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Comparative Study of Haemodynamic Effects of Intravenous Ketamine-fentanyl and Propofol-fentanyl for Laryngeal Mask Airway Insertions in Children Undergoing Herniotomy under General Anaesthesia in a Nigerian Tertiary Hospital

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Abstract

Background: Insertion of laryngeal mask airway (LMA) with propofol in children may cause hypotension, laryngospasm and apnoea. Ketamine and fentanyl have been combined separately with propofol to prevent depression of cardiovascular system during LMA insertion, especially in paediatric patients. Ketamine-fentanyl and propofol-fentanyl combinations have analgesic effect, prevent coughing and apnoea and regarded as agents of choice for LMA insertions. However, the cardiovascular effects of the two admixtures for LMA insertions have not been fully assessed in children. We compared the haemodynamic effects of ketamine-fentanyl and propofol-fentanyl combinations for LMA insertion in paediatric patients who underwent herniotomy in our facility. **Patients and Methods:** This comparative study was conducted on 80 children aged 1–15 years, ASA physical Statuses I and II, who had herniotomy under general anaesthesia. The patients were randomised into two groups (A and B) of 40 patients each and LMA was inserted following administrations of the two different drug combinations. Patients in Group A received pre-mixed ketamine 2 mg/kg and fentanyl 2 µg/kg while the patients in Group B received pre-mixed propofol 2.5 mg/kg and fentanyl 2 µg/kg. The blood pressure and incidence of apnoea were determined in the two groups during and after the LMA insertion. **Results:** The haemodynamic states of the patients were not comparable statistically as the heart rate, systolic, diastolic and mean arterial blood pressure were significantly higher and stable in the ketamine-fentanyl group than the propofol-fentanyl group ($P < 0.05$). The incidence of apnoea was significantly lower in the ketamine-fentanyl group compared with propofol-fentanyl group ($P = 0.045$), but post-anaesthesia discharge scores were similar, with no significant difference in both groups ($P = 0.241$). **Conclusion:** The use of ketamine-fentanyl combination for LMA insertion in paediatric patients was associated with better haemodynamic changes and lower incidence of apnoea when compared with propofol-fentanyl combination.

Keywords: Haemodynamic parameters, herniotomy, ketamine-fentanyl, laryngeal mask airway, propofol-fentanyl

INTRODUCTION

Laryngeal mask airway (LMA), one of the commonly used supraglottic airway devices, is used to maintain airway patency during surgical procedures under general anaesthesia to prevent hypoxic injury. The device was developed by Dr. Archie I. J. Brain in 1983^[1] and is widely used in children for procedures that are done under general anaesthesia following its proven efficacy and safety in adults airway management.^[2,3] Although

it is not a definitive airway device, it has revolutionised anaesthetic practice due to its ease of insertion and ability to

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maintain excellent airway patency without the need for jaw thrust, chin lift and laryngoscopy.

LMA insertion produces less sympathetic stimulation and lower haemodynamic changes because its insertion requires no visualisation of the vocal cords nor penetration of larynx.^[4] The pathophysiology of the haemodynamic response to airway stimulation is believed to be a reflex sympathetic and sympathoadrenal response to airway stimulation or irritation, the afferent limb of the reflex arc is through the cranial nerves of the upper airway, while the efferent limb is through the sympathetic nerves.^[5] Thus, obtundation of airway reflexes is essential for LMA insertion and use of either intravenous (IV) or inhalational induction agent is required to suppress the airway reflexes. Till date, several adjuncts have been added to induction agents for LMA insertion, but the ideal combination that provides the best insertion conditions with minimal side effects has not been identified particularly in children.^[6]

Due to its predominant upper airway reflexes depressant action, propofol has been used as a sole induction agent to facilitate LMA insertion. However, unwanted responses such as drop in blood pressure, coughing, laryngospasm and movement may occur either due to a higher dose which can cause reduction of sympathetic tone or lighter plane of anaesthesia following inadequate dose of propofol.^[7,8] These observations stimulated interests in searching for another induction agent, either administered solely or pre-mixed with an adjunct, would reduce or eliminate propofol-induced unwanted effects.

Ketamine, a phencyclidine derivative,^[9] produces dissociative anaesthetic state by blocking the connection between the thalamic and limbic regions of the brain from processing external stimuli.^[9] When used as a single induction agent, emergence phenomenon, hallucination, elevations of heart rates (HR), blood pressure and increased intracranial pressure can occur.^[10] It is known that emergence phenomenon and hallucination are not common occurrences in children following ketamine induction.^[11] These discriminatory effects of ketamine in children and its indirect stimulatory action on the sympathetic nervous system make it an alternative induction agent for LMA insertion in children. For LMA insertion in children, use of adjuncts such as fentanyl as a co-induction agent with either propofol or ketamine has been advocated during LMA insertions in order to reduce induction agents-associated side effects.

Several studies have suggested possible existence of synergistic interactions between ketamine and opioids.^[12-14] Inferentially, when fentanyl, a synthetic, strong and rapid onset opioid analgesic that is 50–100 times more potent than morphine, is used as a pre-treatment drug for LMA insertion, the required dose of induction agent like ketamine is expected to reduce. Except for its cardiovascular stimulation, ketamine has an added advantage of maintaining patent airway when used as a co-induction agent, even when subanaesthetic doses are administered.^[15]

We evaluated the haemodynamic changes that occurred when ketamine-fentanyl and propofol-fentanyl combinations are used as induction agents for insertion of LMA in paediatric patients scheduled for herniotomy.

