Original research article

Prospective randomized clinical comparative study of Desflurane with Isoflurane under low flow anaesthesia

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Abstract

Background: Safety and economy are the main concerns while using low- flow anaesthesia with newer inhalational agents.

Aim: to compare characteristics of Desflurane with Isoflurane under low flow anaesthesia using equilibration time.

Material and methods: This prospective study was done the Department of Anaesthesia ICARE Institute of Medical Science and Research, Haldia, West Bengal, India, for six months. 100 healthy patients of either sex scheduled for routine surgeries, American Society of Anaesthesiologists' (ASA) physical status I and II, age 20–60 years, and hemoglobin more than 10 g/dL were include in this study. Patients were randomly allocated to two groups. Group I received desflurane as the inhalational anesthetic agent with minimal flow anesthesia (n=50). Group II received isoflurane as anesthetic agent with minimal flow anesthesia (n=50).

Results: 100 adult patients were studied. The groups were randomly divided into two groups of 50 patients each. Mean of time taken for equilibration of the volatile anesthetic agent in the desflurane group was 5.23 ± 1.63 min and in the isoflurane group was 17.011±9.64 min, and the difference was statistically significant (P <0.001). At 5, 20, 60, and 120 min, mean end-tidal concentrations (in kPa) of desflurane were not changed much and were 4.68 ± 0.80, 4.78 ± 0.62, 4.38 ± 0.61 and 4.15 ± 0.62, respectively. In the isoflurane group, variation were significant over time and were 0.77 ± 0.17, 0.93 ± 0.17, 0.73 ± 0.19 and 0.74 ± 0.19 at 5, 20, and 120 min intervals, respectively. 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 to be 0.77 ± 0.14 in 5 min duration and 0.96 ± 0.03 by 12 min. Nitrous oxide concentration also fell over the time, and it was difficult to maintain nitrous oxide at 66 vol.% . It ranged between 42.30 ±4.57 and 61.20 ± 4.56. 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. **Conclusion:** we concluded that, 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

Introduction

There is increasing interest in low-flow anaesthesia (LFA) in clinical practice because of its obvious advantages such as a reduction in the cost of expensive agents like desflurane and sevoflurane and prevention of environmental pollution. Availability of better monitoring devices and newer agents with low blood/gas solubility has facilitated a reduction in the fresh gas flow (FGF) after the initial 'wash-in' period. Various techniques and endpoints are in use to shift from high-flow to low-flow anaesthesia. One of the techniques includes giving high

FGF of 6–10 L/min initially for about 3–6 min to reach a high level of alveolar gas concentration to achieve surgical anaesthesia (loading) which is followed by a reduction in total gas flows during maintenance.[1] An alternative technique is using low FGF from the beginning with very high vaporiser setting to achieve target alveolar concentration.[2] Inhaled volatile anesthetics remain the most widely used drugs for maintenance of general anesthesia because of their ease of administration and predictable intraoperative and recovery characteristics. Management of hemodynamic stability and early recovery is the most important part of a standardized balanced technique. Given the low blood–gas partition coefficients of isoflurane (1.4) and desflurane (0.42), a more rapid emergence from anesthesia is expected compared with traditional inhalation anesthetics.[3] Isoflurane is an inhalational anesthetic whose low solubility (blood–gas partition coefficient equals 1.4) enables a rapid induction of and recovery from anesthesia. Th e mild pungency of isoflurane may limit the rate of induction, although excessive salivation or tracheobronchial secretions do not appear to be stimulated. The level of anesthesia may be altered rapidly with isoflurane. Pharyngeal and laryngeal reflexes are readily and easily obtunded.[4] Desflurane (2,2,2-trifl uoro-1-fluoroethyldifl uoromethyl ether) is a highly fluorinated methyl ethyl ether used for maintenance of general anesthesia. It is gradually replacing Isoflurane for use in humans. It has the most rapid onset and off set of the volatile anesthetic drugs used for general anesthesia because of its low solubility in blood.[5] The aim of the present study was to comparing characteristics of Desflurane with Isoflurane under low flow anaesthesia using equilibration time.

Material and methods

This prospective observational study was done the Department of Anaesthesia ICARE Institute of Medical Science and Research, Haldia, west Bengal, India, for six months, after taking the approval of the protocol review committee and institutional ethics committee.100 healthy patients of either sex scheduled for routine surgeries were include in this study.

Inclusion criteria

American Society of Anesthesiologists (ASA) physical status I and II, age 20–60 years, and hemoglobin more than 10 g/dL.

