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Evaluation of Low Dose Fentanyl-Midazolam Premedication on Sevoflurane Induction for Ease of LMA Insertion in Adults

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Abstract

Background: Sevoflurane, a halogenated volatile anesthetic agent and premedication with fentanyl and midazolam are both helpful in deepening the plane of anaesthesia. When used in synergism, these can aid in a smooth laryngeal mask airway (LMA) insertion. *Materials and Methods:* 80 patients of ASA I and II status, posted for minor elective surgery were randomized in a double-blind study to compare the conditions for LMA insertion following premedication with fentanyl 0.6µg/kg and midazolam 9µg/kg with Sevoflurane (Group I) and Sevoflurane alone (Group II). The time to loss of eye reflex, time for LMA insertion, ease of LMA insertion was noted and hemodynamic variables (heart rate, mean arterial blood pressure) were recorded prior to induction of anaesthesia, prior to LMA insertion and every minute after LMA insertion for 5 minutes. Secondary outcomes included evaluation of adverse effects in two groups. *Results:* The groups were comparable with respect to the demographic profile and baseline parameters. The time to loss of eye reflex as well as time taken for insertion of LMA was significantly lower in the study group as compared to the control group ($p<0.001$). The composite scoring system (comprising Jaw opening, ease of insertion, coughing, gagging, laryngospasm, movement at insertion) was higher in the study group, demonstrating better LMA insertion conditions in the study group as compared to control group, even though it is not statistically significant. Adverse effects like apnea, movement, cough, nausea, shivering were comparable in both the groups. *Conclusion:* Addition of low dose fentanyl and midazolam intravenously preceding vital capacity induction with Sevoflurane *8%* in O2 6l/min provides better conditions for LMA insertion with insignificant hemodynamic effects.

Keywords: Volatile Induction; Sevoflurane; LMA; Premedication; Midazolam; Fentanyl.

Introduction

The laryngeal mask airway (LMA) is a popular alternative to the face mask or endotracheal tube for securing the airway in patients undergoing elective surgery under general anaesthesia [1,2]. The advantages include less invasion of the respiratory tract, avoidance of laryngoscopy, endobronchial or esophageal intubation. However, satisfactory insertion of the laryngeal mask airway after induction of anaesthesia requires sufficient depth for suppression of airway reflexes else, it may lead to coughing, gagging and laryngeal spasm. Propofol is commonly used for LMA insertion but it is associated with hypotension, apnea and pain on injection.

The introduction of volatile anaesthetic agent sevoflurane, led to resurgence of interest in Inhalational induction of anaesthesia in adults [3-5]. Sevoflurane is a halogenated volatile anesthetic agent with a pleasant odour and low blood gas solubility which allows rapid, smooth inhalational induction with excellent recovery. Induction of comparable to intravenous propofol

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[6]. Sevoflurane, when used as maintenance anaesthesia allows rapid recovery and is associated with an acceptably low incidence of post-operative nausea and vomiting [6,7].

Various adjuvants when added to propofol have shown to further improve LMA insertion conditions. These include lignocaine, midazolam, low dose of muscle relaxant and opioid [8-13]. Concomitant administration of opioids such as fentanyl, alfentanyl improved conditions for LMA insertion [14,15]. Benzodiazepines like midazolam lowers anxiety levels in addition to deepening the plane of anaesthesia.

We conducted this study with the objective to compare the effect of low dose fentanyl and midazolam premedication on the ease of insertion of LMA during sevoflurane induction.

Materials and Methods

This was a randomized, double blind, comparative, prospective study. After approval from the institutional ethical committee and written informed consent, eighty adult patients in the age group of 18 to 75 years, of either sex and of ASA (American Society of Anaesthesiologists) [1] grade I or II, posted for minor elective surgery under general anaesthesia were randomly allocated into two groups using computer generated randomization list.

Group I (FM): Patients received premedication with fentanyl 0.6 µg/kg and midazolam 9 µg/kg to which normal saline was added to obtain a volume of 2.5 ml given intravenously, five minutes before tidal volume sevoflurane (8%) induction with 6L/min O2.

Group II (Placebo): Patients received 2.5 ml of normal saline given intravenously, five minutes before tidal volume sevoflurane (8%) induction with 6L/min O2.

