REPUBLIC OF TÜRKİYE

DUZCE UNIVERSITY

FACULTY OF MEDICINE

DEPARTMENT OF ANESTHESIOLOGY AND REANIMATION

Comparison of Changes in Total Oxidant and Total Antioxidant Capacities in Low-Flow and High-Flow General Anesthesia Protocols: Study Protocol

(NCT05590312)

DUZCE-2022

(Translation in English: 16.01.2025)

Comparison of Changes in Total Oxidant and Total Antioxidant Capacities in Low-Flow and High-Flow General Anesthesia Protocols

General Information/ Background

General anesthesia is a complex physiological state characterized by reversible loss of consciousness, whole-body analgesia, amnesia, and muscle relaxation. The term low-flow anesthesia describes inhalation anesthesia techniques that are administered with a semi-closed rebreathing system and have a rebreathing rate of at least 50%. The high standard of anesthesia machines, the existence of monitors that analyze the anesthetic gas composition continuously and in detail, and the increased knowledge about the pharmacodynamics and pharmacokinetics of inhalation anesthetics have greatly facilitated the safe administration of low-flow anesthesia. The terminology associated with low-flow anesthetic techniques may be based on rebreathing or fresh gas flow rates. The fresh gas flow rate is the most critical factor determining the rebreathing rate. Most patients can have low-flow anesthesia when modern re-breathing systems are used; the fresh gas flow rate is reduced to less than 2 L/min. Oxidative stress is accepted as a pathological mechanism. Oxidative stress is a state of oxidative damage that occurs when the critical balance between free radical production and antioxidant defense systems is disrupted. Oxidative stress is beneficial in certain physiological conditions. For example, it can strengthen biological defense mechanisms during appropriate physical exercise and ischemia. However, its benefits are limited to these specific situations, and in many other cases, high levels of oxidative stress cause cell death and, thus, cell and tissue damage through necrotic or apoptotic mechanisms. If damage continues at the cell and tissue level, it causes various organ damage and disease onset and progression. In our study, the amount of inspired oxygen is expected to be low due to keeping the gas supplied to the system low in low-flow anesthesia applications. Accordingly, the oxidative stress will be less. Therefore, this study will investigate whether low-flow anesthesia positively contributes to the total oxidant/antioxidant balance.

Keywords: General anesthesia, low flow anesthesia, oxidative stress

Introduction

It is reported that the use of high-flow anesthesia in operating room practice is still over 80%. Low-flow anesthesia is associated with a less inflammatory response in the postoperative period than high-flow anesthesia. In addition, the low-flow anesthesia technique maintains the temperature and humidity of the respiratory system with less effect on mucociliary clearance. It preserves tracheobronchial physiology better than high-flow anesthesia. This technique also reduces the amount of waste gases released into the environment and atmospheric pollution, as well as health risks for operating room personnel, and better preserves the ecological balance. One of the most essential advantages of using low current is cost reduction.

Many risk factors can cause oxidative stress, including alcohol, drugs, environmental pollutants, intense exercise, inflammation, and sepsis. Biological targets most exposed to oxidative damage include enzymes, cell membranes, and DNA. Oxygen radicals have been implicated as an essential cause of mechanisms that can lead to the rapid degradation of proteins. Free radical-induced changes in proteins increase the degradation of enzymes. Oxidative damage to protein products can affect the activity of enzymes, receptors, and transporter proteins. Oxidatively damaged protein products may contain reactive groups that can damage the cell membrane and many cellular functions. Peroxidation of lipids occurs when biological membranes react with unsaturated fatty acids and proceed by radical chain reaction. Oxidative events cause changes in the physical-chemical properties of membranes and thus alter fluidity and permeability, with membranes disintegrating with swelling of intracellular organelles. DNA and RNA are sensitive to oxidative damage. DNA is thought to be the main target, especially in aging and cancer. Oxidative nucleotides such as glycol, thymidine glycol, and 8-hydroxy-2- deoxyguanosine have increased during oxidative damage to DNA by UV radiation or free radical damage. Mitochondrial DNA has been reported to be more susceptible to oxidative damage in many diseases, including cancer.

In our study, two groups will be formed: low flow group and high flow group. Vitamin D, albumin, CRP, TAS, and TOS values will be checked from all patients before and during the operation. During the operation, 1 L/min fresh gas flow will be given to the low-flow group, 4 L/min fresh gas flow will be given to the high-flow group, and the processed EEG values of all patients will be monitored, and the same depth of anesthesia will be ensured. Albumin, CRP, TAS, and TOS values from the postoperative blood samples of the patients taken to the ward after the operation will be rechecked, and these values will be compared with the previous values.

