

## Assessment of Intubating Conditions with Different Doses of Propofol without Muscle Relaxant in Children

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### Abstract

**Background:** The aim of our study was to assess of tracheal intubation by different doses of propofol preceded by fentanyl for successful tracheal intubation and to see its effectiveness in blunting pressors response in children aged 2-10 years.

**Methods:** This prospective, blind, randomized study was conducted on 120 ASA grade I and II children, between 2 and 10 years undergoing elective surgery who were divided into three groups. The children received different doses of propofol (group I, 2.5 mg/kg; group II, 3.0 mg/kg; and group III, 3.5 mg/kg) preceded by a fixed dose of fentanyl (2 µg/kg) 5 min earlier. The tracheal intubating conditions were graded based on scoring system devised by Helbo-Hensen et al. with Steyn modification which includes five criteria; ease of laryngoscopy, degree of coughing, position of vocal cords, jaw relaxation, and limb movement and graded on a 4-point scale. Heart rate (HR) and mean arterial pressure (MAP) changes were also noted.

**Results:** Tracheal intubating conditions were acceptable in 65% of the patients in group I, while significantly higher ( $P < 0.001$ ) in group II (97.5%) and in group III (100%). The pressor response was not effectively blunted in group I (17% increases in HR), while effectively blunted in groups II and III. A fall in hemodynamic was seen in group III indicated by a decrease in MAP (16%) and HR (11%). No airway complications were noted.

**Conclusions:** Propofol 3.5 mg/kg (group III) preceded by fentanyl 2 µg/kg is the excellent dose combination in our study. It provides acceptable intubating conditions in 100% patients, blunts pressor response to intubation without significant cardiovascular depression.

**Keywords:** Tracheal intubation; Propofol; Fentanyl; Intubating conditions; Pressor response

### Introduction

The concept of tracheal intubation without the use of neuromuscular blocking drugs is well established in children [1]. This technique found its place in situations where there is contraindication to both depolarizing agents (hyperkalemia, burns, plasma cholinesterase deficiency, and penetrating eye injury) and nondepolarizing muscle relaxants (myopathies, and known allergic reactions). It is also useful in conditions where tracheal intubation is required but prolonged muscle relaxation is not, such as in ENT or short gynecologic procedures, and as a part of total intravenous anesthesia [2,3].

Several workers have successfully used a combination of propofol and a short-acting opioid to facilitate tracheal intubation in children [1,4-6]. Most of the studies revealed improvement in intubating conditions with increasing dosages of either propofol [5] or opioid [1]. Increasing dose of short-acting opioids may cause muscle rigidity, prolonged apnea and delayed recovery, while increasing dose of propofol can lead to cardiovascular depression. Therefore, We evaluated the effects of different doses of propofol preceded by a fixed dose of fentanyl on quality of tracheal intubation in children undergoing elective surgery.

### Patient and Methods

After approval from hospital ethical committee, this prospective, blind, randomized study was conducted during the period from October 2015 to December 2016. Based on the available data for the various study parameters [7] with 95% confidence and 85% power, minimum sample size was calculated as 26 in each group to obtain statistically significant results. Hence, this study was conducted in 120 patients of American Society of Anesthesiologists (ASA) I and II, aged 2-10 years undergoing inguinal and umbilical hernias, hypospadias, orthopedic and cleft surgeries, after taking consent from parents.

Patients with anticipated difficult intubation, increased risk of regurgitation, history suggestive of cardiorespiratory illness, and known sensitivity to the drugs used were excluded from this study. Patients were randomly allocated into three groups, Groups 1, II and III, by a closed envelope technique the opening of envelope by the senior resident and the preparation of propofol by another one with dilution by normal saline in fixed volume 15 ml. After a thorough preanesthetic checkup, children were kept nil per oral for 2 hours for clear fluids, and 6 hours for feeds and solids. EMLA cream was applied to potential sites of venous cannulation 1 hour prior to induction. In the preanesthesia room, an intravenous (IV) cannula of 22 or 24 G was inserted and patients were shifted into the operating theater and preinduction monitoring initiated with monitors like non-invasive blood pressure, pulse oximetry, and electrocardiogram. All patients

