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RESEARCH ARTICLE

Comparison between Low Flow and High Flow Sevoflurane Isocapnic Technique to Achieve Early Recovery after Surgery (ERAS)

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Abstract

Objective: the purpose of this study was to compare recovery time between low flow and high flow sevoflurane isocapnic anesthesia techniques, as well as the total consumption of sevoflurane. Design: This study was an observational single-blind randomized trial setting Operating room. Patients: Total 40 patients from gender, 18 to 60 years old, BMI 18.5-29.99 kg/m^2 with physical status ASA I or II, that scheduled for elective surgery under general anesthesia approximately between 3-5 hours were selected for this study. Intervention Selected patients divided randomly into two groups (n=20 each). First group was given low flow sevoflurane, delivered with initial flow 6 L/min until MAC 0.9 or expiration level of sevoflurane 2.2 vol% then reduced flow to 0.5 L/min; second group with high flow technique 4L/min after induction. Measurement The duration of operation, duration of anesthesia, time reaching of BIS 75, eye-opening with command, extubation, moving into the recovery room and when reaching Modified Aldrete score 10. Main Results: Based on statistics, sample characteristics, hemodynamic conditions, length of anesthesia and number of fentanyl were not significantly different. There was a significant difference on post anesthesia recovery time between low flow and high flow anesthesia time BIS 75: 1.7 (± 0.801) vs 7.05 (± 3.956), p<0.001, eye-opening time: 5.45 (± 3.82) vs. 14.86 (± 7.945), p<0.001, extubation time: 5.8 (± 2.783) vs. 15.29 (± 8.776), p<0.001, moving into recovery room: 15.35 (± 5.133) vs. 23.52 (± 12.213), p=0.021, time reaching modified aldrete 10: 8.95 (± 4.211) vs. 29 (± 18,091), p<0.001). Conclusion: Recovery time after general anesthesia using low flow sevoflurane isocapnic anesthesia technique is faster than the high flow anesthesia technique with less sevoflurane consumption.

Keywords: *ERAS, Low flow, Modified Aldrete, End-tidal gas concentration, Bispectral index, Isocapnic.*

Introduction

Development in medical sciences, that encourages us to cut expense, to achieve a better result, arise efficient thinking to reach ERAS (early recovery after surgery).ERAS becomes the main topic in the last decade. The purposes of ERAS are decreasing time of hospital admission, early mobilization and eventually to reduce the whole cost with a better outcome[1, 3].

As we know that ecosystem impact of inhalation agent could hazard the ozone layer. Hence, the decreased of inhalation agent consumption, will reduce the harm to surrounding include to the medical team [4]. The low flow anesthesia technique that reduces fresh gas flow rate will decrease the consumption of inhalation agents and the cost of anesthesia. This study aims to evaluate recovery time after anesthesia and to compare sevoflurane consumption between low flow and high flow technique [3, 6].

Material and Methods

This observational single-blind randomized trial was conducted after approval from our institutional ethics committee and written informed consent from all subjects. Patient from both gender, aged between 18 to 60 years old, BMI between 18.5-29.99 kg/m^2 with physical status ASA I or II, that scheduled for elective surgery under general anesthesia approximately between 3-5 hours were selected for this study. They with allergy history of any drugs that used in this study, brain injury, brain tumor, asthma, COPD, chronic use of opioid or benzodiazepine, contraindication of sevoflurane, bleeding more than 1500 ml were excluded from this study. The total patients were 40 patients.

They were randomized single-blind used coin manner to decide which will receive low flow either high flow technique (*n* =20 each). Initially after arrived at operating theater, catheter vein access was secured. Put on a cardiac monitor, non-invasive blood pressure measurement, pulse oximetry, and an electrode for BIS monitoring on the forehead. Both techniques included premedication with dexamethasone 10 mg IV, diphenhydramine 10 mg IV, induction with propofol, followed by fentanyl 2 µg/kg BW IV, atracurium 0.5 mg/kg BW IV and ketorolac 30 mg IV if no contraindication.

