Original Article

Randomized double-blind trial comparing effects of low-flow vs high-flow anesthesia on postoperative lung functions using respirometer

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Abstract

Background and Aims: Modern anesthetic practice utilizes low-flow anesthesia with evolving evidence on its pulmonary effects. Studies comparing measurement of vital capacity and inspiratory reserve volume using respirometer in both low-flow and high-flow anesthesia are sparse. We evaluated the effects of low-flow and high-flow anesthesia on postoperative pulmonary functions using respirometer.
Material and Methods: This was a prospective randomized double blind study wherein One hundred and ten patients undergoing peripheral surgeries under general anesthesia were allocated into two groups Group I- Low-flow anesthesia with O2 + N2O + Sevoflurane (0.5L + 0.5L + 3.5%) and Group II- High-flow anesthesia with O2 + N2O + Sevoflurane (2L + 2L + 2%). The difference in vital capacity (VC), inspiratory reserve volume (IRV), and peak expiratory flow rates (PEFR) from the preoperative period were compared in both the groups postoperatively.
Results: The difference in VC, IRV, and PEFR measured in both the groups between the preoperative and postoperative period were found to be similar and statistically insignificant (*P* - 0.173, 1.00 and 0.213 respectively). The difference in single breath count (SBC), breath holding time (BHT), and respiratory rates (RR) were also similar in both the groups (*P* – 0.101, 0.698, and 0.467) respectively.
Conclusions: The pulmonary effects of low-flow anesthesia are comparable with the high-flow ones in patients undergoing elective surgeries under general anesthesia.

Keywords: Inspiratory reserve volume, general anesthesia, peak expiratory flow, vital capacity

Introduction

Postoperative pulmonary complications (POPC) contribute significantly to overall perioperative morbidity and mortality. Such complications account for about 25% of deaths occurring within 6 days of surgery. The frequency rate of these complications like atelectasis, infection (bronchitis, pneumonia), prolonged mechanical ventilation, bronchospasm, and underlying chronic lung disease varies between 5%–70%. This wide range is due to variation in definition of POPC, variation in patients, and procedure related factors.[1] Anesthetic agents are associated with marked alterations in respiratory drive thereby causing diminished response to both hypoxemia and hypercapnia. The respiratory effects of general anesthesia cause diaphragm and chest wall relaxation, which results in a

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marked reduction in the functional residual capacity (FRC) and thereby thoracic volume. This decrease in lung volume promotes atelectasis though it is clinically insignificant most of the times. This altered compliance, impaired regional ventilation, and retained airway secretions contribute to atelectasis in the dependent lung regions and persists for more than 24 hours in 50% of patients. Consequently, this can lead to arterial hypoxemia from V-Q mismatching and increased shunt fraction.[1] Loss of lung volume as a result of atelectasis causes inspiration-expiration cycles to commence from lower FRC resulting into increased work of breathing. Deep breathing and effective cough can clear the mucus plugs and secretions leading to recruitment of collapsed alveoli.[2,3] However, the loss of lung volume can reduce the capacity of maximum breathing and effective cough, which is measured by vital capacity (VC).

Besides low-flow anesthesia technique being proven beneficial in reducing mucus blocking and subsequent collapse of alveoli, it is preferred choice over high-flow for various reasons like being economical and reduction in theatre pollution. This effect was proved earlier by measuring forced vital capacity (FVC) and forced expiratory volume in the first second of expiration (FEV1), which was lower in high-flow anesthesia groups.[4] Maximal sustained inspiration (MSI) through respirometer is recommended in immediate postoperative period to reduce respiratory complications. However, the ability to perform this maneuver is based on VC, which can be reduced due to existing atelectasis.

