

Comparison of Two Initiation Techniques of Low-Flow Anaesthesia and Their Effect on Time to Reach Steady State: A Randomized Comparative Study

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ABSTRACT

Background and Aims: Low-flow anaesthesia (LFA) offers environmental and cost benefits; however, optimal initiation strategies remain unclear. The present study compared two LFA initiation techniques one using high fresh gas flow (FGF) with moderate sevoflurane concentration, and the other one using low FGF with high sevoflurane concentration to assess differences in time to reach steady state and agent consumption.

Methods: Ninety-eight patients aged 18–60 years undergoing elective surgeries under general anaesthesia were randomised into two groups H & L, based on gas flow. Group H received 4 L/min FGF with 3% sevoflurane until the minimum alveolar concentration (MAC) of 1.3 was achieved, while Group L received 1 L/min FGF with 8% sevoflurane until the same MAC was attained. After achieving MAC 1.3, both groups were maintained on 0.6 L/min FGF and 2% sevoflurane. Time to steady state (T₂), defined as five consecutive stable F_i/F_e ratios of sevoflurane, and agent consumption were recorded. Statistical analysis included Mann–Whitney U test and t-test where appropriate.

Results: Both groups were comparable in age, sex, and BMI. Group H achieved steady state significantly (P=0.034) faster (7.87 ± 1.67 min) compared to that of group L (8.61 ± 1.48 min). Sevoflurane consumption and cost were comparable (Group H: 2.67 ± 0.58 mL, ₹93.00; Group L: 2.68 ± 0.67 mL, ₹93.41; P > 0.05). Hemodynamic parameters showed no significant differences.

Conclusion: Both high and low initiation techniques are effective and safe. While the high-flow technique achieves a steady state faster, the low-flow overpressure method could be a viable alternative with similar consumption and cost.

Keywords: Low-flow anaesthesia, sevoflurane, steady state, volatile agent consumption, overpressure technique

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How to cite this article: Chand A, Sivachalam SN, Sathyaprabu V, Hemanth Kumar VR. Comparison of Two Initiation Techniques of Low-Flow Anaesthesia and Their Effect on Time to Reach Steady State: A Randomized Comparative Study. *Int J Drug Deliv Technol.* 2026;16(70s): 1622-1628. DOI: 10.25258/ijddt.16.70s.177

INTRODUCTION

Low-flow anaesthesia is a technique that aims to reduce the consumption of anaesthetic agents, which can help decrease the cost of anaesthesia, as well as reduce environmental pollution. The initiation technique of inhalation anaesthesia usually involves initial administration of anaesthetic agent with a fresh gas flow (FGF) equivalent to circuit volume is usually done to achieve MAC and steady state faster. FGF is then decreased to maintain a suitable level of anaesthesia.⁽¹⁾ The concentration of inhalational anaesthetic agent administration is also an essential factor in low-flow anaesthesia, as it can influence the time it takes to reach a steady state and the total amount of agent used during anaesthesia. One common technique for initiating inhalation anaesthesia is to administer the anaesthetic agent sevoflurane at 3% dial setting, typically with 4-8 L/min of fresh gas flow (FGF). This is known as a high-flow technique, which allows for the rapid induction of anaesthesia.⁽²⁾

An alternate method for inducing inhalational anaesthesia is the overpressure technique. This technique involves administering a higher concentration of a volatile anaesthetic, such as sevoflurane, at the beginning of the procedure. This elevated dose swiftly increases the alveolar concentration, accelerating the rise in brain partial pressure and thereby facilitating a quicker onset of anaesthesia. Once the desired depth is attained, the concentration is gradually reduced to maintain a steady-state level, minimizing the risk of excessive accumulation and associated side effects.^{(3) (4)}

We proposed an alternative initiation technique for low flow anaesthesia which involves administering the anaesthetic agent at a flow FGF rate of 1 L/min with 8% dial setting of sevoflurane. Our objective was to compare the effects of two different low-flow initiation techniques, focusing on the time to reach a steady state and the consumption of sevoflurane, a commonly used volatile anesthetic agent, sevoflurane. Despite the widespread use of low-flow anaesthesia, limited literature had compared initiation techniques or evaluated their respective advantages and disadvantages. Consequently, evidence addressing the relative benefits and drawbacks of these approaches remained sparse,

which highlighted the need for further research in this area.