preceded by a fixed dose of fentanyl (2 µg/kg) 5 min earlier and atropine 0.01 5 min. before propofol induction. In all Groups, Xylocaine 1.5 mg/kg was injected intravenously before anesthesia was induced with Propofol 2.5,3, 3.5 mg/kg over a period of 30 sec intravenously. Laryngoscopy and intubation were attempted 150 sec after induction of anesthesia and patients were ventilated via face mask with 100% oxygen in the meantime. Additional bolus of 1 mg/kg of propofol was given if laryngoscopy was not possible due to muscle spasm, coughing, or excessive movements. In patients of all groups if intubation was not possible after two attempts, suxamethonium 2 mg/kg body weight was given and intubation was completed and these patients excluded from the study. In all patients laryngoscopy was done using Macintosh blade and trachea was intubated with an appropriate sized uncuffed, preformed South Pole oral endotracheal tube. Intraoperatively patients were ventilated with 100% oxygen, assisted ventilation for 5-10 min on 3% sevoflurane until good spontaneous ventilation then isoflurane 2-3% with gas flow rates of 4-6 l/min using an Ayres T piece circuit.

During laryngoscopy and intubation, each patient was assessed for five variables namely; ease of laryngoscopy, position of vocal cords, degree of coughing, jaw relaxation, and limb movements and scored accordingly [8]. The tracheal intubating conditions were graded based on scoring system devised by Helbo-Hansen et al. [7], which includes three criteria; ease of laryngoscopy, degree of coughing, and position of vocal cords. In addition two further criteria, jaw relaxation, and limb movements were also observed as modified by Steynet al. [9]. The sum of the scores of these five individual variables was computed as the Helbo-Hansen (Steyn's modification, Table 1) score [10]. Total score of 5 was considered to be excellent, 6-10 good, 11-15 poor, and 16-20 bad. Total scores were divided into clinically acceptable and not acceptable scores (total score ≤ 10 acceptable, >10 unacceptable) (Table 1). Heart rate and noninvasive mean arterial pressure (MAP) were noted at different time intervals (preinduction, postinduction and postintubation at 0, 1, 3, 5 and 15 min). Measurements at 1 min after injection of atropine were taken as baseline values.

	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Jaw relaxation	Complete	Slight	Stiff	Rigid
Limb movements	None	Slight	Moderate	Severe (jerky)

**Table 1:** Intubating condition scores (Steyn modification of Helbo-Hansen) [6,7].

Data are presented as mean (SD) or number (%). Statistical analysis was performed with chi-squared test and sign-rank test for non-parametric data and one-way ANOVA with multiple range tests for parametric data, and P-value <0.05 was considered statistically significant.

## Results

Demographic profile was comparable in all the three groups (Table 2).

	Group (2.5) N=40	Group (3) N=40	Group (3.5) N=39	P-value
Age(year)	5.9 (2.87)	5.16 (3.14)	5.8(2.55)	0.459
<b>Sex</b>				
Males	23 (57.5%)	25 (62.5%)	27 (69.2%)	0.27
Females	17 (42.5%)	15 (37.5%)	12 (30.8%)	
Weight(Kg)	19.38 (5.66)	18.2 (6.17)	19.28 (4.9)	0.64
Data are presented as mean (SD) or number (%)				

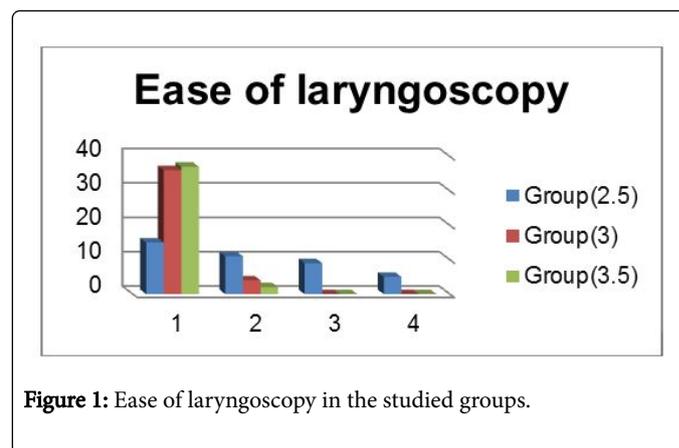
**Table 2:** Demographic data for the studied groups.

