Original Article

Minimal flow anesthesia can be initiated early with the use of higher fresh gas flow to facilitate desflurane "Wash-in"

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Abstract

Background and Aims: More than 80% of delivered anesthetic gases get wasted at high fresh gas flows as they are vented out unused. Use of minimal flow anesthesia is associated with less waste anesthetic gas emission and environmental pollution. There is no approved or validated technique to initiate minimal flow anesthesia and simultaneously achieve denitrogenation of the breathing circuit. We studied the wash-in characteristics of desflurane, when delivered with 50% nitrous oxide, to reach a target end-tidal concentration at two different gas flow rates.

Material and Methods: Patients were allocated randomly to two groups of 25 adults each. In Group A, with the vaporizer dial fixed at 4 vol %, after an initial fresh gas flow of 4 L/min was administered to wash-in of desflurane using the closed-circuit, with 50% N_2O in O_2, and in group B, 6 L/min was used. Minimal flow anesthesia, with 0.5 L/min, was initiated in both groups on attaining a target end-tidal desflurane concentration of 3.5 vol %. After initiation of desflurane delivery, the inspired/expired gas concentrations were noted every minute for 15 min.

Results: In Group A, the target desflurane end-tidal concentration was reached in 499.2 ± 68.6 s±, and in the Group B ($P < 0.001$), it was reached significantly faster in 314.4 ± 69.89 s. Denitrogenation of the circuit was adequate in both groups.

Conclusion: Minimal flow anesthesia can be initiated, without any gas-volume deficit, in about 5 min with an initial fresh gas flow rate of 6 L/min and the vaporizer set at 4 vol%.

Keywords: Desflurane wash-in, low flow anesthesia, minimal flow anesthesia, uptake of inhaled anesthetics

Introduction

High fresh gas flow (FGF) is used in general anesthesia by tradition. More than 80% of the delivered anesthetic gases get wasted at an FGF of 5 L/min and a reduction from 3 L/min to 0.5 L/min results in a 60% reduction in total consumption of any volatile agent.[1] If 6 vol % desflurane is administered at high flows, 94% of the agent is wasted and vented out unused.[2] Environment conservation is the most vital global issue today. Concerns have been raised about pollution by anesthetic gases, and promulgation of guidelines promoting the use of low flow anesthesia (LFA) have resulted from that.[2,3] LFA is associated with low FGF use, significantly lower than the minute volume and results in a significant reduction in waste anesthetic gas (WAG) emission into the operating room environment and the atmosphere. Decision support tools, anesthesia information management systems, and quantified automated inhalation agent delivery systems are being evaluated by anesthesia providers to reduce WAG.[4,5] An FGF <1 L/min is referred to as LFA, while FGF limited to <0.5 L/min is referred to as minimal flow anesthesia (MFA).[6] The use of LFA and MFA dramatically reduces volatile anesthetic cost. We routinely practice MFA at

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our center with FGF of ≤0.5 L/min and use a FGF of 4 L/min before initiation of MFA.

The wash-in of an agent can be accelerated by using high FGF or by increasing the vaporizer dial setting or by taking advantage of the second gas effect of nitrous oxide.[7] A wide range of FGF and dial settings combinations are used by anesthetists to wash-in the inhaled anesthetics, according to habit and personal experience.[5] Most studies in contemporary literature describe wash-in with FGF 4 L/min for 15 min before initiation of MFA. Others describe high dial setting to achieve target end-tidal concentration (EtC) of inhalation anesthetic early and thereby reduce the time taken to convert to LFA and MFA. There is, however, no approved or validated technique to initiate LFA or MFA and simultaneously achieve acceptable denitrogenation of the alveolar gas.

We hypothesized that the use of higher initial fresh gas flow would result in not only faster initiation of MFA but also not result in gas-volume deficit or a fall in EtC of desflurane. We studied the wash-in characteristics of desflurane, when delivered with 50% nitrous oxide, to achieve a target EtC at FGF of 6 L/min vis-à-vis FGF of 4 L/min. We also studied whether this result in a clinically significant reduction in time taken to initiate MFA; whether the target EtC achieved sustains after that during MFA; and whether the agent consumption was similar in the two groups during the study period.

