Difference in two different forms of Sevoflurane for anesthesia maintenance and recovery

SCIENCE

Clinical Research

Key Take-Away:

The original and generic form of sevoflurane were comparable in routine anesthesia practice, but there exist some differences in maintenance period of the anesthesia.

Sevoflurane is a commonly used inhalation anesthetic in anesthesia practice. It is preferred over other known analgesics because its less soluble in blood, less disturbing to the respiratory tract, and also offers a smooth induction and recovery from anesthesia.

ABSTRACT:

Background:

Sevoflurane is a commonly used inhalation anesthetic in anesthesia practice. It is preferred over other known analgesics because its less soluble in blood, less disturbing to the respiratory tract, and also offers a smooth induction and recovery from anesthesia. Different factors can affect the inspirational, alveolar and awakening concentration of Sevoflurane. The inspirational concentration is affected by fresh gas flow rate, the volume of the breathing system and any absorption by the machine or breathing circuit. The alveolar concentration is affected by anesthetic uptake which in turn is dependent on solubility in the blood, alveolar blood flow and the partial pressure difference between alveolar gas and venous blood. The awakening concentration is defined as end-tidal concentration independent of gender, duration of anesthesia and type of surgery. Age and temperature are known to influence minimum alveolar concentration (MAC) and MAC-Awake in humans.

There are two forms of Sevoflurane, one is original, and other is generic form. These two forms are therapeutically equivalent, but differ by synthesis process, formulation characteristics, water content, and conditions of storage. The differences in the water content of these forms are of great clinical importance as it results in different clinical and anesthetic effects of Sevoflurane. The original form of Sevoflurane contains 300 ppm water, while the generic form has <130-ppm water. The water acts as a stabilizer preventing acid degradation of these products, which can cause respiratory irritation if inhaled. It was pointed out in a clinical study of the pediatric population that water content of Sevoflurane affected the fractions of inspired and expired sevoflurane in the awakening period.

Rationale behind the research

There is limited evidence comparing the two forms of sevoflurane. Therefore, this was conducted to examine the differences between two forms of sevoflurane.

Objective

To evaluate the difference between original and generic products of sevoflurane in the time taken to reach 1 MAC level at a fixed vaporizer setting.

Expand section

Methods:
Study Methodology

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<td>Randomization</td>
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<tr>
<td>Blinding</td>
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<td>Duration</td>
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<td>Patient age group</td>
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<td>Main Inclusion Criteria</td>
<td>Patients who were underwent lower abdominal or urological surgery (herniorrhaphy and ureterolithotripsy) under general anesthesia using classic Laryngeal mask airway (LMA) were included</td>
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<td>Dosage/Treatment</td>
<td>In a randomized manner, the patients were divided into two groups: The Sevo Group (N.=35) and the Sojo Group (N.=35). In both groups, sevoflurane was administered to the patients at vaporizer dial to 1.5% concentration in N2O/O2 (50%/50%) mixture.</td>
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STATISTICAL RATING: 3/5

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<tr>
<td>Statistical Methodology</td>
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- **Study outcome measures**
  - Study outcomes include the bispectral index (BIS), time to reach 1 MAC level, percent vaporizer concentration of sevoflurane, additional remifentanil doses, inspired and expired Sevoflurane levels.
  - In the awakening period, decreasing times of MAC 0.5, 0.4, 0.3, BIS levels, sedation-agitation and Aldrete scores were recorded.

- **Time Points**: 2 minutes before anesthesia induction, then at 4, 6, 8, and 10 minutes after induction and subsequently every 5 minutes during anesthesia.

Expand section

Results:
Flow of patients

ASA I or II patients scheduled to undergo lower abdominal & urological therapy under general anesthesia (N=70)

Exclusion criteria
Patients with disorders like cardiac
(BMI) > 35 kg/m²
Time > 2 hr & < 45 min
Usage of medications like neuroleptics

Venipuncture and anesthesia monitoring

Anesthesia induction with Propofol 3 mg/kg,
Rocuronium bromide 0.4 mg/kg and remifentanil 1 µg/kg

LMA insertion after 2 minutes

Sevo group (N=35)  Sojo group (N=35)

Those patients were excluded in which LMA insertion does not take place in the 2nd attempt

Remaining Patients

Sevoflurane administration

Statistical analysis of study outcomes like time to reach 1 MAC level after and during anesthesia induction at different time intervals

SAS and Alderate score calculation in awakening period
Study Outcomes

- No considerable differences reported between the groups in demographic data, duration of anesthesia, HR, NIBP, SpO₂, and EtCO₂ (p>0.05)
- The time to reach 1MAC level was shorter in Group Sevo (6.3±2.4) than in Group Sojo (8.5±5.2) {Fig 1}
- Inspired and expired sevoflurane fractions were observed to be higher in the original form than in the generic form
- No differences were recorded in the above-explained parameters between the two groups in the awakening period and postoperatively

![Fig 1](image.png)

**Fig 1:** Time to reach 1 MAC level after anesthesia induction

**Conclusion:**

The present study reported that the time to reach 1 MAC level was shorter and that the fractions of inspired and expired sevoflurane were higher in the original product compared with the generic product. The results of the previous studies are quite the opposite to what the current research had shown. A survey by Tomal et al., studied two different forms of sevoflurane (with 300-ppm water or 260-ppm propylene glycol as a stabilizer) on a pediatric population and it was found that a significant number of children required an extra bolus of Sevoflurane to keep the same anesthesia level in the generic group. Despite the same concentration in vaporizer dial, the median fractions of inspired and expired Sevoflurane were higher and BIS levels were lower in the original Sevoflurane group than in the generic sevoflurane group.

A standardized anesthesia regimen was used in this study with effective control on depth of anesthesia by keeping a check on BIS levels. The different factors that were affecting the inspirational concentration of sevoflurane, such as fresh gas flow rate and the volume of the breathing system, and thermodynamics and respiratory parameters were similar between the two groups.

The SAS and Alderate scores were also found to be similar in both groups of sevoflurane in the awakening and recovery period. There were no significant signs of respiratory tract irritation such as coughing, laryngospasm or breath holding determined between the two groups. There was no measurement of time to eye-opening or of the fraction of inspired and expired sevoflurane after discontinuation of sevoflurane in both groups. The time to decrease MAC and BIS level from 0.5-0.3 were observed that tends to be longer in original form. The differences observed in time to reach MAC were not significant.