Section: Anaesthesiology

Original Research Article

POST-OPERATIVE LUNG FUNCTIONS AFTER LOW-FLOW VERSUS HIGH-FLOW ANAESTHESIA: A RANDOMIZED, DOUBLE BLIND COMPARATIVE STUDY

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Abstract

Background: Low-flow anaesthesia is prevalent in modern Anaesthetic practice due to its advantages like less operating room pollution, preservation of heat & humidity of the respiratory system and reduction in the costs. Not many studies have been done to compare the vital capacity (VC), inspiratory reserve volume (IRV) and peak expiratory flow rate (PEFR) measurements in both low-flow & high flow anesthesia. We evaluated the effects in both scenarios on the Pulmonary functions using respirometer, before and after General Anaesthesia (GA). **Materials and Methods:** A prospective randomized double-blind study was conducted in eighty patients, belonging to American Society of Anesthesiologists physical status class 1 or 2, undergoing elective peripheral surgeries under GA. The patients were divided into two groups, Group 1- Low-flow Anaesthesia with oxygen (O_2) (0.5L) + nitrous oxide (N_2O) (0.5L) + Sevoflurane (2.5%) and Group 2 - High-flow Anaesthesia with O_2 (2L)+ N_2O (2L) + Sevoflurane (1.5%). The preoperative values of VC, IRV and PEFR were compared with their postoperative values after GA in both the groups. **Result:** Both groups showed similar differences in VC, IRV and PEFR which were statistically not significant (p - 0.172, 0.98 and 0.212 respectively). The variation in breath holding time, single breath count and respiratory rates was also found to be similar in both the groups (p-0.687, 0.101 and 0.457 respectively). **Conclusion:** The pulmonary functions in postoperative period remained unchanged with respect to intraoperative flow rates in patients undergoing peripheral surgeries under General Anaesthesia.

INTRODUCTION

Postoperative pulmonary complications (POPC) are the primary cause of overall peri-operative morbidity and mortality. These complications range from bronchospasm, atelectasis, infection (tracheobronchitis, pneumonia) to prolonged mechanical ventilation. Anaesthetic agents are known to suppress the respiratory drive and as a result show diminished responses to both hypoxemia and hypercapnia. Relaxation of the diaphragmatic and chest wall muscles during general anaesthesia (GA) causes significant reduction in the functional residual capacity (FRC). This reduction in lung volume is the cause of atelectasis following GA, but quite often it is clinically insignificant. Together, the altered compliance, retained airway secretions and impaired ventilation cause atelectasis in the dependent lung regions which in almost 50% of the patients may persist for over 24 hours. The resultant ventilation-perfusion (V-Q) mismatch and increased shunt fraction can lead to arterial hypoxemia.[1] Recruitment of the collapsed alveoli can happen with measures like deep breathing and effective cough which help to clear out the secretions and mucus plugs.[2,3] The capacity of maximum breathing and effective cough, measured in terms of vital capacity (VC) however gets reduced due to the loss of effective lung volume because of atelectasis.

Low-flow anaesthesia technique has been found to be beneficial in reducing the mucus blocking the small airways and resulting alveolar collapse, thereby causing less impairment of the pulmonary function. It is also preferred over high-flow anaesthesia for other benefits like better protection of heat and humidity of the respiratory system, reduction in both cost as well as operating room (OR) pollution.[4,5] These advantages make low-flow anaesthesia more acceptable.[4,6] The effect was earlier proved by measuring forced expiratory volume in the first second of expiration (FEV1) and forced vital capacity (FVC), both found to be lower in the high-flow anaesthesia groups.[7] To reduce the respiratory complications, it has been recommended to use respirometer for maximal sustained inspiration (MSI) in the immediate postoperative period. But existing atelectasis post GA causes reduced VC which affects the patient's ability to perform MSI.

