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Title: Comparison of the effects of sevoflurane and desflurane on thiol-disulfide homeostasis in patients undergoing laparoscopic cholecystectomy

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INTRODUCTION

Laparoscopic cholecystectomy is being increasingly performed. This method has many advantages. However, due to the creation of pneumoperitoneum, increase in intraabdominal pressure causes liver, splanchnic vessels to undergo mesenteric hypoxia, ischemia reperfusion injury and associated increase in oxidative stress [1]. Enzyme systems, ischemia modified albumin, protein carbonyl content, protein sulfhydryl, malondialdehyde, lipid peroxides and total antioxidant capacity (TAC) were measured in order to understand the impact at tissue level and gastric pH values were measured to determine oxidative status [2,3]. One of these methods is to measure the thiol disulfide balance. It could be measured thiol at only one side of this balance, Erel et al. [4]. have succeeded in measuring this balance through thiol disulfide hemostasis. Given the advances in technology, it is obvious that a number of abdominal surgical procedures can be performed with laparoscopic or robotic surgery. Selection of anesthetic agents in these patients is particularly critical. The protective effect of sevoflurane on cardiac and cerebral ischemia has been established. The effects of anesthetic volatile agents on oxidative and cytotoxic mechanisms have been previously studied, but their effects on thiol-disulfide homeostasis has not yet been investigated [5].

In this study, we aimed to investigate the effect of general anesthetic drugs such as sevoflurane and desflurane on thiol disulfide homeostasis in patients undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS

This study was approved by the university ethics committee (Approval No:26379996/238 number 231 and performed in accordance with the Declaration of Helsinki. All patients were informed by a written consent form.

After obtaining approval from the local ethics committee, we included 71 patients aged between 20-60 years with ASA (American Society of Anesthesiologist) physical status classification I-II in the study.

Patients with diabetes mellitus, coronary artery disease, conditions unsuitable for general anesthesia, emergency surgical interventions, smokers, patients with hepatic renal cerebral neurological disease, alcohol and drug abusers, those diagnosed with cancer and neuromuscular disease and patients with difficult intubation expected, and high BMI [>25] were excluded from the study. Prior to induction of anesthesia, all patients divided to the

two group randomly it was determined by drawing lots from an envelope with equal numbers of papers on which the group was specified. Before the operation the patients' heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressures (MBP) and peripheral O₂ saturation (SpO₂) were monitored.

Intravenous vascular access was provided using a 20 gauge (G) and 5-10 ml/kg/h 0.9% sodium chloride (NaCl) infusion was initiated. For the induction of anesthesia, 1 mg/kg lidocain (Aritmal 2%, Osel), 1 µcr/kg remifentanil (Ultiva 5 mg, GlaxoSmithKline) and 2 mg/kg propofol and 0.6 mg/kg rocuronium iv. were administered to patients. After preoxygenation carried out by administration of 100% O₂ with face mask for 3 minutes, orotracheal intubation was performed when adequate muscle relaxation was observed and the patient was ventilated with Dräger (Lübeck, Germany) anesthesia device so as to provide a tidal volume of 10 ml/kg and frequency of 12/min. Soda-lime (Sorbo-lime, Berkim, Turkey) was used as CO₂ absorbent. Storz (Gentec Ltd. Tuttlingen, Germany) electronic laparoflator was used to maintain the abdominal pressure at 14 mmHg by during the surgery. Among the patients randomly divided into two groups, maintenance of anesthesia was provided with 6% desflurane (Forane, Abbott Lab. UK) in patients in the first group and 2% sevoflurane in patients in the second group mixed with 40% O₂ and 60% air. Remifentanil infusion was administered at 0.25 µcr/kg/min in the maintenance in both groups. At the end of the operation, decurarisation was provided in all patients with 0.5 mg atropine and 1.5 mg neostigmine. In all groups, 0.5 mg of atropine was given when the heart rate dropped below 40 and 10 mg ephedrine was administered when the MAP was below 50 mg, and the infusion dose is reduced. Thirty minutes before the end of the operation, all patients received iv 1mg/kg tramadol and 10 mg methocloropropamide. Hemodynamic and respiratory parameters (SBP, DBP, MAP, HR, SpO₂, etCO₂) were recorded at baseline and at the time of induction, intubation, 5th min, 10th min, 15th min, 30th min, extubation and reperfusion. Blood samples were taken before induction (T1) (before the anesthesia), 30th minute of insufflation (T2) (30th min of ischemia) and 30th minute of postdeflation (30th min of reperfusion) (T3). Blood samples were centrifuged at 3600 rpm for 10 min, serum plasma samples were removed and stored at -80°C until analysis. A new spectrophotometric technique used to established thiol/disulfide homeostasis which was previously described by Erel and Neselioglu [4].