Material and Methods

A prospective randomized control study was conducted on fifty adult patients, in American Society of Anesthesiologists (ASA) functional class I-III, undergoing general anesthesia using desflurane, after approval of the institutional scientific and ethics committee (vide Institutional Ethical Committee Max Smart Super Speciality Hospital, Saket, Delhi approval letter No TS/MSSSH/GMMH/IEC/ANAES/17-07 dated 02 Jan 2018). The study was registered with the Clinical Trial Registry India and assigned number CTRI/2018/07/015031. Written informed consent was taken from all patients recruited for the study. Patients with pulmonary disease, moderate or severe obesity, history of previous thoracic surgery and patients with anticipated difficult airway were excluded. Patients underwent a routine pre-anesthetic evaluation, and a routine 6-h fasting protocol was followed.

An internet search of contemporary literature did not reveal a study of similar nature and so a pilot study was conducted, with 5 patients in each group, to determine the number of subjects required to have an adequately powered study. In the pilot study, the mean time to achieve desflurane EtC of 3.5 vol % was 476.2 ± 113.29 s in the 4 L/min group and was 357 ± 72.85 s in the 6 L/min group. On the basis of this, a total of 23 subjects per group were needed for a study power of 95% and a confidence limit of 95%. We recruited 25 patients in each group to cater for possible dropouts due to technical errors. The consort flow diagram of the study is exhibited in Figure 1.

Patients were allocated to two groups of 25 each by random computer draw. In Group-4L, MFA was initiated after wash-in of desflurane with 50% N_2O using an FGF of 4 L/min. In Group-6L, MFA was initiated after a wash-in of desflurane with 50% N_2O using an FGF of 6 L/min. A Dräger Fabius Plus anesthesia workstation with a Dräger D-Vapor vaporizer (Drägerwork AG and Co, Lubeck, Germany), and a closed-circuit breathing system was used in all cases. Patients were preoxygenated for 3 min before induction of anesthesia. A standardized anesthesia induction protocol was followed i.e. administration of intravenous (IV) fentanyl (2 mcg/kg) followed by propofol (1.5–2 mg/kg) after about 3–5 min. All patients were administered atracurium IV for neuromuscular blockade. In both groups, ventilation (FiO_2 0.5) was supported after the subject fell asleep, using a face mask. The airway was secured by an appropriate sized oral endotracheal tube (ETT) after ensuring the onset of adequate neuromuscular block. A 30–40 mg IV bolus of propofol was administered before intubation to ensure adequate depth of anesthesia during laryngoscopy and intubation.

