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STUDY OF SEVOFLURANE IN INDUCING OXIDATIVE STRESS IN PATIENTS UNDERGOING GENERAL ANESTHESIA

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ABSTRACT

Sevoflurane is frequently used for general anaesthesia and earlier many studies have shown that this anaesthetic drug has an impact on oxidative stress and antioxidative defence mechanisms. This study was planned to evaluate the effects of sevoflurane, in general anaesthesia on the oxidant and antioxidant systems of patients undergoing laparoscopic cholecystectomy and appendectomy. A total of 12 patients between 29 and 47 years with planned laparoscopic cholecystectomy and appendectomy under general anaesthetic were selected for this study. Same numbers of normal control persons were recruited in this study. For inducing and maintenance of general anaesthesia experimental group was ventilated with 2% sevoflurane. One hour before induction of general anaesthesia and one hour after the surgery venous blood samples were taken to evaluate the levels of lipid profile, total oxidants and antioxidants. The general physical characteristics of the subject were also recorded with simple questionnaire were matched with control group. In the post-anaesthesia period we observed that sevoflurane induced general anaesthesia increased total oxidants level and antioxidants by a statistically significant level, this indicates that sevoflurane induced general anaesthesia increases formation o free radicals and thus cause an oxidative stress in subject.

INTRODUCTION

Sevoflurane (1, 1, 1, 3, 3, 3-hexafluoro-2-(fluoromethoxy) propane, is used as an inhalational anaesthetic for induction and maintenance of general anaesthesia. It is one of the most commonly used volatile anaesthetic agents, particularly for outpatient anaesthesia, Sevoflurane has an excellent safety record but it is under review for low frequency liver injury and potential neurotoxicity [1]. Free radicals are formed in case of oxidative stress; these highly reactive radicals were oxidizing biological molecules such as the body's building blocks of carbohydrate, protein, lipid and nucleic acids, on the other side these free radicals can also work against the oxidative system as part of the body's natural antioxidant defence system. This situation is balanced under normal physiological conditions [2-4]. However in a situation of meeting any stress, as a result of increasing antioxidant consumption or free radical creation, many oxidative stresses increase [4,5]. Many antioxidant molecules are found in the blood to prevent or inhibit the harmful effects of free oxygen radicals. Measurement of total antioxidant and oxidant levels in plasma can be used to determine the oxidative stress reaction.

An increasing attention has been paid to oxidative stress blaming it as an important causative factor for complications. It is well documented that several diseases like diabetes mellitus, neurodegeneration, cancer and cardiovascular are known to generate reactive species. The commonly using agents like sevoflurane, desflurane, halothane and isoflurane during anesthesia also plays an vital role in production of leucocytes release inflammatory

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mediators and ROS. Damage to membrane lipids by ROS is implied by the appearance of lipid peroxidation products (e.g. MDA) during general anesthesia. Sevoflurane is frequently used for induction of general anaesthesia and earlier studies have shown that many of these anaesthetics cause a variety of changes to the oxidative stress and antioxidative defence mechanisms in human body [6, 7].

In this study we aimed to evaluate the levels of lipid profile, total oxidants and antioxidants after induction of general anaesthesia with sevoflurane, in patients undergoing laparoscopic appendectomy, cholecystectomy.

MATERIALS AND METHODS

Subject Selection

This study comprised of 12 general anaesthetized patients undergoing laparoscopic appendectomy, cholecystectomy (age 38± 9 years) and 35 sex- and age-matched non-anaesthetized persons as a control group (age 37±7 years), with no known history of any disease. The study has got the approval from Institutional Ethics Committee; Informed Consent was obtained from every individual who has participated in this study. Using an in-house designed questionnaire, background information was gathered from the subjects.

Anthropometric measurements

All subjects underwent a clinical examination; weight, height has been measured. Blood pressure was recorded by auscultatory methods with mercury sphygmomanometer according to the American Heart Association guidelines. Prior to the surgery, patient's routine monitoring with electrocardiogram (ECG), peripheral oxygen saturation (SPO_2) was done. Patients were anaesthetized by using appropriate intubation tube ventilation with 2% sevoflurane, 50% air and 50% O_2 mix at 6 L/min flow. After the surgery, with extubation the patient was taken to recovery.

Blood sampling:

Venous blood was collected from all the patients before and after anaesthesia and processed for evaluation of total oxidant status, total antioxidant levels. Fasting blood samples were also collected from both subject's group for an estimation of lipid profiles.

Estimation of lipid profile

This assay was performed by using standard kit in the semi auto analyzer. The activities of serum alanine and aspartate aminotransferases (ALT and AST) were assayed by the combined methods of Mohun and Cook [8] and Reitman and Frankel [9].

Measurement of the Total Oxidant Status

The total oxidant status of the serum (or plasma) was determined using an automated colorimetric measurement method for total oxidant status developed by Erel [10]. The results are shown in point of micromolar hydrogen peroxide equivalent per litre (μmol H_2O_2 Equiv./L).

Measurement of the Total Antioxidant Status

The total antioxidant status of the serum was determined using an automated colorimetric measurement method for total antioxidant status developed by Erel [11]. The results are shown as the micromolar trolox equivalent per litre.