Exclusion criteria

Patients with cardiac diseases, lung disorders, pregnancy and patients undergoing laparoscopic surgery

Patients were randomly allocated to two groups. Group I received desflurane as the inhalational anesthetic agent with minimal flow anesthesia (n=50). Group II received isoflurane as anesthetic agent with minimal flow anesthesia (n=50). 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). Patients were preoxygenated with 100% oxygen. Anesthesia was induced by administering intravenous (IV) fentanyl 2 mcg/kg, propanol 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 propanol 20 mg IV were given. Boluses of propanol 20mg 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 (Fe) to inspired (Fi) 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 Fe to Fi inhalational agent concentration became 0.8 (uptake of the volatile inhalational anesthetic agent reaches: 80% – Fe/ Fi = 0.8) was defined as the "equilibration point" of the inhalational anesthetic agent. During maintenance phase of anesthesia, a minimum inspired oxygen concentration (FiO2) 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 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.

Results

100 adult patients were studied. The groups were randomly divided into two groups of 50 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)

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

Demographic Profile	Group I, Desflurane	Group II, Isoflurane	P value
Age (years, mean ± SD)	38.88 ± 12.94	37.04 ± 13.15	0.77
Body weight (kg, mean ± SD)	65.23 ± 12.88	72.03 ± 14.06	0.055
Height (m, mean ± SD)	1.55 ± 0.13	1.59 ± 0.23	0.15
BMI (kg/m^2, mean ± SD)	26.45 ± 3.56	27.94 ± 4.63	0.18

Table 2: Mean of "equilibration time" of volatile anesthetic agent

	Group 1	Group 2	P value

	Desflurane ($n = 50$)	Isoflurane ($n = 50$)	P value
Mean equilibration time	5.23 ± 1.63 min	17.011±9.64 min	< 0.001)

Mean of time taken for equilibration of the volatile anesthetic agent in the desflurane group was 5.23 ± 1.63 min and in the isoflurane group was 17.011±9.64 min, and the difference was statistically significant (P <0.001)

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

Time (min)	Group I, Desflurane	Group II, Isoflurane	P value
	(n = 50)	(n =50)	
5	4.68 ± 0.80	0.77 ± 0.17	0.00
20	4.78 ± 0.62	0.93 ± 0.17	0.00
60	4.38 ± 0.61	0.73 ± 0.19	0.00
120	4.15 ± 0.62	0.74 ± 0.19	0.00
P value	0.072	0.001	

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 4.68 ± 0.80, 4.78 ± 0.62, 4.38 ± 0.61 and 4.15 ± 0.62, respectively. In the isoflurane group, variation were significant over time and were 0.77 ± 0.17, 0.93 ± 0.17, 0.73 ± 0.19 and 0.74 ± 0.19 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], 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 42.30 ±4.57 and 61.20 ± 4.56 vol.%. The oxygen level varied between a minimum of 33.96 ± 2.95% and a maximum of 46.20 ± 4.23% . At no point of time, the concentration fell below 30%. There was an initial rise in the oxygen level, but drifted down later.

Table 4: Recovery time (min)

	Group I, Desflurane	Group II, Isoflurane	P value
Mean ± SD of recovery time (min)	5.88 ± 2.84	8.13 ± 3.28	0.003

Table 5: Recovery score

Recovery score	Group I, Desflurane	Group II, Isoflurane	P value
2	5	33	0.000
3	45	17	

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 to be 0.77 ± 0.14 in 5 min duration and 0.96 ± 0.03 by 12 min. Nitrous oxide concentration also fell over the time, and it was difficult to maintain nitrous oxide at 66 vol.% . It ranged between 42.30 ±4.57 and 61.20 ± 4.56. 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 0.78 ± 0.12 while that of isoflurane 0.61 ± 0.11 and the difference found was statistically significant. By 20 min, the Fe/Fi ratio of desflurane increased to 0.95 ± 0.05 while that of isoflurane was 0.77 ± 0.08.

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 2.69 ± 1.79times in the desflurane group and 2.39 ± 1.48 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 5.88 ± 2.84 min in the desflurane group while 8.13 ± 3.28 min in the isoflurane group ($P = 0.003$) [Tables 4 and 5]. Patients had a clear-headed recovery in the desflurane group: 45 patients out of 50 were alert and awake and 5 were drowsy but arousable. In the isoflurane group: 33 patients out of 50 were drowsy but arousable and 17 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.[7-9]

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 propanol were used at 1 min intervals after the initial induction as recommended.[10] 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 Fi and Fe agent concentrations is defined as the time to reach a Fe/Fi ratio of 80%.[7,10,11] 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.[10] 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.[10] In the earlier studies, change over from high to low FGF was done after 10–20 min, as recommended by Baum.[10,12,13]

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 propanol, esmolol, etc.[14]

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).[14]

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.[15] 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.[16] 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.[11]

Conclusion

We concluded that, 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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