

## Low-flow Sevoflurane Anesthesia in Laparoscopic Cholecystectomy

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**Background:** Anesthetists participating in laparoscopic cholecystectomy (LC) with CO<sub>2</sub> pneumoperitoneum has been cautious about adapting low-flow anesthesia (LFA). We investigated the efficacy of LFA compared to high-flow anesthesia (HFA) in LC.

**Methods:** Eighty patients undergoing LC were randomly assigned to one of the two groups (n = 40 each). In LFA, 1 L/min (50% O<sub>2</sub> and N<sub>2</sub>O) of the total fresh gas flow (FGF) was used, whereas 4 L/min of the total FGF was used for HFA. Inspiratory and expiratory concentrations of O<sub>2</sub>, N<sub>2</sub>O, CO<sub>2</sub>, and sevoflurane were serially measured. Subjects were monitored for heart rate, blood pressure, and any procedural complications.

**Results:** None of the patients experienced any episodes of hypoxia, hypercapnia, and arrhythmia in both groups. The maximal end-tidal CO<sub>2</sub> was 40.9 ± 3.9 mmHg in LFA and 38.2 ± 3.6 mmHg in HFA, respectively. The minimal O<sub>2</sub> saturation was 98.3 ± 0.6% in LFA and 98.8 ± 0.7% in HFA, respectively. The inspiratory CO<sub>2</sub> concentrations in both groups were all less than 1 mmHg throughout the anesthesia.

**Conclusions:** In conclusion, LFA with sevoflurane using FGF of 1 L/min with setting of 50% O<sub>2</sub> and N<sub>2</sub>O for LC could be performed safely without the risk of complications like hypercapnia, hypoxia, or arrhythmia compared to HFA. (Korean J Anesthesiol 2005; 49: S 1~5)

**Key Words:** fresh gas flow, laparoscopy, sevoflurane.

### INTRODUCTION

There has been a revival of interest in low-flow anesthesia (LFA) techniques over the past decade or so, primarily driven by the introduction of newer anesthetic agents with low solubility and relatively higher costs. The advantages of LFA include a reduction in the consumption of anesthetic gases, reduced operating room and environmental pollution, and the conservation of heat and humidity within the respiratory tract of patients.<sup>1-3)</sup> Historically, most anesthesiologists have been trained to use high-flow anesthesia (HFA), and the anesthetic equipment and available anesthetic agents have not been suitable for LFA. HFA techniques, however, have the potential for inducing hypoxia and/or hypercapnia, administration of an over- or underdosage of anesthetic gases, and the accumulation of potentially toxic degradation

products.<sup>4-7)</sup>

Laparoscopic cholecystectomy (LC) with intra-abdominal CO<sub>2</sub> insufflation has a special anesthetic consideration in that it may induce hypercapnia, acidemia, and depressed hemodynamics.<sup>8)</sup> A number of studies have been published evaluating the use of LFA in a wide variety of surgical procedures, including gastrointestinal, gynecological and general surgery.<sup>9-11)</sup> Despite many advantages of the LFA as mentioned above, few studies have actually been done using LFA with sevoflurane in LC. One likely explanation is the potential for hypercapnia with LFA resulting from rebreathing exhaled CO<sub>2</sub> coupled with an increase in arterial CO<sub>2</sub> from the intraperitoneal CO<sub>2</sub> insufflation.

The purpose of this study was to investigate whether the LFA is safe and compatible with the LC involving abdominal CO<sub>2</sub> insufflation.