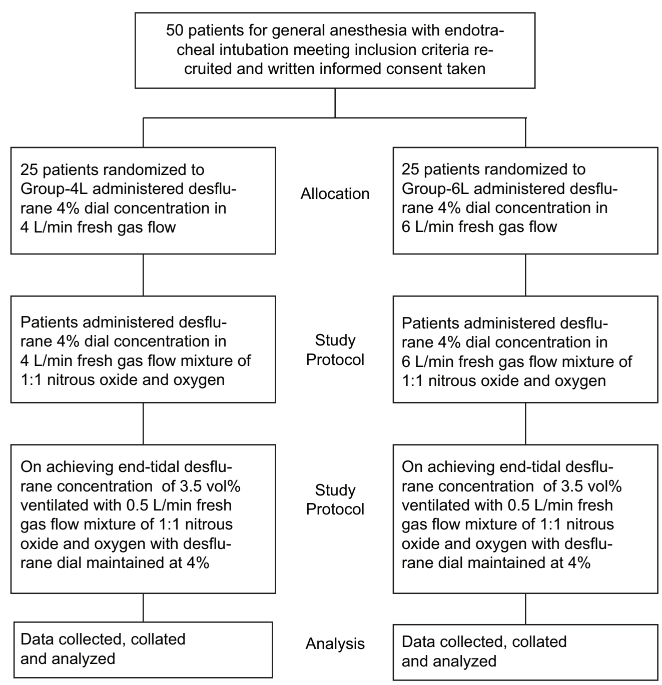

Figure 1: Consort flow diagram of study

In Group-4L, after confirmation of ETT placement, lungs were ventilated with an FGF of 4 L/min (50–50 mixture of nitrous oxide and oxygen), with the desflurane vaporizer dial set (F_D) at 4 vol %. In Group-6L, after confirmation of ETT placement, lungs were ventilated with an FGF 6 L/min (50–50 mixture of N_2O and O_2), with the desflurane F_D at 4 vol %. The anesthesia ventilator was set to deliver volume control ventilation in both groups with a tidal volume of 8 mL/kg and a respiratory rate of 12 bpm, to maintain end-tidal carbon dioxide ($EtCO_2$) between 30–40 mm Hg. The inspired concentration of O_2, N_2O, and desflurane were recorded every 1 min after initiating delivery of the above anesthetic mixture. The EtC of desflurane and its MAC displayed were also recorded. When a target EtC desflurane of 3.5 vol % (about 0.8 MAC in 50% N_2O) was reached, MFA was initiated with total FGF of 0.5 L/min (0.25 L/min each of both N_2O and O_2). No change in F_D of desflurane or alveolar ventilation settings were made during the study period.

The inspired and expired anesthetic gas concentrations were continued to be recorded every minute for 15 min after initiation of desflurane and N_2O delivery in breathing gases, to determine fall in gas concentration and MAC after the onset of MFA. The above parameters were noted by the investigator with the monitor screen facing sideways in such a way that the gas flow meters were not visible to him. The study was terminated 15 min after initiation of desflurane. The breathing circuit was not disconnected during the study period. Consumption of desflurane during the study period was calculated later using the Ehrenworth and Eisenkraft equation i.e., agent consumption (in mL per hour) = 3 * FGF in L/min * F_D of the agent in Vol %.[8]

Inspired and expired gases were analyzed by a respiratory gas monitor (Phillips IntelliVue G7, Phillips Medizine Systeme, Boeblingen GmbH, Germany). Gases were sampled at the distal end of the ETT through a sampling port on the angle-piece. Gases drawn by the respiratory gas analyzer were redirected, after analysis, to the closed-circuit through the expiratory limb. All measurements were made using the same anesthesia machine and respiratory gas monitor.

Anesthesia was maintained with desflurane in N_2O and O_2 titrated to maintain a FiO_2 of 0.5 at all times. Atracurium was administered for maintenance of neuromuscular blockade during the surgical procedure. At the end of the procedure, neuromuscular blockade was reversed and trachea extubated after ensuring adequate recovery.

Results

A total of 50 patients (25 in each group) were recruited and all of them completed the study. The demographic profile and the baseline vitals of the subjects are shown in Table 1. Demography of the subjects of both groups was statistically similar. There was no reactive airway response (signs of bronchoconstriction, laryngospasm, or rise in airway pressure) during the study period in any patient.

The measured clinical and anesthetic gas parameters are shown in Table 2. The set tidal volume and respiratory rates in the two groups were similar. The target EtC of desflurane achieved was similar in the two groups. The target EtC of desflurane was achieved in 499.2 ± 68.67 s in Group-4L, whereas it was achieved more rapidly in Group-6L (314.4 ± 69.89 s), and this difference in time was statistically significant ($P < 0.001$).

Adequate denitrogenation of the alveolar gas (residual nitrogen 6.32 ± 1.41 vol % in the Group-4L and 5.56 ± 1.36 vol% in Group-6L) was achieved in both groups. Marginally, higher nitrogen concentration was seen in Group-6L, but the

Table 1: Demographic variables and Baseline Vital Parameters

	Group-4L (*n*=25)	Group-6L (*n*=25)	*p*
Age (yrs) Mean+SD	40.52+15.16	39.92+13.05	0.88
Sex (Male/Female)	13/12	16/9	0.47
Weight (kg) Mean+SD	65.40+11.13	67.32+10.21	0.53
ASA Grading I/II/III	9/9/7	11/11/3	0.37
Baseline Heart Rate (bpm)	85.1+15.39	81.72+10.7	0.38
Baseline Systolic Blood Pressure (mm Hg)	137.7+14.9	138.1+16.8	0.93
Baseline Diastolic Blood Pressure (mm Hg)	77.04+9.1	78.52+7.9	0.54
Baseline Oxygen saturation (%)	99.28+0.98	99.16+1.3	0.72

