Haemodynamic and ventilatory effects of preoperative epidural analgesia during laparoscopic hysterectomy using NICO™

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ABSTRACT

Introduction: The pneumoperitoneum and the head-down tilt positions required for laparoscopy may induce pathological, haemodynamic and ventilatory changes that complicate anaesthetic management. The purpose of the study was to evaluate the effect of preoperative epidural analgesia on intraoperative haemodynamic and ventilatory parameters during laparoscopic hysterectomy using the non-invasive cardiac output with partial carbon dioxide rebreathing technique (NICO).

Methods: 50 female patients were enrolled in this study. One percent lidocaine 15 ml with epinephrine and 2 mg morphine were administered via an epidural catheter before the induction of anaesthesia in the epidural group (n = 25), but not in the control group (n = 25). NICO was connected and monitored to the ventilatory circle. We also compared the quality of postoperative pain control.

Results: The blood pressures in the epidural group were significantly lower than the control group immediately after the Trendelenburg position. Stroke volume, cardiac output, and cardiac index were significantly higher in the epidural group, than in the control group during the entire surgery. Dynamic compliances after gas exsufflation were significantly higher, and production of carbon dioxide was lower after pneumoperitoneum in the epidural group, than in the control group. In the epidural group, the postoperative pain scores and the additional analgesic requirements were significantly lower than in the control group.

Conclusion: We concluded that preoperative epidural analgesia provides not only more effective postoperative pain control, but also offer higher cardiac output and cardiac index, higher dynamic compliance, and lower production of carbon dioxide during the laparoscopic hysterectomy.

Keywords: epidural analgesia, haemodynamic, laparoscopic hysterectomy, non-invasive cardiac output, partial carbon dioxide rebreathing technique, ventilator parameters

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INTRODUCTION

In recent years, more extensive and prolonged gynaecological procedures have been performed using the laparoscopic surgical technique.[1,2] The adverse effects of the laparoscopy are mainly related to the insufflation of the peritoneal cavity with carbon dioxide (CO_2) and the postural changes needed for surgery. Although the changes in cardiac output (CO) and preload are still matters of debate, many studies have found a marked increase in systemic vascular resistance (SVR).[3,4] Diaphragmatic excursion, limited by the pneumoperitoneum, may be further aggravated by the Trendelenburg position, and consequently, compromising ventilatory parameters.[5]

Recently, a new device, the non-invasive cardiac output using partial carbon dioxide rebreathing technique (NICO™) has been developed to measure CO noninvasively using partial CO_2 rebreathing.[6,7] This device uses periodic partial CO_2 rebreathing to create a CO_2 disturbance, which is then used in a differential Fick CO_2 equation to calculate CO. CO measured by this technique has correlated fairly well with that measured by the thermodilution method.[8-10] The purpose of this study was to evaluate the effects of preoperative lumbar epidural analgesia on the intraoperative haemodynamic and ventilatory stability during laparoscopic hysterectomy using the NICO™.

METHODS

We obtained approval from the institutional ethics committee of our hospital and informed consent from individual patients. Patients with cardiac (hypertension or ischaemic heart disease), pulmonary, or endocrinological disease, or severe obesity, were excluded from the study.

50 female patients (American Society of Anesthesiologists physical status I or II), aged 29–57 years, scheduled for elective laparoscopic total hysterectomy were enrolled in this study. On the preoperative visit by the anaesthesiologist, patients were taught how to complete the visual analogue scale (VAS; 0: no pain and 10: worst-possible pain) for the postoperative pain interview, and were introduced to two patient-controlled analgesic methods. No premedication was administered. They were randomly assigned to one of two groups, patient-controlled epidural analgesia or patient-controlled intravenous analgesia. The randomisation schedule was computer-generated.

In the epidural group (n = 25), with the patient in the lateral decubitus position, the epidural catheter (Portex®; Kent, England) was inserted at L1–2 vertebral level, cranially directed for about 5 cm, before the induction of anaesthesia. 5 ml of 1% lidocaine with 1:200,000 epinephrine was administered as the test dose, followed by 10 ml or more, and 2 mg morphine for the attainment of T6-level sensory block. Blood pressures and heart rates were monitored every 2.5 min during and after the epidural procedure. Prophylactic intravascular volume expansion was not given routinely. However, hypotension (defined as a decrease of systolic blood pressure greater than 20% of the baseline value) was treated with rapid infusion of Ringer's lactate solution and increments of ephedrine 10 mg as needed; hypertension (defined as an increase of systolic pressure greater than 30% of the baseline value) was treated with repeated dose of nicardipine 1 mg.

