ORIGINAL ARTICLE

Changes Associated with Facilitation of Endotracheal Intubation with Either Fentanyl or Suxamethonium in Children

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ABSTRACT

Background: Endotracheal intubation usually aided by the muscle relaxant suxamethonium can elicit responses and changes which are hazardous in some patients including children; suxamethonium is also contraindicated in some patients. Fentanyl, a short-acting opioid may be a suitable alternative with varying results. **Objective:** This study compares the changes associated with the facilitation of endotracheal intubation with either the commonly used suxamethonium or fentanyl. **Methods:** Eighty two American Society of Anaesthesiologist (ASA) physical status classification I and II patients aged between 3 and 12 years scheduled for surgeries requiring general anaesthesia with endotracheal intubation received either 3 µg/kg fentanyl (group F) or 1.5 mg/kg suxamethonium (group S) following induction of anaesthesia with propofol. Haemodynamic parameters: pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were assessed post-intubation at 1, 3, 5 and 10 minutes respectively. The incidence of side effects and post-intubation upper airway events were also observed. **Results:** Patients in group S experienced a significant increase in HR when compared to baseline values (p=0.0001). The SBP and DBP were significantly lower than baseline values in patients in group F (p<0.023). MAP increased in group S and declined in group F at all study timings. However, the post-intubation MAP was significantly lower than the baseline only at the 5th minute (p=0.026). There were no records of postoperative upper airway injuries, hypotension, bradycardia, desaturation, masseter spasm and malignant hyperthermia in the two study groups. **Conclusion:** Propofol-Fentanyl produced more stable parameters compared to propofol-suxamethonium. No significant difference in terms of side effects between Propofol-Fentanyl and propofol-suxamethonium.

Key words: Fentanyl, Suxamethonium, Propofol, Facilitation, Endotracheal intubation

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Introduction

Suxamethonium is a widely used neuromuscular blocking agent to aid endotracheal intubation during general anaesthesia. Some of its unique properties such as a fast onset of muscle paralysis and spontaneous neuromuscular block reversal make suxamethonium a preferred choice for the facilitation of endotracheal intubation.[1]

However, the agent may be associated with side effects such as bradycardia, prolonged paralysis, masseter spasm, postoperative myalgia, arrhythmias, cardiac arrest, increases in intraocular and intragastric pressure and malignant hyperthermia (MH).[2] In children, the incidence of easily treatable side effects such as bradycardia, muscle pain, and an increase in intraocular or intragastric pressure is high. Asystole leading to death has been reported in children given suxamethonium and that has led to criticism of its use in this age group.[3] The risk of hyperkalemia has also been highlighted in patients with unsuspected muscle disorders; primarily Duchenne's muscular dystrophy. It is for these reasons that it has been suggested that suxamethonium be contraindicated for routine use in children and adolescents except for

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emergency tracheal intubation or in instances where immediate securing of the airway is necessary.[2,3]

Agents such as thiopentone, propofol, fentanyl, remifentanyl, alfentanyl, lidocaine, and inhalational agents such as halothane or sevoflurane have been used either solely or in combination to facilitate tracheal intubation without the use of a muscle relaxant.[4,5]

Fentanyl, a fast-acting synthetic μ receptor-stimulating opioid has been commonly prescribed in preventing sympathetic stimulation during intubation.[6] Direct laryngoscopy and endotracheal intubation during general anaesthesia are known to induce clinical changes in the patient's haemodynamic parameters.[7] This haemodynamic stress response to airway manipulation is characterized by an increase in heart rate and blood pressure.[7] Researchers have studied the combination of fentanyl with propofol to facilitate tracheal intubation in children.[4,8] Most of these studies demonstrated improvement in intubating conditions with increasing doses of opioids. Increasing the dose of opioids may however be associated with chest wall rigidity, prolonged apnea, and delayed recovery.[6] This study examines the haemodynamic changes and side effects associated with fentanyl and suxamethonium when used for the facilitation of endotracheal intubation following induction with propofol in children.