Our study will compare the changes in total oxidant and total antioxidant systems in general anesthesia methods applied with 1 lt/min and 4 lt/min flows. Studies show patient-based advantages of low-flow anesthesia, such as respiratory functions and inflammatory response in the postoperative period. However, very few studies show its effects on oxidative stress, and a comprehensive study evaluating total oxidant/antioxidant systems was not found in our literature review. Therefore, our study will contribute to the literature.

Material and Methods

Inclusion criteria:

Patients older than 18 years and younger than 60 years to be operated under general anesthesia

Patients in the I and II risk groups, according to the American Society of Anesthesiologists (ASA) classification

Exclusion criteria:

ASA III and above patients,

Patients for whom an Intensive Care Unit (ICU) indication is foreseen

Chronic obstructive pulmonary disease,

A personal or family history of malignant hyperthermia,

Morbid obesity,

Alcohol or drug addiction,

History of liver or kidney disease,

With coronary artery disease or heart failure,

Significant anemia or hemoglobinopathy,

Hypotension, hypovolemia, sepsis.

After the patients who meet the specified criteria are informed about the study, volunteers who agree to participate and sign an informed consent will be included. Vitamin D, albumin, CRP, Total Antioxidant Status (TAS), and Total Oxidant Status (TOS) levels will be measured in the blood samples obtained from all volunteers' preoperative routine blood samples. After all volunteers are admitted to the operation room, they will be monitored with electrocardiography, pulse oximetry, non-invasive blood pressure, end-tidal carbon dioxide, temperature probe, and processed electroencephalogram- -bispectral index (BIS) without any medication. Baseline peak heart rate (HR), peripheral oxygen saturation (SpO2), systolic (SBP) and diastolic blood pressure (DBP), end-tidal carbon dioxide (ETCO2), body temperature, and BIS will be recorded. All measurements will be repeated and recorded at 5-minute intervals during the operation.

Volunteers will be divided into low-flow group (D) and high-flow group (Y). D group will receive 1 L/min fresh gas flow, and Y group will receive 4 L/min fresh gas flow. Processed EEG values of all patients will be monitored during the operation and ensured they are at the same depth of anesthesia. Albumin, CRP, TAS, and TOS values will be rechecked in the postoperative blood samples of the patients during and after the operation and compared with the previous values.

Management Scheme

Executive Researcher: Ass. Prof. Dr. ÖEK: Contacting the volunteers, explaining the study, obtaining informed consent, keeping records, evaluating the data, interpreting statistical analysis, and converting the results into an article.

Researcher: Dr. GS: Contacting the volunteers, explaining the study, obtaining informed consent, evaluating the data, interpreting the statistical analysis, and converting the results into an article.

Success Criteria and Alternative Plan

The project will be considered successful when all procedures of 6 volunteers are completed each week. Since the researchers will carry out all measurements if the operation dates of the volunteers change or there is disruption due to the work intensity/excuse of the researcher, the disrupted time will be compensated by performing the procedures of more than 6 volunteers per week.

Statistical Analysis Plan

The Shapiro-Wilk test will be used to check the normal distribution of the numerical data, and the kurtosis and skewness coefficients will also be examined. Variance homogeneity will be analyzed using Levene's test. Independent samples t-test, Welch test, or Mann-Whitney U test will compare the groups depending on the data distribution. Depending on the expected value rule, categorical variables will be analyzed using Pearson chi-square, Fisher's exact, or Fisher-Freeman-Halton tests. A comparison of the values measured at different periods during the operation will be performed using repeated measures ANOVA. Pearson correlation or Spearman's rho will be used in correlation analyses depending on the data distribution. Descriptive statistics will be given as mean±standard deviation or median, quartiles, and minimum-maximum values depending on the data distribution, and categorical variables will be summarized as numbers and percentages. Statistical analyses will be performed using SPSS v.22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) package program, and the significance level will be taken as 0.05.

Ethical Board Approval

Duzce University Non-Invasive Health Research Ethics Committee; Date: 25.04.2022; Number: 2022/61

Funding

Duzce University Scientific Projects Coordination Office; Project Number: 2022.04.02.1335