Oxidative Stress Index

The percentage ratio of total oxidant status levels to total antioxidant status levels were accepted as oxidative stress index (OSI) [12]. OSI values were calculated with the help of below mentioned formula:

$$\text{Oxidative stress index (arbitrary unit)} = \frac{\text{Total oxidant status (micromolar hydrogen peroxide equivalent per L)}}{\text{Total antioxidant status (micromolar trolox equivalent per L).}}$$

Statistical Analysis

The data obtained was analysed for its statistical significance by one way ANOVA using SPSS. $P<0.05$ was considered the level of significance.

RESULTS

The result shown in Table 1 indicates the general physical and anthropometric characteristics of selected subject, in which subject's age and gender almost matching in both the group.

ALT: alanine aminotransferase, AST: aspartate aminotransferase, TG: triglycerides, TC: total cholesterol, LDL-C: low-density lipoprotein-cholesterol and HDL-C: high-density lipoproteincholesterol,

The results in Table 2 indicate the comparison between different biochemical indicators in Control, Pre- and Post-anaesthesia group, there is significant variation in lipid profile among control group and post-anaesthesia group. The results in Table 3 indicate the comparison between evaluate total oxidant status, total antioxidant status, lipid peroxidation levels in Control, Pre- and Post-anaesthesia group, there is significant variation in all those parameters among control group and post-anaesthesia group.

Table 1. General anthropometric characteristics of control and anaesthetized group

Parameter	Control Group	Anaesthesia Group
Age	37±7	38± 9
Gender (M/F)	7/5	8/4
BMI (kg/m^2)	23.6 ± 1.2	24.8 ± 1.4
Smoker	5 %	7%
Systolic Blood Pressure	122 ± 8.48	126 ± 10.52
Diastolic Pressure	76 ± 4	78 ± 6

The Subjects (n) in each group, n= 12. The values are expressed as mean ±SD.

Table 2. Comparison of biochemical indices between control and anaesthetized group

Parameter	Control Group	Pre-Anaesthesia Group (Prior to Surgery)	Post- Anaesthesia Group (After Surgery)
ALT (IU/L)	127±14.7	156±11.8	169±19.7
AST (IU/L)	265±21.4	215±8.7	241±22.3
TG (mg/dL)	121.1 ± 12.69	237.7 ± 28.16	259.0 ± 14.05*
TC (mg/dL)	95.5 ± 4.18	162.7 ± 7.82*	149.3 ± 6.14
LDL-C (mg/dL)	68.2 ± 6.22	109.4 ± 4.87	131.1 ± 7.93*
HDL-C (mg/dL)	29.2 ± 4.15	19.6 ± 3.28*	13.2 ± 1.98*

Values are means ± SD; *significantly different from control ($P < 0.05$).

Table 3. Comparison of oxidant status between control and anaesthetized group

Parameter	Control Group	Pre-Anaesthesia Group(Prior to Surgery)	Post- Anaesthesia Group (After Surgery)
TAS (nmol Troloks/L)	3.39±0.8	4.1±0.75	5.42±1.34
TOS (µmol H_2O_2 Equiv./L)	9.2±0.43	13.75±1.2*	30.62±2.89*
OSI	0.3±0.2	3.96±0.8*	6.39±0.9*

Values are means ± SD; *significantly different from control ($P < 0.05$).
TAS=Total Antioxidant Status, TOS= Total Oxidant Status, OSI= Oxidative Stress Index

DISCUSSION

Free radicals are more highly activate and potential damaging than molecular oxygen. Inhalation of anaesthetic drugs increases free radical formation and imbalance in body's antioxidative defence mechanism [4-5]. Earlier different studies also shown that general anaesthesia might lead to excess generation of reactive oxygen species, which causes the acute oxidative stress [2-5]. Inflammatory factor levels and oxidative stress product concentration could predict the chance of complications after anaesthesia. The risk of these kinds of complications should be evaluated in patients.

It has been shown that poor recovery after anaesthesia might deteriorate oxidative stress and predict postoperative mortality. Different studies illustrated the role of oxygen toxicity, adults' respiratory distress syndrome, and halothane in free radical injuries in patients who underwent surgery with general anaesthesia. Sevoflurane induced general anaesthesia could reduce lipid peroxidation in surgeries [13-15].

In this study we observed that sevoflurane increases oxidative stress. Anaesthetic drugs and anaesthetic duration used in general anaesthesia, together with the stress of surgical trauma, are important factors that disrupt the body's immunological and antioxidant defence systems. [16, 17]. General anaesthesia also disrupts the immunological defence mechanisms and induces an inflammatory reaction in the body. In generalized inflammatory reactions results in membrane damage caused by free radicals as observed lipid peroxidation products formation increases. Previous studies have shown that a variety of medications used in anaesthesia have effects on the oxidant-antioxidant system [17-20]. However the surgical stress of laparoscopy with inhalation of sevoflurane increased total oxidant capacity and reduced total antioxidant capacity. The effect on the antioxidant system of the inhalation anaesthetic sevoflurane has not been fully studied, so the exact mechanism of increased oxidative stress during sevoflurane induced general anaesthesia is not yet known.

CONCLUSION

This study propose an idea that in general anaesthesia, to minimise the adverse effects oxidative stress the agent that will least damage the antioxidant system should be chosen. Further research into the physical health, body composition of patients receiving general anaesthetic and the relationship between oxidant/antioxidant systems are required.

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