Methods

Ethical approval: Ethical approval for this study was obtained from the ethical committee of Aminu Kano Teaching Hospital.

Eighty two children aged 3 to 12 years, belonging to American Society of Anaesthesiologists (ASA) status I and II, and scheduled to undergo various elective surgical procedures for which endotracheal intubation was required were selected for this study. Children excluded from the study include those with suspected difficult intubation, patients undergoing an ophthalmic or neurosurgical procedure, patients with a full stomach, a history of reactive airways such as asthma, or upper respiratory tract infection and patients with a history of upper gastro-intestinal tract reflux.

The investigator reviewed patients a day before surgery, and relevant investigation results were reviewed and recorded. Demographic parameters such as age, sex, weight, height, and body mass index (BMI) were recorded. On the day of surgery, patients were randomly allotted to either group F (fentanyl) or group S (suxamethonium) after picking uniformly sized sheets of paper from a large box. The patient's file number was written on a sheet of paper bearing the group to which the patient belonged and kept in a sealed separate envelope that was opened after the collection of data. Both the investigator and the patient remained blinded to the group allocation.

Intravenous access was secured, an anaesthetic machine and oxygen source were checked, and appropriate sizes of endotracheal tubes (ETT), oropharyngeal tubes and laryngoscopes were made available. Baseline vital signs including non-invasive blood pressure (NIBP), Pulse Rate (PR), Mean Arterial Pressure (MAP), Respiratory Rate (RR), Peripheral Oxygen Saturation (SPO_2) and Electrocardiography (ECG) were taken with a multi-parameter patient monitor. All patients had 4.3% dextrose/0.18% saline for fluid maintenance based on calculated fluid requirements. Patients were premedicated using IV midazolam 0.05 mg/kg and IV atropine 0.02 mg/kg prior to induction. Patients were preoxygenated with 100% oxygen using a face mask via Ayre's T-piece for patients less than 25 kg and Bain circuit for patients above 25 kg for 3-5 minutes.

Induction of anaesthesia was with IV bolus propofol 3 mg/kg (0.2 mg/kg plain lidocaine added to prevent injection pain) given by a research assistant over 30 seconds. Group F then received fentanyl 3 mcg/kg while group S received 1.5 mg/kg of suxamethonium both made up to 5mls, the researcher who had been behind a screen and unaware of administered drugs then carried out a laryngoscopy and intubation using appropriately sized Macintosh laryngoscope and ETT, the ETT was then connected to the breathing circuit.

Vital signs including HR, NIBP, MAP, SpO_2 and electrocardiograph (ECG) were taken and recorded 10 minutes after the administration of 0.05 mg/kg IV bolus midazolam and atropine 0.02 mg/kg IV, this was regarded as the baseline, then immediately after induction, and post-intubation 1, 3, 5 and 10 minutes respectively. Maintenance of anaesthesia was with 1-2% volume of isoflurane in 100% oxygen. Intraoperative monitoring included capnography, ECG, SpO_2, PR and SBP, DBP and MAP measurement every 5 minutes throughout the surgery. Intraoperative fluid management continued

using 4.3% dextrose/0.18% saline. Analgesia was provided by administering top-up doses of fentanyl (1-2 mcg/kg). At the end of the surgery, the patient was extubated while awake and transferred to the recovery room.

Data on demographic characteristics and post-intubation adverse events such as bradycardia, hypoxia (SpO_2< 90%), apnea, hypotension (a 30% fall in baseline MAP), masseter spasm, and malignant hypertension were recorded using a data collection form. Bradycardia was taken as HR < 100 beats per minute (bpm) and treated with supplemental 100% O_2 via face mask and IV 0.02 mg/kg atropine, hypoxia was treated with 100% O_2 via face mask.

Complications like laryngospasm, stridor, hoarseness, and odynophagia were recorded. Laryngospasm was treated by deepening anaesthesia with halothane and 100% O_2 with or without IV suxamethonium 0.1 mg/kg.