The patients were induced with 2 mg/kg propofol, fentanyl 1 μg/kg, and 0.5 mg/kg rocuronium. After tracheal intubation, general anaesthesia was maintained with enflurane in 50% oxygen in oxygen/nitrous oxide, with additional doses of rocuronium when the T1 of the train-of-four exceeded 15%. After peritoneal closure, 1% lidocaine with 0.1 mg/ml morphine was administered via epidural catheter for two days using a PCEA pump (ANAPA plus®, E-WHA International Inc, Korea) at a basal rate of 2 ml/h, demand dose of 2 ml, and lockout interval of 15 min. In the control group (n = 25), patients received patient-controlled intravenous analgesia for postoperative pain control by the same pump using fentanyl 15 μg/ml and ketorolac 1.5 mg/ml per demand dose of 2 ml, lockout time of 15 min, with basal rate of 2 ml. If patients complained of pain more than VAS 4 in spite of the PCA, 50 mg intramuscular pethidine was administered repeatedly.

We measured CO using NICO™ (fast mode, Novametrix Medical Systems Inc, Wallingford, CT, USA). This procedure has been presented in detail elsewhere.[6,7] Briefly, on a breath-by-breath basis, CO_2 production (V_{CO_2}) was calculated from the flow and CO_2 concentration at the airway opening. Then, to establish the relation between V_{CO_2} and CO, the Fick principle was applied as follows:

$$V_{CO_2} = CO \times (Cv_{CO_2} - Ca_{CO_2}) \quad (1)$$

where Cv_{CO_2} and Ca_{CO_2} represent the CO_2 content in mixed venous and arterial blood, respectively. In the NICO™ system, CO_2 rebreathing is performed for 50 s every 3 min using a disposable sensor (Novametrix Medical System). A brief period of CO_2 rebreathing caused a change in arterial CO_2 pressure (Pa_{CO_2}) and a change in V_{CO_2}, but little or no change in Cv_{CO_2} in anaesthetised dogs,[6] probably because the quantity of CO_2 stores in the body was large, and new equilibrium levels were attained after 20–30 minutes.[11] Assuming that CO and Cv_{CO_2} remained constant during the CO_2 rebreathing procedure, the following equation can be substituted for the previous one:

$$\Delta V_{CO_2} = CO \times (-\Delta Ca_{CO_2}) \quad (2)$$

where ΔV_{CO_2} is the change in V_{CO_2} between normal breathing and CO_2 rebreathing, and $\Delta Caco_2$ is the change in arterial CO_2 content. Assuming here that dead space fraction (VD/VT) remained constant during the CO_2 rebreathing and that ΔCa_{CO_2} was proportional to changes in the Pa_{CO_2} and end-tidal CO_2 pressure (PET_{CO_2}), the following equation can be formulated:

$$CO = \Delta V_{CO_2}/S \times \Delta PET_{CO_2} \quad (3)$$

where ΔPET_{CO_2} is the change in PET_{CO_2} between normal breathing and CO_2 rebreathing, and S is the slope of the CO_2 dissociation curve from haemoglobin. The constant S can be expressed as a function of haemoglobin concentration and Pa_{CO_2} as follows:

$$S = (1.34 \times [Hb] + 18.34)/(1 + 0.193 \times Pa_{CO_2})$$
$$[ml\ CO_2\ /L\ blood\ /\ mmHg] \quad (4)$$

