ORIGINAL ARTICLE

Biochemical Effects of Low Gas Flow Anaesthesia with Inhalational Agent Sevoflurane in Patients Undergoing Laparoscopic Abdominal Surgery

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Abstract

Background: The low-flow anaesthesia with sevoflurane is preferred in laparoscopic abdominal surgeries due to its advantage of less anaesthetic consumption, decreased atmospheric pollution and cost effectiveness. ***Purpose:*** To investigate the effects of low-flow anaesthesia with volatile anaesthetic sevoflurane on renal and hepatic functions in patients undergoing laparoscopic abdominal surgery. ***Material and Methods:*** Forty patients with ASA I or II (American Society of Anaesthesiologists Classification) physical scores were included in the study to receive sevoflurane at a fresh gas flow rate of 1 L/min. Blood samples were obtained before anaesthesia and at 24 and 48 hours after the anaesthesia for serum biochemical analysis. ***Results:*** There was no significant difference in renal and hepatic function tests 24 and 48 hours after laparoscopic abdominal surgery as compared to preoperative levels. ***Conclusion:*** Biochemical parameters were similar in the preoperative and post-operative period ($p > 0.05$).

Key words

Biochemical parameters, Volatile anaesthetics, Low-flow anaesthesia

Introduction

Various intraabdominal surgical procedures are being performed by laparoscopy where the type of inhalational agent and fresh gas flow rate is important as it affects organ systems. Differences emerge from the blood/gas and tissue/blood solubility coefficients of the drug (1,2). The low-flow anaesthesia with sevoflurane is preferred in laparoscopic surgeries due to its advantage of less anaesthetic consumption, decreased atmospheric pollution and cost effectiveness. Sevoflurane has not shown any adverse effects on hepatic and renal function (3,4). Few studies have reported that in vivo and in vitro degradation of sevoflurane produces inorganic fluoride and vinyl ether (Compound A), which has the potential to harm renal and hepatic function however, its damage on human kidney is not established.

In rats, it was shown that both degradation products from 150 to 300-ppm/h concentrations could injure rat kidneys and compound A (CpA) caused cortico-medullary tubular necrosis localized to the proximal tubule (5). The few studies of the renal effects of sevoflurane given with fresh gas flows of d" 2 L/min have not demonstrated nephrotoxicity. In a previous study, it was indicated that the fluoride resulting from sevoflurane anaesthesia at a higher fresh gas in flow rate (normal range: 2–6 liter/min) did not produce renal injury in humans (6). The present study was designed to investigate the effects of low-flow anaesthesia (1 L/min) with inhalational agent Sevoflurane on renal and hepatic functions in patients

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undergoing laparoscopic abdominal surgery.

Material and Methods

This was a self-control study to investigate the effects of low-flow anaesthesia with volatile anaesthetic sevoflurane on renal and hepatic functions in patients undergoing laparoscopic abdominal surgery. We included forty patients undergoing laparoscopic abdominal surgery with an ASA I-II (the American Society of Anaesthesiologists Classification) physical score after obtaining consent from each patient. Ethical approval was obtained from hospital ethical committee. The study was conducted between January 2019 and December 2019.

The demographic characteristics of all subjects such as age, height, weight, and body mass index (BMI) were recorded. Patients who had any metabolic, endocrine, hepatic, or renal disease were excluded from the study. Forty patients were selected randomly to receive sevoflurane at a fresh gas flow rate of 1 L/min. Fresh sodalyme (GE Avance CS2 anaesthesia work station) was placed into the canister immediately before the anaesthesia. The patients were premedicated 0.004 mg/kg glycopyrrolate 30 min before the induction of anaesthesia.

Anaesthesia was induced with propofol (2–2.5 mg/kg), butraphanol (0.2 mg/kg) and vecuronium bromide (0.1 mg/kg) at 100% oxygen. After tracheal intubation, the fresh gas flow rate was set to 4.4 L/min. After 5 minutes the total fresh gas flow was reduced to 1.0 L/min. The ratio of oxygen to airflow rates was adjusted to maintain the oxygen concentration in the inspiratory limb at 30%. The anaesthetic concentration was adjusted to maintain 1.5–2.0% for sevoflurane with systolic blood pressure within ± 20% of baseline. An intravenous maintenance dose of 0.02 mg/kg vecuronium bromide was added in 30 min periods. Ventilation was controlled with a tidal volume of 10 ml/kg and the respiratory rate was adjusted to maintain an end-tidal carbon dioxide (EtCO2) value between 35 and 45 mmHg. The anaesthetic device used was GE Avance CS2 Anaesthesia work station.