METHODS

This randomised comparative study was conducted at Mahatma Gandhi Medical College and Research Institute, Puducherry, from August 2023 to August 2024, with Institutional Ethics Committee approval. Written informed consent, including the use of patient data for research and educational purposes, was obtained from all participants prior to enrolment. The study was conducted in accordance with the principles of the Declaration of Helsinki (2013) and Good Clinical Practice guidelines. Ninety-eight patients of both gender of ASA I/II & aged between 18–60 undergoing elective surgery under general anaesthesia were enrolled in this study. Patients with a known allergy to sevoflurane or related agents, unable or unwilling to provide informed consent; Body Mass Index (BMI) greater than 30 were excluded from the study. The study involved a total of 92 patients based on the statistical part of the methods. Participants were randomized into 2 groups: Group H (High-flow)-FGF 4 L/min + 3% sevoflurane until MAC 1.3. Group L (Low-flow Overpressure)- FGF 1 L/min + 8% sevoflurane until MAC 1.3. Once MAC 1.3 (T1) was reached, both groups were maintained at FGF 0.6 L/min and 2% sevoflurane. Time to steady state (T2) was defined as 5 consecutive stable Fi/Fe sevoflurane ratios. Sevoflurane consumption was calculated using Ehrenwerth's formula. Patients were recruited using consecutive sampling, and informed consent was obtained from all participants before their enrolment in the study.

Patients were randomized to receive one of two techniques through computer-generated randomization: Group H or Group L. After patients were transferred to the operating room, intravenous access and monitors were established. The patient's age, weight, and height parameters were entered into the monitor. Patients in both groups were premedicated with intravenous (IV) midazolam 0.05 mg/kg and IV morphine 0.1 mg/kg. Patient was induced with a bolus of 2 – 2.5 mg/kg of IV propofol, and IV succinylcholine 2 mg/kg was administered after confirming adequate mask ventilation. Tracheal

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intubation was performed after 90 seconds of succinylcholine administration. The inhalational agent (sevoflurane) was administered only after the confirmation of endotracheal tube placement with capnograph. After intubation, patients were connected to a semi-closed circle system on a ventilator (GE Datex Ohmeda-9100c, Madison, WI, USA) with a tidal volume of 6-7 mL/kg and a respiratory rate of 12-14 breaths per minute to maintain an end-tidal carbon dioxide level between 35 and 40 mmHg. The patient's vital signs were monitored using GE monitors. The anaesthetic gas module measures, displays, and stores agent concentration data. The gas module utilized the Non-Dispersive Infrared (NDIR) Gas Concentration measurement technique to measure the concentration of gases. The accuracy of the analyzer for sevoflurane, as claimed by the manufacturer, is 0.15 vol% $\pm$ 15.0% relative; the range is 0-8.5 vol%, and the rise time was 500 ms. Measurement resolution is 0.05 vol%.

Following intubation, Group H received an FGF of 4 L/min with sevoflurane at 3% and nitrous oxide at 50% till MAC of 1.3 was achieved, and this time was noted as T1, and then FGF was reduced to 0.6 L/min (300 ml/min of O₂ and 300 ml/min of N₂O) and the dial setting to 2%. In group L, patients will receive an FGF of 1 L/min with 50% N₂O and 8% sevoflurane until T1. The FGF was reduced to 0.6 L/min (300 ml/min of O₂ and 300 ml/min of N₂O), and the dial setting was adjusted to 2%. The fraction of inspired (Fi) and end-tidal (Fe) sevoflurane were recorded every 30 seconds for 5 minutes, then at one-minute intervals for 15 minutes from the time of intubation. The time to reach a steady state was noted as T2 in both groups. A steady state was defined as the equilibration of the circuit, alveolar, and vessel-rich groups. It was identified when the Fi/Fe ratio of sevoflurane remains constant for five consecutive readings taken at one-minute intervals. The sevoflurane consumption in both groups till T2 was calculated using the following formula, Ehrenwerth and Eisenkraft. [20] · Sevoflurane consumption in ml = FGF (ml/min) *Dial Concentration*Duration in mins/ 184*100

Heart rate and blood pressure were recorded every 5 minutes from induction till the completion of the Study. Hypotension is defined as mean arterial pressure < 60mmHg or more than 20% decrease of mean arterial pressure (MAP) from baseline and was treated with Injection mephentermine 3 mg

IV bolus. Bradycardia is defined as a heart rate of less than 50 beats/min, associated with hypotension, and treated with an intravenous bolus of 0.6 mg atropine.