Before the start of the study protocol, the NICO™ system was calibrated to zero CO_2 by opening the system to the atmosphere, according to the manufacturer's instructions. The baseline data was obtained after the epidural injection and before induction of anaesthesia (T0) in self-respiration with 50% oxygen mask connected to the NICO™. After tracheal intubation, it was connected to the ventilatory circle to monitor the variables. Stroke volume (SV), cardiac index (CI), CO, minute ventilation (V_E), peak inspiratory pressure (PIP), V_{CO_2}, airway resistance (R_{aw}), and dynamic compliance (C_{dyn}) were collected after intubation (T1), and again after turning the patient to the Trendelenburg position of 15 degrees (T2). Pneumoperitonium was created in the Trendelenburg position with a Veress needle using a CO_2-insufflator (OP-PNEU Electronic *Semm* system®, WISAP GmbH, Sauerlach, Germany), and intra-abdominal pressure (IAP) was maintained automatically at 12 mmHg. Haemodynamic and ventilatory measurements using the NICO™ were made after the beginning of insufflation (T3), at 10 and 20 minutes after insufflation (T4, T5), and 30-min intervals thereafter during the surgery (T6, T7). After deflation, measurements were repeated within a few minutes in the Trendelenburg position (T8), and five minutes after turning the patient to the supine-lithotomy position (T9).

Table I. Subject and intraoperative data of the control and epidural groups.

Parameter	Control group (n = 25)	Epidural group (n = 25)
Age (years)	44.3 ± 6.3	43.2 ± 5.6
Weight (kg)	61.0 ± 8.6	58.6 ± 8.0
Height (cm)	159.0 ± 4.4	158.9 ± 5.2
Body mass index (kg/m2)	19.5 ± 1.6	20.1 ± 2.0
Duration of surgery (min)	112.6 ± 28.6	100.1 ± 30.3
Amount of CO_2 insufflated (L)	659.1 ± 23.0	628.7 ± 41.3
Total fluid intake (ml)	1720 ± 287	1950 ± 314
MAC·hour	3.1 ± 0.6*	2.2 ± 0.5

Values are expressed as mean ± SD.

MAC·hour was higher in the control group than in the epidural group.

*p < 0.05

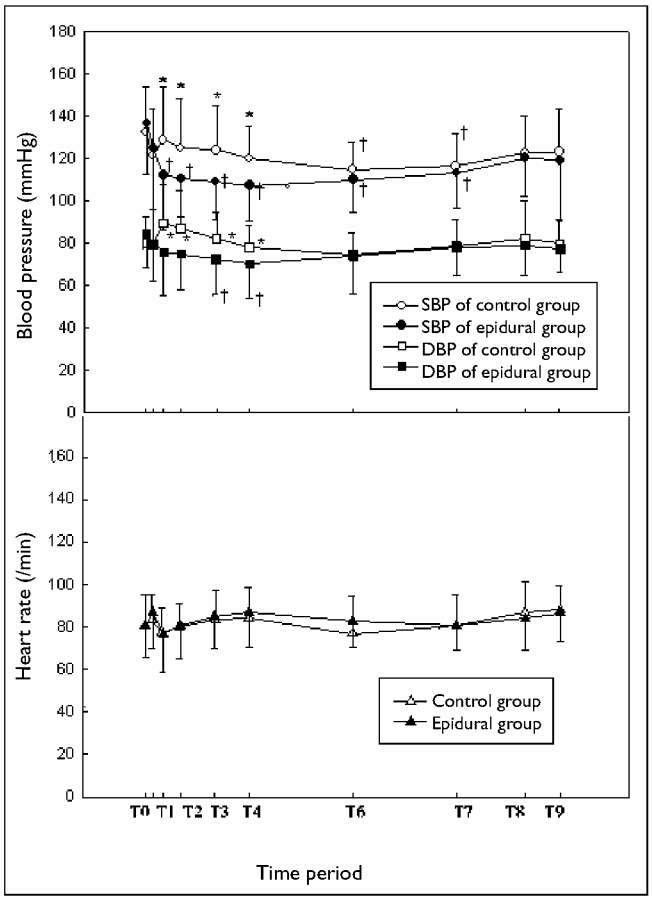

Fig. 1 Line charts show blood pressures and heart rates during laparoscopic hysterectomy.

Data is expressed as mean ± SD. T0: before the induction of anaesthesia; T1: after intubation; T2: after turning the patient into the Trendelenburg position of 15°; T3: after insufflation of CO_2; T4 and T5: respectively at 10 and 20 minutes after insufflation; T6 and T7: respectively at 30-min intervals thereafter during the surgery; T8: after deflation; T9: five minutes after turning the patient to the supine-lithotomy position. Systolic and diastolic blood pressures of the patients in the epidural group were significantly lower than the control group after Trendelenburg position, CO_2 insufflation, and until 20 minutes after pneumoperitoneum. Heart rates at every time period showed no significant differences between the groups.