All patients were monitored by electrocardiography (ECG) for noninvasive blood pressure (BP), peripheral oxygen saturation (SpO2) and end-tidal CO2. During anaesthesia, the end-tidal CO2 concentration and inspired and end-tidal anaesthetic concentrations were monitored by mass spectrometry (GE Avance CS2 Anaesthesia work station). Finally, the duration of anaesthesia and surgery was recorded. The radial artery was cannulated to permit blood samples to be obtained for serum biochemical analysis before and after anaesthesia. Blood samples were obtained before anaesthesia and at 24 and 48 hours after the anaesthesia for measurement of blood urea nitrogen (BUN), serum urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), direct bilirubin, total bilirubin levels.

All serum urea, creatinine, blood urea nitrogen (BUN), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT), direct bilirubin and total bilirubin analyses were performed by a central commercial laboratory fully automated auto analyzer Siemens RXL MAX. Creatinine levels and AST, using commercial kits supplied by Siemens Diagnostics. Creatinine clearance was interpreted by the Cock Croft-Gault formula (estimated creatinine clearance = [[140 – age in years] × weight in kilograms]/ [72 × serum creatinine concentration in milligrams per deciliter]; multiplied by 0.85 for women).

Data are given as mean values ± standard deviation. Comparison of preoperative and postoperative serum biochemical concentrations was performed using paired sample t-test. A p-value < 0.05 was considered statistically significant.

Results

Demographic characteristics of the patients studied, mean duration of anaesthesia and surgery are listed in *Table 1*. Renal function parameters such as urea, BUN and creatinine did not show significant differences at 24 and 48 hours compared to baseline levels whereas creatinine clearance levels were found to be low at postoperative 24 (135.62 ± 24.95) and 48 hours (122.35 ± 40.39) compared to the baseline level (135.95 ± 36.03) but statistically not significant as listed in *Table 2.*

Table 1: Demographic Characteristics of Patients

Characteristics	Sevoflurane (n= 40)
Age (years)	43.7 ± 7.67
Height (cms)	163.8 ± 4.10
Weight (kgs)	71.7 ± 7.30
BMI	27.2 ± 3.05
ASA I/II	14/06
Duration of Anaesthesia (mins)	105.5 ± 18.02
Duration of Surgery (mins)	93.0 ± 17.02

All values are expressed as mean ± standard deviation; BMI: Body mass index

Table 2: Comparison of Renal Functions Preoperatively and Postoperatively

Renal Function Parameters	Sevoflurane (n = 40)		
	Baseline	24 hours Postop.	48 hours Postop.
BUN (mmol/L)	11.75 ± 3.35	12.07 ± 3.71	12.83 ± 3.52
Urea (mmol/L)	24.80 ± 8.09	25 ± 7.18	25.40 ± 7.91
Creatinine (Umol/L)	0.62 ± 0.11	0.61 ± 0.07	0.72 ± 0.14
Creatinine Clearance (ml/min)	135.95 ± 36.03	135.62 ± 24.95	122.35 ± 40.39

All values are expressed as mean ± standard deviation; BUN: blood urea nitrogen

Table 3: Comparison of Hepatic Functions Preoperatively and Postoperatively

Hepatic Function Parameters	Sevoflurane (n= 40)		
	Baseline	24 hours Postop.	48 hours Postop.
AST (U/L)	23.00 ± 7.7	24.50 ± 9.2	24.50 ± 9.2
ALT (U/L)	20.00 ± 7.1	20.70 ± 7.9	22.10 ± 7.3
GGT (U/L)	13.40 ± 3.3	12.90 ± 3.6	13.5 ± 2.8
LDH (U/L)	357.40 ± 63.3	341.20 ± 82.7	353.50 ± 71.7
Dr. Bil (umol/L)	0.15 ± 0.07	0.17 ± 0.08	0.16 ± 0.09
T. Bil (umol/L)	1.01 ± 1.4	0.61 ± 0.2	1.06 ± 1.7

All values are expressed as mean ± standard deviation; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma glutarmyl tranferase; LDH: lactate dehydrogenase; Dr. Bil: direct bilirubin, T. Bil: total bilirubin

Hepatic effects of low-flow anaesthesia were tested by serum AST, ALT, GGT, LDH, direct bilirubin and total bilirubin concentrations. The preoperative and postoperative levels of hepatic function parameters are listed in *Table 3*. There was no significant change from baseline to 24 and 48 hours postoperatively. Thus, preoperative and postoperative values of biochemical parameters were similar ($p > 0.05$).