Vital capacity (VC) and inspiratory reserve volume (IRV) measurement is an easy and simple way to monitor postoperative pulmonary functions. Many studies gave mixed or controversial results regarding the effects of high-flow and low-flow on pulmonary functions postoperatively.[4,5] Previous studies have validated the use of spirometry in assessing lung functions in terms of FVC and FEV1. Even in the presence of atelectasis,[6] the spo2 was maintained between the high-flow and low-flow groups indicating that the available alveolar exchange is sufficient to maintain oxygenation.[5] Incentive spirometry (IS) is designed to encourage breathing in over tidal volumes, such volumes tend to fall after abdominal surgeries, and this helps patients to take long, deep, and slow breaths to increase lung inflation. Hence, IS can be used as a simple mean to follow lung function, especially IRV, in the postoperative period in spontaneous breathing.

Peak expiratory flow meter (PEFR) is used to detect maximal effort of patients in forceful exhalation and any obstruction due to atelectasis. It is used as a marker of adequacy of lung function in the postoperative period. There are very limited studies on effects of anesthesia and atelectasis on VC, and none comparing effects of low-flow vs high-flow on VC.

The primary aim of our study was to compare the effects of low-flow and high-flow anesthesia on VC and IRV using respirometer. The secondary aim was to compare other parameters like PEFR, Single breath count (SBC), Breath holding time (BHT), and respiratory rates (RR) of both the groups.

Material and Methods

This was a randomized double-blinded study conducted over 6 months period, after obtaining approval from the Institutional Ethical Committee (IEC No. 2017/343 Dt 09/01/2019). The trial was registered in the Clinical Trial Registry- India, before starting enrollment of patients (CTRI/2019/07/020304). One hundred and ten adult patients between 18 and 60 years of age of physical status American Society of Anesthesiologist (ASA) class 1 and 2 posted for elective peripheral surgeries under general endotracheal anesthesia were included in the study Patients with physical status ASA class 3 and above, those posted for emergency surgeries, thoracic abdominal surgeries, and those not willing to participate in the study were excluded from the study [Figures 5 and 6]. The study protocol was explained to all patients in their own language and informed valid consent was obtained. All patients enrolled were randomized into two groups by computer generated list of random numbers into Group A- Low-flow anesthesia and Group B- High-flow anesthesia. All patients were monitored with planet 60/star 60 monitor, SANKRAY Technologies Pvt. Ltd, India.

Procedure to perform breath holding time (BHT) and spirometry was explained to the patients in detail where patients were made to sit up straight or lean forward and instructed to exhale, letting to breathe out. Then they were instructed to close their lips around the mouth piece of spirometer (Smart PFT CO transfer S/N; EC0715-00028). The patients were instructed to inhale slowly, breathing in until unable to do so. The patients were asked to hold the breath for two to three seconds then exhale slowly, which would help to maintain maximal inspiration and reduce the risk of progressive collapse of individual alveoli. They were asked to take out the mouth piece and breathe out slowly and normally for few seconds. After completion, the patients were instructed to take a deep breath and cough out to clear the mucous. Patients were asked to repeat the same procedure thrice, and the best of the three readings were noted. This procedure of spirometry was carried out preoperatively as well as postoperatively to assess the inspiratory flow rate (IFR) thereby assessing the lung functions along with performing the BHT, and PEFR (AIRZONE PEAK EXP FLOW METER). BHT was recorded by asking the patient to take normal inspiration and hold the breath as much they can, and the time they can hold was recorded as number in minutes. Best of those three readings was taken as BHT. Similarly single breath count parameter was done by asking the patient to count numbers as far as possible after taking in a deep breath, and the best of three readings were noted. Peak expiratory flow was done by asking the patient to hold flowmeter in hand, ask them to blow air into the mouthpiece, and a small plastic arrow moves in the flowmeter, measurement taken as best of three readings where the arrow stops moving. If patients cough or sneeze the procedure was repeated again.

All patients were fasted for a period of 6 hours prior to surgery and were pre-medicated with Tab. Ranitidine 150 mg at the night prior and morning of surgery and Tab. Alprazolam 0.25 mg night before the surgery. Patients were randomized by computer generated list of random numbers. On the day of surgery, patients were shifted to operation theatre complex and large bore IV access 18 G was established and Ringer lactate solution (10 ml/kg) was given.