The Procedure of Low Flow Technique Anesthesia

Induction started with propofol 1-2 mg/kg BW titrated until loss of eyelash reflex and ventilated using a face mask, a rebreathing system with minimal leak and carbon dioxide absorber at fresh gas flow 6 L/min (2: 4; air: oxygen). Followed by 1.5-2 vol% of sevoflurane until expiratory sevoflurane level at 2.2 vol% or MAC 0.9, then the gas flow reduced to 0.5 L/min. (0.4-0.1: oxygen-air). For intubation facilitation was atracurium 0.5 mg/kg BW and intubation were executed 3 minutes after that.

Maintenance intra-operative, sevoflurane vaporizer dialed at 2-3.5 vol% to reach bispectral index between 40-55, and MAC 0.9 with the end-expiratory level of sevoflurane 2.2 vol%. The minute volume of respiration set until end-tidal carbon dioxide around 30-45.

The Procedure of High Flow Technique Anesthesia

Protocol for induction and intubation in high flow anesthesia was not different with low flow anesthesia. The difference was the gas flows were set to 4 L/min. Minute volume set to reach end-tidal carbon dioxide 30-45. In both groups, fentanyl gave intermittently or when there was increase heart rate more than 20% than basal. Also, the muscle relaxant gave a base on need. At the end of surgery, residual of muscle relaxant reversed with neostigmine 1 mg iv, accompanied by sulfas atropine 0.5 mg IV. After the muscle relaxant effect was gone, stopped the vaporizer, and then increased the gas flow to 10 L/min of oxygen.

Time from induction until closed the vaporizer was noted (time of anesthesia). Time from incision until the wound closed with gauze (time of operation) was noted too. After finish the operation, and the vaporizer closed, the clock was recorded and noted when BIS reach 75, patient opened their eyes on command, extubation, move to the recovery room, and modified Aldrete 10.

Total consumption of sevoflurane was noted from anesthesia machine's log book. Total consumption of fentanyl also recorded. To compare both groups, demographic data including gender, age, body mass index, duration of operation, duration of anesthesia, ASA physical status was calculated statistically.

Shapiro-will test was used for normality test, followed by t-test for normal distribution data and Mann-Whitney test for abnormal distribution data. Numeric data were analyzed using chi-square test. The level of significance was noted as $p<0.05$ for the study. Based on a study of accelerated recovery from sevoflurane anesthesia, the standard deviation is 4.4, α of 0.05, power 0.90, we calculated the minimum sample size for each group were 17 and added by the 20% drop out probability, the sample size for each group were 20 patients.

Results

After single-blind randomized, 20 patients were included in high flow anesthesia technique and 20 patients in low flow anesthesia technique. Both groups were compared based on their demographic parameters (age, gender, BMI, ASA physical status, duration of operation, duration of anesthesia) (Table 1). Mean arterial pressure and pulse basal, intra operation, before extubation between two groups also comparable (Table 2). Doses of opioid were comparable (Table 3).

Table 1: Demographic data and duration of surgery

Variable	Group		P value
	Low Flow Anesthesia N = 20	High Flow Anesthesia N=20	
Sex	M 35% (7) F 65.0% (13)	M 38.1% (8) F 61.9% (13)	0.837[a]
Age (years old)	42 (19 - 59)	40 (19 - 59)	0.737[c]
BMI (kg/m^2)	22.85 (17.57 – 30.47)	21.60 (19.05 – 30.42)	0.548[b]
Duration of operation (min)	176 (133 – 370)	186 (135 – 285)	0.147[b]
Duration of anesthesia (min)	195 (148 – 408)	205(170 – 309)	0.219[b]
ASA physical status	I : 50% (10) II : 50% (10)	I : 52.4% (11) II : 47.6% (10)	0.879[a]

- Chi Square test, $p < 0.05$ significant
- Mann Whitney test, $p < 0.05$ significant
- ct test, $p < 0.05$ significant