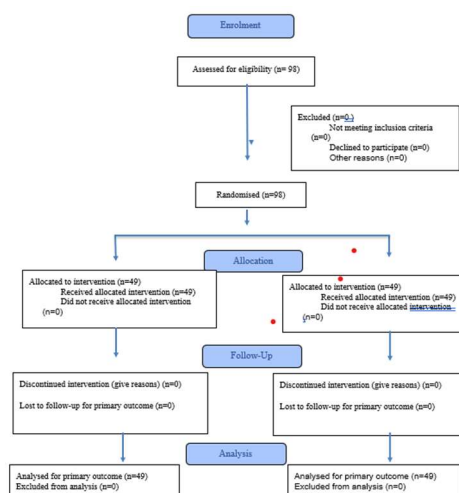
Based on a previous study by Tyagi et al,^[3] the sample size for this non-inferiority study was calculated using a standard deviation of 1.2 and a non-inferiority margin (delta) of -1.0. This calculation indicated that a total of 92 participants (46 in each group) would be required to demonstrate non-inferiority with a significance level (α) of 0.05 and a power of 99%. In the referenced study, the mean time to achieve 1.0 MAC with the standard low-flow anesthesia (LFA) technique was 2.5 $\pm$ 1.2 minutes, compared to 3.5 $\pm$ 1.1 minutes using an alternative method. Accounting for possible dropouts, we recruited 49 patients in each group, resulting in Group H (n = 49) and Group L (n = 49). The primary outcome was the mean time to achieve steady-state anesthesia, while the secondary outcome was the mean amount of sevoflurane consumed.

Data were analyzed using JASP version 0.8.5.1. Continuous variables were assessed for normality, and appropriate statistical tests were applied accordingly. For normally distributed data, the independent *t*-test was used, while the Mann-Whitney *U* test was applied for non-normally distributed data. A *P*-value of <0.05 was considered statistically significant.

RESULTS

All 98 participants were assessed for eligibility and none were excluded, resulting in 98 subjects being randomized equally into two groups (49 in each). All participants in both groups received the allocated intervention, with no losses to follow-up or discontinued interventions. Finally, all 49 participants in each group were analyzed for the primary outcome, with none excluded from analysis.

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The demographic characteristics of the study population were comparable between the two groups. The mean age in Group H was 41.80 ± 14.41 years, while in Group L it was 38.25 ± 13.89 years ($p = 0.410$), indicating no statistically significant difference. In terms of sex distribution, Group H comprised 17 males (34.69%) and 32 females (65.30%), whereas Group L included 20 males (40.81%) and 29 females (59.18%). The mean body mass index (BMI) was 24.97 ± 1.08 kg/m² in Group H and 24.75 ± 0.90 kg/m² in Group L, with no significant difference between the groups ($p = 0.533$). These findings suggest that the two groups were demographically comparable at baseline.

The T1 (time to achieve MAC 1.3) distribution in both study groups was shown in Figure 1. The mean T1 in Group H was 3.31 ± 1.13 minutes, and in Group L, it was 4.21 ± 1.46 minutes. The p-value was <0.001 , indicating a statistically significant difference, with Group H achieving MAC 1.3 faster than Group L.

The T2 (time to achieve steady state) distribution in both study groups was shown in Figure 2. The mean T2 in Group H was 7.87 ± 1.67 minutes, and in Group L, it was 8.61 ± 1.48 minutes. The p-value was 0.034, indicating a statistically significant difference, with Group H reaching steady state faster than Group L.

The sevoflurane consumption (in mL) between the two groups was shown in Figure 3. The mean consumption in Group H was 2.67 ± 0.58 mL, and in Group L, it was 2.68 ± 0.67 mL. The p-value was 0.797, indicating no statistically significant difference, with both groups showing similar sevoflurane usage.

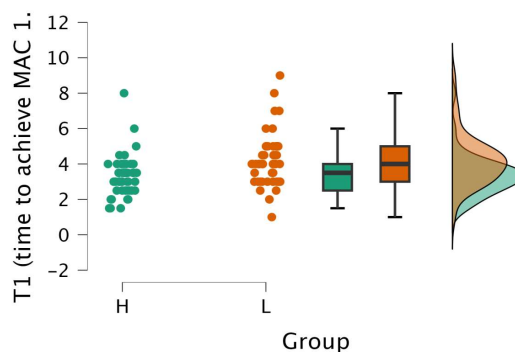


Figure 1: comparison of time to achieve MAC 1.0 between Group H and Group L.