Postoperative pulmonary functions (POPF) can be measured in an easy way by measuring VC and Inspiratory Reserve Volume (IRV). Several studies have given controversial or mixed results regarding POPF when low-flow and high-flow anaesthetic techniques are used.[7,8] The use of spirometry for assessing the lung functions in terms of FEV1 and FVC has been validated in previous studies. Despite the presence of atelectasis,[9] haemoglobin oxygen saturation (SpO_2) was found to be maintained between the high-flow and low-flow groups, suggesting that oxygenation is well maintained even with the available alveolar exchange.[8] Incentive spirometry (IS) encourages breathing in over the tidal volumes. The lung volumes generally have a tendency to fall after abdominal surgeries. IS helps patients to take slow, long and deep breaths to increase the lung inflation. IS therefore can be used as a simple means to improve the lung function especially IRV during spontaneous breathing in the postoperative period.

Peak expiratory flow rate (PEFR) is a marker of the lung function in the postoperative period. A simple hand-held device, Peak expiratory flowmeter is easily used to detect the maximal effort made by a patient during forceful exhalation and any obstruction in the airways.

The main aim of this study was to compare the effects of low-flow versus high-flow anaesthesia on IRV and VC using respirometer. The secondary objective was to compare other parameters like Single Breath Count (SBC), Breath holding time (BHT), Respiratory Rate (RR) and PEFR in both the groups.

MATERIALS AND METHODS

This was a randomised double-blinded study conducted after obtaining approval from the Institutional Ethics Committee. Eighty-eight patients aged between 18 and 60 years of age, belonging to American Society of Anaesthesiologists (ASA) physical status class 1 or 2, posted for elective peripheral surgeries under GA with endotracheal intubation were included in the study. Exclusion criteria was - patients ASA physical status class 3 and above, emergency surgeries, thoraco-abdominal surgeries and those unwilling to participate in the study. A written informed consent was obtained from all participant patients as per the tenets of Helsinki's Declaration, after explaining the study protocol to them. All the enrolled patients were randomly grouped into Group 1: Low-flow anaesthesia and Group 2: High-flow anaesthesia group. Randomisation was done by lottery system using opaque envelopes.

Use of spirometer and breath holding procedure was explained to all participating patients before anaesthesia and surgery. BHT was recorded after asking the patient to take a deep breath and hold it for as long as they could, in sitting posture. The time for which they could hold the breath was recorded in seconds. Best of those 3 readings was taken as BHT. It was recorded both pre- & post-operatively.

Similarly, the patient was asked to count numbers after taking in a deep breath. The count until as far as the patient could, was noted as SBC. The best of 3 readings was noted. PEFR was measured by asking the patient to blow air into the mouthpiece of the Wright's flowmeter held in his hand and noting the value where the small plastic arrow stops moving. The best of three readings was recorded. Inspiratory Flow Rate (IFR) was recorded after proper instructions to the patient .The patient was instructed to inhale in sitting posture . After closing the lips around the mouthpiece of the Wright's flowmeter, the patient was instructed to slowly inhale until unable to breathe-in more. They were then asked to hold the breath for two to three seconds then exhale slowly and normally for a few seconds after removing the mouthpiece. This enables to maintain maximal inspiration thereby reducing the risk of progressive collapse of individual alveoli. After completing this procedure, the patients were asked to cough out to clear any mucus and take a deep breath. The same procedure was repeated thrice with the patients and the best of the three readings was noted. This procedure of spirometry was conducted both pre & postoperatively for assessment of IFR. Hence the lung functions were assessed using IFR, BHT, PEFR, SBC. In case of accidental cough or sneeze during the procedure, it was repeated.

All patients were kept nil per orally (NPO) for 8 hours prior to surgery and received a premedication with tab Alprazolam 0.25mg at night before surgery and on morning of surgery (with a sip of water). On the day of surgery, after being shifted to the operation theatre complex, an intravenous (i.v.) line was secured with 20G cannula and an infusion of Ringer Lactate was started @2ml/kg/hr for the patient. Randomisation was done by lottery system using opaque envelopes for both the groups. All routine monitoring like electrocardiography (ECG) for heart rate (HR), Non-invasive Blood pressure (NIBP) and haemoglobin peripheral oxygen saturation (SpO_2) was initiated.

