

A randomized prospective study of desflurane versus isoflurane in minimal flow anesthesia using “equilibration time” as the change-over point to minimal flow

Tanuja Mallik, S Aneja, R Tope, V Muralidhar

Department of Anaesthesiology and Intensive Care Unit, Indraprastha Apollo Hospital, New Delhi, India

Abstract

Background: In the administration of minimal flow anesthesia, traditionally a fixed time period of high flow has been used before changing over to minimal flow. However, newer studies have used “equilibration time” of a volatile anesthetic agent as the change-over point.

Materials and Methods: A randomized prospective study was conducted on 60 patients, who were divided into two groups of 30 patients each. Two volatile inhalational anesthetic agents were compared. Group I received desflurane ($n = 30$) and group II isoflurane ($n = 30$). Both the groups received an initial high flow till equilibration between inspired (F_i) and expired (F_e) agent concentration were achieved, which was defined as $F_e/F_i = 0.8$. The mean (SD) equilibration time was obtained for both the agent. Then, a drift in end-tidal agent concentration during the minimal flow anesthesia and recovery profile was noted.

Results: The mean equilibration time obtained for desflurane and isoflurane were 4.96 ± 1.60 and 16.96 ± 9.64 min ($P < 0.001$). The drift in end-tidal agent concentration over time was minimal in the desflurane group ($P = 0.065$). Recovery time was 5.70 ± 2.78 min in the desflurane group and 8.06 ± 31 min in the isoflurane group ($P = 0.004$).

Conclusion: Use of equilibration time of the volatile anesthetic agent as a change-over point, from high flow to minimal flow, can help us use minimal flow anesthesia, in a more efficient way.

Key words: Desflurane, equilibration time, fixed time, isoflurane, minimal flow, volatile anesthetic agent

Introduction

Minimal flow anesthesia was defined by Simionescu as the fresh gas flow (FGF) rate of 250–500 mL/min.^[1] Its popularity has varied over the years, with resurgence of interest over the last few years because of economic concern, environmental factors, and advances in monitoring and introduction of new expensive anesthetics.

Minimal flow anesthesia is commonly instituted after delivery of high FGF for 10–20 min, which precludes the efficient use

of the circle system for large proportion of anesthetics that are of short duration. There is no general agreement as to what constitutes an adequate alveolar concentration before the flow can be reduced. However, recent studies have used the “equilibration point” of the inhalational agent as the switch-over point.^[2] The physical and chemical characteristics of individual agents influence the initial high FGF period. A number of techniques of minimal flow anesthesia are described in the literature. There are a number of reports that desflurane achieves adequate alveolar concentration faster than agents with comparatively lesser blood gas solubility like isoflurane, thus requiring lesser duration of high FGF and causing less environmental pollution.^[3] The role of an end-tidal volatile agent, in evaluating the effect of FGF on achieving a suitable depth, can be explained by the Gas Man simulation^[4] and Mapelson hypothesis.^[5]

Address for correspondence: Dr. Tanuja Mallik,
Anaesthesia and Intensive Care Unit, Indraprastha Apollo Hospital,
Sarita Vihar, New Delhi, India.
E-mail: mallik_nmc@yahoo.com

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Materials and Methods

After obtaining approval from hospital ethics committee and informed consent from patients, this study was conducted on 60 healthy patients of either sex scheduled for routine surgeries. Inclusion criteria were American Society of

Anesthesiologists (ASA) physical status I and II, age 20–60 years, and hemoglobin more than 10 g/dL. Patients with cardiac diseases, lung disorders, pregnancy and patients undergoing laparoscopic surgery were excluded.

A routine preanesthetic checkup was conducted one day prior to surgery. No preanesthetic medication that could affect the total anesthetic agent requirement and recovery profile (recovery time and recovery score) was administered. Patients were randomly allocated to two groups depending on the volatile anesthetic agent being used, using concealed envelopes. Group I received desflurane as the inhalational anesthetic agent with minimal flow anesthesia ($n = 30$). Group II received isoflurane as anesthetic agent with minimal flow anesthesia ($n = 30$).

An Aestiva anesthesia workstation (Datex Ohmeda, Madison, USA) was used in all patients. A special connector for return of sampling gas back to the breathing circuit was used (one end of this connector was attached to the exhaust port of the respiratory gas monitor and the other end was attached to the expiratory limb of the breathing circuit) [Figure 1a and 1b].