## Comparison of the intubating conditions in the studied groups

**Laryngoscopy:** In group I, laryngoscopy was easy (score 1) in 37.5% of children, fair (score 2) in 27.5% of children, difficult (score 3) in 22.5% of children and impossible in 12.5%. In group II, laryngoscopy was easy (score 1) in 85% of children and fair (score 2) in 15% of children and in group III, laryngoscopy was easy (score 1) in 94.9% of children and fair (score 2) in 5.1% of children, as illustrated in Table 3 and Figure 1.

	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
Score 1	15 (37.5%)	34 (85%)	37 (94.9%)	<0.001
Score 2	11 (27.5%)	6 (15%)	2 (5.1%)	
Score 3	9 (22.5%)	0	0	
Score 4	5 (12.5%)	0	0	

**Table 3:** Ease of laryngoscopy in the studied groups.



**Figure 1:** Ease of laryngoscopy in the studied groups.

**Position and movement of vocal cords:** In group I, vocal cords were open (score 1) in 32.5% of children, moving (score 2) in 37.5% of children, closing (score 3) in 15% and was closed (score 4) in the remaining 15% of children. In group II, vocal cords were open (score 1) in 87.5% of children, moving (score 2) in 10% of children and closing (score 3) in the remaining 2.5% of children. In group III, vocal cords were open (score 1) in 94.9% of children and moving (score 2) in the remaining 5.1% of children, as illustrated in Table 4 and Figure 2.

	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
Score 1	13 (32.5%)	35 (87.5%)	37 (94.9%)	<0.001
Score 2	15 (37.5%)	4 (10%)	2 (5.1%)	
Score 3	6 (15%)	1 (2.5%)	0	

Score 4	6 (15%)	0	0	
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Table 4: Vocal cord position of the studied groups.

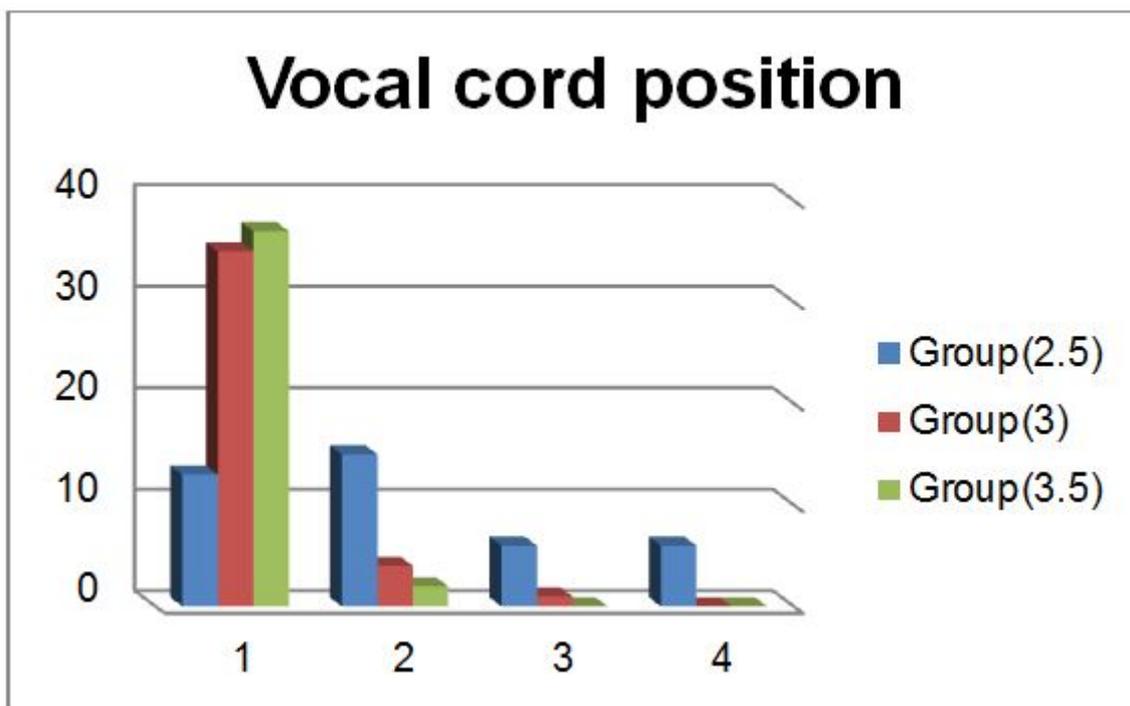


Figure 2: Vocal cord position of the studied groups.