All patients were induced with Inj. Fentany l 2 mcg/kg, Inj. Propofol 2 mg/kg after adequate preoxygenation and paralyzed with Inj. Vecuronium 0.1 mg/kg and were intubated with appropriate size cuffed endotracheal tube, and tube position was confirmed by auscultation and end tidal carbon dioxide trace.

In Group A – Low-flow anesthesia was maintained with O2 + N2O + Sevoflurane (0.5L + 0.5L + 3.5%).

In Group B – High-flow anesthesia was maintained with O2 + N2O + Sevoflurane (2L + 2L + 2%).

Intraoperative hemodynamic monitoring was done every 30 min (pulse rate (PR), noninvasive blood pressure (NIBP), Oxygen saturation (SPO2), respiratory rate (RR), End tidal carbon dioxide (ET CO2), fraction of inspired oxygen (FiO2)). Duration of surgery was noted and at the start of closure all benzodiazepines, opioids, and muscle relaxants were avoided. At the end of surgery, the residual neuromuscular blockade was reversed with Inj. Glycopyrrolate 20 mcg/kg and Inj. Neostigmine 50 mcg/kg and extubated after regaining consciousness and return of the airway protective reflexes. All patients were shifted to post anesthesia care unit (PACU) and monitored for 1 hour. Inj. Ketorolac 30 mg IV was given to all patients postoperatively for pain along with appropriate regional analgesic blocks. If in case of persistent pain short acting opioids was given based on requirement. All patients were monitored SpO2, ETCO2, RR and postoperative spirometry was performed at the first 30 min, first, second, sixth, and 24th hour along with BHT, SBC and PEFR. One anesthesiologist performed the study and another anesthesiologist recorded and evaluated the data, which was done to blind the group allocation.

Statistical analysis

Statistical analysis was done using software SPSS version 23 using Student's t-test and paired t-test. Based on previous study with difference in VC of 400 ml and SD of 700 ml,[4,7] sample size of 55 patients per group was needed for significance of 5%, power of study of 80%, and attrition of 10%.

All the results were expressed as mean ± SD of patients and were evaluated at a 95% confidence interval at a significance level of $P < 0.05$.

Results

Among the 115 who were screened for eligibility, 110 patients were enrolled into two groups, 55 patients in Group A and 55 patients in Group B. Five patients who had operations lasting more than two hours were excluded from the study because of the specific surgical problems, which might impact their postoperative pulmonary functions.

Demographic parameters were comparable between both the groups [Table 1].

No significant differences were found between two groups in terms of heart rate (HR), Mean Arterial Blood Pressure (MABP), SPO2, and ETCO2 during anesthesia. ETCO2 was maintained between 30 to 35 mm Hg intraoperatively in both the groups, few patients had lesser ETCO2 of 25–30, but that didn't cause any change in SpO2 or any other hemodynamic perturbations [Figures 1-4].

Preoperative and postoperative pulmonary function tests results were similar in both the groups. In both the group of patients, the difference in VC and IRV from the preoperative values were comparable in the postoperative period at all time points till the first 24 hours after surgery. The difference in VC at end of 30 minutes found to be similar between groups with the P value of 0.173 [95% confidence interval (566.51-879.56)] and IRV with the P value of 0.93 [95% confidence interval (386.33-577.80)]. The difference in PEFR from the preoperative value in both the groups were also similar at the first

30 minutes postoperatively (*P*-0.213). [95% confidence interval (106.50-135.04)] [Tables 2-4].

The difference in respiratory rates, SBC, BHT from the preoperative values were not statistically significant in the first 30 min postoperatively (*P*-0.467, 0.101, 0.698 respectively) [Table 2].

There was no contamination whereby the protocols were altered for any procedures in either low-flow group or high-flow group. None had any complaints or side effects related to the study procedures.

Discussion

The present study has shown that the pulmonary effects of low-flow anesthesia is comparable with high-flow anesthesia in patients undergoing elective peripheral surgeries under general anesthesia.