Reducible disulfide bonds were reduced to create free functional thiol groups. Unused reductant sodium borohydride was eliminate using formaldehyde and all thiol groups

including native and reduced groups were identified after the reaction with 5, 50 - dithiobis-(2- nitrobenzoic) acid. The amount of dynamic disulfide was then calculated by taking half of the difference between the native thiol and the total thiols. After the native thiol (-SH) and total thiols (-SH+SS) were determined, amounts of disulfide (-SS), disulfide/native thiol percent ratios (-SS/-SH), disulfide/total thiol percent ratios (-SS/-SH+SS), and -SH/total thiol percent ratios (-SH/-SH+SS) were calculated [4]. When undergoing an operation, decreased native and -SH+SS levels mean that these compounds have been consumed due to oxidative stress during surgery. If -SS/-SH+SS decrease, it means antioxidant mechanism is effective. The major oxidative parameters that we measured were -SH, -SH+SS and -SS.

Measurements were carried out by utilizing an automated clinical chemistry analyzer (Cobas 501, Roche Diagnostics, Mannheim, Germany). Serum thiol/ disulfide homeostasis values are expressed as $\mu\text{mol/L}$.

Sample Size Estimation: The primary aim of this study was to compare by the differences in percentage changes in total oxidative stress parameters (i.e. -SH, disulfide, -SH+SS) between desflurane and sevoflurane groups. A sample size of 34 per group was required to detect at least 20% difference in percentage change of in any oxidative stress parameter between groups with a power of 90% at the 1.67% significance level regarding for Bonferroni Correction. The difference of 20% was taken from both pilot study and also our clinical experiments. Sample size estimation was performed by using G*Power (Franz Faul, Universität Kiel, Kiel, Germany) version 3.0.10.

Statistical Analysis: Data analysis was performed by using IBM SPSS Statistics version 17.0 software (IBM Corporation, Armonk, NY, USA). Whether the continuous variables were normally distributed or not were determined by using Kolmogorov Smirnov test. Descriptive statistics for continuous variables were shown as mean \pm SD or median (25th-75th) percentiles, where applicable. Categorical data were expressed as number of cases and percentages. While, the mean differences between groups were compared by Student's t test, otherwise, Mann Whitney U test was applied for the comparisons of not normally distributed variables. Categorical data were analyzed by continuity corrected Chi-square test. Whether the differences among measurement times within groups regarding for total oxidative stress parameters were statistically significant or not was evaluated by Friedman test. When the p-values from the Friedman test statistics were statistically significant to know which measurement time differ from which others by using Wilcoxon Sign Rank test.

The repeated measurements of ANOVA by Wilks' Lambda test was applied for determining whether the mean differences in hemodynamic parameters among follow-up times were statistically significant or not. When the p values from the Wilks' Lambda test were statistically significant to know which measurement time differ from which others by using Bonferroni Adjusted multiple comparison. A p value less than 0.05 was considered statistically significant. However, all possible multiple comparisons, the Bonferroni Correction was applied for controlling Type I error.

RESULTS

The mean age was 49.0 ± 9.5 years in desflurane group and 47.7 ± 11.0 years in sevoflurane group. Distribution of males and females was statistically similar between the groups ($p=0.473$) (see Table 1). Data; were shown as median 25th / 75th percentiles, † Intra – groups comparisons, Friedman test, according to the Bonferroni Correction a p value less than 0.025 was considered as statistically significant, ‡ The comparisons between groups within each measurement time, Mann Whitney U test, according to the Bonferroni Correction a p value less than 0.0167 was considered as statistically significant, a: Preoperative vs intraoperative ($p<0.001$), b: Preoperative vs postoperative ($p<0.0083$). In the desflurane group, intraoperative and postoperative levels of -SH were significantly lower than preoperative values ($p<0.001$ and $p=0.003$; respectively). However, no statistically significant changes were observed in the sevoflurane group ($p=0.080$). All patients the intraoperative and post-operative levels of -SH+-SS were decreased compared to preoperative values ($p<0.001$ and $p<0.001$; respectively). No significant changes were observed in disulfide levels between the desflurane and sevoflurane groups at the preoperative, ischemia and reperfusion times. ($p=0.110$, $p=0.219$). SS-SH levels were similar in the desflurane group ($p=0.053$). Whereas, within the sevoflurane group, SS-SH levels were statistically decreased intraoperatively ($p<0.001$). There was no statistically significant difference between the desflurane and sevoflurane groups in terms of mean SBP values over Bonferroni correction ($p> 0.0056$) (Table 2). In the repeated measures, as the result of variance analysis, DBP, MBP, HR and SpO₂ were similar between the desflurane and sevoflurane groups ($p=0.571$, $p=0.751$, $p=0.113$, $p=0.723$; respectively).