*p < 0.05 compared to the control group.

During anaesthesia, the minute volume was adjusted to maintain the end-tidal CO_2 (ET_{CO2}) between 30 and 35 mmHg, by changing the frequency and keeping the tidal volume (TV) using a respirator (Remus A, Drägerwerk AG, Lubeck, Germany) in a semiclosed circle system with fresh gas flow of 4 L and CO_2-absorber in the circle. Repeated arterial blood gas analysis was performed at the every time period, T0–T9. Postoperative pain was self-assessed by the patient using VAS at 1, 3, 6, 12, and 24 hours after surgery. The incidence of intra- and postoperative side-effects (i.e. nausea, vomiting, pruritus, shivering or others) were recorded and treated appropriately. Severe nausea and vomiting was treated with ondansetron 4 mg intravenously, and shivering was treated with pethidine 25 mg intravenously.

A power analysis was performed to determine sufficient sample sizes required to establish a significant difference in CO and CI based on the results of the preliminary study, using a α-value of 0.05, and power of 0.9. The calculated number of total subjects required is at least 47 for the two groups. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA). The differences between the two groups were evaluated by multiple *t*-test, Mann-Whitney rank sum test, and Fisher's exact test, if appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

The two groups were similar with regard to demographic characteristics and intraoperative variables (Table I). The results of haemodynamic measurements using NICO™ are shown in Figs. 1 and 2. Systolic and diastolic blood pressure of the patients in the epidural group were significantly lower than in the control group after Trendelenburg position, CO_2 insufflation, and until 20 minutes after pneumoperitoneum ($p < 0.05$, Fig. 1). Heart rates at every time period showed no significant differences between the groups. Significant intergroup differences are

