

# An observation from an online survey: is fresh gas flow used for sevoflurane and desflurane different from isoflurane based anesthesia?

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## Abstract

Minimal uses of fresh gas flow (FGF) during volatile inhalational agents based anesthesia are gaining popularity for many reasons. However, the practice pattern is not uniform. Even the same anesthesiologist uses different FGF for different agents. The present study was aimed to evaluate the variation in the practice pattern of FGF used in context to volatile agents used. With departmental approval, the present study was conducted by reviewing the data of a previously conducted cross-sectional survey. The survey was conducted from January 2018 to May 2018 using SurveyMonkey®. Anesthesiologists working in different organizations across India were approached through e-mail and WhatsApp and anonymous responses were collected. The responses which contained FGF data for isoflurane and for at least one of either sevoflurane and/or desflurane were included. A total of 236 eligible responses were analyzed. The FGFs used by different anesthesiologists were very much inconsistent; only 5.1% used FGF < 600 mL/min and 19.1% used 600–1000 mL/min consistently for all three agents. There was a significant variation of FGF used for sevoflurane and desflurane as compared to isoflurane. Use of FGF of < 1000 mL/min was significantly higher for the desflurane as compared to both isoflurane and sevoflurane. The uses of lower FGF greatly vary both at intrapersonal as well as interpersonal level. The possibility of using FGF < 1000 mL/min is significantly higher with desflurane as compared to isoflurane. Volatile anesthetic agent appears to be a factor for the decision making on the use of low flow anesthesia.

**Key words:** isoflurane; sevoflurane; desflurane; low flow anesthesia; anesthesia machine; economics; pharmaceutical; health care costs; anesthetics; inhalation

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## INTRODUCTION

Minimal use of fresh gas flow (FGF) during volatile anesthetic based general anesthesia (GA) reduces anesthetic gas consumption, which makes it more economical.<sup>1</sup> It also benefits in terms of heat and humidity preservation by recirculating the rebreathing gases. With the advancement of Anesthesia workstation and monitoring of anesthesia gas concentrations, low flow anesthesia (LFA) can be safely used. However, survey data show that the use of higher FGF is still prevalent.<sup>2</sup> Moreover, the practice is also not uniform. Even the same anesthesiologist uses different FGF when using different volatile agents. While using volatile anesthetics, the cost of the volatile agent invariably comes in the mind of the anesthesiologist. We hypothesized that: the volatile anesthetic used will affect FGF and the subconscious alertness of cost may prompt the anesthesiologist in using lower FGF while using costlier volatile anesthetic agents like sevoflurane and desflurane. Therefore, the present study was aimed to evaluate the interpersonal and intrapersonal variation in the practice pattern of FGF used in context to different volatile agents. It was also aimed to know whether the costlier volatile agents (*i.e.* sevoflurane and desflurane) when used, affects the use of FGF as compared to less costly (*i.e.* isoflurane) based GA.

## DATA AND METHODS

### Data collection

With approval from the affiliated institute with an exemption

for consent, the present analysis was conducted by reviewing the data of a previously conducted cross-sectional survey. The survey was created and conducted using online survey software and questionnaire tool service from SurveyMonkey® (SurveyMonkey Inc., San Mateo, CA, USA; <https://www.surveymonkey.com>). Requests for responding to the online survey was sent during January 2018 to May 2018 through an electronic link to the online survey, using emails and WhatsApp ([www.whatsapp.com](http://www.whatsapp.com); Menlo Park, CA, USA), a social media platform services. Anesthesiologists working in different organizations (*i.e.*, teaching medical colleges/institutes, corporate teaching hospitals, and private and public sector non-teaching hospitals) across India, whose e-mails were available in public domain and were part of a few WhatsApp discussion groups (known to the investigators), were approached. Reminder emails and messages were also sent to potential responders if no reply was received after 2 weeks of the original email/message request. Any person practicing in the field of anesthesiology was taken as eligible for taking up the survey.

The present analysis was planned with data from a previous survey where the use of LFA was found to be 73%.<sup>3</sup> We hypothesized that there will be + 10% variation of FGF use in context to volatile anesthetic agent use and calculated the sample required as 147 per group with Fleiss method using an online epidemiological tool ([www.openepi.com](http://www.openepi.com)). However, as the sampling (survey) was cross-sectional, a design effect

of 1.4 was applied and the minimum participant required for 80% power with 5% precision was found as 206. As the same participant acted as the control, so the minimum total number of participant required was also 206.