DISCUSSION

Thiol, which is also known as a mercaptan, contains a hydrogen atom bound to a carbon atom and a sulfur atom and is a functional group of sulfhydryls [6].

Dynamic thiol/disulphide rate plays critical role in antioxidant defense, apoptosis,

detoxification, transcription, regulation of enzyme activities and mechanisms of cellular signal transduction [7,8]. The proteins' sulfhydryl groups turn into a reversible pattern of disulphides under oxidative conditions. In turn, disulphide bonds can be reduced again to thiol groups. When undergoing an operation, decreased native and -SH+-SS levels mean that these compounds have been consumed due to oxidative stress during surgery. If -SS/-SH+-SS decrease, it means antioxidant mechanism is effective. Antioxidant activity was found to be significantly higher during ischemia as the -SS/-SH+-SS value dropped in the sevoflurane group. Whereas in the desflurane group, -SH showing antioxidant activity was significantly decreased in both intraoperative ischemia and reperfusion period compared to preoperative value. Independent of both anesthetic agents, laparoscopic surgery was shown to shift thiol homeostasis towards oxidation [9]. It is known that anesthesia triggers inflammatory processes in patients. This process, which begins with the production of leukocytes in the alveolar macrophages, continues with the emergence of inflammatory mediators and free radicals. As a result, this process also causes peroxidation products to occur in general anesthesia due to the formation of membrane damage [10]. In addition, during laparoscopic procedures, the organ perfusion and portal venous flow could be reduced because of the decrease of cardiac output and accompanying mesenteric vasoconstriction [11]. Polat et al.[12] showed decreased levels of sulfhydryl during laparoscopic surgery. In another study, the levels of -SH, -SH+-SS, and disulfide were found to be intraoperatively fall during laparoscopic surgery [13]. The effect of many anesthetic drugs on oxidative stress during surgery has been studied. Desflurane and sevoflurane are the most recently developed and widely used anesthetic agents. Antiinflammatory and antioxidant properties of these agents have been previously studied. Schilling et al.[14]. demonstrated that, desflurane and sevoflurane suppress proinflammatory cytokine release following re-ventilation after single lung ventilation. In studies performed with the human heart, protective effect of desflurane occurs by modulating mitochondrial K[ATP]. channels and adenosine A1 receptors when preconditioning was performed. It is thought that, desflurane is more effective than sevoflurane in the late period, because it also has adrenoceptor modulation [15]. The application of sevoflurane in preconditioning and postconditioning forms has been shown to protect against ischemia-reperfusion injury in vital organs such as the heart, lung, and kidney [16]. Although the antioxidant properties of sevoflurane and propofol were statistically significant, an elevation in the oxidative status was observed in the desflurane group compared to the preoperative level [5]. In another study conducted

with rats, sevoflurane was found to have high antioxidant activity during cerebral ischemia reperfusion [17]. Sevoflurane postconditioning concentration-dependently significantly increased blood and brain superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) and glutathione reductase (GR) activities. Sevoflurane postconditioning concentration-dependently decreased blood and brain malondialdehyde (MDA) and increased reduced glutathione (GSH) concentrations.

Sivaci et al. [18]. also demonstrated that, desflurane increases MDA and protein carbonyl content, and as a result, desflurane increases free oxygen radicals more than sevoflurane during laparoscopic surgery. In this study, MDA levels and protein carbonyl contents of desflurane group went up and SH groups were reduced. These parameters of sevoflurane group did not change.

Yalçın et al. [19]. also found that desflurane was more associated with oxidative stress when used in thoracic surgery.

Consistently with the literature, in our study, we also observed that the antioxidant properties of sevoflurane were statistically higher. The protective properties of volatile agents have been determined in terms of cerebral, cardiac, renal, thoracic, and ischemia reperfusion injury. In animal studies, xanthine oxidase activity was elevated in rabbit colonic tissue after only 20 min of laparoscopic insufflation [20]. And also human studies, level of thiobarbituric acid-reactive substances were significantly higher in laparoscopic versus open cholecystectomy; this was seen only at 5 min post deflation, with no significant difference at 24 h [21]. In open and laparoscopic procedure at the end of the surgery in all groups observed higher levels of MDA and advanced oxidation protein products.