### MATERIALS AND METHODS

After obtaining Institutional Review Board approval and written informed consent from each patient, 80 patients, ASA I or II status, who were to undergo elective LC under general anesthesia were

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**Table 1.** Patient Demographics

	LFA (n = 40)	HFA (n = 40)
Age (yr)	50.0 ± 11.5	48.9 ± 12.3
Sex (m/f)	18/22	20/20
Weight (kg)	64.8 ± 9.5	61.9 ± 10.4
Anesthetic duration (min)	67.0 ± 11.3	70.4 ± 12.3

Data are mean ± SD except sex (number). LFA: low-flow anesthesia, HFA: high-flow anesthesia.

enrolled. The patients were randomly assigned to one of two groups, LFA or HFA (n = 40 in each group), depending on fresh gas flow (FGF) settings. Patients with cardiopulmonary disease, previous adverse reactions to inhaled agents, intravenous anesthesia, obesity, smoking history, and where the procedure was subsequently changed to open cholecystectomy were excluded from the study. Age, gender, and weight were recorded for all subjects. There was no statistically difference in patient demographics (including age, gender, weight, and anesthetic duration) between the two groups (Table 1).

All anesthetic procedures were performed by one of the two authors, who was experienced in the application of the LFA. All patients were premedicated with midazolam (7.5 mg orally), the night before the operation, and intramuscular 2-2.5 mg midazolam and 0.2 mg glycopyrrolate, 30 min before entering the operating room (OR).

After arrival in the OR, baseline hemodynamic parameters were recorded after a 5 min stabilization period on the operating table. Before anesthetic induction, all patients breathed 100% O<sub>2</sub> for 3 min, FGF 6 L/min, using a face mask connected to a semiclosed breathing circuit (Datex Ohmeda 7,000 ventilator, Datex-Ohmeda, USA). After preoxygenation, 2 mg/kg propofol, 0.6 mg/kg rocuronium bromide, and 1-2 µg/kg fentanyl were administered intravenously. Tracheal intubation was followed by mechanical ventilation with a tidal volume of 10 ml/kg at 10 breaths/min. Inspiratory/expiratory ratio was set as 1 : 2. These respiratory parameters were not modified during the procedures. All procedures were performed using the same circle breathing system and vaporizer (Vapor 2000, Dräger, Germany) with sevoflurane under standard operating room conditions. The accuracy of the flowmeters was verified by passing the FGF through a dry gas meter (Parkinson-Cowan, Birmingham, UK).

Lead II of an electrocardiogram on the patient's back and saturation via pulse oximetry (SpO<sub>2</sub>) at patient's finger were con-

tinuously monitored. An automated blood pressure cuff was applied to the right arm. To ensure uniform conditions, same patient monitoring equipment was used in all cases. Electrocardiography, oscillatory blood pressure, and pulse oximetry was monitored using Agilent M1205A (Agilent technologies Co., Germany). Peak airway pressure was measured using anesthesia machine (Datex Ohmeda 7,000 ventilator, Datex-Ohmeda, USA). Tidal volume and minute ventilation were measured using 5420 volume monitor (Ohmeda, USA). We also serially measured inspiratory and expiratory fractional concentrations of the O<sub>2</sub>, N<sub>2</sub>O, CO<sub>2</sub>, and sevoflurane using a multi-gas monitor (Capnomac Ultima, Datex-Ohmeda, Finland). The accuracy of multi-gas monitor was tested before the study (accuracy for ± 10%). Fresh soda lime (Sodasorb<sup>®</sup>, W.R. Grace & Company, USA) was used during each individual anesthesia procedure.

Variables were measured immediately prior to CO<sub>2</sub> pneumoperitoneum and every 5 minutes thereafter until the end of surgery but were presented 10 (T1), 20 (T2), 30 (T3) minutes after CO<sub>2</sub> pneumoperitoneum and immediately before emergence from anesthesia (T4). Neuromuscular transmission was monitored by train-of-four stimulation (TOF Watch, Organon Teknika, Netherlands).