**Statistical analysis**

The responses were collected anonymously and were directly downloaded in Excel format. Further to suit the objective of the present study, data were sorted out to exclude those responses which were grossly incomplete, where having only data of halothane and isoflurane. A final master chart was prepared with the responses which contained FGF data for isoflurane and for at least one of either sevoflurane and/or desflurane and were analyzed. The data were expressed in absolute number (percentage) scale. Data were further compared using Fisher’s exact test and chi-square test of independence, and INSTAT software (GraphPad Prism Software Inc., La Jolla, CA, USA) was used for the statistics;  $P < 0.05$  was considered as significant.

**RESULTS**

Out of the total 251 responses received in the survey, 236

response contained FGF data for at least sevoflurane or desflurane along with isoflurane and were included for analysis. One hundred and sixty (67.8%) anesthesiologists were from hospitals associated with teaching program and 209 (88.6%) were using workstations. The Boyle’s machines were common in use in non-teaching hospitals; 27.63% vs. 3.75% in non-teaching *versus* teaching hospitals.

Analysis of the variation of the FGF used for sevoflurane and desflurane by the same anesthesiologist in context to the FGF used for isoflurane (intrapersonal variation) showed a significant difference in the FGF used for the agents; variability was highest for  $FGF < 600$  mL/min while using sevoflurane,  $P < 0.0001$ . The variation was lowest for  $FGF < 600$  mL/min used for isoflurane and desflurane; 76.9% time used the same flow as of isoflurane, but, the variation was still statistically significant;  $P = 0.02$  (Table 1). Similarly, an intrapersonal variation of FGF used for desflurane based GA in context to sevoflurane based GA were also significantly different (Table 2).

Analysis of the variation of the FGF used for sevoflurane and desflurane among the different anesthesiologists in context to

**Table 1: Intrapersonal variation of fresh gas flow use with sevoflurane and desflurane as compared to isoflurane tested using Fishers exact test**

Variation with context to fresh gas flow	Isoflurane [n (%)]	Sevoflurane [n (%)]	P value	Desflurane [n (%)]	Two-tailed P value
< 600 mL/min			< 0.0001		0.022
No	26 (100)	14 (53.8)		20 (76.9)	
Yes	0	12 (46.2)		6 (23.1)	
600 – 1000 mL/min			< 0.0001		< 0.0001
No	91 (100)	65 (71.4)		57 (62.6)	
Yes	0	26 (28.6)		34 (37.4)	
1000 – 2000 mL/min			< 0.0001		< 0.0001
No	80 (100)	52 (65.0)		33 (41.2)	
Yes	0	28 (35.0)		47 (58.8)	
> 2000 mL/min			0.0002		< 0.0001
No	38 (100)	26 (68.4)		20 (52.6)	
Yes	0	12 (31.6)		18 (47.4)	

**Table 2: Intrapersonal variation of fresh gas flow use with sevoflurane and desflurane tested using Fishers exact test**

Variation with context to fresh gas flow	Sevoflurane [n (%)]	Desflurane [n (%)]	P value
< 600 mL/min			0.021
No	22 (100)	16 (72.7)	
Yes	0	6 (27.3)	
600–1000 mL/min			< 0.0001
No	90 (100)	60 (66.7)	
Yes	0	30 (33.3)	
1000–2000 mL/min			< 0.0001
No	85 (100)	38 (44.7)	
Yes	0	47 (55.3)	
> 2000 mL/min			< 0.0001
No	39 (100)	21 (53.8)	
Yes	0	18 (46.2)	

the FGF used for isoflurane (interpersonal variation) showed no significant difference in the FGF used for the isoflurane vs. sevoflurane (Table 3). However, the variation was significantly different for desflurane vs isoflurane for the  $FGF < 600$  mL/min and 1000–2000 mL/min group (Table 3). Similarly, an intrapersonal variation of FGF used for desflurane based GA in context to sevoflurane based GA were also significantly different for the  $FGF < 600$  mL/min and 1000–2000 mL/min group (Table 4).