After adequate preoxygenation, all patients were given Inj. Midazolam 1mg i.v., Inj. Fentanyl 1-2 mcg /kg body weight (b.w.), Injection Propofol 2 mg/kg b.w. and after check ventilation, the patient was paralysed with injection Vecuronium 0.1mg/kg b.w. and the trachea was intubated with disposable polyvinyl chloride, cuffed Endotracheal Tube (ETT) size 7mm (in females) and 7.5mm (in males). The ETT position was confirmed by end tidal carbon-dioxide ($EtCO_2$) trace and auscultation to confirm bilateral equal air entry before securing the ETT with

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a tape. A heat-moisture exchanger was used between the breathing system and the ETT.

In group 1- Low-flow anaesthesia was maintained with O_2 (0.5L) + N_2O (0.5L) + Sevoflurane (2.5%). In group 2- High-flow anaesthesia was maintained with O_2 (2L) + N_2O (2L) + Sevoflurane (1.5%) Intraoperative monitoring like HR, NIBP, fraction of inspired oxygen (fiO_2), RR, SpO_2 along with $EtCO_2$ were done at every 5 min. Surgical duration was noted and at least 20 min prior to closure, no opioid, benzodiazepine or muscle relaxant was repeated. The residual neuromuscular blockade at the end of surgery was reversed with Inj. Neostigmine 50 mcg/kg b.w. and Inj. Glycopyrrolate 20 mcg/kg b.w. The trachea was extubated after the patient regained consciousness and airway protective reflexes were found to have returned. Post-surgery all patients were shifted to post anaesthesia care unit (PACU) for monitoring. Injection diclofenac sodium 75mg i.v. as infusion was given to patients postoperatively for pain relief. Maximum of 2 doses at 12 hourly interval were given in 24 hrs. In case further analgesic was required, Inj. Paracetamol 1gm i.v. infusion was given. All patients were monitored for HR, NIBP, SpO_2, RR. Postoperative spirometry was performed at first, second, eighth and 24th hour. SBC, BHT, IRV, VC and PEFR were recorded. In order to blind for the group allocation, the study was performed by a different anaesthesiologist whereas recording and evaluation of the data was performed by another one. The anaesthetist who recorded and evaluated the data was blind to the group allocation.

Statistical Analysis

Statistical analysis of the data was done using software version SPSS 20.0 (IBM Corp., Armonk, NY USA). Based on previous study comparing the effects of low-flow and high-flow inhalational anaesthesia on PFT,[10] a minimum sample size of 40 per group was required for 95% confidence interval and power of study 80%. Intergroup comparison of PFT and the operative time was done using Student's t-test. Haemodynamic parameters were evaluated using repeated measures analysis of variance (ANOVA). All results for continuous variables were expressed as mean ± SD, for categorical variables the results were expressed in numbers (percentages) and were evaluated at a 95% confidence interval with a significance level of $P < 0.05$.

RESULTS

From the eighty-five patients screened for eligibility, eighty patients were enrolled into 2 groups; forty patients in group 1 and group 2 each. Five patients whose surgery lasted for more than 1.5 hours were excluded from the study.

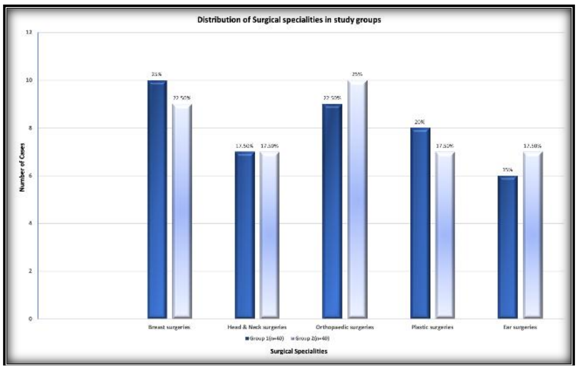

Figure 1: Distribution of number of surgeries in different Surgical specialities in both the study groups

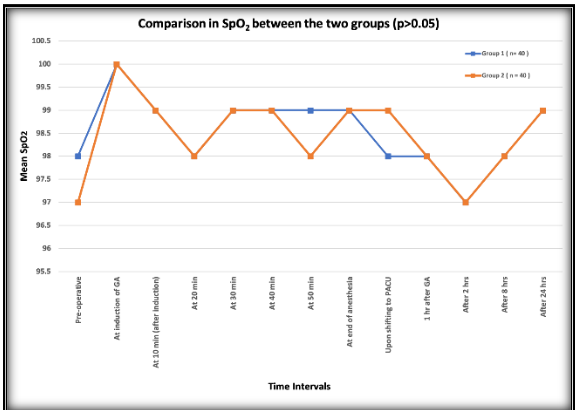

Figure 2: Comparison in SpO_2, between the two groups (p>0.05)