After tracheal intubation, O<sub>2</sub> and N<sub>2</sub>O flow was 2 L/min and 2 L/min, respectively. These parameters were maintained throughout the duration of anesthesia in HFA group. The initial inspiratory sevoflurane concentration was 2.6 vol% in HFA group. In LFA group, initial FGF was 4.5 L/min, 1.5 L/min O<sub>2</sub> and 3.0 L/min N<sub>2</sub>O, and an inspiratory sevoflurane concentration was 2.6 vol%. This initial high flow phase lasted 10 min to allow for initial rapid uptake of N<sub>2</sub>O and elimination of nitrogen. Thereafter, FGF was reduced to 1 L/min, 500 ml/min O<sub>2</sub> and 500 ml/min N<sub>2</sub>O, and the vaporizer dial of sevoflurane was set at 3.0 vol%. During the CO<sub>2</sub> pneumoperitoneum, the intra-abdominal pressure was maintained between 12 and 15 mmHg by CO<sub>2</sub> insufflator.

In both groups, sevoflurane concentration was adjusted throughout the anesthesia to maintain systemic arterial blood pressure and heart rate (HR) within ± 30% of baseline values. Light anesthesia was defined as tachycardia (HR > + 30% of baseline values or HR > 110 beats/min) or hypertension (mean arterial pressure [MAP] > + 30% of baseline values or MAP > 100 mmHg). The occurrence of hypoxia and hypercapnia was noted throughout the anesthesia. Hypoxia and hypercapnia were defined as SpO<sub>2</sub> less than 90% and end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>) more than 50 mmHg, respectively.

Whenever the inspiratory concentration of O<sub>2</sub> was noted to be

low 30%, O<sub>2</sub> flow was increased by 10% of the total FGF, while reducing the N<sub>2</sub>O flow by the same amount. At the end of surgery, the vaporizer dial of sevoflurane was turned off and the O<sub>2</sub> flow was increased to 6 L/min along with discontinuation of N<sub>2</sub>O administration. Residual neuromuscular block was antagonized at the start of skin closure by the administration of pyridostigmine and glycopyrrolate. Patients were extubated upon awakening.

Prior to the study, a power analysis was performed to determine population size based on the 3% incidence of hypercapnia during CO<sub>2</sub> pneumoperitoneum as reported by Qureshi EA.<sup>12)</sup> We presumed that a  $\pm 10\%$  incidence of hypercapnia in LFA group would be as effective and safe as the HFA group. This required recruitment of 36 patients in each group, as noted above.

Data was presented as mean  $\pm$  standard deviation (SD). Data analysis was performed using the SPSS statistical Package program version 11.0 (SPSS Inc., Chicago, USA). Statistical analysis for demographics, maximal ET-CO<sub>2</sub>, and minimal SpO<sub>2</sub> was done by using independent sample t-test. We used GLM (General Linear Model) repeated measures procedures to analyze the changes in hemodynamics and concentrations of O<sub>2</sub>, N<sub>2</sub>O, CO<sub>2</sub> and sevoflurane between two groups. Statistical significance was set at five percent level.

## RESULTS

Maximal ET-CO<sub>2</sub> was  $40.9 \pm 3.9$  mmHg in LFA group and  $38.2 \pm 3.6$  mmHg in HFA group. The minimal SpO<sub>2</sub> was  $98.3 \pm 0.6\%$  (range 97-100%) in LFA group and  $98.8 \pm 0.7\%$  (range 98-100%) in HFA group ( $P = 0.005$ ). In both groups, the inspiratory O<sub>2</sub> concentration never dropped below 30% on the multi-gas monitor. None of the patients experienced episodes of hypoxia, hypercapnia, and arrhythmia requiring treatment in either group.

The changes in concentration of gases are presented in Table 2. The inspiratory O<sub>2</sub> concentrations were significantly lower in LFA group than in HFA group at T1 and T2 ( $P = 0.004$ ). There were no statistical differences in inspiratory O<sub>2</sub> concentrations at T3 and T4 between two groups. The inspiratory N<sub>2</sub>O concentrations in LFA group were significantly higher in LFA group than in HFA group at T1, T2, and T3 ( $P = 0.007, 0.003$  and  $0.001$ , respectively).