**Coughing:** In group I, there was no coughing (score 1) in 15% of children, 40% of children had a slight cough (score 2), 30% of children had moderate cough (score 3), and 15% of children had severe cough (score 4). In group II, no coughing (score 1) occurred in 85% of children, slight cough (score 2) in 15% of children, and moderate cough (score 3) in 0% of children. In group III, 92.3% of children had no cough (score 1), 7.7% of children had slight cough (score 2), and 0% of children had moderate cough (score 3), as illustrated in Table 5 and Figure 3.

	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
Score 1	6 (15%)	34 (85%)	36 (92.3%)	<0.001
Score 2	16 (40%)	6 (15%)	3 (7.7%)	
Score 3	12 (30%)	0	0	
Score 4	6 (15%)	0	0	

Table 5: Coughing in the studied groups.

**Jaw relaxation:** In group I, jaw relaxation was complete (score 1) in 35%, slight (score 2) in 35% and stiff (score 3) in 22.5% of children and rigid (score 4) in 7.5%. In group II, jaw relaxation was complete (score

1) in 100% children and slight (score 2) in 0% children. In group III, jaw relaxation was complete (score 1) in all children, as illustrated in Table 6 and Figure 4.

**Limb movements:** In group I, there was no limb movements (score 1) in 25% children, slight (score 2) in 32.5% children and moderate (score 3) in 20% of children and severe (score 4) in 22.5%. In group II, 87.5% of children showed no limb movement (score 1) and 10% had slight limb movement (score 2) and 2.5% of children had moderate (score 3) limb movements. In group III, there was no limb movements (score 1) in 92.3% of children and slight (score 2) in 7.7% of children, as illustrated in Table 7 and Figure 5.

	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
Score 1	14 (35%)	40 (100%)	39 (100%)	<0.001
Score 2	14 (35%)	0	0	
Score 3	9 (22.5%)	0	0	
Score 4	3 (7.5%)	0	0	

Table 6: Jaw relaxation in the studied groups.

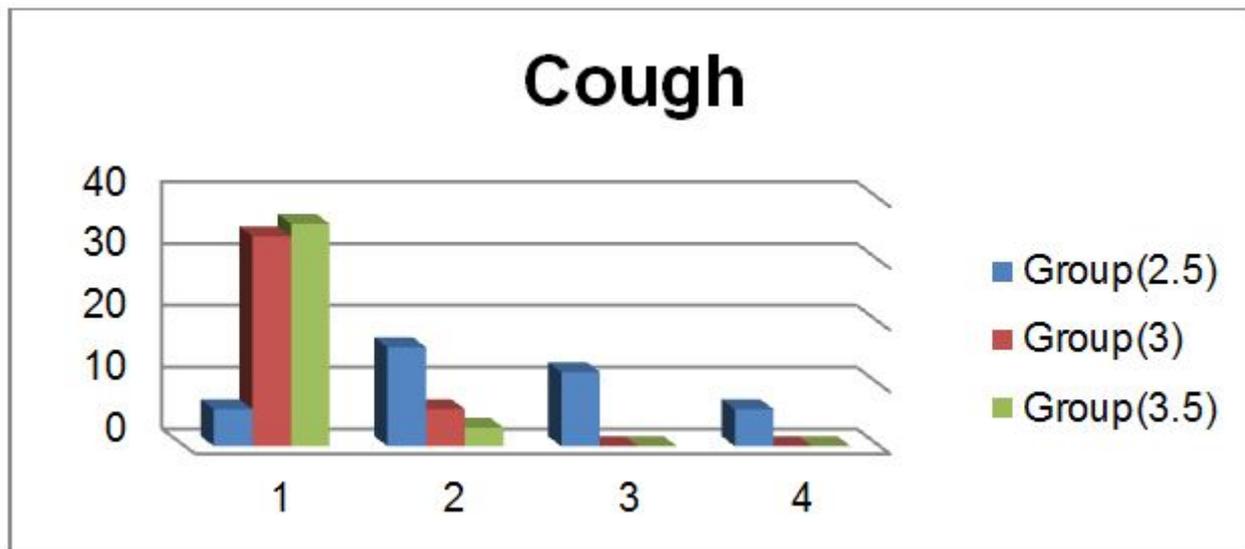


Figure 3: coughing in the studied groups.