Data collected was analyzed using Statistical Package for Social Sciences (SPSS) version 21.0 windows statistical software. Numerical values which are normally distributed were expressed using means and standard deviation (SD), while values that are not normally distributed were expressed using range and median and the test of association between the groups using the student's t-test for the quantitative variables. Intragroup changes in hemodynamic variables (HR, SBP, DBP and MAP) were compared with baseline values using paired t-test. The test of association for qualitative variables was done using the Chi-square test or Fisher's exact test where appropriate. The results are presented in the form of tables and graphs. The level of statistical significance was taken as p-value < 0.05

Results

Data obtained showed that there was no statistically significant difference in the demographic parameters between the two groups concerning age, BMI and sex distribution as seen in table I.

As shown in table II, the baseline means SBP of the patients in group S (98.74 ± 16.00 mmHg) and group F (103.98 ± 12.87 mmHg) were comparable (p = 0.102). Post intubation, SBP values progressively increased in group S but a progressive decline from baseline was observed in group F at all study timings. The difference in SBP values between groups S and F became significant at the 3rd, 5th and 10th minute after intubation (p = 0.048, p = 0.003, p = 0.008 respectively). No significant difference was found in the baseline mean DBP of the patients in groups S (58.55 ± 17.97 mmHg) and F (63.60 ± 11.54 mmHg). At all study timings, a drop from baseline mean DBP was noticed in both groups but no significant difference was noticed (comparing the two groups).

An increase in the mean MAP of patients in group S was observed after intubation at all study timings. There was a decline in MAP values compared to baseline post-intubation at all study timings in group F. The difference in MAP values in the two groups was however significant at the 5th (p = 0.015) and 10th (p = 0.042) minute after intubation. The difference in baseline mean HR of the patients in group S and group F was not statistically significant (p = 0.238). After endotracheal intubation, the mean heart rate of patients in group S progressively increased. Patients in group F post-intubation had an initial drop in HR values but later rose to baseline value at the 10th minute. The difference in mean HR in the two groups was significant at the 3rd, 5th, and 10th minute after intubation (p = 0.001, p = 0.0001, p = 0.0001 respectively).

There was a highly significant increase in heart rate compared to baseline at all the study timings in group S post-intubation (p = 0.0001). The SBP and MAP increased above the baseline values but only significantly at the 5th minute (p=0.005). A significant drop in DBP was observed at the 1st and 3rd minutes (p = 0.039 and 0.043 respectively) but later rose towards the baseline at the 5th and 10th minutes. Patients in group F experienced a drop in HR and the difference from baseline was only significant at the 5th-minute post-intubation (p=0.044). There was a significant drop in SBP and DBP values at all the study timings (p<0.023). The post-intubation MAP was however significantly lower than the baseline only at the 5th minute (p=0.026) (Table III).

Table IV shows that at all study timings post insertion of the endotracheal tube, the mean SpO_2 of patients in group S was comparable to those in Group F

Figure 1 shows the incidence of the study drug's side effects (apnea, hypotension, bradycardia, masseter spasm, malignant hyperthermia) in both study groups. Apnea was observed in all patients (100%) in group S and 41 patients (97.6%) in group F and the difference was not statistically significant (p = 0.786).

No incidence of hypotension, bradycardia, masseter spasm and malignant hyperthermia was observed in the two study groups.