Table 2: Study data

	Group	Mean+SD	*p*
Set Tidal Volume (ml)	A (*n*=25)	502.80+59.28	0.53
	B (*n*=25)	513.12+54.46	
Respiratory Rate (bpm)	A (*n*=25)	12.60+1.83	0.79
	B (*n*=25)	12.48+1.33	
Duration of high flows (s)	A (*n*=25)	499.20+68.67	<0.001
	B (*n*=25)	314.40+69.89	
Target expired anaesthetic concentration achieved (vol %)	A (*n*=25)	3.5+0.01	0.56
	B (*n*=25)	3.5+0.014	
Nitrogen concentration at the end of high flows (vol %)	A (*n*=25)	6.32+1.41	0.06
	B (*n*=25)	5.56+1.36	
Inspired desflurane concentration at 15 min (vol %)	A (*n*=25)	3.26+0.2	0.65
	B (*n*=25)	3.29+0.23	
Expired desflurane concentration at 15 min (vol %)	A (*n*=25)	2.89+0.18	0.45
	B (*n*=25)	2.93+0.24	
Decrease in end-tidal Desflurane (%)	A (*n*=25)	17.52+5.17	0.25
	B (*n*=25)	15.76+5.50	
Volume of Desflurane consumed (ml)	A (*n*=25)	6.9+0.82	0.19
	B (*n*=25)	7.26+1.12	

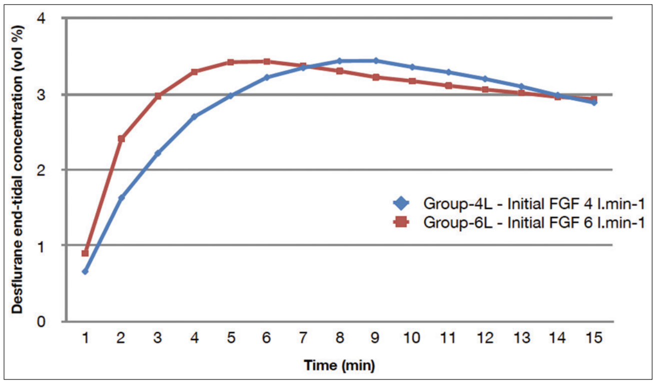

Chart 1: Wash-in of desflurane in the two groups

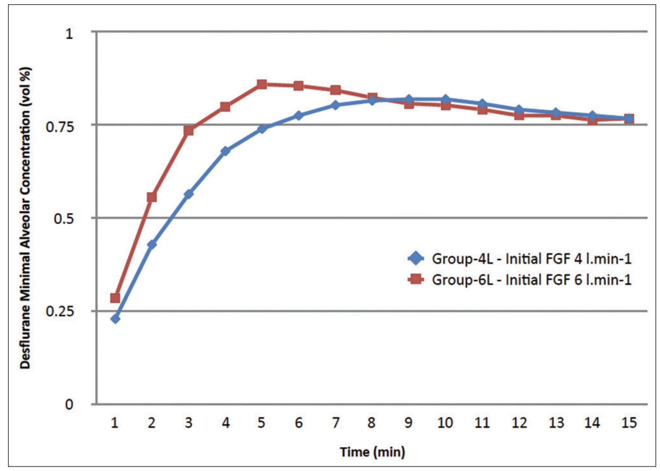

Chart 2: Minimum alveolar concentration in the two groups during wash-in

difference, with group-4L, was not statistically or clinically significant. Charts 1 and 2 respectively display the change in EtC and MAC of desflurane during the study period. There was a small fall in EtC and MAC of desflurane after initiation of MFA in both the groups, but it was not significant clinically. The extent of fall was less in Group-6L as compared to Group-4L, but the difference between the groups was not found to be statistically significant (p 0.25). The consumption of desflurane was marginally higher in Group-6L during the study period, but it was not statistically significant and did not result in any relevant increase in cost.