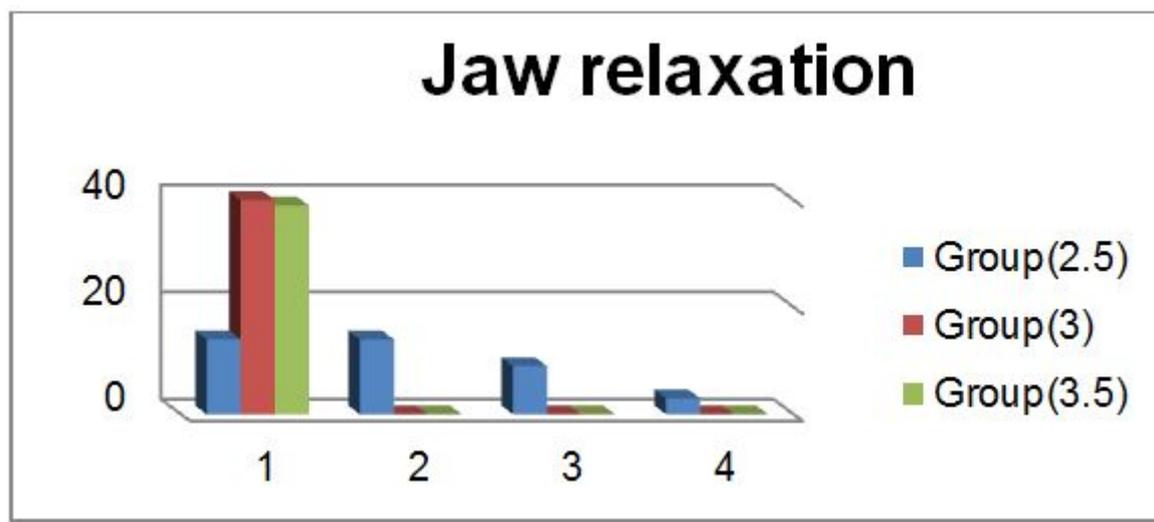


Figure 4: Jaw relaxation in the studied groups.

	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
Score 1	10 (25%)	35 (87.5%)	36 (92.3%)	<0.001
Score 2	13 (32.5%)	4 (10%)	3 (7.7%)	
Score 3	8 (20%)	1 (2.5%)	0	
Score 4	9 (22.5%)	0	0	

Table 7: limb movements in the studied groups.

The total score of the tracheal intubating conditions were considered adequate in 65% of patients in group I, 97.5% of patients in group II, and in 100% of patients in group III. There was a statistically significant difference in total score between groups I and II, and groups I and III ( $P < 0.001$ ), as illustrated in Table 8 and Figure 6.