No incidence of postoperative upper airway injuries nor sequelae was recorded in the two groups

TABLE I: Patients' Demographic data and Clinical Characteristics

	Group S (*n = 42*)	*Group F* (*n = 42*)	*p – value*
Age (years)	6.52 ± 2.75	7.00 ± 3.32	0.476
Gender (Male:Female)	23:19	24:18	0.826
BMI (kg/m^2)	21.98 ± 3.87	21.88 ± 4.51	0.918

Table II: Intergroup comparison of Haemodynamic Changes at Different Time Intervals

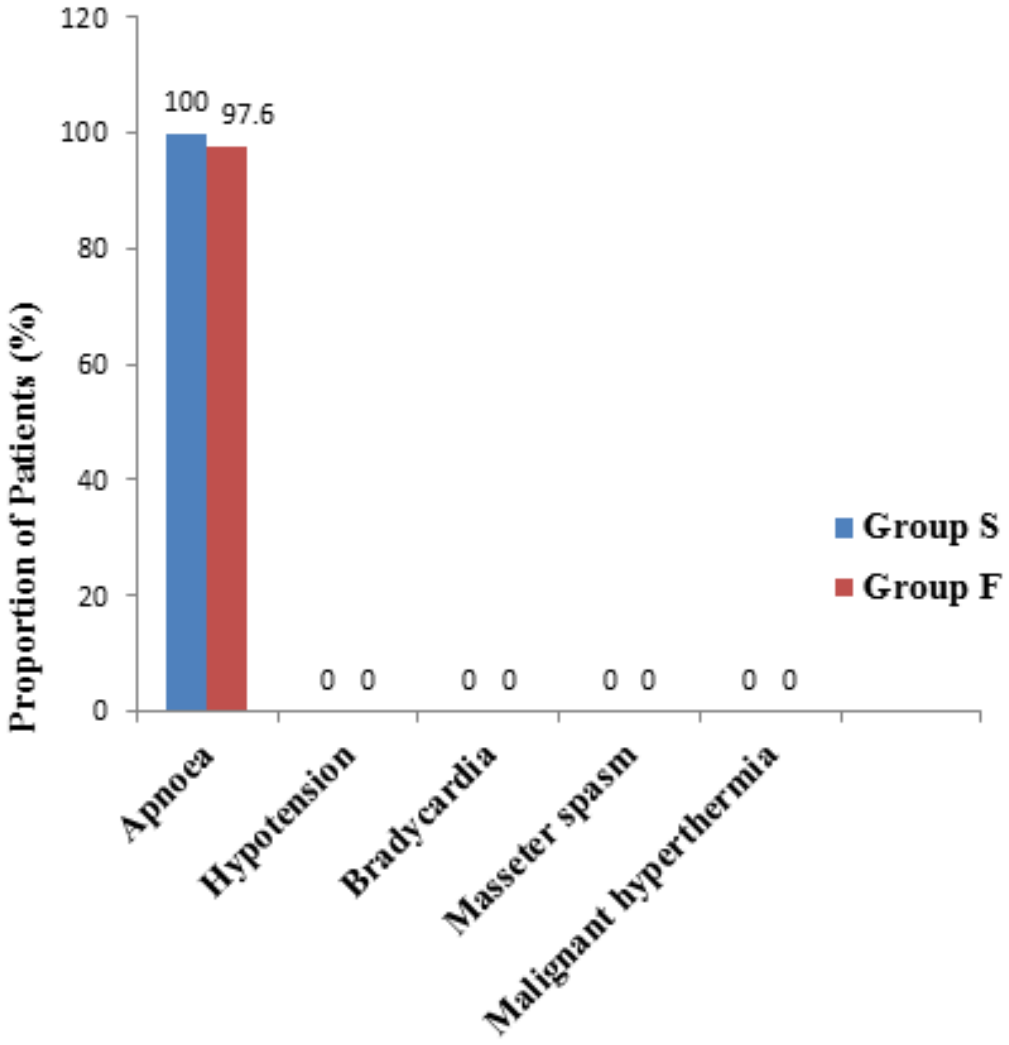
Haemodynamic Variable		*Group S Mean ± SD*	*Group F Mean ± SD*	*P-value*
SBP (mmHg)	Baseline	98.74 ± 16.00	103.98 ± 12.87	0.102
	1 minute post intubation	98.12 ± 11.13	98.64 ± 13.50	0.847
	3 minute post intubation	100.60 ± 13.34	94.86 ± 12.83	0.048
	5 minute post intubation	105.45 ± 13.77	97.07 ± 11.25	0.003
	10 minute post intubation	104.95 ± 12.80	97.55 ± 11.99	0.008
DBP (mmHg)	Baseline	58.55 ± 17.97	63.60 ± 11.54	0.129
	1 minute post intubation	53.67 ± 9.26	56.83 ± 9.91	0.134
	3 minute post intubation	53.69 ± 9.88	55.50 ± 9.90	0.404
	5 minute post intubation	55.79 ± 9.96	52.12 ± 8.52	0.073
	10 minute post intubation	56.33 ± 9.59	53.40 ± 9.26	0.158
MAP (mmHg)	Baseline	67.81 ± 10.28	73.69 ± 16.29	0.051
	1 minute post intubation	68.93 ± 9.24	71.17 ± 10.10	0.292
	3 minute post intubation	69.38 ± 9.99	69.26 ± 10.17	0.957
	5 minute post intubation	72.71 ± 10.79	67.36 ± 8.79	0.015
	10 minute post intubation	72.88 ± 9.54	68.50 ± 9.92	0.042
HR (beats/minute)	Baseline	124.29 ± 16.47	128.69 ± 17.50	0.238
	1 minute post intubation	132.29 ± 14.69	127.76 ± 15.91	0.179
	3 minute post intubation	137.76 ± 10.90	126.81 ± 16.46	0.001
	5 minute post intubation	140.17 ± 13.70	125.00 ± 16.04	0.0001
	10 minute post intubation	143.60 ± 13.90	128.21 ± 13.81	0.0001

