STUDY PROTOCOL

Official Title

Infection Risk Associated with Minimal-Flow Anesthesia: A Randomized Controlled Trial

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1. Background and Rationale

Inhalational anesthesia is commonly administered using fresh gas flows of 2–6 L/min. A fresh gas flow of 1 L/min is defined as low-flow anesthesia, whereas a flow of 0.5 L/min is defined as minimal-flow anesthesia.

In the high-flow technique, fresh gas flows of 2–6 L/min ensure a continuous abundance of fresh gas within the breathing system. Since the patient inhales only a small portion of this gas, most of it is discharged into the anesthetic gas scavenging system. This allows rapid adjustment of gas concentrations, including oxygen and anesthetic agents. However, because the heat and moisture released from the patient's lungs are removed by the carbon dioxide absorber, the gas within the system remains relatively cold and dry. In addition, a considerable amount of inhalational anesthetic agent is wasted.

The use of fresh gas flows of 1 L/min or lower reduces the amount of fresh gas delivered from the vaporizers to the breathing system. Consequently, the system responds more slowly to changes in gas concentrations. Low-flow and minimal-flow anesthesia provide significant advantages by humidifying and warming the inspired gases, thereby protecting the respiratory tract. Compared with ventilation using cold and dry gases, mucociliary clearance is improved, epithelial damage is reduced, and the release of inflammatory mediators decreases.

Low-flow anesthesia is considered a safe and beneficial technique for patients. It also offers financial and environmental advantages. The use of minimal-flow anesthesia reduces heat loss from the airways and prevents drying of mucosal surfaces. Furthermore, it significantly decreases the amount of fresh gas and inhalational anesthetic waste released into the atmosphere. These benefits may contribute to lower rates of airway inflammation and infection, reduced environmental pollution, and lower healthcare costs.

Modern anesthesia workstations support the safe administration of low-flow anesthesia through leak-resistant breathing systems, humidity management, accurate flow measurement technology, advanced ventilator systems, precise anesthetic agent delivery, and reliable gas monitoring.

The primary aim of this study is to determine whether the increased humidity and temperature associated with minimal-flow anesthesia lead to microbial colonization within the anesthesia breathing circuit.

2. Study Objectives

Primary Objective

To determine whether minimal-flow anesthesia increases microbial contamination and colonization within the anesthesia breathing circuit compared with high-flow anesthesia.

Secondary Objectives

- To evaluate the relationship between circuit temperature, humidity, and microbial growth.

- To compare contamination rates between inspiratory and expiratory circuit limbs.
- To investigate the association between anesthesia duration and microbial contamination.
- To identify the microorganisms isolated from anesthesia circuit samples.

3. Expected Benefits and Risks

This study is expected to clarify whether prolonged circulation of gases within the breathing circuit during minimal-flow anesthesia theoretically increases microbial accumulation and whether the increase in temperature and humidity promotes bacterial growth.

The findings may help evaluate concerns regarding infection risk during minimal-flow anesthesia and contribute to wider acceptance of this technique. Since studies specifically investigating the relationship between minimal-flow anesthesia and microbial contamination are limited, this study is expected to provide valuable data to the literature.

No additional risks beyond routine clinical practice are anticipated. Minimal-flow anesthesia is already routinely performed in our institution.

4. Study Design

This study is designed as a randomized, prospective, double-blind clinical trial.

Following approval by the Ankara City Hospital Clinical Research Ethics Committee, a total of 140 patients scheduled to undergo elective surgical procedures will be enrolled.

Eligible participants will be adults aged 18–65 years of either sex and classified as American Society of Anesthesiologists (ASA) physical status I–II. Written informed consent will be obtained from all participants before enrollment.

Participants will be randomized using a sealed-envelope method into one of two groups:

Group 1: High-Flow Anesthesia Group (fresh gas flow 2 L/min)

Group 2: Minimal-Flow Anesthesia Group (fresh gas flow 0.5 L/min)

5. Study Population

A total of 140 adult patients undergoing elective surgery at Ankara Bilkent City Hospital will be enrolled.

Baseline demographic and clinical data including age, body weight, ASA classification, and comorbid conditions will be recorded before surgery.

