IJPSR (2019), Volume 10, Issue 5 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 15 August 2018; received in revised form, 17 November 2018; accepted, 25 November 2018; published 01 May 2019

COMPARISON OF 3%, 5% AND 8% CONCENTRATIONS OF SEVOFLURANE FOR INDUCTION AND INTUBATION IN ADULTS WITHOUT USING NEUROMUSCULAR BLOCKING AGENTS

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Keywords:

Anaesthetic technique, Sevoflurane, Inhalation, Mask induction, Tracheal intubation without neuromuscular agents

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ABSTRACT: Introduction: Tracheal intubation is commonly facilitated by the use of muscle relaxants. Sevoflurane fulfills the criteria for successful rapid & smooth inhalational induction when muscle relaxants are contra-indicated. **Aim:** To compare the success rate of intubation characteristics, hemodynamic changes, the effectiveness of the trapezius squeezing test for an adequate condition for intubation. **Method:** A total of 150 patients of ASA grade I and II undergoing elective surgical procedures of aged 20-60 years were included in our study. Patients on MAO-inhibitors, antidepressants, and B-blockers were excluded. 50 patients in each group; were randomized to groups A, B, and C with sevoflurane dial concentration of 3%, 5%, and 8% respectively. Before induction, priming of the circuit with allotted group done with 3 times bag full and empty cycles. Once the trapezius squeeze test is negative, IPPV (intermittent positive pressure ventilation) was continued for another one minute. Mean arterial pressure (MAP) and heart rate (HR), jaw relaxation, body movements vocal cord position; complications were recorded for all patients. **Results:** The incidence of successful intubation in the first attempt was 72%, 94%, 100% in groups A, B, and group C respectively (P≤0.0001). 14/50 patients in group A and 3/50 patients in group B required a second attempt for intubation due to the stiff jaw or moderate to severe body movement. In all groups, induction time is maximum in group A p-value <0.0001. Significant increase in mean blood pressure and pulse was present from laryngoscopy to 4 min after intubation in groups A, and group B. Cardiovascular stability is seen in group C. **Conclusion:** Higher concentration 8% sevoflurane (group C) has a faster and more successful induction with cardiovascular stability and lesser incidence of body movements, cough compare to 5% sevoflurane (group B). TST is used as an indicator of anesthesia depth, which also seems adequate and simple to perform.

INTRODUCTION: Tracheal intubation is commonly facilitated by the use of muscle relaxants. Intubation without muscle relaxants required in situations like hyperkalemia, burns, plasma cholinesterase deficiency, penetrating eye injury and myopathies.

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DOI: 10.13040/IJPSR.0975-8232.10(5).2230-35

The article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(5).2230-35

It is also advantageous in cases where intubation is necessary but neuromuscular block is not required to facilitate surgical access [1, 2]. Among all inhalation agents, Sevoflurane has a low blood gas partition coefficient, and the relative absence of pungency, the non-irritant effect on the airways, less hypotension [3], a pleasant smell makes successful rapid and smooth induction inhalation induction without using neuromuscular blocking agents [4].

Adequate depth of anesthesia must be necessary before intubation; otherwise it may lead to complications such as airway hyperreactivity or

physical injury to the patient. So, there should be a simple, repeatable, and accurate maneuver or indicator for it [5]. We have applied the trapezius squeezing test because it is a superior indicator of an adequate condition for LMA insertion compared to the jaw thrust maneuver in adults under sevoflurane anesthesia [6].

Aim: Our study aimed to compare the different concentration of sevoflurane as 3%, 5%, and 8% groups to compare the success rate of intubation, hemodynamic changes, and cough response and limb movement. We also want to compare the effectiveness of the trapezius squeezing test for an adequate condition for intubation.

Method: In this prospective, randomized, single-blinded study of 150 patients, scheduled for elective surgery, aged between 25-70 years, with ASA grading I and II with MPG-I&II required oral intubation were included in the study. Patients with associated co-morbidities like diabetes mellitus, hypertension, respiratory or cardiovascular disease, renal-hepatic or neurological diseases were excluded from the study. Patient with any anticipated difficult intubation was also excluded. Patients on MAO-inhibitors, antidepressants and β-blockers, history of malignant hyperthermia, body mass index more than 35, smokers were also excluded from the study.