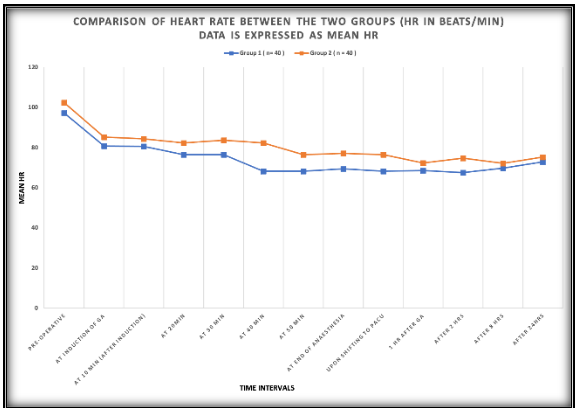

Figure 3: Comparison of heart rate(HR) between the two groups (HR in beats/min) (data is expressed as mean HR)

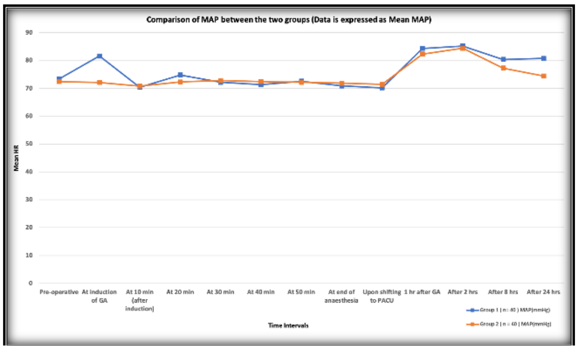

Figure 4: Comparison of mean arterial pressure(MAP) between the two groups (Data is expressed as mean MAP)

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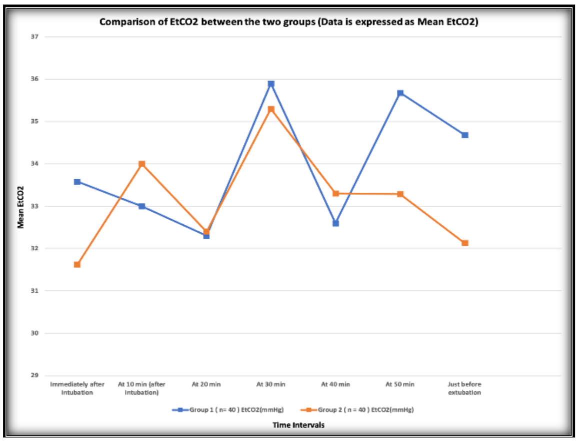

Figure 5: Comparison of end tidal carbondioxide ($EtCO_2$) between the two groups (Data is expressed as Mean $EtCO_2$).

Demographic parameters were comparable amongst the two groups [Table 1]. Different types of surgeries (numbers/percentages) are depicted in [Figure 1]. Intraoperatively SpO_2, HR, mean arterial pressure (MAP) & $EtCO_2$ were monitored and the results were found to be comparable between the two groups and these are depicted in [Figures 2-5] respectively. During surgery, the ventilation was adjusted to maintain $EtCO_2$ between 30-35 mmHg in both the groups.

Both the groups showed similar results with respect to preoperative and postoperative PFT. The difference in the postoperative values of VC and IRV in either group were found to be comparable from 1 hour after the surgery till the first 24 hours postoperatively and these are presented in Tables 2 & 3 respectively. The difference in pre-operative and at 1 hour post-operative values of VC and IRV between the two groups were found to be statistically insignificant with 'p' value of 0.172 and 0.98 respectively [Table 4]. The difference in PEFR values between the two groups was also found to be similar at 1 hour post-operatively with a 'p' value of 0.212 [Table 4].