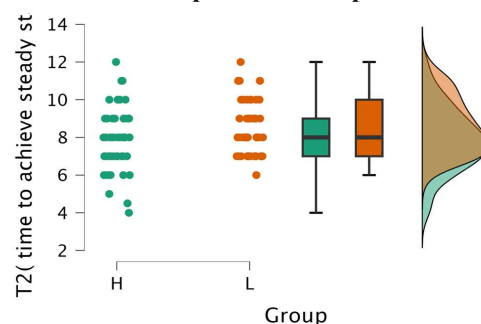


Figure 2: Comparison of time to achieve steady state (T2) between two groups group H and group L.

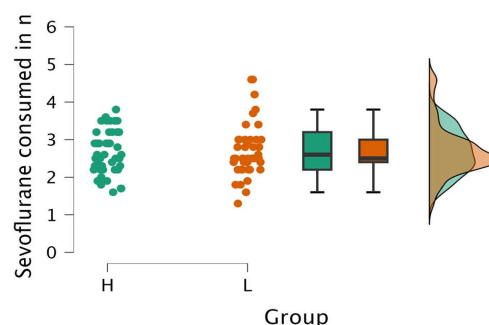


Figure 3: Comparison of sevoflurane consumption between two groups, with Group H and Group L

The mean cost of sevoflurane was comparable between the groups, with ₹93.00 $\pm$ 20.27 in Group H and ₹93.41 $\pm$ 23.74 in Group L ($p = 0.778$). Baseline mean arterial pressures (MAP) were similar in both groups (~ 90 mmHg), with a sharp initial decline of approximately -26.5% following induction. Overlapping error bars indicated no statistically significant difference in hemodynamic response between the groups. While significant differences were observed in T1 and T2 values, there were no significant differences between the groups in terms of age, BMI, sevoflurane consumption, cost, or MAP changes.

Parameter	Group H	Group L	p-
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			value
Age (years)	41.80 ± 14.41	38.25 ± 13.89	0.410
BMI (kg/m ²)	24.97 ± 1.08	24.75 ± 0.90	0.533
T1 (MAC 1.3 time)	3.31 ± 1.13	4.21 ± 1.46	<0.001
T2 (Steady state time)	7.87 ± 1.67	8.61 ± 1.48	0.034
Sevoflurane Consumption (mL)	2.67 ± 0.58	2.68 ± 0.67	0.797
Cost (INR)	₹93.00 ± 20.27	₹93.41 ± 23.74	0.778
MAP Change (%)	19.2% ± 6%	17.3% ± 5%	>0.05

Table 1: Comparison of Demographic Variables, Anaesthesia Induction Times, Sevoflurane Consumption, Cost, and Hemodynamic Response Between Group H and Group L

DISCUSSION

The practice of low-flow anaesthesia offers several advantages, including reduced anaesthetic consumption, lower costs, and a minimized environmental impact. Traditional protocols for initiating low-flow anaesthesia typically involve high fresh gas flows (FGF) of 4–6 litres per minute for an initial period, usually 10 minutes, to achieve circuit and patient equilibration before reducing the flow.⁽⁴⁾⁽⁵⁾ These protocols emphasize fresh gas flow as the primary mechanism for circuit saturation and often recommend longer times for establishing a steady state at low flows. However, there is potential for optimization by modulating the concentration of the volatile agent rather than relying solely on high FGF⁽⁶⁾⁽⁷⁾⁽⁸⁾. In our Study, we investigated whether using a higher concentration of sevoflurane (8%) at a lower initial flow rate (1 L/min) could achieve similar equilibration in a shorter timeframe compared to the traditional high-flow rate method.

The primary findings of the Study highlight that Group H achieved a steady state slightly faster, in 7.9 ± 1.7 minutes, compared to Group L, which took 8.6 ± 1.5 minutes. Although this difference was statistically significant, it was not considered clinically relevant, implying that either group's anaesthetic induction technique is acceptable in practice. Intriguingly, both the groups consumed comparable amounts of sevoflurane (2.6 ± 0.579 ml in Group H vs. $2.7 \pm$

0.7 ml in Group L), leading to similar cost implications (₹93 ± ₹20.3 for Group H and ₹93.4 ± ₹23.7 for Group L). The faster attainment of steady state in Group H did not compromise anaesthesia depth or safety, thus supporting the use of low-flow initiation even when the time to steady state is marginally longer.