A day before surgery pre-anesthetic checked up and patient's recent laboratory investigation accessed. Premedication was given as Tab. Lorazepam 0.01 mg/kg on 10 pm before surgery and deprived of any oral intake for at least 10 h. After patient comes in operation theatre, baseline pulse, NIBP recorded, 18 gauze IV cannula secured, and Ringer lactate solution started as per patient's fluid requirement was started.

A total of 150 patients, with 50 patients in each group; were randomized to groups A, B, and C with sevoflurane dial concentration of 3%, 5%, and 8% respectively, with oxygen at the flow rate of 6 L/min as a carrier gas. Before inhalation induction, priming of the circuit with allotted group inhalational concentration of sevoflurane was done with 3 times of bag full and empty cycles *via* closing and opening the patient's end of the circuit. Inj. Glycopyrrolate 0.04 mg/kg IV and Inj. fentanyl citrate 2 µg/kg diluted in 10cc, IV over 30 sec was given. Induction was started using a closed circle absorber breathing circuit and appropriate size face mask attached, sealed fit and tight over the patient face, without elevating the jaw and patient ask to take deep inspiration to full vital capacity spontaneously at a rate of 12-16 per min.

Spontaneous ventilation was first assisted and then IPPV was given at the rate of 12-16 breath/min to maintain an end-tidal carbon dioxide pressure of 33-40 mmHg. Pulse, non-invasive blood pressure, SpO_2, respiration recorded as baseline values. Similarly, end-tidal sevoflurane concentration values recorded as minimum alveolar concentration (MAC), inspiratory and expiratory sevoflurane values. All timings were recorded using the same mobile stopwatch every time.

Values were recorded on event-based as baseline, at the time of pre-oxygenation, placing the mask, loss of eyelash reflex (LOELR), at the time of trapezius squeeze test (TST) comes negative, at the time of laryngoscopy, during intubation, 1 min after intubation, 2 min after intubation,4 min after intubation. The 'loss of eyelash reflex' was assessed every 5 seconds by gentle brushing of the eyelashes of one eyelid with a finger. With the loss of eyelash reflex, trapezius squeeze test (TST) performed at every 15-sec interval.

In trapezius squeeze test, a right side trapezius muscle at the shoulder is squeezed between thumb and index finger to full thickness and full power by the intubating anesthesiologist for every 10 sec and observed for any body movement or motor response.

Once trapezius squeeze test is negative, IPPV (intermittent positive pressure ventilation) was continued for another one minute as per allocated sevoflurane group concentration with $ETCO_2$30-35 mm of Hg. Laryngoscopy is performed by an anesthesiologist, who is more than 10 years of experienced Patient intubated with a polyvinyl chloride endotracheal tube no. 7 for female and no. 8 for male respectively. We had compared cough response, vocal cords position, Jaw relaxation or any body movement. Effective ventilation was determined by observing chest wall movement, auscultation, and capnography.

In case of any moderate to severe body movement or coughing, Inj. propofol 2 mg/kg was given IV. Intermittent positive pressure ventilation (IPPV) given to prevent oxygen desaturation. After 30 seconds, the second attempt at laryngoscopy was performed. Induction time was estimated as the time taken from sevoflurane inhalation mask placed to one minute of the trapezius test become negative. Induction side effects like SPO_2<94%, breath holding, hiccup, laryngospasm, excessive salivation were also noted. Anesthesia was maintained as per patient and surgical requirement.

Statically Analysis: Results were expressed as mean± standard deviation (SD) for normally distributed quantitative variables and as frequencies with percentages for categorical variables. The groups were compared using the one-way analysis of variance (ANOVA) for continuous variables and the Chi-square, Fisher exact and Kruskal-Wallis tests were used as appropriate. The analysis of covariance (ANCOVA) was used as the multivariate analysis to evaluate the differences in hemodynamic parameters between the three groups in the presence of confounding factors; repeated measures ANOVA was performed to evaluate the differences between the variables being measured. P-values of <0.05 were considered statistically significant. All data analyses were performed using SPSS statistics for Windows version 20.0 (Armonk NY: IBM Corp).