In the laparoscopic group oxidative parameters had essentially normalized at 24h. The level of the oxidative stress in the laparoscopic group related with the volume of gas and the duration of insufflation [22]. So, in this study it was decided to take blood samples at the same time of the insufflation and the post deflation for all patients because it was planned not to compare the open procedure with laparoscopic surgery, to compare the volatile anesthetics.

The limitations of our study may be the lack of comparison with different oxidative parameters that gives long-term oxidation information.

In conclusion, for the first time in the literature, it was demonstrated that sevoflurane has more protective effects on thiol-disulfide homeostasis compared to desflurane.

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REFERENCES

1. Neseek-Adam V, Vnuk D, Rasić Z, Rumenjak V, Kos J, Krstonijević, Z. Comparison of the effects of low intraabdominal pressure and pentoxifylline on oxidative stress during CO₂ pneumoperitoneum in rabbits. *Eur. Surg. Res.* 2009; 43: 330–337.
2. Biler A, Yucebilgin S, Sendag F et al. The effects of different intraabdominal pressure protocols in laparoscopic procedures on oxidative stress markers and morphology in rat ovaries. *Adv Clin Exp Med* 2014; 23: 885–892.
3. Sammour T, Mittal A, Loveday BP et al. Systematic review of oxidative stress associated with pneumoperitoneum. *Br J Surg* 2009; 96: 836–850.
4. Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. *Clin Biochem* 2014; 47: 326-32.
5. Erbas M, Demiraran Y, Yildirim H.A et al Comparison of effects on the oxidant/antioxidant system of sevoflurane, desflurane and propofol infusion during general anesthesia *Rev Bras Anesthesiol* 2015; 65: 68-72.
6. Sen CK, Packer L. Thiol homeostasis and supplements in physical exercise. *Am J Clin Nutr* 2000; 72: 653- 69.
7. Circu ML, Aw TY. Reactive oxygen species, cellular redox systems, and apoptosis. *Free Radic Biol Med* 2010; 48: 749–62.
8. Biswas S, Chida AS, Rahman I. Redox modifications of protein-thiols: emerging roles in cell signaling. *Biochem Pharmacol* 2006; 71: 551-564.
9. Polat M, Ozcan O, Sahan L et al. Changes in Thiol-Disulfide Homeostasis of the Body to Surgical Trauma in Laparoscopic Cholecystectomy Patients *Journal of Laparoendoscopic Adv Surg Tech* 2016; 26: 992-996.
10. Koksall GM, Sayilgan C, Aydin S, Uzun H, Oz H. The effects of sevoflurane and desflurane on lipid peroxidation during laparoscopic cholecystectomy. *Eur J Anaesth* 2004; 21:217-220.
11. Jakimowicz J, Stultiens G, Smulders F. Laparoscopic insufflation of the abdomen reduces portal venous flow. *Surg Endosc* 1998; 12: 129–132.
12. Polat C, Kahraman A, Yilmaz S et al. A comparison of the oxidative stress response and antioxidant capacity of open and laparoscopic hernia repairs.

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13. Schilling MK, Redaelli C, Krahenbuhl L, Signer C, Buchler MW. Splanchnic microcirculatory changes during CO₂ laparoscopy. *J Am Coll Surg* 1997; 184: 378-382.
14. Schilling T, Kozian A, Senturk M et al. Effects of volatile and intravenous anesthesia on the alveolar and systemic inflammatory response in thoracic surgical patients. *Anesthesiology* 2011; 115: 65-74.
15. Sivanna U, Joshi S, Babu B, Jagadeesh AM. A comparative study of pharmacological myocardial protection between sevoflurane and desflurane at anaesthetic doses in patients undergoing off pump coronary artery bypass grafting surgery. *Indian J Anaesth* 2015; 59: 282-286.
16. Luo C, Yuan D, Zhaon W et al. Sevoflurane ameliorates intestinal ischemia-reperfusion-induced lung injury by inhibiting the synergistic action between mast cell activation and oxidative stress. *Molecular Medicine Reports* 2015; 12: 1082-1090.
17. Zhang Y, Zhang F, Meng C et al. Inhibition of Sevoflurane Postconditioning Against Cerebral Ischemia Reperfusion-Induced Oxidative Injury in Rats. *Molecules* 2012; 17, 341-354.
18. Sivaci R, Kahraman A, Serteser M, Sahin DA, Dilek ON. Cytotoxic effects of volatile anesthetics with free radicals undergoing laparoscopic surgery. *Clin Biochem* 2006; 39: 293-298.
19. Yalçın Ş, Özgencil E, Serdaroglu H, Oba Ş, Enön S, Demiralp S. Anesthetics modulate oxidative stress during one-lung ventilation in lung cancer patients: Comparison of target-controlled propofol infusion and desflurane. *Afr. J. Pharm. Pharmacol.* 2012; 6: 407-411.
20. Emir H, Akman M, Belce A, Gumustas K, Soylet Y. Is intestinal ischemia a risk of laparoscopy? An experimental study in rabbits. *Eur J Pediatr Surg* 2001; 11: 158–162.
21. Glantzounis GK, Tselepis AD, Tambaki AP et al. Laparoscopic surgery-induced changes in oxidative stress markers in human plasma. *Surg Endosc.* 2001; 15: 1315-13159.
22. Bentes de Souza AM, Rogers MS, Wang CC, Yuen PM, Ng PS. Comparison of peritoneal oxidative stress during laparoscopy and laparotomy. *J Am Assoc Gynecol Laparosc.* 2003; 10: 65-74.