Discussion

We evaluated the hepatic and renal effects of low flow anaesthesia with inhalational agent Sevoflurane 24 and 48 hours postoperatively who have undergone laparoscopic abdominal surgery. Low-flow anaesthesia (1–1.5 L/min) reduces the inhalation anaesthetics consumption by nearly 40%–75%, compared to the circle system under high-flow anaesthesia (2–6 liter/min). In addition, carbon dioxide (CO2) absorbents, which have been used in anaesthesia rebreathing circuits, reduce the consumption of inhalation anaesthetics (7). Sevoflurane has advantages over other volatile anaesthetics: the lower solubility which provides improved control of delivery and faster rates of recovery as compared with isoflurane or enflurane (8).

Suttner *et al.* (9) showed that hepatic function was well preserved in elderly patients anesthetized with sevoflurane. On the contrary, metabolites of sevoflurane and breakdown products from its reaction with carbon dioxide absorbents theoretically can result in hepatic and renal damage. Nephrotoxicity of sevoflurane comes from direct alkylation of CpA, but such toxicity has not occurred despite extensive medical use. We found that sevoflurane did not alter the hepatic enzyme levels. Although BUN and serum creatinine are the most commonly used indicators of injury in the studies of sevoflurane nephrotoxicity, they have not revealed renal injury.

Ryoji *et al*. (10) and Kharasch *et al*. (11) demonstrated that BUN and serum creatinine did not increase after low-flow Sevoflurane anesthesia, which is consistent with previous results from studies using volunteers or clinical studies and thus no abnormality in the standard biomarkers was seen for low-flow sevoflurane anesthesia. Creatinine clearance a marker of renal metabolic function is used in renal toxicity. Several studies have shown that sevoflurane anaesthesia in open surgery at various fresh gas rates (1–4.4 L/min) was found to be safe in patients with normal renal function.

Sivaci *et al*. (3) and Eger *et al*. (12) have suggested that sevoflurane anaesthesia can cause transient dysfunction of several parts of the human nephron. Albuminuria and slightly greater proteinuria indicate glomerular injury. Therefore, it has been suggested that low-flow sevoflurane anaesthesia (<1 L/min) would not be safe in patients with renal impairment. Patients with preexisting renal disease are at an increased risk for further postoperative deterioration of function and CpA

nephrotoxicity may add to this risk.

In a study conducted by Reichle *et al*. (13), it was reported that plasma inorganic fluoride concentrations were regularly increased after sevoflurane anaesthesia and were not associated with nephrotoxicity. Histological examination in horses revealed that sevoflurane anaesthesia was associated with mild microscopic changes in the kidney involving mainly the distal tubule, but no remarkable alterations in hepatic tissue. These results indicate that horses can be maintained in a systemically healthy state during unusually prolonged sevoflurane anaesthesia with minimal risk of hepatocellular damage from this anaesthetic. In human studies, sevoflurane was found to have no adverse hepatic effects.

In the study conducted by Fatih *et al.* (4), they did not find any deterioration in hepatic functions. It was shown that pneumoperitoneum of 10 mmHg, resulting from the laparoscopic surgery technique, caused a 70% decrease in GFR. It was also suggested that the pneumoperitoneum reduced the hepatic portal blood flow, although it did not alter the clinically important postoperative hepatic transaminases. In these patients, selection of the anaesthetic agent, which has minimal or no effect on renal and hepatic functions, and a low fresh gas flow rate are very important. CO2 insufflated during the pneumoperitoneum period is absorbed into circulation, which may cause many side effects.

During low-flow anaesthesia reduced CO2 is produced due to lower metabolism of the anaesthetic agent. Thus, low-flow anaesthesia may minimize the total amount of CO2 in the pneumoperitoneum by reducing gas consumption resulting from anaesthetic agent metabolism (4). The present data shows that the choice of low flow anaesthesia with volatile anaesthetics is associated with a better outcome after laparoscopic surgery. In addition, low flow anaesthesia did not affect the biochemical parameters and may be a good alternative to the conventional high flow anaesthesia techniques.

Conclusion

Low-flow sevoflurane anaesthesia does not alter renal and hepatic functions in patients undergoing laparoscopic abdominal surgeries. The biochemical parameters of hepatic and renal functions are not altered when checked 24 and 48 hours postoperatively as compared to preoperative values.

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Conflicts of Interest

There are no conflicts of interest.

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