RESULTS: All 150 patients were intubated successfully in our study. There were no differences in patient demographic characteristics between the group's **Table 1**. Baseline means blood pressure and pulse rate parameters were similar in all groups **Table 2, 3**.

TABLE 1: DEMOGRAPHICS

	Group A (n=50)	Group B (n=50)	Group C (n=50)	p value
Age	50.1 ± 10.11	48.54 ± 10.13	48.12 ± 10.32	0.593
Sex (M: F)	25:25	25:25	25:25	1.000
Weight	56.1 ± 8.46	54.16 ± 7.98	55.12 ± 7.55	0.482

P-value <0.05 is significant. Data are expressed as mean and SD. All demographic data were similar in all groups. P-value <0.05 is significant. Variables are expressed as mean ± SD values

TABLE 2: MEAN ARTERIAL PRESSURE

	Group A (n=50)	Group B (n=50)	Group C (n=50)	p value
Baseline	99.88 ± 6.42	98.58 ± 6.15	98.9 ± 5.87	0.430
Pre O_2	97.22 ± 5.50	95.26 ± 6.21	96.68 ± 4.37	0.297
Mask Placed	95.88 ± 4.85	96.33 ± 5.00	95.64 ± 5.74	0.815
Loss of eye lash reflex (LOELR)	92.96 ± 4.18	92.02 ± 4.20$^{\neq}$	88.24 ± 4.41$^{\$}$	0.000
Trapezius squeeze test (TST)	90.56 ± 4.66*	88.15 ± 3.45	86.94 ± 3.11$^{\$}$	0.000
Laryngoscopy	104.34 ± 4.01*	95.26 ± 3.68$^{\neq}$	92.6 ± 6.87$^{\$}$	0.000
Intubation	107.12 ± 5.09*	97.55 ± 4.01$^{\neq}$	93.94 ± 4.95$^{\$}$	0.000
After 1 min	91.22 ± 3.10*	93.79 ± 3.02$^{\neq}$	94.68 ± 2.96$^{\$}$	0.000
After 2 Min	99.26 ± 5.07*	92.48 ± 2.48$^{\neq}$	95.28 ± 2.94$^{\$}$	0.000
After 4 Min	97.48 ± 5.56*	90.29 ± 3.51$^{\neq}$	96.92 ± 4.32$^{\$}$	0.000

P-value <0.05 is significant. Variables are expressed as mean ±SD values* = Significance between Group A- Group B, ≠ = Significance between Group B- Group C, $= Significance between Group C- Group A Mean arterial pressure (MAP) remains raised in group A from laryngoscopy till 4min of intubation. Significant hypotension in group C compared to group B.

TABLE 3: PULSE RATE

	Group A (n=50)	Group B (n=50)	Group C (n=50)	p value
Baseline	84.52 ± 11.43	85.48 ± 9.36	86.14 ± 9.50	0.725
Pre O_2	84.66 ± 6.87	83.50 ± 9.38	83.14 ± 8.08	0.642
Mask Placed	83.28 ± 6.63	82.66 ± 9.06	82.11 ± 8.08	0.774
Loss of eye lash reflex(LOELR)	82.96 ± 7.66	80.73 ± 7.48$^{\neq}$	80.98 ± 8.06	0.168
Trapezius squeeze test (TST)	82.16 ± 4.64	80.34 ± 6.50	80.18 ± 8.03$^{\$}$	0.1344
Laryngoscopy	100.44 ± 5.26*	84.04 ± 4.64$^{\neq}$	80.64 ± 6.97$^{\$}$	0.000
Intubation	103.48 ± 7.99*	88.8 ± 6.64$^{\neq}$	82.48 ± 5.24$^{\$}$	0.000
After 1 min	94.8 ± 7.03*	84.68 ± 4.05	82.04 ± 6.82$^{\$}$	0.000
After 2 Min	92.78 ± 4.63*	84.92 ± 4.30	82.16 ± 4.09$^{\$}$	0.008
After 4 Min	90.78 ± 7.13*	80.92 ± 7.91$^{\neq}$	82.84 ± 8.81$^{\$}$	0.000