The difference from the pre-operative values in SBC, BHT and RR between the two groups at 1 hour post-operatively was also found to be statistically insignificant [Table 4]. No side effects or complaints were noticed in the study groups.

Table 1: Demographic profile of patients and Operative Time (continuous variables are expressed in mean ± SD, categorical variables are expressed in numbers)

Parameters	Group 1 (n=40)	Group 2 (n=40)	P
ASA physical status (1/2) 'n'	31/9	30/10	-
Age (years)	36.97± 12.41	40.45 ±16.69	0.12
Sex (male/female) 'n'	25/15	27/13	-
Weight (kg)	57.05± 6.59	55.6 ± 7.83	0.520
Height (cm)	157.43± 4.70	159.04 ± 3.9	0.35
Operative Time (min)	63.50 ± 14	65.7 ± 15.6	0.519

ASA-American Society of Anesthesiologists, n=numbers, SD=standard deviation

Table 2: Difference in VC between the two groups in the post-operative period at different time points (Data is expressed as Mean ± SD)

Parameter	Time- point	Group 1 (n=40)	Group 2 (n=40)	P value
VC (ml)	1 hr	802.28 ± 420.94	699.08 ± 405.35	0.172
	2 hrs	804.02 ± 602.12	596.04 ± 449.89	0.122
	8 hrs	730.15 ± 614.89	562.70 ± 458.32	0.089
	24 hrs	638.46 ± 635.26	428.35 ± 414.10	0.068

VC – vital capacity, SD – standard deviation

Table 3: Difference in IRV between the two groups in the post-operative period at different time points (Data is expressed as Mean ± SD)

Parameter	Time point	Group 1 (n= 40)	Group 2 (n= 40)	P
IRV Difference (ml)	1 hr	497.90 ± 371.64	497.90± 371.93	1.0
	2 hrs	446.02 ± 348.28	484.37± 376.64	0.96
	8 hrs	473.37 ± 371.64	473.35± 371.64	1.0
	24 hrs	341.39 ± 358.90	345.08± 363.91	0.98

IRV – inspiratory reserve volume, SD – standard deviation

Table 4: Difference of different variables between the two groups in pre-operative and post-operative period at 1 hr (Data is expressed as Mean ± SD)

Parameters (Difference)	Group 1 (n= 40)	Group 2 (n= 40)	'P' value
SBC (number)	7.72 ± 6.29	5.81 ± 6.31	0.101
BHT (seconds)	4.36 ± 4.58	4.67 ± 4.16	0.687
IRV (ml)	497.90 ± 371.93	497.78 ± 370.88	0.98
RR (rate/min)	0.44 ± 2.19	0.12 ± 2.29	0.457
PEFR (Litre/min)	119.66 ± 420.94	108.12 ± 43.49	0.212
VC (ml)	802.28 ± 420.94	699.08 ± 405.35	0.172

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SBC – single breath count, BHT - breath holding time, IRV – inspiratory reserve volume, RR – Respiratory Rate, PEFR – Peak expiratory flow rate, VC – Vital capacity

DISCUSSION

The contemporary low-flow anaesthesia makes use of sevoflurane, isoflurane and desflurane as volatile anaesthetic agents.[11-14] The present study showed that the pulmonary effects of low-flow and high-flow anaesthesia are comparable in the patients undergoing peripheral surgeries under GA.

GA is known to interfere with the gas exchange and lung dynamics during intra-operative period which plays an important role in pulmonary complications after surgery.[15] Study by Rock and Rich reported decrease in VC and Functional Residual Capacity (FRC) after upper abdominal surgeries.[16] We, in our study, included only the patients undergoing peripheral surgeries like orthopaedic limb surgeries, ear surgeries etc [Figure 1] to exclude surgery related pulmonary complications.

To optimise the respiratory muscle function in the post-operative period, it is a norm to use different methods like respirometer or the incentive spirometry. These methods help in deep breathing exercises to avoid POPC after GA. These respiratory exercises should ideally be started in the pre-operative period. If regularly performed, these procedures serve to maintain the small airways' patency, hence minimising atelectasis and POPC.[17] We followed it for patients in our study from the time of being seen in the Pre-anaesthetic clinic prior to scheduled surgery.