With the vaporizer dial (FD) set at 4, the inspired concentration of desflurane was 3.68 ± 0.2 vol % at 5 min in Group-4L, whereas it was 3.97 ± 0.11 vol % at 5 min in Group-6L. The agent delivery error was 8% at the FGF of 4 L/min and only 0.75% at FGF of 6 L/min. MFA was administered in both groups after the initial high FGF. The inspired concentration of desflurane was found to be 3.28 ± 0.21 vol % at 15 min in the groups with the F_D set at 4 and the set at FGF 0.5 L/min i.e., a vaporizer delivery error of 18% during MFA with FGF of 0.5 L/min. The EtC desflurane at 15 min was 2.89 ± 0.18 vol % in Group-4L and 2.93 ± 0.24 vol % Group-6L and were statistically similar. The mean EtC of desflurane was found to be 2.91 ± 0.21 vol % at 15 min in the two groups with the F_D set at 4 and the FGF 0.5 L/min i.e., 17% less than the target EtC. The EtC of desflurane after 15 min was between 2.9–3.8 vol % during the maintenance phase, but the data is not presented as the study objective was limited to "wash-in" of the agent.

Using the study protocol, we estimated EtC of desflurane at the different time points on the Gas Man software.[9] Gas Man estimated the desflurane alveolar concentration at the initiation of MFA as 3.2 vol % in Group-4L and 3.1 vol % in Group-6L. The estimated EtC of desflurane at 15 min was estimated as 3.0 vol % in Group-4L and 2.9 vol % in Group-6L.

Discussion

This study was conducted to determine a better technique of desflurane "wash-in" before initiating MFA. MFA was initiated when EtC of desflurane reached 3.5%.We found that using an FGF of 6 L/min with an F_D set at 4 vol % was associated with a faster wash-in. The mean time required to initiate MFA was about 3 min less with an FGF of 6 L/min flow vis-à-vis an FGF of 4 L/min, and the difference was statistically highly significant (*P* value <0.001).

To initiate MFA, high FGF is maintained to wash-in the anesthetic agent till its desired EtC is achieved within the breathing system and the alveoli thereafter. The wash-in of an agent to achieve the desired EtC depends on its solubility and pharmacokinetics.[10] MFA can be initiated when the target EtCor minimum alveolar concentration (MAC) is achieved.

The FGF and F_D combination used for delivery of inhaled anesthetics to reach a target EtC varies from physician to physician.[11] Habits and personal preferences are responsible for the extensive range of FGF – F_D combinations used to wash-in inhaled anesthetics. Some anesthetists use a high FGF to shorten the wash-in time constant, whereas others use a lower FGF with a higher F_D to compensate for the longer wash-in time constant. The use of high FGF for a more extended period, than needed, may increase agent consumption,[12] negate the savings offered by closed-circuit anesthesia machine use,[13] and may increase wastage of anesthetic gases. Anesthetists should aim to follow a protocol based FGF/F_D setting to achieve the target EtC without wasting potent inhaled anesthetic agents and causing operating room pollution.

By tradition, initiation of LFA and MFA follows a 10–20 min phase of high FGF anesthesia. Most trials, in contemporary literature, to evaluate methods for early wash-in of desflurane before initiation of LFA, have used low FGF with high F_D. To achieve a 1 MAC EtC of desflurane and to ensure low gas consumption during wash-in, Leijonhufvud *et al.* described an optimal FGF of 4 L/min, with the F_D fixed at 3 vol %.[14] Sathitkarnmanee *et al.* achieved EtC of desflurane of 1, 2, 3, 4, 5, and 6 vol % using FGF of 2 L/min with F_D set at 12% at 0.6, 1, 1.5, 2, 3, and 4 min, respectively.[15] Delivery of desflurane to patients in high concentration, above the threshold for respiratory irritation (1–1.5 MAC), can lead to irritation of the airway, coughing, breath-holding, and laryngospasm.[16] We targeted an EtC of desflurane of 3.5% with the dial set at 4% to avoid possible airway irritation by delivery of high inspired concentration of desflurane but achieved the target EtC of desflurane to initiate MFA in a short period. We set a EtC based target, instead of a MAC based one, as monitors round off MAC up to the first decimal place (a range of EtC is labeled as the same MAC) and so an EtC based target is more accurate.

The faster wash-in of desflurane was also associated with adequate denitrogenation of the closed-circuit in both the groups. The fall in EtC of desflurane after initiation of MFA (recorded at 15 min after starting desflurane) was 17.52 ± 5.17% in Group-4L and 15.77 ± 5.5% in Group-6L, but the difference was not statistically significant ($P = 0.25$) but was possibly clinically significant.