Patients were preoxygenated with 100% oxygen. Anesthesia was induced by administering intravenous (IV) fentanyl 2 mcg/kg, propofol 3 mg/kg, and atracurium 0.5 mg/kg. Lungs were hand ventilated with help of a facemask using FGF of oxygen 6 L/min for 3 min. Intermittent boluses of propofol 20 mg IV were given. Boluses of propofol 20 mg were used thus at 1 min intervals (without nitrous oxide and inhalational agent) after induction of anesthesia. Trachea was intubated 3 min after administration of atracurium. The patient was connected to the anesthesia machine with a Y-piece connector of the breathing circuit. A high FGF mixture of 6 L/min (oxygen 2 L/min and nitrous oxide 4 L/min) was delivered initially with a volatile inhalational anesthetic agent after tracheal intubation.

The volatile inhalational anesthetic agent was set at 1.3 times the agent minimum alveolar concentration (MAC), i.e. 1.5% for isoflurane or 8% for desflurane. Once the ratio of expired (F_e) to inspired (F_i) volatile inhalational agent concentration (isoflurane/desflurane) became 0.8, high FGF was reduced to the minimal FGF mixture, i.e. 300 mL/min of oxygen and 200 mL/min of nitrous oxide. The point when the ratio of F_e to F_i inhalational agent concentration became 0.8 (uptake of the volatile inhalational anesthetic agent reaches: $80\% - F_e/F_i = 0.8$) was defined as the “equilibration point” of the inhalational anesthetic agent.

During maintenance phase of anesthesia, a minimum inspired oxygen concentration (F_iO_2) of 0.3 was maintained in the minimal FGF mixture. The vaporizer dial setting was changed, if needed, after flow reduction to maintain MAC of 1 or more as required depending on the type of surgery, but keeping the FGF constant. Top-up doses of atracurium 0.1 mg/kg IV were given every 15 min and morphine 0.15 mg/kg IV was given at time of incision. Diclofenac 1 mg/kg IV, in 100 mL normal saline, was given to all patients as a part of the multimodal approach to analgesia.

The inhalational anesthetic vaporizer was switched off after the end of the surgery. The neuromuscular block was reversed with neostigmine 0.5 mg/kg and glycopyrolate 0.01 mg/kg IV administered 20 min of the last dose of relaxant or if the patient started spontaneously breathing. Thereafter, nitrous oxide was stopped and only oxygen 6 L/min was given. The trachea was extubated once extubation criteria were met, and the patient transferred to the postoperative recovery room. Before discharging the patient from the recovery room, the patient was interviewed for intraoperative awareness.

“Recovery time” was defined from the time of discontinuation of the inhalational anesthetic agent (vaporizer switched off) to



Figure 1: Special connector for return of sampling gas used. (a) One end of the connector attached to the expiratory limb of breathing circuit. (b) Second end of connector attached to the exhaust of respiratory gas monitors (RGM)

the time the patient opened his/her eyes on verbal command while recovering from anesthesia. During recovery, patient recovery characteristics were defined by a recovery score (1 = No response to painful stimuli; 2 = Drowsy but arousal by verbal command; and 3 = Awake and responding to command at extubation).^[6]

The following parameters were recorded: hemodynamic characteristics (mean change in the heart rate, systolic, diastolic and mean blood pressure, oxygen saturation, nasopharyngeal temperature); mean equilibration time of the volatile inhalational agent (mean was taken at 5, 10, 15, 30 min, and thereafter at 30 min interval till the time of extubation); mean end-tidal volatile anesthetic partial pressure; recovery time and score; and any critical event if occurred and measures taken to tackle the problem.

Statistical analysis was done, and all values were expressed as mean \pm standard deviation (SD). The sample size was decided by determining its power of study, which was 0.8 for the primary outcome variable. Equilibration time of the volatile anesthetic agent was taken as a primary outcome variable. Independent continuous data (example heart rate, blood pressure, and mean end-tidal agent concentration, ratio between inspired and expired agent concentration, recovery time, and recovery score) were analyzed using an analysis of variance (ANOVA) or unpaired *t*-test and the *P* value of less than 0.05 was considered statistically significant. Mann–Whitney *U*-test was used for nonparametric (mean consumption of volatile agent concentration), skewed (non-normal) distribution for test of significance.