Patient with upper respiratory tract infection, anticipated difficult airway,morbid obesity BMI > 32 kg/m2, full stomach or taking opioids, sedatives or antiepileptics were excluded. Surgeries requiring full relaxation, shared airway and head and neck surgeries were excluded.

All patients were kept eight hours fasting and given tab Ranitidine 150 mg and T. Metoclopromide 10mg HS. In the operating room, before induction of anaesthesia, intravenous access was secured and crystalloid infusion was commenced. Standard monitoring included ECG, non-invasive blood pressure, SpO2 and EtCO2.

Patients were randomized into one of the two groups of 40 each and premedication was given as per group allocation. Magill's circuit was primed with sevoflurane 8% and O2 (flow rate 6L/min) for 30 seconds. Patient was asked to exhale maximally and the primed circuit was then connected to the face mask. They were asked to take vital capacity breaths (Vital capacity technique). Loss of consciousness was defined as the time the patient stops rhythmically tapping their fingers and was confirmed by loss of the eyelash reflex. After loss of consciousness, muscle tone of the patient's jaw was assessed at every 10 seconds. The LMA was inserted by an experienced anaesthesiologist who was blinded to the drugs used. The position of the LMA was confirmed. LMA insertion conditions were graded on a 3 point scale using 6 variables and the overall conditions for LMA insertion was assessed.

Table 1: Grading of conditions for Laryngeal Mask Airway insertion

Introduction of the LMA	**3**	**2**	**1**
Jaw opening	Full	Partial	Nil
Ease of insertion	Easy	Difficult	Impossible
Patient response	**3**	**2**	**1**
Coughing	Nil	Minor	Severe
Gagging	Nil	Minor	Severe
Laryngospasm	Nil	Partial	Total
Patient movement	Nil	Moderate	Vigorous
Total score			
18	Excellent		
16-17	Satisfactory		
<16	Poor		

If the first attempt was unsuccessful, repeat administration of sevoflurane was used to deepen the plane of anaesthesia before reattempting LMA insertion. Successful insertion of the LMA denotes the end of induction of anaesthesia and commencement of the maintenance phase.

The time of induction i.e. the time (in sec) taken from induction of anaesthesia to the loss of eye lash reflex, and the time for LMA insertion was recorded in both the groups. Heart rate (HR), mean arterial pressure (MAP),Respiratory (RR), and oxygen saturation (SpO2) was recorded prior to induction of anaesthesia, prior to LMA insertion and every minute after LMA insertion for 5 minutes in both the groups. Hereafter, anaesthesia was maintained at the discretion of the anaesthesia care provider.

Bradycardia, hypotension or any other significant complications was recorded.

Statistical Analysis

The data collected was tested for normalcy. Normally distributed parametric data was analyzed using unpaired Student'st test while Chi square test was performed for categorical data. The data for which the distribution was not normal 'Mann-Whitney test was used. For comparison within the group, ANOVA test was used. p value <0.05 was considered statistically significant.

Observation and Results

The demographic variables and baseline hemodynamic parameters (HR, MAP) were statistically comparable in both thegroups (Table 2, 3).

Grading of conditions for LMA insertion was noted. Adequate jaw relaxation and low incidence of coughing, gagging was found in both the groups. Limb movements followed a similar trend. No incidence of laryngospasm was noted in either group (Table 4).

On comparing the overall condition for the LMA insertion in betweenthe two groups, it was found to be poor (<16) in 2 patients in group I and 4 patients in group II. However, it was satisfactory