Table III: Intragroup comparison of changes in haemodynamics with Baseline values

Group S			Group F		
Hemodynamic Variable	Post intubation	p value	Hemodynamic Variable	Post intubation	p value
Baseline HR (beats/min)	1 min (132.29±14.69)	**0.0001**	Baseline HR (beats/min)	1 min (127.76±15.91)	0.389
124.29 ± 16.47	3 min (137.76±10.90)	**0.0001**	128.69 ± 17.50	3 min (126.81±16.46)	0.091
	5 min (140.17±13.70)	**0.0001**		5 min (125.00±16.04)	**0.044**
	10 min (143.60±13.90)	**0.0001**		10 min (128.21±13.81)	0.542
Baseline SBP (mmHg)	1 min (98.12±11.13)	0.504	Baseline SBP (mmHg)	1 min (98.64±13.50)	**0.001**
98.74±16.00	3 min (100.60±13.34)	0.604	103.98±12.87	3 min (94.86±12.83)	**0.0001**
	5 min (105.45±13.77)	**0.005**		5 min (97.07±11.25)	**0.002**
	10 min (104.95±12.80)	0.077		10 min (97.55±11.99)	**0.023**
Baseline DBP (mmHg)	1 min (53.67±9.26)	**0.039**	Baseline DBP (mmHg)	1 min (56.83±9.91)	**0.0001**
58.55±17.97	3 min (53.69±9.88)	**0.043**	63.60±11.54	3 min (55.50±9.90)	**0.0001**
	5 min (55.79±9.96)	0.114		5 min (52.12±8.52)	**0.0001**
	10 min (56.33±9.59)	0.164		10 min (53.40±9.26)	**0.0001**
Baseline MAP (mmHg)	1 min (68.93±9.24)	0.543	Baseline MAP (mmHg)	1 min (71.17±10.10)	0.308
67.81±10.28	3 min (69.38±9.99)	0.491	73.69±16.29	3 min (69.26±10.17)	0.087
	5 min (72.71±10.79)	**0.007**		5 min (67.36±8.79)	**0.026**
	10 min (72.88±9.54)	**0.027**		10 min (68.50±9.92)	0.117