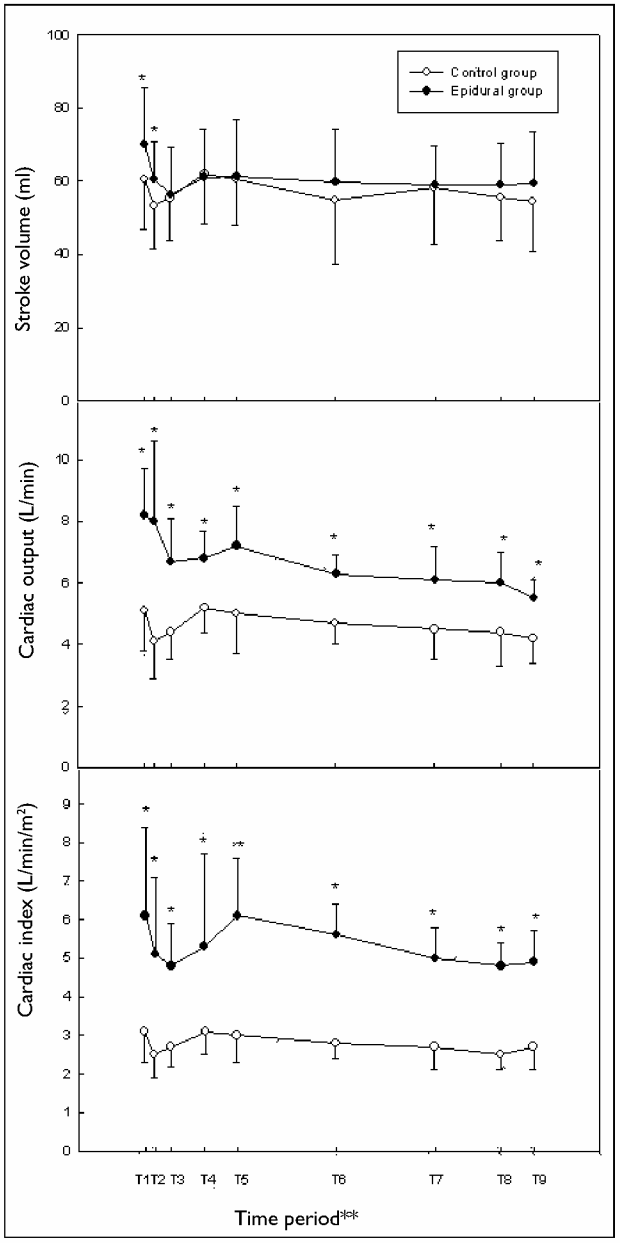

Fig. 2 Line charts show haemodynamic measurements using NICO™.
Data is expressed as mean ± SD. Stroke volume (SV) after intubation and Trendelenburg position, cardiac output (CO) and cardiac index (CI) during the entire surgery were significantly higher in the epidural group than in the control group.
*p < 0.05 compared to the control group. **See Fig. 1 legends for T1–T9 descriptions.

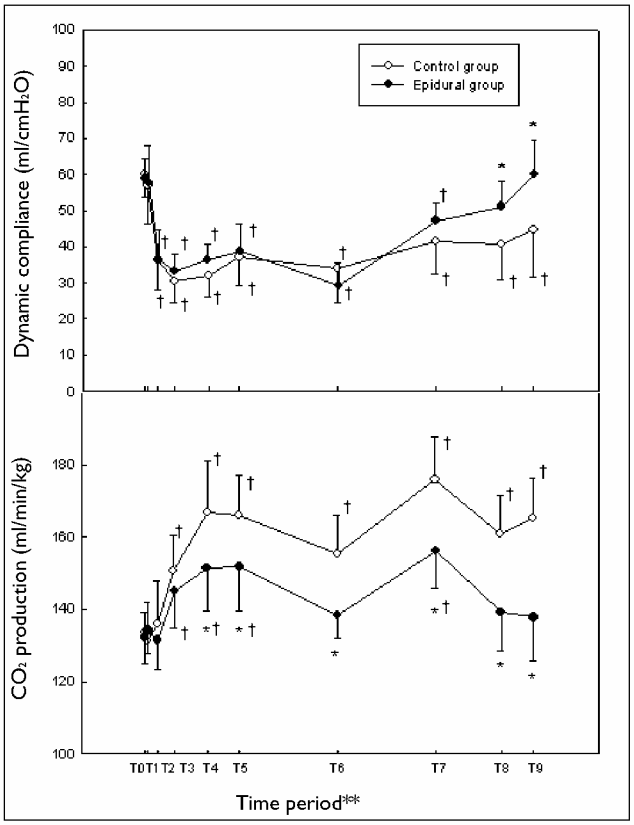

Fig. 3 Line charts show ventilatory measurements using NICO™.
Data is expressed as mean ± SD. C_{dyn} were higher in the epidural group after gas exsufflation and after neutral positioning than in the control group. V_{CO2} of the epidural group were significantly lower from 20 minutes after gas insufflation to the end of surgery compared to the control group. PIP during and after pneumoperitoneum were significantly lower in the epidural group than in the control group. V_E and R_{aw} showed no differences between the two groups during the surgery.
*p < 0.05 compared to the control group. **See Fig. 1 legends for T1–T9 descriptions.

found with respect to SV, CO, and CI during the surgery ($p < 0.05$, Fig. 2). The ventilatory parameters are presented in Fig. 3. In the epidural group, C_{dyn} was higher than the control group after neutral positioning ($p < 0.05$). V_{CO2} were significantly lower in the epidural group than the control after gas insufflation ($p < 0.05$). PIP, V_E and R_{aw} showed no differences between the two groups at every time period during the surgery (Fig. 4). There were neither intra- or intergroup differences in the measured blood gas analysis.

Pain scores at 1, 3, 6, and 12 hours after surgery were significantly higher in the control group than in the epidural group ($p < 0.05$, Fig. 5). Significantly more patients in the control group, compared to the epidural group, complained of a pain level of more than VAS 4, in spite of the PCA (9/25, 36% vs. 2/25, 8%; $p = 0.041$), and they were administered 50 mg pethidine intramuscularly. Total amount of pethidine were 1,150 mg in the control group and 100 mg in the epidural group ($p < 0.05$). During the surgery, more patients in the epidural group required ephedrine for treatment of hypotension, even with rapid fluid administration during surgery (6/25, 24%), compared with the control group (2/25, 8%; $p < 0.05$). On the other hand, seven patients (28%) developed hypertension that required incremental doses of nicardipine in the control group, and three patients (12%) in the epidural group ($p < 0.05$). The postoperative side effects are presented in Table II. There were significantly more patients developing postoperative vomiting and headache in the control group, compared to the epidural group ($p < 0.05$). Incidence of pruritus was significantly more frequent in the epidural group than in the control group ($p < 0.05$). All the side effects were managed properly in the recovery room.