P-value <0.05 is significant. Variables are expressed as mean ±SD values; * = Significance between Group A- Group B, ≠ = Significance between Group B- Group C, $= Significance between Group C- Group A; Pulse remains raised in group A from laryngoscopy till 4 min of intubation

The incidence of successful intubation in the first attempt was 36/50 (72%) and 47/50 (94%), 50/50 (100%) in groups A, B, and group C respectively (P ≤0.0001). In group A14/50 patients and 3/50 patients in the group, B required a second attempt for intubation due to the stiff jaw or moderate to severe body movement. They have given propofol 2 mg/kg IV as rescue drug **Table 5**.

In all groups, induction time is maximum in group A. (p-value <0.0001) **Table 4**.

Moderate to severe body movement was seen in 28% patients in group A, and 6% patients in group B. Cardiovascular stability is seen in group C. Complications such as laryngospasm and hypoxia are absent in all groups.

TABLE 4: DURATION OF INDUCTION CHARACTERISTICS

	Group A (n=50)	Group B (n=50)	Group C (n=50)	p value
Mean duration of Loss of eye lash reflex	152.4 ± 10.21	132.6 ± 9.32	115.3 ± 2.67	0.00018
Mean duration of Trapezius squeeze test (TST) negative	174.8 ± 13.84	148.2 ± 11.57	121.7 ± 2.21	0.0001
Mean Duration of Induction	184.8 ± 13.84	158.2 ± 11.57	131.7 ± 4.21	0.0001

Induction time is minimum in group C and maximum in group A

TABLE 5: INTUBATION CONDITIONS, RESPONSES, AND RESCUE DRUG GIVEN DURING LARYNGOSCOPY

	Group A (n=50)	Group B (n=50)	Group C (n=50)	p value
Jaw Relaxation				
Fully	8	26	44	<0.0001
Partial	28	21	6	<0.0001
Stiff	14	3	0	<0.0001
Vocal Cords position				
Open	4	20	44	<0.0001
Moving	32	27	6	<0.0001
Closed	14	3	0	<0.0001
Body Movement				
None	5	37	46	<0.0001
Mild	31	10	4	0.0028
Moderate	12	2	0	0.0010
Severe	2	1	0	0.3604
Cough	12	7	4	0.0157
propofol 2 mg/kg I.V given (rescue drug)	14	3	0	<0.0001

Better jaw relaxation and lesser coughing incidence observed in group B and C, in comparison to group A. Good intubating condition of the vocal cord is seen in group C. Full jaw relaxation is maximum in group C. Moderate to Severe body movements is maximum in group A.

DISCUSSION: This prospective, randomized, single-blinded study with 3%, 5% and 8% of sevoflurane to premeditated adult patients provides a safe, successful and pleasant induction. More acceptable intubating conditions with minimal side effects with a concentration of sevoflurane 5% and 8%.

Majority of anesthetist uses inhaled anesthetic is mainly for maintenance. The benefit of the volatile agent's cardiac protection should start from induction and adding the advantage of minimizing vapor concentration difference during the transition from intravenous to inhaled agents, what is, in effect called, a "second induction." Inhalation induction is advantageous in all cases [4, 7].

According to Stefan De Hert *et al*., [8] sevoflurane should be administered throughout the surgical procedure for acquiring the cardio-protective effects of it. The advantages of inhalation induction of anesthesia in adults were an avoidance of apnea, drug anaphylaxis and less hypotension as compared to IV induction [4]. Thwaites *et al*., [9]showed that cost of induction with 8% sevoflurane was significantly cheaper compared to propofol.

The induction time was significantly earlier in Yurino [10] study (118+/-25 sec) to that our study group B (184.8+/-13.8). They had taken eyelash reflex, and no intubation tried while we had used additional trapezius squeeze test for getting adequate depth for intubation.

