are validated methods. The pressure (8 mm Hg) and duration (210 min) of the carbon dioxide insufflation used simulated common conditions in advanced laparoscopic surgery. The study CI was significantly lower in PP from 60 min to the study end. Central venous oxygen saturation (Svo₂) decreased after insufflation and was significantly lower in PP from 210 min to the study end when compared with the control group and baseline. The changes in CI and Svo₂ between 210 and 240 min correlated significantly (Pearson correlation, r=0.69, P<0.05). Total blood volume decreased in PP and was significantly lower at the study end. In the control group total blood volume remained constant (Table 1 and Fig. 2). Global end-diastolic volume (GEDV) increased in PP after insufflation and decreased thereafter (P=0.09, baseline vs 60 min), but there were no significant differences between the groups or against baseline (Table 1).

Acid–base

At baseline acid–base parameters were comparable in both groups. During the study HCO₃ concentrations and BE decreased in PP and was significantly lower from 180 min to the study end. In the control group pH, HCO₃ concentration and BE remained constant (Table 1 and Fig. 2).

Fig 1 Ventilatory and arterial carbon dioxide changes during pneumoperitoneum (PP) lasting 210 min (carbon dioxide, pressure 8 mm Hg. *P<0.05, PP vs control).

baseline and the study end. In PP-group cardiac index (CI) increased initially after insufflation from baseline to 30 min and decreased thereafter firstly from 30 to 60 min and secondly after abdominal decompression. During the
shows that prolonged (>120 min) low pressure pneumoperitoneum is tolerated by small organisms but can lead to significant changes in haemodynamics, acid–base balance and total blood volume. First, we found an initial increase in CI after insufflation of carbon dioxide and we attribute this finding to a blood volume shift from intra-abdominal to intrathoracic possibly caused by a compression of intraabdominal blood vessels. Second, there was a continuous decrease in total blood volume during the study. Because veins are more compressible than arteries, we hypothesize that this is possibly because of the fact, that the prolonged increase in IAP may lead to an intestinal venous congestion with resulting venous hypertension and intestinal oedema. Third, surprisingly the release of the pneumoperitoneum did not restore CI and total blood volume to baseline values suggesting a backward shift of blood volume from intrathoracic to intra-abdominal spaces caused by a decompression of intraabdominal blood vessels. These findings were homogeneous in all animals with pneumoperitoneum. The changes in GEDV were not significant possibly because of the small number of animals and the low end-diastolic volume in rabbits. Kuntz and colleagues showed in a rat model that carbon dioxide pneumoperitoneum decreases intra-abdominal pH in a pressure-dependent way and this tissue acidosis may aggravate fluid shifts especially in prolonged pneumoperitoneum. Kaya and colleagues reported that an increased IAP for 60 min followed by abdominal deflation can lead
to an ischaemia–reperfusion-like injury in the normal small intestine in rabbits (insufflation–deflation injury). The authors stated that one of the most important effects of increased IAP is a reduction in mesenteric arterial blood flow that may cause ischaemia of the small intestine aggravated by venous hypertension and intestinal oedema. Therefore, the metabolic acidosis found in our study during 210 min of increased IAP may be a consequence of reduced intestinal blood flow, tissue acidosis and hypovolaemia.

During the pneumoperitoneum, MV, and PAP was increased in order to avoid hypercapnia and respiratory acidosis. The peritoneum of neonates and small infants is relatively larger and better perfused when compared with adults, and this can cause faster carbon dioxide absorption leading to a higher need for MV. Positive pressure ventilation may diminish left ventricular preload and central blood volume, but in our study the CI increased during peritoneal inflation and raising of ventilation and decreased after peritoneal deflation and a reduction of ventilation. Therefore, we hypothesise that the changes in the CI were primarily a consequence of blood volume shifts induced by altered IAP, whereas total blood volume may be diminished, additionally, by the raised MV during pneumoperitoneum. After abdominal decompression the increased MV was maintained for a while in order to eliminate buffered carbon dioxide. This may be the reason for the difference in arterial carbon dioxide tension at the study end. At all other study points there were no differences in arterial carbon dioxide tension between the groups. Therefore it is unlikely that the decrease in CI in the PP-group was a sequelae of the lower arterial carbon dioxide tension at the study end because arterial carbon dioxide tension remained constant in PP during the whole study.

Other authors have found that short-term pneumoperitoneum has minor effects on CI when IAP is lower than 15 mm Hg. Our study shows that changes in cardiovascular stability and acid–base balance can develop with latency when IAP is increased for several hours. This is of clinical relevance, because advanced laparoscopic surgery may be time-consuming and usually lasts longer than 60 min. Of importance the changes identified in this study cannot be detected using standard monitor setting. Therefore, our animal study suggests that the routine use of extended monitoring including measurement of central venous oxygen saturation and acid–base parameters should be considered during and soon after operation, when pneumoperitoneum will last longer than 2 h. Further clinical studies are warranted to investigate, whether an intermittent release of prolonged pneumoperitoneum or an elevation of CO may be beneficial in neonates and small infants during advanced laparoscopic surgery.

**References**