Results

Sixty adult patients were studied. No patient was excluded. The groups were randomly divided into two groups of 30 patients each. The two groups were comparable with respect to age, weight, height, and body mass index. There was no significant clinical and statistical difference in hemodynamic parameters in between the two groups [Table 1].

Mean of time taken for equilibration of the volatile anesthetic agent in the desflurane group was 4.96 ± 1.60 min and in the isoflurane group was 16.96 ± 9.64 min, and the difference was statistically significant ($P < 0.001$) [Table 2].

Mean end-tidal volatile anesthetic partial pressure (MFe) were calculated at 5, 20, 60, and 120 min intervals, i.e. in wash-in period (5, 20 min) and steady state (60 and 120 min). At 5, 20, 60, and 120 min, mean end-tidal concentrations (in kPa) of desflurane were not changed much and were 4.73 ± 0.83 , 4.83 ± 0.65 , 4.43 ± 0.64 and 4.19 ± 0.65 , respectively. In

the isoflurane group, variation were significant over time and were 0.74 ± 0.15 , 0.90 ± 0.15 , 0.71 ± 0.17 and 0.71 ± 0.17 at 5, 20, and 120 min intervals, respectively. Changes in measured values were statistically significant between the two groups and within the isoflurane group. The changes were, however, not statistically significant within the desflurane group [Table 3 and Figure 2], i.e. there were less drift in mean end-tidal concentration in this group.

We could maintain breathing gas concentration throughout, and no patient had hypoxia any time during anesthesia. The nitrous oxide concentration tended to fall over time. It ranged between 41.90 ± 4.62 and 60.40 ± 4.83 vol.%. The oxygen level varied between a minimum of $34.56 \pm 2.89\%$ and a maximum of $45.80 \pm 4.14\%$ [Figure 3]. At no point of time, the concentration fell below 30%. There was an initial rise in the oxygen level, but drifted down later.

Uptake of nitrous oxide was 80% and above by the time equilibration of any of the agents occurred. In both the groups, end-tidal to inspired nitrous oxide ratio was found

Table 1: Demographic characteristics of patients who received minimal flow anesthesia with desflurane or isoflurane as inhalational anesthetic agent

Demographic data	Group I, Desflurane n = 30	Group II, Isoflurane n = 30	P value
Age (years, mean \pm SD)	38.10 \pm 13.40	36.77 \pm 13.06	0.69
Body weight (kg, mean \pm SD)	64.77 \pm 13.58	71.43 \pm 13.41	0.061
Height (m, mean \pm SD)	1.56 \pm 0.11	1.60 \pm 0.09	0.18
BMI (kg/m ² , mean \pm SD)	26.19 \pm 3.72	27.73 \pm 4.54	0.15

Unpaired *t*-test used. **P* value < 0.05 represent statistically significant

Table 2: Mean of “equilibration time” of volatile anesthetic agent

Mean equilibration time \pm SD	
Group I	Group II
Desflurane (n = 30)	Isoflurane (n = 30)
4.96 \pm 1.60 min	16.96 \pm 9.64 min
	(<i>P</i> value < 0.001*)

Unpaired *t*-test was used for statistical analysis.; **P* value < 0.05 statistically significant

Table 3: Mean end-tidal volatile anesthetic partial pressure (MFe)

Time (min)	Group I, Desflurane (n = 30)	Group II, Isoflurane (n = 30)	P value
5	4.73 \pm 0.83	0.74 \pm 0.15	0.00*
20	4.83 \pm 0.65	0.90 \pm 0.15	0.00*
60	4.43 \pm 0.64	0.7 \pm 0.17	0.00*
120	4.19 \pm 0.65	0.71 \pm 0.17	0.00*
<i>P</i> value	0.065*	0.001*	

ANOVA for within group comparison and unpaired *t*-test for inter group comparison.; **P* value < 0.05 is statistically significant

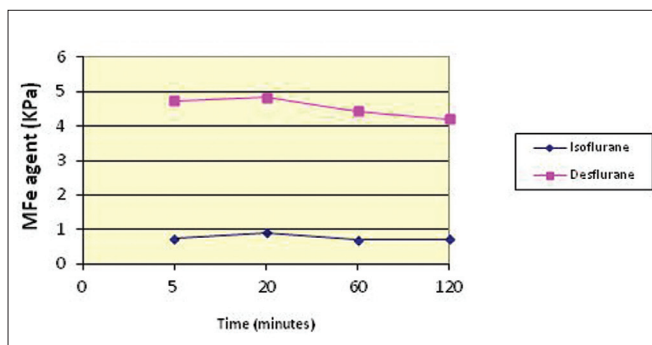


Figure 2: Comparison of mean end-tidal volatile anesthetic partial pressure (MFe) concentration