6. Inclusion Criteria

Participants must meet all of the following criteria:

- Age between 18 and 65 years
- ASA physical status I–II

- Scheduled for elective surgery
- Ability to provide written informed consent
- Willingness to participate in the study

7. Exclusion Criteria

Participants meeting any of the following criteria will be excluded:

- Refusal to participate
- Age below 18 years or above 65 years
- ASA physical status III–V
- Emergency surgery
- Uncontrolled hypertension
- Severe cardiac disease
- Severe pulmonary disease
- Neuromuscular disease
- Uncontrolled diabetes mellitus
- Metabolic disorders
- Immunodeficiency
- Significant anemia
- Bleeding disorders
- Hepatic disease
- Renal disease
- Previous cardiac surgery
- Previous intracranial surgery
- Previous pulmonary surgery
- Previous head and neck surgery
- Anticipated difficult airway
- Alcohol or substance abuse
- Pregnancy or lactation
- Known allergy to anesthetic agents
- Body mass index >30 kg/m^2
- Sepsis or active infection
- Baseline body temperature <35°C or >38°C
- Antibiotic treatment within the previous month
- Active malignancy

8. Anesthetic Management

Before each procedure, anesthesia machines will undergo routine leak testing and gas monitor calibration.

Single-use anesthesia breathing circuits, bacterial filters, and anesthesia masks will be used for all participants. Carbon dioxide absorbent (Sorbo-lime®, Berkim, Turkey) will be replaced daily.

Anesthesia will be administered using a GE Avance CS2 anesthesia workstation.

Routine monitoring will include:

- Electrocardiography (ECG)
- Non-invasive blood pressure monitoring
- Peripheral oxygen saturation (SpO_2)
- Respiratory rate
- End-tidal carbon dioxide ($EtCO_2$)

Body temperature monitoring will also be performed throughout anesthesia.

After preoxygenation with 100% oxygen for 3 minutes using a fresh gas flow of 3 L/min, anesthesia will be induced with:

- Lidocaine 1 mg/kg
- Propofol 2 mg/kg
- Fentanyl 1 μg/kg
- Rocuronium 0.6–1.0 mg/kg

Patients will then be intubated with an appropriately sized endotracheal tube.

Maintenance of anesthesia will be achieved using:

- Remifentanil infusion (0.02–0.2 μg/kg/min)
- Sevoflurane titrated to maintain a MAC value of 1.0

Ventilator settings:

- Tidal volume: 8 mL/kg
- Respiratory rate: 12 breaths/min
- I ratio: 1:2

Fresh gas flow will initially be set at 3 L/min (45% oxygen, 55% air) in both groups.

After the MAC reaches 1.0:

- High-Flow Group: 2 L/min
- Minimal-Flow Group: 0.5 L/min

Ten minutes before completion of surgery, fresh gas flow will be increased to 3 L/min in both groups. Sevoflurane will be discontinued and 100% oxygen administered.

Neuromuscular blockade will be reversed using sugammadex (2–4 mg/kg), followed by extubation.

9. Microbiological Assessment

Nasopharyngeal swab samples will be collected immediately after arrival in the operating room using sterile swabs.

Additional swab samples will be collected from the inspiratory and expiratory ports of the anesthesia machine:

- Before connection of the disposable breathing circuit
- Immediately after completion of anesthesia and disconnection of the circuit

All samples will be transported to the microbiology laboratory in transport media at room temperature.

Samples will be cultured on 5% sheep blood agar and incubated at 35–37°C for 48 hours.

Microorganisms will be identified by a microbiology specialist using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS).

10. Outcome Measures

The following parameters will be recorded:

- Demographic characteristics
- Duration of surgery
- Duration of anesthesia
- Intraoperative vital signs
- Intraoperative body temperature
- Fresh gas flow settings
- Anesthetic agent settings
- Timing and location of microbiological sampling
- Presence or absence of microbial growth
- Type of microorganism identified in positive cultures

11. Withdrawal Criteria

Participants will be withdrawn from the study under the following circumstances:

- Significant intraoperative hemodynamic instability
- Interruption of minimal-flow anesthesia for longer than five minutes
- Accidental disconnection of the anesthesia breathing circuit

Data from withdrawn participants will not be included in the final analysis.

12. Study Completion

The study will be completed after enrollment of 140 participants and collection of all required study data.