DISCUSSION

In haemodynamic stability, there were higher SV, CO, and CI in the epidural group compared to the control group

Table II. Postoperative side effects in the control and epidural groups.

Parameter	Control group (n = 25)	Epidural group (n = 25)
Nausea	12 (48)	10 (40)
Vomiting	9 (36)*	1 (4)
Pruritus	2 (8)	6 (24)*
Dizziness	4 (16)	3 (12)
Headache	5 (20)*	0
Back pain	1 (4)	1 (4)
Shoulder pain	2 (8)	1 (4)
Shivering	0	1 (4)
Delirium	1 (4)	0

Values are expressed as number of patients (%).
The incidence of pruritus was higher in the epidural group than in the control group. The incidences of vomiting and headache were significantly higher in the control group compared to the epidural group. *$p < 0.05$.

during the laparoscopic hysterectomy, compared with the postoperative patient-controlled intravenous analgesia. However, during the surgery, more patients in the epidural group required ephedrine for treatment of hypotension, but more developed hypertension that required nicardipine in the control group than in the other group. In ventilatory stability, there were higher C_{dyn} and lower V_{CO2} in the epidural group than in the control group.

Previous studies reported an increase in SVR during pneumoperitoneum. This can be considered a reflex sympathetic response to decreased CO,[12] and to be mediated by neurohormonal factors.[13] The increase in SVR is also affected by the Trendelenburg position.[14] In our results, preoperative epidural lidocaine improved SV and CI during the whole surgery. A possible mechanism is the decrease in SVR due to the sympathetic block to T6 and the improvement in CO, consequent upon the head-down position and pneumoperitoneum. The cardiovascular effects of epidural blockade during general anaesthesia have previously been reported.[15,16] In these reports, the sympathetic blockade caused BP to decrease, CVP and SVR to increase, and CO to increase. Therefore, the epidural sympathetic block may compensate for the increase sympathetic tone resulting from pneumoperitoneum in a head-down position, including vasomotor constriction of the splanchnic organs and leg muscles with a large vascular capacity. However, the mechanism of decrease of CO during laparoscopy is multifactorial. Increased IAP results in caval compression,[17] and may cause pooling of blood in the legs,[18] and an increase in venous resistance.[19]

With regard to the ventilatory parameters, it has been known that elevated IAP leads to decreased