Table 1: Demographical characteristics of patient groups

	Desflurane (n=35)	Sevoflurane (n=36)	p-value
Age (years)	49.0±9.5	47.7±11.0	0.612†
Sex			0.473‡

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Male	8 (22.9%)	12 (33.3%)
Female	27 (77.1%)	24 (66.7%)

†Student's t test, ‡Continuity corrected chi-square test.

Table 2: Repeated measurements of total oxidative stress parameters

	Preop Mean (Min-Max)	Intraop (Ischemia 30 min) Mean (Min-Max)	Postop (Reperfusion 30 min) Mean (Min-Max)	p-value †
-SH				
Desflurane	368.7 (326.0-432.4) ^{a,b}	324.7 (262.9-383.3) ^a	324.2 (293.5-395.6) ^b	<0.001
Sevoflurane	342.5 (264.4-404.2)	318.5 (257.9-365.0)	323.1 (268.6-382.9)	0.080
p-value ‡	0.035	0.743	0.765	
Disulfide				
Desflurane	15.0 (10.5-19.8)	12.1 (8.4-25.7)	16.6 (12.3-24.3)	0.110
Sevoflurane	17.6 (12.2-23.2)	12.2 (9.0-22.6)	15.9 (10.6-23.9)	0.219
p-value ‡	0.298	0.963	0.476	
-SH+SS				
Desflurane	408.4 (351.4-459.8) ^{a,b}	326.9 (198.5-385.1) ^a	344.5 (273.2-402.4) ^b	<0.001
Sevoflurane	371.7 (302.4-438.1) ^{a,b}	299.0 (190.7-361.6) ^a	320.0 (130.9-374.5) ^b	<0.001
p-value ‡	0.062	0.206	0.155	
SS-SH				
Desflurane	4.3 (2.8-6.2)	4.4 (2.9-5.3)	4.5 (3.8-6.3)	0.053
Sevoflurane	5.5 (3.3-6.8) ^a	3.6 (2.4-4.9) ^a	4.3 (3.2-5.9)	0.017
p-value ‡	0.123	0.262	0.388	
SS-total				
Desflurane	3.9 (2.6-5.5)	4.1 (2.8-4.8)	4.1 (3.6-5.6)	0.053
Sevoflurane	4.9 (3.1-6.0) ^a	3.4 (2.3-4.5) ^a	4.0 (3.0-5.3)	0.017
p-value ‡	0.123	0.262	0.385	
SH-total				
Desflurane	92.1 (88.9-94.7)	91.8 (90.4-94.4)	91.7 (88.9-92.8)	0.053
Sevoflurane	90.1 (88.0-93.7) ^a	93.2 (91.0-95.3) ^a	92.0 (89.4-93.9)	0.017

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p-value ‡ 0.123 0.257 0.388

SH:-SH, SS:disulfide SS-SH: disulfide--SH

Data were expressed in median (25th to 75th) percentiles, †Intra-group comparisons, Friedman test, according to the Bonferroni Correction; a *p* value less than 0.025 was considered statistically significant, ‡Inter-group comparisons within each measurement time point, the Mann-Whitney U test, according to the Bonferroni Correction; a *p* value less than 0.0167 was considered statistically significant, a: Preop vs Intraop (*p*<0.001), b: Preop vs Postop (*p*<0.0083). Pre-op, preoperative; intraop, intraoperative; postop, postoperative.

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