Analysis of the consistency of using the same FGF irrespective of volatile agents used showed that only 5.1%, 19.1%, 15.3%, and 9.7% were using  $FGF < 600$  mL/min, 600–1000 mL/min, 1000–2000 mL/min and  $> 2000$  mL/min consistently, respectively. The difference/inconsistency was extremely significant;  $P < 0.0001$  (chi-square test of independence). The relative risk (95% confidence limit) of using LFA ( $FGF < 1000$  mL/min) with desflurane was 1.33 (1.11–1.59),  $P = 0.002$ , and sevoflurane 1.05 (0.87–1.28),  $P = 0.644$  as compared to Isoflurane; while the relative risk (95% confidence limit) of


**Table 3: Inter-personal variation of fresh gas flow use with sevoflurane and desflurane as compared to isoflurane tested using Fishers exact test**

Variation with context to fresh gas flow	Isoflurane [n (%)]	Sevoflurane [n (%)]	Two tailed P value	Desflurane [n (%)]	Two-tailed P value
< 600 mL/min			0.648		0.015
No	26 (11.0)	22 (9.3)		40 (19.6)	
Yes	210 (89.0)	214 (90.7)		164 (80.4)	
600–1000 mL/min			1		0.769
No	91 (38.6)	90 (38.1)		82 (40.2)	
Yes	145 (61.4)	146 (61.9)		122 (59.8)	
1000–2000 mL/min			0.699		0.047
No	80 (33.9)	85 (36.0)		51 (25.0)	
Yes	156 (66.1)	151 (64.0)		153 (75.0)	
> 2000 mL/min			1		0.895
No	38 (16.1)	39 (16.5)		31 (15.2)	
Yes	198 (83.9)	197 (83.5)		173 (84.6)	

**Table 4: Inter-personal variation of fresh gas flow use with sevoflurane and desflurane compared using Fisher's exact test**

Variation with context to fresh gas flow	Sevoflurane [n (%)]	Desflurane [n (%)]	Two-tailed P value
< 600 mL/min			0.002
No	22 (9.3)	40 (19.6)	
Yes	214 (90.7)	164 (80.4)	
600–1000 mL/min			0.695
No	90 (38.1)	82 (40.2)	
Yes	146 (61.9)	122 (59.8)	
1000–2000 mL/min			0.013
No	85 (36.0)	51 (25.0)	
Yes	151 (64.0)	153 (75.0)	
> 2000 mL/min			0.794
No	39 (16.5)	31 (15.2)	
Yes	197 (83.5)	173 (84.6)	

using LFA with Desflurane was 1.26 (1.05–1.50),  $P = 0.009$  as compared to sevoflurane.

## DISCUSSION

Literature suggests that with our modern anesthesia machines, an FGF of 0.3–0.5 L/min oxygen using third-generation volatile anesthetics is reassuringly safe anesthetic technique.<sup>4</sup> Literature also suggests that the FGF used for volatile agent based GA is decreasing over time. An audit in a teaching hospital found that the average FGF rate at that time was 2 L/min and there was an increasing trend of the use of the more expensive agent, but the FGF used with these expensive agents decreased.<sup>5</sup> The same authors audited the changing trend of FGF used in their department over the period of 2001–2006 and found that the use of FGF decreased by 35% over 4 years.<sup>6</sup> However, the use of LFA is not yet very much prevalent.<sup>2,3,7</sup> A recent study revealed that the mean FGF (L/min) for sevoflurane and isoflurane was 2.55 and 2.33, respectively.<sup>7</sup> Therefore, whether

the use of relatively costlier agents influences the FGF used is yet not clear. In this context, the present study evaluated the FGF used by the anesthesiologists for the three different volatile agents (*i.e.* isoflurane, sevoflurane, and desflurane) where isoflurane is relatively less costly as compared to the other two agents. The analysis of the FGF practice variation in context to these agents both at the intrapersonal and inter-personal level was done, which is likely to reveal the impact of the agent on the decision of FGF use, as the anesthesia machine, work set-up, person, *etc.* remained same.

The decision to use of lower FGF is multifactorial. A relatively shorter time is required to reach the target concentration when a higher FGF rate is used.<sup>8</sup> The anesthesia workstation itself can affect the time required to reach target concentration and thereby physician can use higher FGF to get the effect earlier.<sup>8</sup> Moreover, the manufacturer also recommends using 1–2 L/min of FGF for sevoflurane and 1 L/min for isoflurane. Food and Drug Administration at present indicates lower FGF with sevoflurane only for 2 minimum alveolar concentration  $\times$  hour.<sup>9</sup> These all can affect the FGF used with different inhalational agents. In our analysis, it was hypothesized that the volatile anesthetic agent used in practice will have an impact on the FGF which will be reflected by both intrapersonal and interpersonal variation analysis. The findings of the present analysis indicate that the consistency of using the same FGF irrespective of the volatile anesthetic agent used was very low. Only 5.1% of practitioners were using consistently < 600 mL/min; the lowest consistency, while 19.1% (the highest consistency) was found with FGF with 600–1000 mL/min. This indicates that the volatile anesthetic used is likely to have an impact on the FGF used. It was also found that the intrapersonal variation of FGF used for sevoflurane and desflurane as compared to isoflurane were significantly different. It was also different between sevoflurane and desflurane. This finding re-iterates towards to effect of the volatile anesthetic agent on the decision of FGF use by the anesthesiologist.