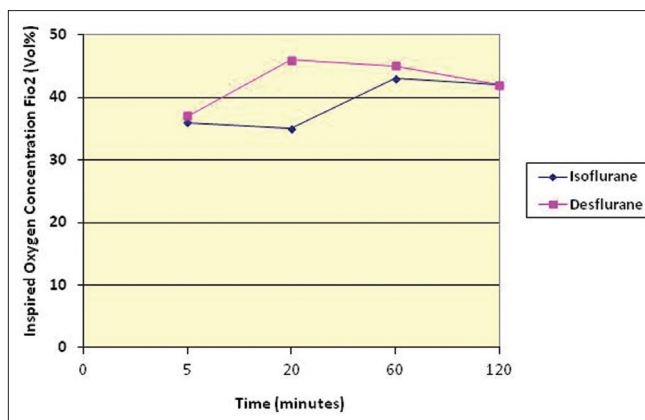


Figure 3: Comparison of mean end-tidal volatile anesthetic partial pressure (MFe) concentration

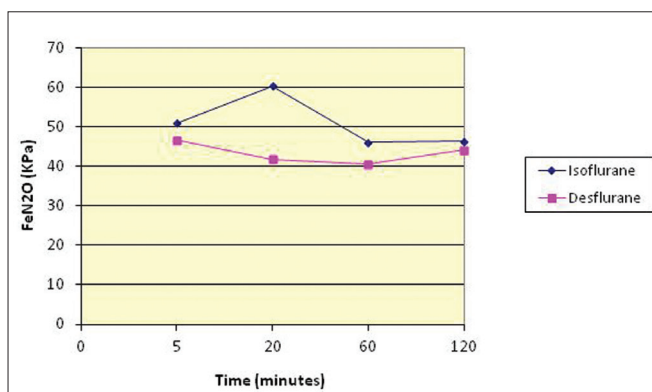


Figure 4: Comparison of end-tidal nitrous oxide concentration over time, while patient receiving minimal flow anesthesia with desflurane or isoflurane as volatile anesthetic agent

to be 0.82 ± 0.12 in 5 min duration and 0.99 ± 0.02 by 12 min. Nitrous oxide concentration also fell over the time, and it was difficult to maintain nitrous oxide at 66 vol.% [Figure 4]. It ranged between 41.90 ± 4.62 to 60.40 ± 4.83 . In long duration, minimal flow anesthesia nitrous oxide end-tidal concentration found to be $<50\%$.

At 80% uptake point of nitrous oxide, uptake of only desflurane was found to be nearly 80% at that time. At 5 min interval, the Fe/Fi volatile anesthetic agent ratio of desflurane was calculated to be 0.80 ± 0.10 while that of isoflurane 0.57 ± 0.08 and the difference found was statistically significant. By 20 min, the Fe/Fi ratio of desflurane increased to 0.92 ± 0.03 while that of isoflurane was 0.76 ± 0.07 .

After the changeover to minimal flows, the frequency of change of dial setting or the number of times dial setting that was changed to achieve the abovementioned goal was not statistically different in the two groups. It was 2.73 ± 1.81 times in the desflurane group and 2.40 ± 1.54 times in the isoflurane group.

Recovery of patients from anesthesia was quicker in the desflurane group, and patients were more alert than those of the isoflurane group. Patients recovered in nearly $5.70 \pm$

Table 4: Recovery time (min)

Group	Mean \pm SD of recovery time (min)	P value
I/Desflurane	5.70 ± 2.78	0.004*
II/Isoflurane	8.06 ± 3.31	

Unpaired t-test was used for statistical analysis.; *P value < 0.05 statistically significant

Table 5: Recovery score

Recovery score	Group I, Desflurane (n = 30)	Group II, Isoflurane (n = 30)	P value
2	2	18	0.000*
3	28	12	

Unpaired t-test was used for statistical analysis.; *P value < 0.05 statistically significant.; Recovery score 2: Drowsy but arousable by verbal command. Recovery score 3: Awake and responding to command at extubation

2.78 min in the desflurane group while 8.06 ± 3.31 min in the isoflurane group ($P = 0.004$) [Tables 4 and 5]. Patients had a clear-headed recovery in the desflurane group: 28 patients out of 30 were alert and awake and 2 were drowsy but arousable. In the isoflurane group: 18 patients out of 30 were drowsy but arousable and 12 patients were alert and awake. The difference between the two groups was statistically and clinically significant. No patient had awareness.