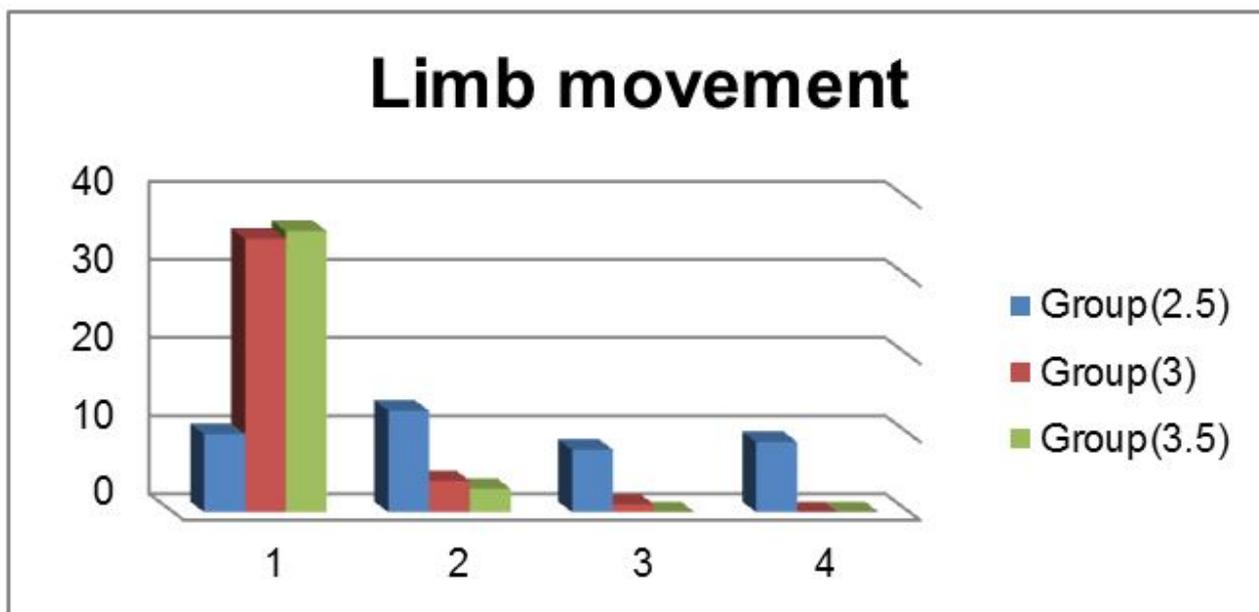


Figure 5: Limb movements in the studied groups.

	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
Excellent	4 (10%)	25 (62.5%)	29 (74.3%)	<0.001
Good	22 (55%)	14 (35%)	10 (25.7%)	
Poor	3 (7.5%)	1 (2.5%)	0	
Bad	11 (27.5%)	0	0	

Table 8: The total score of the studied groups.

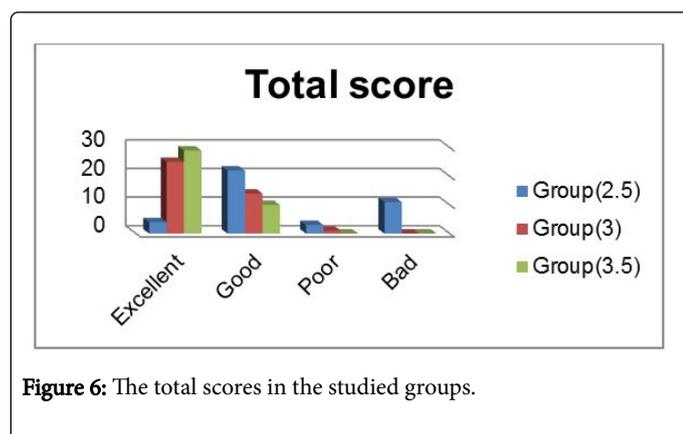


Figure 6: The total scores in the studied groups.

### Hemodynamic variables

**Heart rate:** Group I showed a significant increase in HR from baseline during intubation ( $P<0.001$ ), 1 min after intubation ( $P<0.001$ ), 3 min after intubation ( $P<0.01$ ), and 5 min after intubation ( $P<0.05$ ) (Figure 7).

Group II showed no significant changes in HR from baseline. Group III showed a significant decrease in HR from the baseline after propofol injection ( $P<0.01$ ), during ventilation ( $P<0.01$ ) and Intergroup analysis for HRs between groups I and II showed no statistically significant difference except during laryngoscopy when HR in group I was significantly higher than group II ( $P<0.05$ ). Analysis between groups I and III showed significant difference in HR during ventilation ( $P<0.02$ ), during laryngoscopy ( $P<0.05$ ), during intubation ( $P<0.01$ ), 1 min after intubation ( $P<0.01$ ), 3 min after intubation ( $P<0.01$ ), and 5 min after intubation ( $P<0.01$ ), whereas comparison between groups II and III showed no statistically significant differences in heart rates.