General anesthesia imparts changes in pulmonary functions in the postoperative period by altering the lung volumes and capacities and interferes with gas exchange and overall lung dynamics. We included peripheral surgeries like orthopedics, limb reconstructive, and ear surgeries in order to exclude the surgical component of pulmonary complications.

Various methods of respiratory physiotherapy including inspiratory muscle training and incentive spirometry have been described as effective tools in optimizing the respiratory muscle function. Routinely, in clinical practice respirometer/ incentive spirometry devices are used for deep breathing exercises and as physiotherapy to prevent POPC, which are ideally started in the early preoperative period. This maneuver increases the inspiratory volume and trans-pulmonary pressure thus improving inspiratory muscle function. The pulmonary hyperinflation that is simulated by these procedures if repeated regularly maintains airway patency and minimizes atelectasis and POPC.[8]

Rothen *et al*. explained that the major cause of impaired gas exchange during general anesthesia is atelectasis causing

Table 1: Comparison of demographic parameters and operating time in Group A (*n*=55) and Group B (*n*=55)

Parameters	Group A (*n*=55)	Group B (*n*=55)	Significance
Age (years)	42.34±14.55	37.18±19.07	0.113
Sex (male/female)	36/19	37/18	1.000
BMI (kg m^{-2})	28.62±3.79	29.99±2.84	0.035
ASA Class (1,2)	37/18	42/13	0.788
Operative Time	47.93±4.91	46.28±18.5	0.787