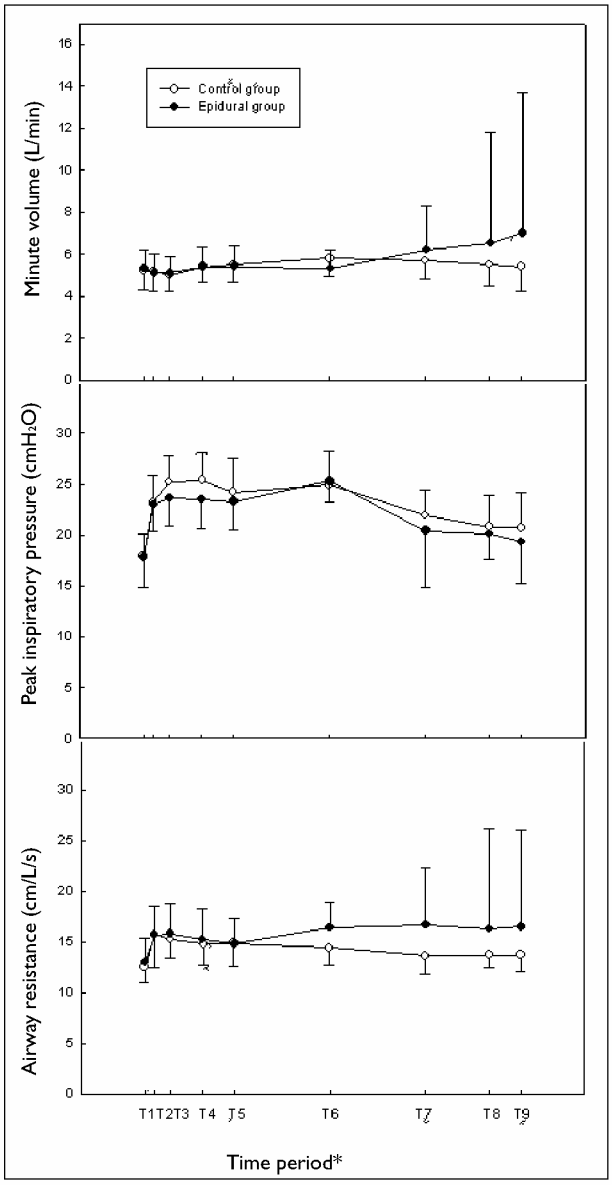

Fig. 4 Line charts show minute volume and airway pressures. Data is expressed as mean ± SD. V_E and R_{aw} showed no differences between the two groups at every time period. * See Fig. 1 legends for T1–T9 descriptions.

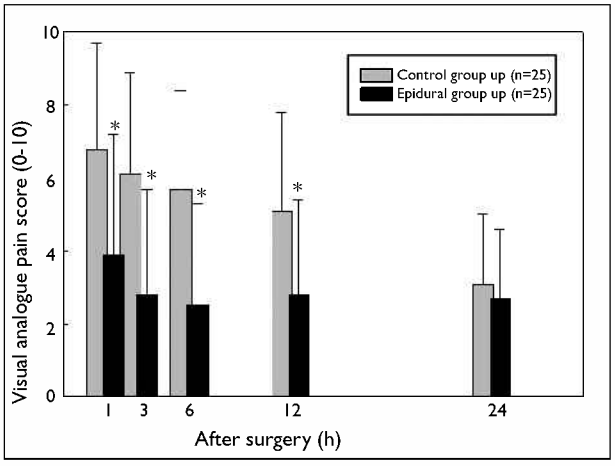

Fig. 5 Bar chart shows the postoperative pain scores.
Data is shown as a box-plot with interquatile ranges. VAS at 1, 3, 6, and 12 hours after surgery were significantly lower in the epidural group than in the control group. *$p < 0.05$ compared to the control group.

thoracopulmonary compliance. Furthermore, steep head-down tilt results in decreased functional residual capacity, total lung volume, and pulmonary compliance. Pneumoperitoneum in the Trendelenburg position decreased dynamic compliance by nearly 50% in both groups in this study. This is consistent with some earlier studies, in which respiratory compliances were reduced by 20%–50%.[20,21] After the head-down tilt position was created and kept constant, compliances in the two groups were not affected further by subsequent insufflation of gas. However, after exsufflation, dynamic compliance returned to the baseline value before the change of position in the epidural group, but not in the control group. The peripheral neural blockade, sympathetic neural blockade, or the systemic effects of local anaesthetics on the myoneural junction were the possible explanations for this observation, although the exact mechanism is unclear.

There are some limitations to this study. The use of CO_2 rebreathing as a measure of CO during CO_2 insufflation may not be accurate, due to small quantities of CO_2 being reabsorbed, which interferes with the NICO™ method. NICO™ only considers that part of the pulmonary blood flow that takes part in the gaseous exchange, and empirically performs a shunt correction based on a preset equation. To circumvent these problems, other monitors could be used.[22,23] The majority of patients evaluated had normal cardiopulmonary functions. Hence, our results could only be extrapolated to a similar population of patients, and would not be applicable to more critically-ill patients with cardiopulmonary dysfunction. In conclusion, preoperative epidural analgesia provides not only effective postoperative pain control, but also offers higher CO and CI, higher C_{dyn}, and lower V_{CO2} during pneumoperitoneum in the Trendelenburg position. With the possibility of hypotension after epidural analgesia, clinicans should consider administering preoperative lumbar epidural analgesia, as this appears to be beneficial in patients undergoing laparoscopic hysterectomy with inhalational anaesthesia.

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