Study by Rothen et al have shown that the resulting pulmonary atelectasis during GA is the major cause of impaired gas exchange which results in pulmonary shunting. Oxygenation can be improved and atelectatic lung areas expand by performance of vital capacity manoeuvre (lung inflation up to 40cmH_2O, maintained for around 15 seconds).[18] Hence is the importance and ease of measurement of lung functions like VC, IRV, PEFR with the help of spirometry, which serves as a very beneficial tool for studying the POPC in patients receiving GA. We used these simple spirometry manoeuvres in our study to assess the result of GA on PFT in the post-operative period.

As stated above, low-flow inhalational anaesthesia has several benefits over the high-flow anaesthesia. But at the same time, there are certain disadvantages too of low-flow anaesthesia like hypoxia, hypercapnia and reaction of the inhalational agent with soda-lime which can be judiciously avoided. Due precautions were taken and adequate monitoring was done and in our study no such complications were noticed. SpO_2 and $EtCO_2$ were well maintained in the Low-flow group [Figures 2 & 5].

Comparison between the low-flow and high-flow anaesthesia techniques by Murat Bigli et al with regard to pulmonary function tests and muco-ciliary clearance in tympano-mastoidectomy patients found that forced vital capacity (FVC) and FEV1 was significantly lower in the high-flow group when compared with the Low-flow group.[7] The results for pulmonary functions while using simple flowmeter in our study were found to be comparable in both the High-flow and the Low-flow groups.

Muco-ciliary clearance helps to get rid of the inhaled particles and microbes from the respiratory tract and forms an integral part of the lung's defence mechanism.[19,20] Impairment of muco-ciliary clearance causes retention of secretions, micro atelectasis and lower respiratory tract infections, thereby causing serious pulmonary complications. GA is known to impair the muco-ciliary clearance.[21,22] Our study had certain limitations. The muco-ciliary clearance was not studied in either of the groups because of the unavailability of required resources. The surgeries lasting for more than one and a half hours were excluded from the study to avoid bias on the pulmonary effects of GA in them.

Cohan Doger et al on comparing low-flow and high flow techniques in laparoscopic abdominal surgeries, found that the results were comparable in terms of FVC and FEV1 between the groups.[8] The results in our study with respect to pulmonary functions were also found to be comparable irrespective of the flows used.

Lai Y et al in their study (limited to lung cancer patients) found a significant correlation between PEFR as a predictor of POPC. They suggested a low preoperative PEFR (PEF value $\leq$ 300 L/min) as a potential independent risk factor for POPC in lung cancer patients undergoing surgery.[10] Our study which included healthy patients without any pulmonary co-morbidity, showed comparable results for difference in PEFR (pre and postoperatively)in both the study groups, indicating that in elective peripheral surgeries, POPC are independent of the intraoperative flow rates being used during GA.

There has been considerable lack of evidence on the specific pulmonary benefits during low-flow anaesthesia techniques in comparison to the high-flow ones due to mixed results from previous randomised control trials (RCTs) in various clinical studies. VC and IRV during the post-operative period have not been compared by most. These easily measured volumes have been compared in our study between the low-flow and high-flow anaesthesia techniques. Both values were studied in the preoperative and postoperative period in the low-flow and high-flow anaesthesia groups and showed a rise in the low-flow group in the postoperative period but the results were statistically insignificant.

Jacek Kupisiak et al in their study with low-flow and high-flow rate general anaesthesia proved that proper oxygenation and hemodynamic stability were maintained in both the groups.[23] Our study showed similar results, with SpO_2, HR, MAP and $EtCO_2$ in

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both the groups remaining statistically insignificant [Figures 2-5].

In order to collect further evidence with respect to pulmonary effects of various fresh gas flows during general anaesthesia, further research is needed in the form of meta-analysis and large multi-centric trials.

CONCLUSION

No change is observed in the pulmonary functions in the post-operative period in relation to the different flow rates being used in patients receiving endotracheal GA for elective peripheral surgeries.