Loss of eyelash reflex test became negative with 5% sevoflurane in 132.6 ± 9.32 sec in our study while it was 147 seconds in another study in children without opioids [11]. This was due to the difference in the flow rate of oxygen gas, age, and opioids are given. Higher inspiratory concentration

is mandatory to determine the optimal concentration and ventilation time for tracheal intubation [12]. In our study, the successive tidal volume ventilation expiratory sevoflurane (5.69 ± 0.21) is at a higher level but did not result in cardiovascular depression. With this, even the increase in HR and SBP after 1 min of intubation was observed in group Cat mean duration of 131.7 ± 4.21 sec. So, we are agreed with Tso-Chou Lin's [12] views that inspiratory sevoflurane concentration, not the expiratory concentration or the MAC values should be considered for tracheal intubation in the future.

In our study, in premeditated patients, HR and MAP is increased in 3% group A at time of laryngoscopy and up to 4 min after intubation. Which are comparable with another study of 6-7% sevoflurane [8]. Group C (8%) shows remarkable hemodynamic stability compared to other groups. The decrease in the MAP with sevoflurane was within 10 mm Hg in group C, and MAP had returned to baseline values within 4 min. Differences in HR and MAP between group A and B, are significant in our study. This data was compared with another study [9].

The end-tidal sevoflurane concentration where the trapezius squeezing test becomes negative was 4.1 volume % in adults having sevoflurane dial concentration of 6% for LMA insertion [6]. In our study, the end-tidal sevoflurane concentration was 5.27 ± 0.23 in group C (8% sevoflurane) and 3.12 ± 0.28 in group B (5% sevoflurane) at a time to TST become negative. A trapezius squeeze test is considered to be a less noxious stimulus than skin incision or laryngoscopy [13]. So, we have given IPPV for 1 min more beyond the TST becomes negative, to increase the depth of induction.

All patients in Group C (8% sevoflurane) and 94% patients in group B (5% sevoflurane) were incubated in the first attempt without propofol requirement. So TST is a quite a perfect predictor of enough depth of anesthesia for intubation in a higher concentration of sevoflurane. Changes in mean arterial pressure and heart rate were noticeably raised during intubation in all groups. In our study, the intubation success rate is higher and additional propofol requirement is minimal in group C only 8%. Although the effectiveness of trapezius squeezing test needs further confirmation with a larger sample of patients.

Consistent with several other reports [9, 14] airway complications rate such as laryngospasm, oral secretion, and cough are comparable to our group C **Table 4**. In our study, 8% (4/50) coughing rate was seen in group C, which was comparable to others [15, 16]. In our study, group C no limb movement was observed in 92% of patients and mild movements in only in 8%. Our data were quite compared with another study [4]. In group 3% and 5% sevoflurane group of our study, moderate body movement was observed in 24% and 4% respectively which is comparable with 6.5% incidence in Yurino [10] study that used 4.5% sevoflurane concentration.

In our study, jaw stiffness observed in 28% in group A,6 % in group B, none in group C, while it was higher in another study like 30% [16], 45% by Tl *et al*., [17] 20% by Mohmand saad [18] using 4% sevoflurane.

CONCLUSION: Sevoflurane 8% (group C) has a faster induction with cardiovascular stability and lesser incidence of body movements, cough compare to 5% sevoflurane (group B). TST is used as an indicator of anesthesia depth, which also seems adequate and simple to perform.

We found that higher concentration 8% sevoflurane for inhalational intubation is more successful at a fresh gas flow of 6 l/min and fentanyl 2 mcg/kg using trapezius squeeze test as an indicator to adequate depth for intubation in adults.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

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How to cite this article:
Khangwal SK, Shah K and Patel BM: Comparison of 3%, 5% and 8% concentrations of sevoflurane for induction and intubation in adults without using neuromuscular blocking agents. Int J Pharm Sci & Res 2019; 10(5): 2230-35. doi: 10.13040/IJPSR.0975-8232.10(5).2230-35.