Owing to the long time-constant of LFA and MFA, the delivery concentration of volatile anesthetics may not match the set vaporizer F_D. The vaporizers thus do not deliver the F_D at extremes of FGF as they are calibrated at FGF rates of 4–6 L/min in 100% O_2. Vaporizer performance error has been calculated to be within ± 5% at an FGF of 2–4 L/min and 7.5% at an FGF of 6 L/min.[17] Weiskopf *et al.* found that at FGF 0.5–10 L/min of O_2, the desflurane delivery in the outflow gas from the Tec 6 vaporizer was within ± 15% relative or ± 0.5% absolute of the F_D, whereas at FGF <2 L/min of O_2, desflurane concentration was about 8% lower than at high FGF. The addition of N_2O to the carrier gas reduces the output of vaporizers. With FGF of 70% N_2O in O_2, the desflurane delivery was found to be 16% lower than that with similar FGF of O_2.[18] At high FGF, there is a reduction in rebreathing and a decrease in vaporizer output, because of cooling, which leads to a lower alveolar anesthetic concentration at high flows.[2]

Honemann *et al.* recommended no change in F_D setting after initiation of LFA with desflurane.[7] We could not find any recommendation, in contemporary literature, about the F_D setting after the introduction of MFA and so followed the protocol of Honemann *et al.* in our study. During MFA, we kept the F_D at 4, to maintain a target EtC of desflurane at 3.5 vol % and achieved an EtC of 3.28 ± 0.21 vol %, which was a bit lower than our target EtC of 3.5 vol %. We used a Drager D-Vapor vaporizer (which has performance properties similar to Tec 6) and found just a 0.75% lower desflurane delivery at the FGF of 6 L/min O_2 but an 8% lower desflurane delivery at the FGF of 4 L/min O_2. At the FGF 0.5 L/min (50% N_2O in O_2) desflurane delivery was 18% lower than the set F_D. From our findings, we suggest that after the institution of MFA with a 50% N_2O in O_2 mixture, the F_D should be set about 18–20% more than the target desflurane EtC.

As a secondary objective, we also calculated the consumption of desflurane in the first 15 min in the respective groups. The consumption of desflurane was marginally lower in the 4 L/min Group-6L, but the difference in volume consumed was both statistically and economically not significant. The other secondary objective was to determine whether the EtC of desflurane fell after early initiation of MFA, in case a stage of equilibrium had not been reached by that time. There was no statistically significant fall in the EtC of desflurane after initiation of MFA implying that uptake and distribution of desflurane by body tissue was minimal by this time.

Honemann *et al.* state that about 600 mL of N_2O gas gets absorbed in an adult even after 10 min of high FGF and if one initiates MFA early gas-volume deficit will be there.[7] We initiated MFA as early as 5–8 min after high FGF without any gas-volume deficit. We could not detect any fall in breathing system volume on the ventilator monitor nor did the ventilator alarm indicate a gas deficit. The Draeger anesthesia ventilator entrains atmospheric air to compensate for the gas-volume deficit, as a safety feature. The nitrogen concentration of the breathing circuit remained static indicating absence of air entrainment in any of our case.

Early reduction of FGF results in cost savings, reduces environmental and workplace pollution by inhalation agents, without altering the amount of drug delivered to the patient.[19,20] Agent consumption is determined the initial FGF; the duration of this FGF; and the maintenance of this FGF. The significance of the initial "wash-in" of the agent during anesthesia is often ignored. The use of higher initial FGF has been shown to have a significant effect on overall agent consumption in an environment that favors low maintenance FGF.[21] In MFA, consumption of agent in the maintenance phase is very low and is mainly dependent on duration of this phase.

The limitations of our study are that although the desflurane EtC values observed in our study matched with those estimated by Gas Man software[9] at the end of 15 min, there was a variance of 9% with the Gas Man forecasts at the time of initiation of MFA. We recommend further studies on different patient population and larger sample size to establish this technique of initiating MFA.

Conclusion

FGF of 6 L/min was associated with a faster wash-in, adequate circuit denitrogenation, and there was no fall in alveolar anesthetic gas concentration after initiation of minimal flow anesthesia.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

Dr Mukul Chandra Kapoor has served as professional speaker for Baxter Inc. The other authors do not declare any conflicts of interest.

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