Table 2: Distribution according to demographic variables

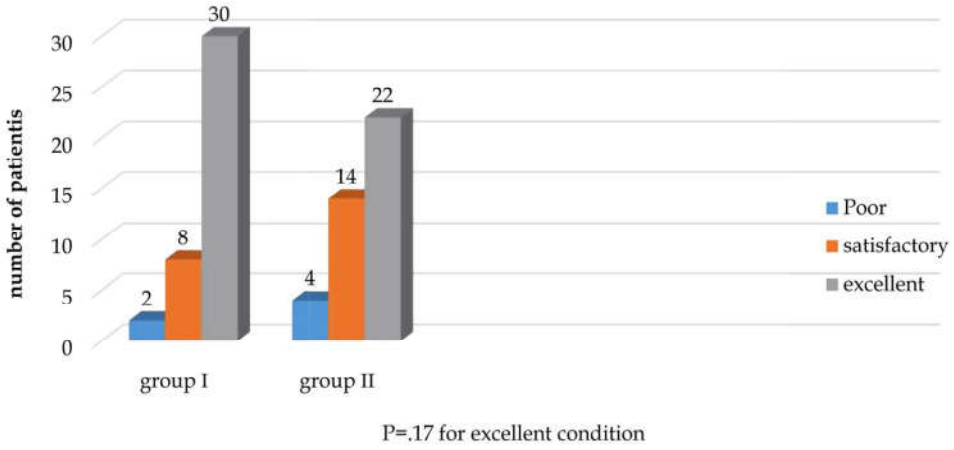
	Group I (N=40) Mean ± SD	Group II (N=40) Mean ± SD	P-value
Age	34.45±14.28	40.7±15.39	.06
Weight	57.73±11.74	61.68±17.21	.23
Height	1.62±0.092	1.51 ± 0.083	.32
BMI	21.77±4.37	22.58±6.72	.53
Sex			
Male	25(62.5%)	20(50%)	0.60
Female	15(37.5%)	20(50%)	

Table 3: Hemodynamic parameters

Heart Rate						
	Time after premedication (in minutes)					
	0	1	2	3	4	5
Group I	98.65±16.75	95.66±15.33	94.50±16.24	93.18±15.63	92.13±15.25	91.10±15.96
Group II	95.28±13.51	94.45±12.84	94.50±13.33	93.95±13.15	94.20±13.47	94.28±13.57
P Value		0.32	0.25	1.00	0.81	0.52
	Time after sevoflurane induction (in minutes)					
		1	2	3	4	5
Group I		92.58±15.37	91.25±16.51	90.38±16.72	90.20±16.47	90.40±18.20
Group II		93.15±13.67	91.78±14.04	90.93±14.56	90.13±15.29	89.40±14.43
P Value		0.34	0.86	0.87	0.88	0.98
Mean Arterial Pressure						
	Time after premedication (in minutes)					
	0	1	2	3	4	5
Group I	96.05±8.01	95.42±7.74	94.74±7.58	94.84±7.25	94.95±7.04	93.00±11.05
Group II	99.18±9.41	97.03±12.32	98.20±9.29	97.50±8.86	97.58±9.14	96.92±9.72
P Value		0.11	0.48	0.07	0.14	0.15
	Time after sevoflurane induction (in minutes)					
		1	2	3	4	5
Group I		90.53±6.64	90.03±6.86	89.03±7.06	88.38±7.29	87.29±7.32
Group II		94.65±9.07	93.21±9.58	91.70±8.27	91.00±9.77	90.93±9.81
P Value		0.02	0.09	0.12	0.17	0.06

Table 4: Grading of conditions for Laryngeal Mask Airway insertion

Score			Group I – Group (n=40)	Group II – Group (n =40)	*P* value
Jaw Opening	1	Nil	2(5.00%)	0 (.000%)	***.82***
	2	Partial	3(7.50%)	6(15.00%)	
	3	Full	35(87.30%)	34(85.00%)	
Ease of Insertion	1	Impossible	2(5.0%)	3 (7.5%)	***.30***
	2	Difficult	1(2.5%)	3 (7.5%)	
	3	Easy	37(92.5%)	34(85.0%)	
Cough	1	Severe	2(5.0%)	2(5.2%)	***.76***
	2	Minor	3(7.3%)	4(10.0%)	
	3	Nil	35(87.5%)	34(85.0%)	
Gagging	1	Severe	0(.0%)	0(0.0%)	***.49***
	2	Minor	0(.0%)	2(5.0%)	
	3	Nil	40(100.0%)	38(95.0%)	
Laryngospasm	3	Nil	40(100%)	40 (100%)	-
	2	Minor	0(0.0%)	0(0.0%)	
	1	Severe	0(0.0%)	0(0.0%)	
Patient movement	1	Vigorous	2(5.0%)	2(5.0%)	***.32***
	2	Moderate	2(5.0%)	6(15.0%)	
	3	Nil	36(90%)	32(80%)	



Graph 1: Overall conditions for Laryngeal Mask Airway Insertion

Table 5:

	Group I (N = 40) Mean± SD (sec)	Group II (N =40) Mean± SD (sec)	P Value
Time to Loss of Eye Reflex	50±0.30	72±0.38	<0.0001
LMA Insertion Time	80±0.45	100±0.35	<0.001

(16-17)in 8 patients in group I as compared to 14 in group II. But 30 patients in group I had excellent insertion condition as compared to 22 in group II. Even though group I had more ease in insertion of LMA than group II, when compared statistically between the groups, it was found to be insignificant (p value >0.05) (Graph 1).