The inspiratory CO<sub>2</sub> concentration in LFA group was significantly higher than in HFA group at T1 ( $P = 0.032$ ). However, the inspiratory CO<sub>2</sub> concentrations in both groups were all less than 1 mmHg throughout the duration of anesthesia. The ET-CO<sub>2</sub> in LFA group were significantly higher in LFA group than in HFA group at T1, T3, and T4 ( $P = 0.016, 0.000$  and  $0.000$ ). The highest

**Table 2.** Changes in Inspiratory and Expiratory Gases during CO<sub>2</sub> Pneumoperitoneum

		T1	T2	T3	T4
Ins-O <sub>2</sub> (%)	LFA	$42.0 \pm 11.0^*$	$46.8 \pm 4.6^*$	$47.7 \pm 2.6$	$47.8 \pm 2.4$
	HFA	$49.5 \pm 7.9$	$50.2 \pm 4.1$	$49.4 \pm 4.3$	$49.3 \pm 5.6$
Exp-O <sub>2</sub> (%)	LFA	$40.3 \pm 11.4^*$	$43.1 \pm 5.3^*$	$43.6 \pm 2.9^*$	$43.7 \pm 2.1$
	HFA	$47.5 \pm 7.4$	$47.1 \pm 2.4$	$46.6 \pm 1.8$	$46.3 \pm 1.8$
Ins-N <sub>2</sub> O (%)	LFA	$53.4 \pm 10.4^*$	$49.1 \pm 4.4^*$	$48.4 \pm 2.6^*$	$48.0 \pm 2.5$
	HFA	$47.3 \pm 5.7$	$46.4 \pm 1.0$	$46.5 \pm 1.1$	$47.1 \pm 1.6$
Exp-N <sub>2</sub> O (%)	LFA	$51.0 \pm 10.6^*$	$48.0 \pm 4.9^*$	$47.2 \pm 2.7^*$	$47.2 \pm 1.9^*$
	HFA	$44.9 \pm 6.0$	$45.1 \pm 1.1$	$45.3 \pm 1.1$	$45.6 \pm 1.1$
Ins-CO <sub>2</sub> (mmHg)	LFA	$0.5 \pm 0.5^*$	$0.2 \pm 0.4$	$0.4 \pm 0.5$	$0.4 \pm 0.5$
	HFA	$0.2 \pm 0.4$	$0.1 \pm 0.4$	$0.2 \pm 0.4$	$0.3 \pm 0.5$
Exp-CO <sub>2</sub> (mmHg)	LFA	$32.6 \pm 3.9^*$	$35.6 \pm 4.8$	$40.0 \pm 4.1^*$	$41.1 \pm 3.5^*$
	HFA	$29.4 \pm 6.0$	$33.7 \pm 4.2$	$36.1 \pm 3.3$	$36.8 \pm 3.0$
Ins-Sevo (vol%)	LFA	$2.0 \pm 0.4^*$	$2.0 \pm 0.4^*$	$2.1 \pm 0.3^*$	$2.2 \pm 0.2$
	HFA	$2.3 \pm 0.3$	$2.4 \pm 0.5$	$2.3 \pm 0.3$	$2.4 \pm 0.3$
Exp-Sevo (vol%)	LFA	$1.7 \pm 0.3^*$	$1.7 \pm 0.3^*$	$1.9 \pm 0.3^*$	$1.8 \pm 0.2^*$
	HFA	$1.9 \pm 0.4$	$2.1 \pm 0.4$	$2.0 \pm 0.3$	$2.0 \pm 0.3$

Values are mean  $\pm$  SD. LFA: low-flow anesthesia, HFA: high-flow anesthesia, Ins: inspiration, Exp: expiration, Sevo: sevoflurane. T1, T2, and T3: 10, 20, and 30 minutes after carbon dioxide pneumoperitoneum, T4: immediately before emergence of anesthesia. \*:  $P < 0.05$  compared to HFA.