Our present Study and that by Joshiraj et al,⁽⁹⁾ share a common goal: improving the efficiency and sustainability of low-flow anaesthesia induction using sevoflurane. While Joshiraj and co-workers⁽⁹⁾ examined an over-pressure wash-in method with an ultra-low fresh gas flow (0.5 L/min) combined with a high sevoflurane concentration (8%). Our Study compared a more moderate low-flow approach (1 L/min) against a high-flow technique (4 L/min) to assess time to steady state, agent consumption, and safety.

Both studies found that lower FGF strategies tend to prolong the time to reach a steady state compared to higher flows; however, this difference was clinically acceptable given the significant benefits in terms of anaesthetic consumption and system stability. Joshiraj and co-workers⁽⁹⁾ demonstrated markedly reduced oxygen, air, and sevoflurane usage with their over-pressure method, aligning with our findings that low-flow anaesthesia provides economic and environmental advantages without compromising hemodynamic stability or patient safety.

Together, these findings reinforce that carefully designed low-flow anaesthesia protocols, whether via over-pressure wash-in or optimized low initial FGF, represent effective, safe, and resource-conserving alternatives to conventional high-flow induction⁽¹⁰⁾⁽¹¹⁾⁽¹²⁾. Our Study complements and extends this evidence by confirming the clinical equivalence of 1 L/min low-flow induction to high-flow techniques in a controlled surgical setting.

The randomized controlled trial by Tyagi et al.⁽³⁾ involved 45 adult patients scheduled for approximately one-hour elective surgeries, assigned to one of three groups comparing sevoflurane delivery techniques: (1) low-flow with propofol induction and an initial FGF of 6 L/min reduced to 0.5 L/min, (2) low-flow at a constant 1 L/min, and (3) sevoflurane used for both induction and maintenance. The current study affirms the previous report by Tyagi et al., (3) Study affirms on the clinical safety and feasibility of low-flow anaesthesia techniques, with no significant adverse hemodynamic effects. Tyagi et al.,^[3] concluded

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that using sevoflurane for both induction and maintenance is the most cost-effective approach when considering combined drug costs. In contrast, low-flow techniques demonstrate cost savings primarily by reducing the wastage of anaesthetic agents.

Another study by Tribuddharat et al.,⁽⁴⁾ on 1-1-8 scheme demonstrates swiftness (achieving FAS of 1–3.5% within 1–5 minutes), while our Study identifies resource and time efficiencies with low-flow techniques. While the study reported hemodynamic stability as FAS increases, which is consistent with our findings that low-flow techniques do not compromise patient safety. They also demonstrated significant reductions in oxygen and sevoflurane consumption with low-flow methods.

Our present Study shares significant methodological and conceptual similarities with previous work by Charath et al.,⁽¹³⁾ which investigated the use of the “equilibration point” as a physiologically guided changeover from high-flow to low-flow anaesthesia during sevoflurane and isoflurane administration. Both studies emphasize the importance of identifying the steady-state or equilibration point—defined as the stabilization of inspired and end-tidal anaesthetic concentrations—to ensure effective anaesthetic delivery while minimizing agent waste. In line with Charath et al., who reported a mean equilibration time for sevoflurane of approximately 8.22 minutes, our Study found comparable times to steady state (7.9 ± 1.7 minutes in the high-flow group and 8.6 ± 1.5 minutes in the low-flow group), supporting the reliability and reproducibility of this parameter in clinical settings.

While Charath et al.,⁽¹³⁾ focused on comparing isoflurane and sevoflurane equilibration times and their implications for hemodynamic stability and recovery profiles, our Study extends these findings by directly comparing high-flow and low-flow induction techniques for sevoflurane anaesthesia concerning anaesthetic consumption, cost, and safety parameters during the critical wash-in phase. Our results reinforce that low-flow techniques, guided by the equilibration point, do not compromise clinical efficacy or hemodynamic stability and offer comparable sevoflurane consumption and cost-effectiveness.

Together, these studies advocate for the use of the equilibration point as a physiologically sound, individualized marker to guide adjustments in fresh gas flow during volatile anaesthesia. This approach maximizes resource

efficiency, reduces environmental pollution, and maintains patient safety, key priorities in contemporary anaesthetic practice.

CONCLUSION

Low-flow initiation technique is a viable alternative to high-flow technique, offering similar outcomes and reduced theatre pollution, contributing to more sustainable anaesthesia practices

Declaration of Ethics and Consent

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants.

Financial Support and Sponsorship

None.

Conflicts of Interest

None declared.

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