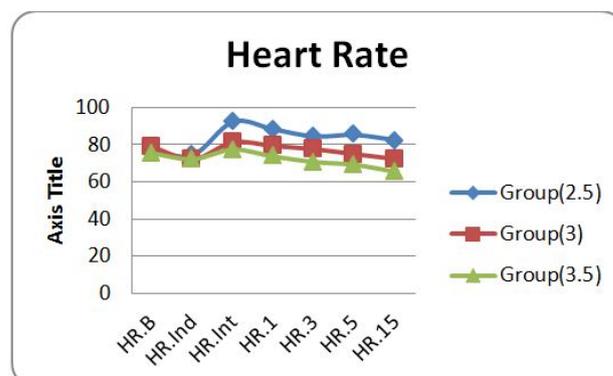
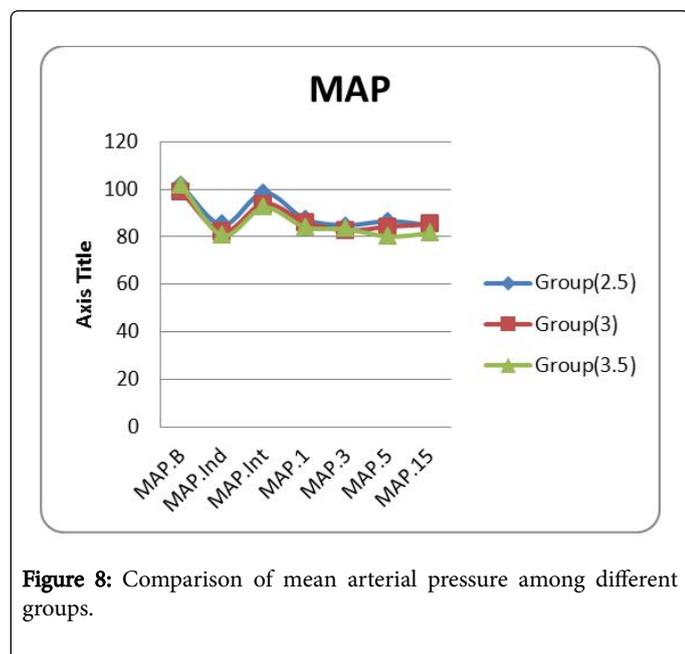


Figure 7: Comparison of heart rate among different groups.

**Mean arterial pressure:** The horizontal, i.e. intragroup analysis versus baseline showed a significant decrease in MAP from 3 min after fentanyl injection until 5 min after intubation in all three groups

(Figure 8). There was no statistically significant difference in MAP among the three groups at various time intervals.

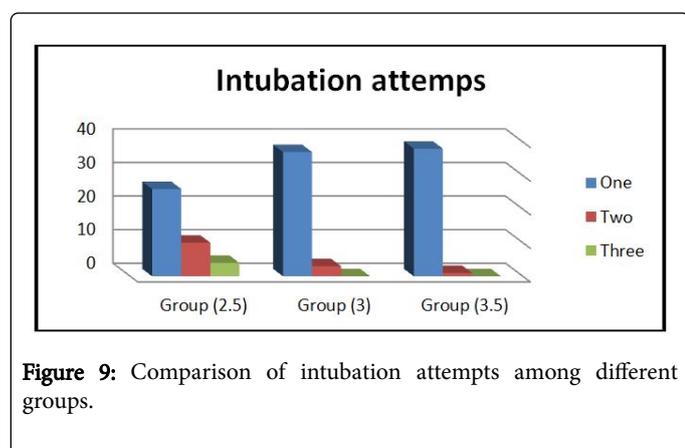


**Figure 8:** Comparison of mean arterial pressure among different groups.

Intubation was successfully performed at the first attempt in 65% of patients in Group I, 92.2% of patients in Group II and in 97.4 % of patients in Group III , with no serious airway complications, i.e. laryngospasm, bronchospasm, desaturation (SpO<sub>2</sub><90%) or emesis was seen in any patient Table 9 and Figure 9.

Intubation attempts	Group I (2.5)	Group II (3)	Group III (3.5)	P-value
One	26 (65%)	37 (92.5%)	38 (97.4%)	<0.001
Two	10 (25%)	3 (7.5%)	1 (2.6%)	
Three	4 (10%)	0	0	

**Table 9:** Comparison of intubation attempts among different groups.



**Figure 9:** Comparison of intubation attempts among different groups.

## Discussion

Laryngoscopy and tracheal intubation are essential skills associated with the practice of anesthesia. Succinylcholine is the muscle relaxant of choice for tracheal intubation in short procedures and for rapid sequence induction when there is risk of aspiration. Undesirable side effects such as muscle pain, hyperkalemia, cardiac arrhythmias, and increase in intraocular and intracranial pressure have limited its use. The incidence of prolonged apnea, masseter spasm, malignant hyperthermia, and even cardiac arrest related to succinylcholine is not insignificant among children [11].