Table IV: Comparison of changes in Mean SpO_2 at Different Time Intervals

		Group S Mean ± SD	Group F Mean ± SD	p-value
SPO_2 (%)	Baseline	99.80 ± 0.41	99.65 ± 0.48	0.136
	1 min after intubation	99.50 ± 0.51	99.58 ± 0.76	0.245
	3 min after intubation	98.90 ± 0.96	99.00 ± 0.91	0.632
	5 min after intubation	97.40 ± 2.41	98.10 ± 1.60	0.129
	10 min after intubation	98.00 ± 1.92	98.30 ± 1.02	0.386



Discussion

Data from this study shows that patients who received fentanyl following induction of anaesthesia with propofol had significant drops in SBP and DBP compared to baseline values at all the study timings ($p< 0.001$). These findings could be explained by the ability of fentanyl, a short-acting opiate to obtund pressor response to laryngoscopy. That might also have been accentuated by the hemodynamic depressant effect of propofol. We also saw a significant decrease in HR and MAP compared to baseline values at the 5th minute post-induction ($p = 0.044$ and $p = 0.026$ respectively). Stimulation of the upper respiratory tract during tracheal intubation under general anaesthesia causes activation of the sympathoadrenal system and results in hypertension, tachycardia and also an increase in intracranial pressure.[9] These may be harmful in patients with cardiovascular diseases.

Fentanyl has been advocated for the obtunding of sympathetic response to laryngoscopy and intubation.[9] The blunting of the sympathetic response is dose-dependent with 6 mcg/kg completely abolishing the response while at 2 mcg/kg it significantly attenuates the arterial pressure and heart rate increases during laryngoscopy and intubation.[9] Our patients received 3 mcg/kg of fentanyl which might have accounted for significant drops seen in blood pressure values when compared to baseline values.

Similar to our observation, Shaikh and Bellagali[10] reported that their propofol-fentanyl combination was associated with a significant decrease in PR and SBP post-intubation compared with the baseline values at all their study timings ($p<0.001$). In the study by Rizvanovic *et al*,[11] they also experienced significant decreases in SBP, DBP and MAP at 1 and 3 minutes post-intubation in their fentanyl group when compared to baseline values ($p< 0.005$).

Thippeswamy *et al*[12] reported that low-dose fentanyl (2 µg/kg) when given effectively, masked the haemodynamic response to intubation. Fentanyl at a dose of 3 μg/kg when used in combination with 3mg/kg propofol for endotracheal intubation has also been reported to be the best combination to reduce intubation responses, without great falls in mean arterial pressure and heart rate.[13]

Only one patient who received the propofol-fentanyl combination retained his spontaneous ventilatory effort throughout the study period. Others in that group and all those that received the propofol-suxamethonium combination went apneic after induction. However, the SpO_2 of all patients remained relatively stable throughout the period of our investigation because ventilation was assisted immediately after the airway was secured and the patients were maintained on 100% oxygen. Similar to our finding, Salawu and colleagues[14] also observed that none of their patients who had propofol-suxamethonium desaturated to $SpO_2< 90\%$ post-intubation.

Other side effects like hypotension, bradycardia, masseter spasm and malignant hyperthermia were not seen in both of our study groups, a similar trend was also reported by Salawu *et al*[14]. Paediatric patients are however more sensitive to potential side effects such as malignant hyperthermia when suxamethonium is administered compared to adults; this is due to differences in postsynaptic nicotine receptor structure and functional insufficiency of the neuromuscular junction. The risk of hyperthermia increases in children when neurologic and muscle diseases coexist.[15]

None of the intubations in this present study was associated with laryngeal morbidity. Mencke *et al*[16] suggested that the quality of tracheal intubation has a direct correlation with the incidence of post-intubation upper airway sequelae and that excellent intubations are less frequently associated with postoperative hoarseness. Suxamethonium is known to provide excellent airway relaxation thus patients are unlikely to suffer laryngeal injuries.[16]

Conclusion

Hemodynamically, propofol-fentanyl-induced anaesthesia produced more stable parameters compared to propofol-suxamethonium, there were no significant differences in terms of side effects between propofol-fentanyl and propofol-suxamethonium.

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