Table 2: Hemodynamic basal, intraoperative, extubation

Hemodynamic	Group		P value
	Low Flow Anesthesia (N = 20)	High Flow Anesthesia (N = 20)	
MAP basal	93 (83-116)	93 (53-116)	0.814[b]
Pulse Basal	84± 1	80 ± 2	0.433[a]
MAP intra-op	86 ± 1	88 ± 9	0.580[a]
Pulse intra-op	85 ± 1	82 ± 2	0.814[b]
MAP ekstube	92 ± 1	88 ± 10	0.250[a]
Pulse ekstube	89 ± 1	82 ± 1	0.069[a]

- t test, $p < 0.05$ significant
- Mann-Whitney test, $p<0.05$ significant

Table 3: Sevoflurane and fentanyl consumption in both groups

Variable	Groups		P value
	Low Flow Anesthesia (N = 20)	High Flow Anesthesia (N = 20)	
Sevofluran consumption	21 (18 – 32)	74 (19 - 111)	<0.001[a]
Fentanyl	225 ± 6.69	236 ± 8.00	0.893[b]

- *Mann Whitney*, $p < 0.05$
- *t-test*

Consumption of sevoflurane was higher in high flow group than low flow group (21.8 ± 3.7ml vs. 75.9 ±1.8ml) with p-value< 0.01

The low flow group had a shorter time to emerge (BIS >75, eye-opening, extubation, move to RR, modified Aldrete 10) compare to high flow group (Table 4).

Table 4: Emergence time in average (SD) on both groups

Variable	Groups				Nilai p
	Low Flow Anesthesia (N = 20)	95% CI	High Flow Anesthesia (N = 20)	95% CI	
BIS_75	1.7 (±0.801)	1.32-2.08	7.05(±3.956)	5.25-8.85	<0.001 [a]
Open eye	5.45(±3.82)	3.66-7.24	14.86(±7.945)	11.24-18.47	<0.001 [a]
Extubation	5.8(±2.783)	4.50-7.10	15.29(±8.776)	11.29-19.28	<0.001 [a]
Move to RR	15.35(±5.133)	12.95-17.75	23.52(±12.213)	17.96-29.08	0.021 [a]
Modified aldrete10	8.95(±4.211)	6.98-10.92	29(±18.091)	20.76-37.24	<0.001[a]

Mann Whitney, $p < 0.05$

There were no differences in opiates consumption statistically. In this study, we used fentanyl. The amount of muscle relaxant was not analyzed, because before stop the sevoflurane vaporizer, we make sure that the residual effect of muscle relaxant fulfills the extubation criteria.

Discussion

Inhalation anesthesia technique is a technique that uses volatile agent main agent in general anesthesia. This inhalation technique has been done for centuries started from Nitrous oxide until sevoflurane and desflurane recently, even before intra-vein agent found. Sevoflurane is known as a volatile agent with a lower blood-gas coefficient that makes it more rapid for induction but with a high cost as stated by Ebert in 1998 [7,8].

Anesthesia cost is really important for the institution that will impact to anesthesia service that forced us to use drugs efficiently. We chose this technique in this study because the lower blood-gas coefficient of sevoflurane will reduce the time for induction and emergence [9, 11].

Because of the high price of the sevoflurane, we chose low flow anesthesia that will reduce consumption of sevoflurane significantly. In this study, participants that fulfill inclusion criteria were picked by consecutive sampling then will be fixed which will be handling with low flow or high flow anesthesia then follow the work procedure that stated before. The characteristic of the sample which contains 20 samples from high flow anesthesia with 10 samples ASA 1 and 10 samples ASA 2, 20 samples from low flow anesthesia group which contain 10 samples ASA 1 and 10 samples ASA 2. Continuous data displayed in mean ± SD.

Independent test for comparing body weight, age, anesthesia duration, and the duration of operation. While Pearson's chi-square test used for ASA physical status and sex, after Shapiro's Wilk test, an only age that distributes normally in both group, so we continued t-test for age and Mann-Whitney for another variable. From demographic data, found that there is no differential significantly between two groups, which mean could be compared. We also noted the hemodynamic pre-anesthesia, durante operative and the time of extubation. Then from analysis, we conclude that the hemodynamic not different statistically between two groups.