Rapidly acting nondepolarizing muscle relaxants such as rocuronium may provide good intubating conditions in 90 sec; however, they have prolonged duration of action which could be troublesome in a difficult airway. Moreover histamine release and anaphylaxis are also known side effects with these agents. Propofol, one of the most frequently used induction agent, has favorable depressant effect on the pharyngeal and laryngeal reflexes [12] and the muscle tone [13,14]. The induction with propofol is quick and smooth, with rapid awakening during recovery [15]. With the adjuvant of short-acting opioids, their use in combination with propofol for tracheal intubation without neuromuscular blocking agents has been well documented [1,4-6]. Numerous studies have stressed the advantages of propofol, such as a low cumulative effect which offers fast recovery of consciousness after surgery, an antiemetic effect, a diminished pressor response to laryngoscopy and tracheal intubation, and a lower incidence of airway complications, in adults and pediatric patients [16,17]. However, a larger apparent volume of distribution for propofol is consistent with a higher induction dose requirement in children than in adults [18].

Various scoring system for assessing intubating conditions have been used in the past. Scoring systems of Alcock et al. [19], Saarnivaara and Klemola [12] and Scheller et al. [13] have considered only local factors such as jaw relaxation, cord movement, ease of mask ventilation, coughing, etc. However, we used the scoring system of Helbo-Hansen with Steyn modification [6], which included both local as well as distal factors, limb movements for better assessment. This scoring system has also been used earlier by Blair et al. [1] and Robinson et al. [4] for assessing intubating conditions with propofol and remifentanyl or alfentanil.

In our study, comparing varying doses of propofol preceded by a fixed dose of fentanyl (2 mg/kg), acceptable intubating conditions were seen in 65% of patients in group I (propofol 2.5 mg/kg), which was significantly lower than in groups II and III (P<0.001). Intubating conditions were found acceptable in 97.5% of patients in group II (propofol 3.0 mg/kg) and 100% in group III (propofol 3.5 mg/kg) with no statistically significant difference between the two groups. De Fatima et al. [5] with the same dose combination, found acceptable intubating conditions in 20%, 75%, and 80% of patients in each group. However, they used only three criteria for assessing the intubating conditions: (i) the degree of difficulty in laryngoscopy; (ii) intensity of coughing; (iii) and the presence of vocal cord movement.

Comparing the pressor response to intubation, we found that the response was not obtunded in group I as evidenced by 17% increase in HR, while it was effectively blunted in groups II and III, where there was no significant increase in HR from baseline after intubation. Blair et al. [1] found a significant increase in HR in response to intubation with remifentanyl 1 mg/kg and propofol 3 mg/kg, while Robinson et al.

[4] found the pressor response effectively blunted with remifentanyl 1 mg/kg in combination with propofol 4 mg/kg.

In our study, a consistent and similar fall in MAP (16-18%) was seen in all the three groups, but in group III (propofol 3.5 mg/kg), it was also associated with fall in HR (11%) implying a fall in cardiac output. Klemola et al. [10] also found a 12% fall in MAP and 8% fall in HR with a dose combination of 4.0 mg/kg remifentanyl and 3.5 mg/kg propofol, while de Fatima et al. [5] did not find any significant changes in hemodynamics. This fall in cardiac output may not be well tolerated in high-risk patients, where it could become significant. This decrease in HR and MAP after fentanyl and propofol is due to the synergistic action of the two drugs. Fentanyl blunts hemodynamic responses to laryngoscopy and intubation and propofol decreases sympathetic nervous activity [20]. Also baroreceptor reflex control of HR may be depressed by propofol [15]. The possible development of severe hypotension is the limiting factor with the use of propofol although Schrumet al. [21] demonstrated that it was transient in healthy, normovolemic children. Topical laryngeal spraying of lidocaine as suggested by Abouleish et al. [22] can be used as an adjunct to the technique of tracheal intubation without muscle relaxant for further improving the intubating score with no effects on hemodynamics. To conclude, on the basis of relative comparison between our three groups, we recommend a combination of 2 mg/kg fentanyl and 3.5 mg/kg propofol as the safest option, as it provides acceptable intubating conditions in all of patients (100%), effectively blunts pressor response and lead to minimal cardiovascular depression.

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