The time to loss of eye reflex in group I was 50±0.30 sec whereas in group II, it was found to be 72±0.38 sec. This was highly significant with a p value of < 0.0001 when compared statistically. Similarly, the mean time taken for LMA insertion was found to be statistically significant with a p value < 0.001. The mean time taken was 80±0.45 sec in group I and 100±0.35 sec in group II. (Table 5).

There was no statistically significant difference in the complications or adverse events observed during the study.

Table 6: Complications on insertion of LMA

	Group I (N =40)	Group II (N=40)	P value
No complication	19 (47.5%)	23 (57.5%)	0.37
Apnea	7 (17.5%)	4 (10%)	0.15
Cough	3 (7.5%)	3 (7.5%)	1
Movement	7(17.5%)	8 (19.5%)	0.76
Nausea	2 (5%)	2(5%)	1
Shivering	2(5%)	0	0.49
Inadequate depth of anaesthesia	0	2 (5%)	0.49

Discussion

The present study was done to determine the effect of premedication on sevoflurane induction in adults and to evaluate the conditions for the insertion of LMA. Premedication with Fentanyl (.06µg/kg) and midazolam (9µg/kg) with 8% sevoflurane were used in the study group and 8% sevoflurane was used in the control group.

In the study group i.e. FM group, the overall condition for LMA insertion was found to be better when compared to placebo group, where two patients required deepening of anaesthesia again for the insertion of LMA. In the study group, LMA was inserted in all patient in the 1st attempt where as in the control group 7 patients required a 2nd attempt for insertion of LMA. Similar findings were noted by Sivalingam et al [16] where alfentanyl was used as a premedication with sevoflurane or propofol induction. Excellent condition for LMA placement were noted in the alfentanyl – sevoflurane group followed by alfentanyl –propofol group.

In our study,the time from induction to loss of eye reflex in FM group was reduced by 22 seconds and the time required for LMA insertion was reduced by >20 seconds. These findings were highly significant when compared to the placebo group. The synergistic action of low dose fentanyl and midazolam with sevoflurane was supported inthe various studies done by Muziet al [5], Lesage et al [17], Paris et al [18], and Ben-shlomo et al [5]. They demonstrated that fentanyl and midazolam act synergistically in such a way that 25% of ED50 of fentanyl was required in combination with 23% of ED50 of midazolam to achieve the ED50 for the combination. The time to loss of eye reflex varied from 35 to 90 sec in the previous studies. This difference was attributed to the different ways of induction such as single breath inhalation technique, normal breathing technique, or the vital capacity technique.

LMA was used in our study instead of tracheal intubation which was used by Muzi et al [5]. Therefore, lower dosage of fentanyl and midazolam could be used in LMA insertion as it is less stimulating than direct laryngoscopy and endotracheal intubation.

The adverse effect profile was comparable in both the groups (apnea, cough, and movement). However, apneic episodes were noted in the FM group. Similar episodes were reported by Kelly et al [19] during desflurane inhalational induction with or without fentanyl- midazolam premedication. These episodes of apnea may be attributed to hyperventilation by the patient and lowering of arterial $PaCO_2$ below respiratory threshold. The combined effect of sevoflurane and hypocarbia could have provoked apnea. After loss of consciousness, none of the patients required assisted ventilation as breathing resumed spontaneously.

The intravenous FM combination attenuates the pressor response of LMA insertion. Premedication during sevoflurane induction lowers the heart rate and blood pressure but within normal limit [16,20,21,22]. This fall in heart rate and Blood pressure is attributed to the opioid usage. Asystolic episodes on use of sufentanyl [23] and remifentanyl [24,25] have been reported but none with fentanyl.

Conclusion

A low dose combination of intravenous fentanyl-midazolam premedication administered before sevoflurane induction accelerates loss of consciousness and facilitates LMA insertion .This combination results in minimum hemodynamic variability and fewer side effects like apnea, cough, and movement

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