ETCO<sub>2</sub> level was observed at T4 in both groups. The inspiratory and expiratory sevoflurane concentrations were lower in LFA group than in HFA group throughout the duration of anesthesia ( $P < 0.05$ ).

## DISCUSSION

The LFA was first introduced by Foldes et al.<sup>13)</sup> in 1952. Since then, the technique has been variously defined by different authors.<sup>1,14)</sup> The purpose of this study was to examine the efficacy of LFA with sevoflurane in LC with CO<sub>2</sub> pneumoperitoneum.

Traditionally, anesthetists participating in LC have been quite cautious about adapting LFA due to the potential for inducing hypoxia, hypercapnia, and accumulation of toxic degradation products such as compound A by sevoflurane due to the exhaled CO<sub>2</sub> rebreathing and administration of small amount of oxygen less than 500 ml/min.<sup>4-7)</sup> However, it has several benefits, including the reduced consumption of anesthetic gases, reduced environmental pollution, and conservation of heat and humidity within the respiratory tract.<sup>1-3)</sup>

In the present study, a semiclosed-circuit with a soda lime absorbent was used as the CO<sub>2</sub> absorbent. All our patients were operated as the first case of the day. Therefore, the fresh soda lime absorbent was used during each anesthesia. The inspiratory CO<sub>2</sub> concentrations in LFA and HFA groups were less than 1 mmHg throughout the anesthesia and there in no case did the ETCO<sub>2</sub> increase more than 50 mmHg in LFA group. The duration of anesthesia was short in all our patients (mean 67.0 min in LFA and 70.4 min in HFA). These findings suggest that the clinically significant CO<sub>2</sub> rebreathing is not developed in patients undergoing LC with a brief period of anesthesia with intraperitoneal CO<sub>2</sub> insufflation if fresh soda lime is used in the circuit.

One another important barrier to LFA acceptance is the possibility of hypoxia resulting from inspiration of low O<sub>2</sub> concentrations during rebreathing. This may be one of the major disadvantages associated with the use of LFA. In our present study, the minimal SpO<sub>2</sub> in LFA group was  $98.3 \pm 0.6\%$  and this result was similar to that of HFA group ( $98.8 \pm 0.7\%$ ), although it was noted to be statistically significant. No patients experienced hypoxia defined as decrease in SpO<sub>2</sub> less than 90% in the LFA group.

Sajedi et al.<sup>15)</sup> reported that the LFA could be used with relative safety in anesthetic management of patients during LC. However, they used halothane as an inhalation agent. Sevoflurane has a number of properties that allow for the full realisation of the

benefits of LFA. The lower solubility of sevoflurane compared to halothane results in more rapid alveolar equilibration and tissue elimination, and this property is particularly well suited for use during LFA. However, the potentially toxic degradation products may be accumulated during the LFA with sevoflurane.<sup>16)</sup> The flow rate is one of the most important factors in determining the rate at which Compound A is produced. Although we did not directly check the Compound A concentrations in our present study, none of our patients revealed any postoperative renal dysfunction clinically significant or postoperative blood urea nitrogen concentrations that would suggest potentially toxic Compound A production.

We presumed the hypercapnia as ETCO<sub>2</sub> without direct checking the arterial CO<sub>2</sub> tension (PaCO<sub>2</sub>). The diversity has been shown between PaCO<sub>2</sub> and ETCO<sub>2</sub> during LC.<sup>17)</sup> However, Bhavani-Shankar et al.<sup>18)</sup> demonstrated that the difference between PaCO<sub>2</sub> and ETCO<sub>2</sub> was only  $2.6 \pm 1.2$  mmHg during CO<sub>2</sub> pneumoperitoneum in 8 pregnant women undergoing LC. They concluded that capnography is adequate to measure CO<sub>2</sub> status and to guide ventilation during laparoscopic surgery. This was our justification not to directly measure PaCO<sub>2</sub> in our patients.

In conclusion, LFA with sevoflurane using FGF of 1 L/min with setting of 50% O<sub>2</sub> and N<sub>2</sub>O for LC is safe without any significant likelihood of risks such as hypercapnia, hypoxia, and arrhythmia.