BMI - Body Mass Index, ASA - American Society of Anaesthesiologists

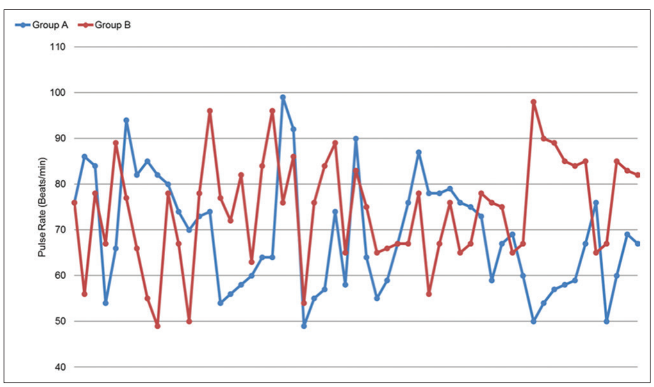

Figure 1: Comparison of Heart Rate between the two groups

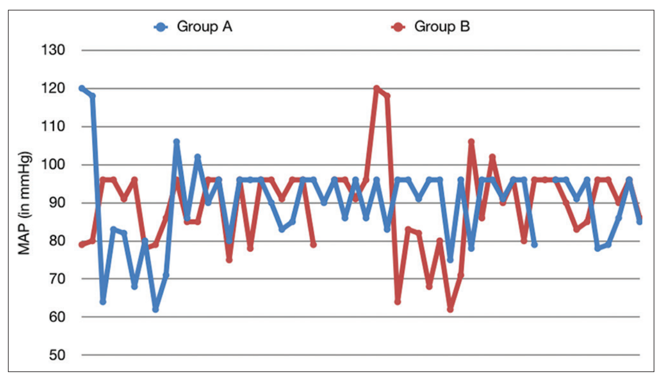

Figure 2: Comparison of MAP between the two groups

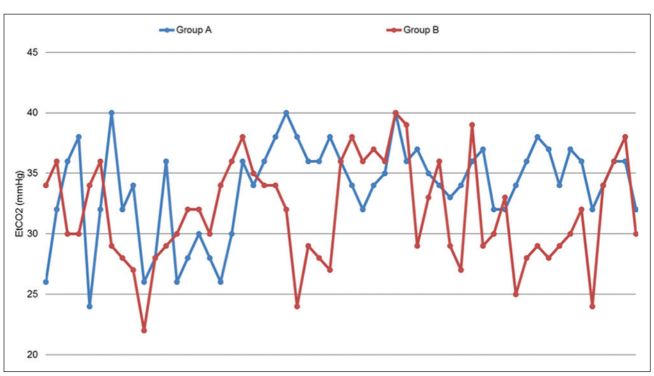

Figure 3: Comparison of EtCo2 between the two groups

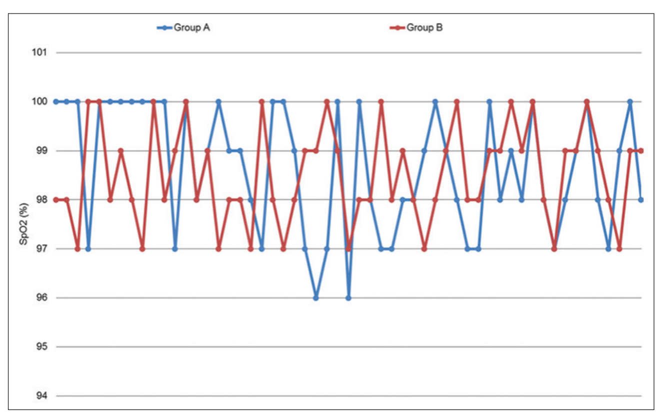

Figure 4: Comparison of SpO2 between the two groups

pulmonary shunting and vital capacity maneuver (inflation of lung up to 40 cm H2O, maintained for 15 seconds) re-expands atelectasis and improves oxygenation.[9]

Hence, spirometry maneuvers (IRV, VC, PEFR) and its measurement becomes an easier and beneficial tool to study the POPC in patients undergoing general anesthesia.

The beneficial effects of low-flow inhalational anesthesia over high-flow techniques are innumerable as stated above, though limited by availability, timely servicing of the equipment, and their associated cost. Low-flow anesthesia also has disadvantages in the form of hypoxia, hypercapnia, and reaction of gases with dry CO2 absorbents.

Murat Bilgi *et al*. compared the low-flow and high-flow techniques on mucociliary activity and pulmonary function tests. They found the forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV 1) were significantly lower and the saccharin clearance time was significantly longer in high-flow group compared to low-flow.[4]

Cihan Doger *et al*. found comparable results with low-flow and high-flow techniques on postoperative pulmonary functions in terms of FVC and FEV 1 in laparoscopic abdominal surgery.[5]

Table 2: Comparison of Difference in preop and post-operative parameters at 30 min in Group A (*n*=55) and Group B (*n*=55)

Parameters	Group A (*n*-55)	Group B (*n*=55)	Significance
VC Difference (ml)	803.27±421.25	695.09±405.45	0.173
IRV Difference (ml)	630.54±366.83	498.90±373.83	1.00
BHT Difference	4.69±4.17	4.36±4.61	0.698
RR Difference (rate min^{-1})	0.436±2.27	0.118±2.30	0.467
SBC Difference	7.82±6.32	5.82±6.35	0.101
PEFR Difference (L min^{-1})	120.77±52.79	109.10±44.57	0.213

VC - Vital Capacity, IRV - Inspiratory Reserve Volume, BHT - Breath Holding Time, RR - Respiratory Rate, SBC - Single Breath Count, PEFR - Peak Expiratory Flow Rate

Table 3: Difference between two Groups in Vital Capacity in Postoperative period at Times

Parameter	Time in minutes	Group A (*n*=55)	GroupB (*n*=55)	Significance
Vital Capacity Difference (ml)	30	803.27±421.25	695.09±405.45	0.173
	60	806.00±605.23	586.00±451.78	0.133
	180	732.36±625.97	542.90±558.32	0.097
	360	683.27±657.30	437.45±425.12	0.072
	1440	608.54±654.16	345.09±364.92	0.088

Table 4: Difference between two Groups in Inspiratory Reserve Volume in Postoperative period at Times

Parameter	Time in minutes	Group A (*n*=55)	Group B (*n*=55)	Significance
IRV Difference (ml)	30	630.54±366.84	625.09±374.01	0.93
	60	498.90±373.83	498.90±373.83	1.00
	180	484.36±382.74	484.36±382.74	1.00
	360	446.00±349.29	446.00±349.29	1.00
	1440	341.45±360.70	345.09±364.92	1.00