The time to shift towards low flow also needs special attention in the practice of LFA. Use of equilibration time of the volatile anesthetic agent as the change-over point can help



the anesthesiologists in the use of minimal flow anesthesia, in a more efficient way.<sup>10</sup> A study using Smart Anesthesia Manager™ and Anesthesia Information Management System to notify the anesthesia team if FGF exceeds 1 L/min found that real-time notification is an effective way to reduce excess FGFs.<sup>11</sup> However, such an advanced system is not widely available in most of the developing countries. Therefore, to change the practice, we have to address the practitioners attitude and behavior. Changing the practice patterns of physicians' is difficult but possible and use of interventions like academic detailing with enhanced education and individualized feedback is an inexpensive and effective tool to do so.<sup>12</sup> A study evaluating the attitudes and behaviors toward LFA, using educational seminars for the anesthetists found a good effect and increasing use of LFA.<sup>13</sup> So, it is clear that the practice of LFA needs good knowledge and insight of the pharmacokinetics of volatile anesthetics. Increasing the understanding of the anesthesiologists towards the basic principles with regards to the volatile agent used alteration of FGF and vaporizer dial settings along with suitable monitoring and its interpretation can take away the concerns related to the LFA.<sup>14</sup> The impact of such an approach needs to be evaluated in the future.

The present study findings show that, while using desflurane, an anesthesiologist is 1.33 times more likely to use an FGF < 1000 mL/min as compared to isoflurane and 1.26 times more likely than sevoflurane. Desflurane being the costliest inhalational agent in clinical use at present, it is likely that the cost factor led to the use of lower FGF. Desflurane based minimal flow anesthesia has been shown to reduce the cost incurred per minute of anesthesia drastically across the time duration of anesthesia.<sup>15</sup> In this aspect, it also needs attention that sevoflurane is also a costly agent as compared to isoflurane, but the present finding failed to show a significant increase in the lower FGF use with sevoflurane as compared to isoflurane. While the use of LFA with sevoflurane has shown to reduce consumption too.<sup>16</sup> This is probably because of the fear of Compound A accumulation and acute kidney injury with low flow use in sevoflurane-based anesthesia.<sup>17</sup> But, the finding of nearly 48% anesthesiologist using an FGF < 1000 mL/min with sevoflurane also indicates that the practice is influenced by many a factors and cost of sevoflurane may play a role too in decision making.

The present study, although it found extreme significance in the difference for the practice variation at an intrapersonal level and significant variation in interpersonal level, is limited by the fact that multivariate analysis was not done. It is because, although the FGF use in practice is multifactorial, the dependant factors are not yet precisely delineated. Although the sample size was calculated for a minimal power of 80%; considering the survey was being national, the numbers of participants were relatively small to represent the nation. Moreover, a cross-sectional cohort study has its own inherent bias. In the future, an international, multicenter study can give us better data for multivariate analysis and conclusion, and the present study will be helpful in the preparation of hypothesis/research question.

In summary, the uses of lower FGF greatly vary both at intrapersonal as well as interpersonal level. The possibility

of using FGF < 1000 mL/min was significantly higher with desflurane as compared to isoflurane. Volatile anesthetic agent appears to be a factor for the decision making on the use of LFA. However, this conclusion needs to be validated by other national/international observations with larger samples.

#### Author contributions

Design of the study: HMRK, MS, MK; data collection: MK, RD; manuscript writing: HMRK.

#### Conflicts of interest

There is no conflict of interest.

#### Financial support

None.

#### Institutional review board statement

The data was collected through online survey from the participating anesthesiologists. With approval from the affiliated institute with an exemption for consent.

#### Copyright transfer agreement

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#### Data sharing statement

Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices). Study protocol and informed consent form will be available immediately following publication, without end date. Results will be disseminated through presentations at scientific meetings and/or by publication in a peer-reviewed journal. Anonymized trial data will be available indefinitely at [www.figshare.com](http://www.figshare.com).

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