## REFERENCES

1. Baum JA, Aitkenhead AR: Low-flow anaesthesia. *Anaesthesia* 1995; 50: S37-44.
2. Imberti R, Preseglio I, Imbriani M, Ghittori S, Cimino F, Mapelli A, et al: Low flow anaesthesia reduces occupational exposure to inhalation anaesthetics: environmental and biological measurements in operating room personnel. *Acta Anaesthesiol Scand* 1995; 39: 586-91.
3. Kleemann PP: Humidity of anaesthetic gases with respect to low flow anaesthesia. *Anaesth Intensive Care* 1994; 22: 396-408.
4. Liu J, Laster MJ, Eger EI 2nd, Taheri S: Absorption and degradation of sevoflurane and isoflurane in a conventional anesthetic circuit. *Anesth Analg* 1991; 72: 785-9.
5. Hargasser S, Hipp R, Breinbauer B, Mielke L, Entholzner E, Rust M, et al: A lower solubility recommends the use of desflurane more than isoflurane, halothane, and enflurane under low-flow conditions. *J Clin Anesth* 1995; 7: 49-53.
6. Aldrete JA: Compound A concentrations during sevoflurane anesthesia in children depend on fresh gas flow. *Anesthesiology* 1996; 85: 684.
7. Meakin GH: Low-flow anaesthesia in infants and children. *Br J Anaesth* 1999; 83: 50-7.

8. Holzman M, Sharp K, Richards W: Hypercarbia during carbon dioxide gas insufflation for therapeutic laparoscopy: a note of caution. *Surg Laparosc Endosc* 1992; 2: 11-4.
  9. Bito H, Ikeda K: Closed-circuit anesthesia with sevoflurane in humans. Effects on renal and hepatic function and concentrations of breakdown products with soda lime in the circuit. *Anesthesiology* 1994; 80: 71-6.
  10. Bito H, Ikeda K: Degradation products of sevoflurane during low-flow anaesthesia. *Br J Anaesth* 1995; 74: 56-9.
  11. Lu CC, Ho ST, Wang JJ, Wong CS, Tsai CS, Chang SY, et al: Minimal low-flow isoflurane-based anesthesia benefits patients undergoing coronary revascularization via preventing hyperglycemia and maintaining metabolic homeostasis. *Acta Anaesthesiol Sin* 2003; 41: 165-72.
  12. Qureshi FA: Anesthesia related complications of laparoscopic cholecystectomy. *J Coll Physicians Surg Pak* 2003; 13: 369-71.
  13. Foldes FF, Ceravolo AJ, Carpenter SL: The administration of nitrous oxide-oxygen anesthesia in closed systems. *Ann Surg* 1952; 136: 978-81.
  14. Gregorini P: Effect of low fresh gas flow rates on inspired gas composition in a circle absorber system. *J Clin Anesth* 1992; 4: 439-43.
  15. Sajedi P, Naghibi K, Soltani H, Amoshahi A: A randomized, prospective comparison of end-tidal CO<sub>2</sub> pressure during laparoscopic cholecystectomy in low and high flow anesthetic system. *Acta Anaesthesiol Sin* 2003; 41: 3-5.
  16. Morio M, Fujii K, Satoh N, Imai M, Kawakami U, Mizuno T, et al: Reaction of sevoflurane and its degradation products with soda lime. Toxicity of the byproducts. *Anesthesiology* 1992; 77: 1155-64.
  17. Bures E, Fusciardi J, Lanquetot H, Dhoste K, Richer JP, Lacoste L, et al: Ventilatory effects of laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 1996; 40: 566-73.
  18. Bhavani-Shankar K, Steinbrook RA, Brooks DC, Datta S: Arterial to end-tidal carbon dioxide pressure difference during laparoscopic surgery in pregnancy. *Anesthesiology* 2000; 93: 370-3.
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