REFERENCES

1. Yoder MA, Sharma S, Schwer WA. Medscape-Perioperative pulmonary management: E-medicine. Medscape.com/article 284983.
2. Aqino LM, Branco, JN, Bernardelli GF. Short duration transcutaneous electrical nerve stimulation in the post-operative period of cardiac surgery. Arq Bras Cardiol 2010 ; 94 : 325-31.
3. Ray K,Bodenham A, Paramasivam E. Pulmonary atelectasis in anesthesia and critical care. CEACCP 2014;14:236-45.
4. Baum JA, Aitkenhead AR. Low-flow anaesthesia. Anaesthesia 1995; 50 (Suppl):37-44.
5. Baum JA. Low-flow Anesthesia: theory, practice, technical preconditions, advantages and foreign gas accumulation. J Anesth 1999; 13:166-174.
6. Baum J. Clinical applications of low flow and closed circuit anesthesia. Acta Anaesthesiol Belg 1990; 41:239-247.
7. Bigli M, Goksu S, Mizrak A, Cevik C, Gul R, Koruk S, et al. Effects of low flow and high flow inhalational anesthesia with nitrous oxide and desflurane on mucociliary activity and pulmonary function tests. Eur J Anesthesiology 2011;28:279-83.
8. Doger C, Kahveci K. Effects of Low-flow sevoflurane anesthesia on pulmonary functions in patients undergoing Laparoscopic Abdominal Surgery. Biomed Res Int 2016; 2016. Article ID 3068467,5.
9. Pinheiro AC, Novais MC, Neto MG, Rodrigues MV, de Souza Rodrigues E Jr, Aras R Jr, et al. Estimation of Lung vital capacity before and after coronary artery bypass grafting surgery: A comparison of incentive spirometer and ventilometry. J Cardiothoracic Surg 2011;6:70.
10. Lai Y, Wang X, Li P, Li J, Zhou K, Che G. Preoperative peak expiratory flow for predicting postoperative pulmonary complications after lung cancer lobectomy. J Thorac Dis 2018;10:4293-301.
11. Elbert TJ, Arain SR. Renal responses to low-flow desflurane, sevoflurane and propofol in patients. Anaesthesiology 2000; 93:1401-1406.
12. Odin I,Feiss P. Low flow and economics of inhalational anaesthesia. Best Pract Res Clin Anaesthesiol 2005;19:399-413.
13. Hendrickx JF, Coddens J, Callebaut F, et al. Effect of N2O on sevoflurane vaporiser settings during minimal and low-flow anaesthesia.Anaesthesiology 2002; 97:400- 404.
14. Cherian A, Badhe A. Low-flow anaesthesia at a fixed flow rate. Acta Anaesthesiol Scand 2009; 53:1348- 1353.
15. Ferreyra G, Long Y, Ranieri VM. Respiratory complications after major surgery. Curr Opin Crit Care 2009; 15:342-348.
16. Rock P, Rich PB.Postoperative pulmonary complications. Curr Opin anaesthesiol 2003;16: 123-31.
17. Azhar N. Preoperative optimization of lung function. Indian J Anaesthesiology 2015; 59:550-6.
18. Rothen HU, Neumann P, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G. Dynamics of reexpansion of atelectasis during general anesthesia. Br J Anaesth 1999; 82:551-6.
19. Cohen IL, Weinberg PF, Fein IA, Rowinski GS. Endotracheal tube occlusion associated with the use of heat and moisture exchangers in the intensive care unit. Crit Care Med 1988; 16: 277- 279.
20. Antunes MB, Cohen NA. Mucociliary clearance- a critical upper airway host defense mechanism and methods of assessment. Curr Opin Allergy Clin Immunol 2007; 7:5- 10.
21. Martin C, Perrin G, Gevaudan MJ, Saul P, Gouin F. Heat and moisture exchangers and Vaporising humidifiers in the intensive care unit. Chest 1990; 97:144-149.
22. Ledowski T, Manopas A, Lauer S. Bronchial mucus transport velocity in patients receiving desflurane and fentanyl vs. sevoflurane and fentanyl. Eur J Anaesthesiol 2008; 25:752-755.
23. AKupisiak J, Goch R, Polenceusz W, Szyca R, Leksowskic K. Bispectral index and cerebral oximetry in low-flow and high-flow rate anaesthesia during laparoscopic cholecystectomy. Videosurgery and Other Miniinvasive Techniques 2011; 6 (4):226-230.