IRV - Inspiratory Reserve Volume

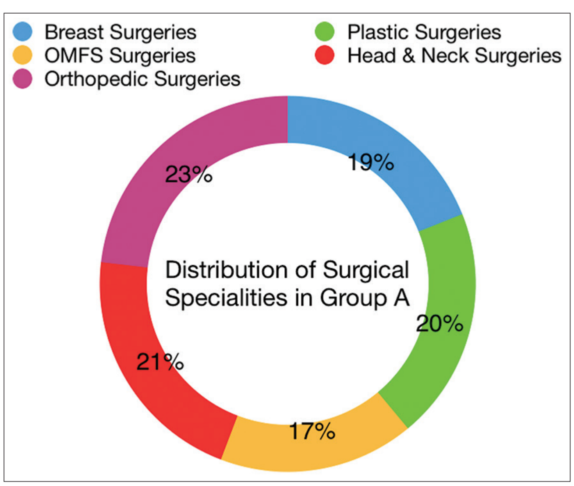

Figure 5: Distribution of surgical specialities in low flow group (group A)

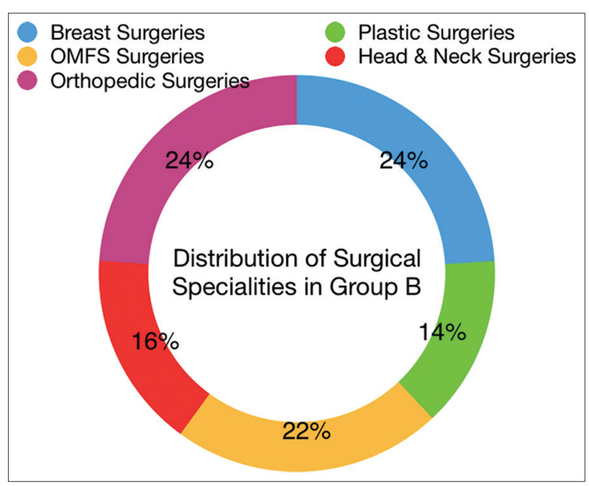

Figure 6: Distribution of surgical specialities in high flow groups (group B)

Due to mixed results from previous randomized control trials (RCTs), there has been a lack of evidence of the definitive pulmonary beneficial effects of low-flow anesthesia over the high-flow ones.

Literally, none compared the VC and IRV between high-flow and low-flow techniques in the postoperative period, which are supposed to be easily measured in such patients.

We studied the differences in (VC) breaths and (IRV) in both the groups from the preoperative values and found that both the values increased in the low-flow group, but were not statistically significant.

Lai Y *et al*. in their study revealed a significant correlation of PEFR estimation as a predictor of POPC and suggested a low preoperative PEFR (PEF value ≤300 L/min) could indicate a potential independent risk factor for occurrence of POPC in lung cancer patients for surgery.[7]

We estimated the difference in PEFR from preoperative and postoperative period in both our study groups and found no significant difference indicating that the occurrence of POPC in elective peripheral surgeries is independent of the flow rates used intraoperatively.

The preservation of hemodynamic stability has been proven by some researches in low-flow anesthesia.[10] However, in our study, hemodynamic stability was well preserved in both the groups with no significant difference between the groups.

There were some limitations of the study. We didn't study the mucociliary clearance in both the study groups due to non availability of resources. We excluded surgeries, which lasted more than two hours where the pulmonary effects of general anesthesia would have been profound because most of the surgeries concluded less than an hour.

Further research in the form of large multi-centric trials and meta-analysis is needed to gather evidence with respect to pulmonary effects of various fresh gas flows of inhalational anesthesia.

Conclusion

There is no change in pulmonary functions in the postoperative period with respect to the flow rates used intraoperatively in patients undergoing elective peripheral surgeries under general endotracheal anesthesia.

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Conflicts of interest
There are no conflicts of interest.

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