Discussion

Minimal flow anesthesia is safe today because of availability of advanced gas monitoring. However, a leak proof machine, gas monitoring, and capnography are essential for conduct of a minimal flow technique.^[1,7,8]

We aimed to compare desflurane and isoflurane in minimal flow anesthesia. Use of mask ventilation with high FGF can lead to the loss of inhalational agent, defeating the purpose of minimal flow and also making it difficult to monitor the

level of inhalational agent used during this period. To prevent this, boluses of propofol were used at 1 min intervals after the initial induction as recommended.^[2] This method is an effective alternative to the use of inhalational agent at this period of time.

Equilibration time is an effective parameter for change over from high flow to minimal flows. Time of equilibration between F_i and F_e agent concentrations is defined as the time to reach a F_e/F_i ratio of 80%.^[1-3] This ratio is an effective change-over point and helps in effective denitrogenation and maintenance of the constant level of desflurane and isoflurane after the change over from high FGF to minimal FGF anesthesia.^[2] Equilibration time with desflurane was found to be shorter than isoflurane, and we could reduce the FGF earlier in the desflurane group as compared to the isoflurane group. Similar findings were obtained by others.^[2] In the earlier studies, change over from high to low FGF was done after 10–20 min, as recommended by Baum.^[2,9,10]

In minimal flow anesthesia, nitrous oxide usually shows an increasing trend while oxygen shows a decreasing trend because nitrous oxide is neither consumed nor metabolized, but oxygen is consumed by the body. Higher flow of oxygen in relation to nitrous oxide is recommended, to prevent undesirable fall in inspired oxygen concentration especially in long duration surgeries. Higher flow of oxygen in relation to nitrous oxide is recommended in first 30–45 min after the start of minimal flow as the nitrous oxide uptake continuously declines and the gas tends to accumulate within the breathing system. In our study, the fall in the level of end-tidal concentration of nitrous oxide was possibly due to maintenance of the FGF flow ratio as per the study protocol and .

MAC is a useful measure because it mirrors brain partial pressure, allows comparisons of potency between agents. Around 1.3 MAC of any of volatile anesthetic has been found to prevent movement in about 95% of patients (an approximation of ED95). We did not use any depth of anesthesia monitoring, but maintained 1MAC or more asked the patient for any history of awareness before discharging from the recovery room. No patient had any awareness. Change in hemodynamics can occur during surgery because of changes in the surgical stimulus level. Hemodynamics can be maintained by regulating the depth of anesthesia (maintaining an adequate MAC/end-tidal concentration) or by the use of rescue medications such as propofol, esmolol, etc.^[11]

The dial setting of volatile anesthetic agent concentration in our study was changed only to maintain adequate MAC. The high FGF, delivered initially, quickly achieved the desired concentration. At minimal flows, the dial was set higher as

it takes longer to achieve the desired concentration. At both low and high FGF rates, the acute hemodynamic response to surgical stimulus was more efficiently treated by increasing the end-tidal concentration of desflurane concentration than isoflurane. Armavov *et al.* could easily control an increase in mean arterial blood pressure by changing the desflurane dial setting even at lower FGF (1 L/min).^[11]

The effects of anesthetic duration on kinetics and recovery characteristics of desflurane and sevoflurane were studied. Awakening to response to command and orientation was found to be almost twice as rapid after anesthesia with desflurane.^[12] We found a more rapid wake-up with desflurane than isoflurane. In the desflurane group, patients had a clear-headed recovery.

Coetzee and Stewart used a wash-in period of 10 min at high FGF, which was less than the usually recommended 15–20 min for minimal flow.^[5] They concluded that even for the most soluble drug-like halothane, a 10 min wash-in period was sufficient and said that for desflurane, a shorter wash-in period will suffice with even greater cost saving. Consumption of soluble agents (such as enflurane and isoflurane) only partially depends on FGF.^[3]

To conclude, with availability of agents like desflurane we can use minimal flow anesthesia more efficiently, with less drift in anesthetic gases and a clear-headed recovery and minimum operating room pollution.

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