We noted mean arterial pressure (MAP), pulse rate. The results are: MAP basal 95 ± 8 vs 93 ± 1 with p=0,990 (p>0, 05), pulse basal 83± 1 vs 80 ± 2 with p = 0.433(p>0, 05). MAP intra-operative 86 ± 1 vs 88 ± 9 with p = 0.580 (p>0, 05), pulse intra-operative 85 ± 9 vs 82 ± 2 with p = 0.814 (p>0, 05). MAP extubation 92 ± 1 vs 88 ± 10 with p = 0.250 (p>0, 05). Pulse extubation 89 ± 1 vs 82 ± 1 with p = 0.069 (p>0, 05).

After the test for normality and homogeneity of the data, we noted that only MAP basal that normally distributes. We continue with a t-2 test for MAP basal and Mann-Whitney for others that distribute not normally. The result displayed that the hemodynamics do not differ significantly in both groups. This condition might be because of the design of the study. In this study, we examined the emergence time after general anesthesia with high flow vs low flow anesthesia. Frost. E.A, in 2014 claimed that many factors that influence the emergence like a high dose of drugs, long anesthesia duration, blood gas solution coefficient, the synergism of the drugs and remnant of the paralyzes drug [9]. For this purpose, we did not use benzodiazepine as premedication, duration of anesthesia between 3-5 hours, BIS monitoring to make sure the depth of the anesthesia (target 40-60) and will make sure the anesthesia drugs are not too exceeded, [12,13] TOF or clinically (capable to lift his or her head for 5 seconds) to makes sure the remnant of the paralyze drugs has gone, [14,15] also maintain the etCO2 at 35-45. As state by Katznelson R et.al in 2008, general anesthesia with et CO2 39+6, the time to emergence is more rapid than lower et CO2.

The consumption of the fentanyl was not significantly different statistically (225 ± 6.69 vs 236 ± 8.00, p = 0.893) between two groups, so we hope it will not affect the recovery time after anesthesia [16]. Katznelson. R et.al in 2008, found that patients with technique high flow anesthesia + etCO2 39±6 will emergence (open eyes by order 13.3±4,4 minute) [16]. In this study, we found that time to emergence between low flow and high flow anesthesia respectively (time to achieve BIS 75: 1.7 (±0.801) vs 7.05(±3.956), open eye by command: 5.45(±3.82) vs 14.86(±7.945), extubation: 5.8(±2.783) vs 15.29(±8.776), move to RR: 15.35(±5.133) vs 23.52(±12.213), modified

Aldrete 10: 8.95(±4.211) vs 29(±18.091)) with p<0.001. So it's mean that with low flow anesthesia technique, we can achieve rapid emergence after anesthesia and in the end, we can fulfill the target to decrease time in the operating room and enhance the possibility of ERAS (early recovery after surgery). For recovery, we used the modified Aldrete score to assess the patient for the possibility to move to the ward [17].

The article by Honemann. C et.al said thatlow flow anesthesia usage will decrease the inhalation agent until 75% that eventually will reduce the effect on the environment and ozone layers [3]. In this study we found the consumption of the sevoflurane between low flow and high flow anesthesia were 21.75 ml ± 3.71 vs 75.95 ml ± 1.82 respectively, p <0.001.

Conclusion

We can conclude that to achieve ERAS, we can use low flow anesthesia technique because with this technique the level of inhalation agent near to consumption of the patient and not exceeded, so in the end, clearance of the inhalant agent will be rapid. If the clearance of the inhalant agent from the patient's circulation is rapid, the recovery time will be quick enough and decrease the time in operating room or recovery room. On the other hand, the low usage of the inhalant agent will decrease the cost and release of the gas to the environment and the result will reduce the impact on the healthcare provider, ozone layer.

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