PATIENTS AND METHODS

After ethical approval was gained on the 17 May 2017 from University of Ilorin Teaching Hospital Ethical Review Committee, in Ilorin, Kwara State; with approval number (ERC PAN/2017/05/1679), and patient informed consent or assents obtained, 80 children aged 1–15 years, American Society of Anesthesiologists (ASA) classes I and II were enrolled into this study. The data collection for the study was commenced on 18 May 2017 and was finally completed on the 20 Oct 2017. The study was done at University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria.

All patients had LMA insertion with either ketamine-fentanyl or propofol-fentanyl as induction agent and were allowed to breath spontaneously throughout the procedure. The number of patients enrolled into this study was calculated with a formula that uses comparison of proportions (equal size group).^[16] A previous study^[17] revealed 36% of the patients experienced excellent LMA insertion conditions, and clinical significance is said to occur if 25% experience good LMA insertion conditions.

$$n = \text{the required sample in each group} = (A + B)^2 \times (P_1 \times [1 - P_1] + [P_2 \times (1 - P_2)]) / [P_1 - P_2]$$

$$P_1 = \text{first proportion} = 0.36$$

$$P_2 = \text{second proportion} = 0.25$$

$$P_1 - P_2 = \text{size of clinical difference} = 0.11$$

$$A = \text{significance level set at 5\% which is equal to 1.96}$$

$$B = \text{power of the study which is 80\% and corresponding value of 0.84}$$

$$n = (1.96 + 0.84)^2 \times [0.36 \times (1 - 0.36)] + [0.25 \times (1 - 0.25)] / (0.36 - 0.25) = 30.04$$

To increase the power of this study, forty patients were recruited per group.

Patients with a history of allergies to propofol, ketamine and fentanyl, those with clinically significant cardiovascular, respiratory, hepatic and renal diseases and those on sedative or analgesic drugs were excluded from the study. Others excluded were patients with oropharyngeal pathology, hiatus hernia, respiratory tract infection, history of seizure disorder, raised intracranial or intraocular pressure, anatomical abnormality of the airway, risk of aspiration and hyperactive airway.

Patients were fasted according to the standard fasting guidelines and were randomised into two groups of forty patients each; Group A (ketamine-fentanyl group) and Group B (propofol-fentanyl group) and the two study drugs were premixed in the operating suite. On arrival in the

operating suite, patients were connected to multiparameter patient monitor (DASH 4000 by GE Medical Systems Information Technology, Inc. 8200w. Tower Ave, Milwaukee USA) and baseline vital signs such as HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), temperature, peripheral arterial oxygen saturation (SpO_2) and electrocardiogram were measured and recorded. Thereafter, IV access was secured with appropriate-sized cannula and IV atropine $0.01 \mu\text{g/kg}$ and IV paracetamol 12.5 mg/kg were given to all patients before induction of anaesthesia. All patients were pre-oxygenated for 5 min, and based on the group of the patients, the study drugs were administered intravenously over 10 s. Both the researchers and patients were blinded by wrapping the syringes containing the study drugs in aluminium foil in order to conceal the milky colour of propofol. Under the cover of drapping, the syringes were unwrapped when the study drugs were being administered to the patients to ensure accurate drugs delivery by research assistant. Using the standard midline approach, appropriate-sized classic LMA was inserted 120 s after the administration of either of the study drugs. The LMA cuff was then inflated with air until effective ventilation was achieved. Following successful insertion, correct LMA position was assessed by observing chest movement and squared-wave capnograph tracing with both spontaneous and assisted ventilation. LMA was properly secured with adhesive tapings and patients were allowed to breathe spontaneously. In case of apnoea (absence of respiration for more than 15 s), patients were manually ventilated to maintain the SpO_2 above 95% till the resumption of spontaneous breathing. Thereafter, under aseptic condition, patients were positioned for caudal block in left lateral position and 0.5 ml/kg of 0.25% plain bupivacaine was injected into the epidural space through sacral hiatus to provide intra-operative and post-operative analgesia.

Anaesthesia was maintained with 1% halothane in 50% oxygen in air; and peripheral arterial SpO_2 , HR, SBP, DBP, mean arterial blood pressure (MAP) and RR were measured and recorded at 1 min, at 3 min, and subsequently at 5-min interval till the end of the surgery. Intra-operative fluid management, using 4-2-1 regimen, was achieved with 4.3% dextrose in 0.18% saline and 0.9% saline for the older patients. At the end of surgery, inhalation agent was turned off, and the hypopharynx was suctioned while the LMA cuff was still inflated, and patients were allowed to breathe on 100% oxygen until fully awake after which the LMA was removed. The patients were then transported in recovery position to the post-anaesthetic care unit for continued monitoring of vital signs, fluid administration and supplemental oxygen administration.

Statistical analysis

Statistical Packages for Social Sciences, SPSS Version 20.0 (SPSS Ltd., Chicago, IL, USA) was used to analyse the data. Values were presented as means standard deviation or frequencies, medians and proportions. Haemodynamic parameters (HR, SBP, DBP and MAP) were analysed using Student's *t*-test for comparisons between means.

Categorical data such as gender and number of attempts of LMA insertions were analysed with the Chi-square test or Fisher's exact test as appropriate. A $P < 0.05$ was considered to be statistically significant.

RESULTS

Eighty children were recruited into the study; all patients were well matched in terms of demographic and anthropometric variables. The demographic characteristics and anthropometric parameters in the two groups are shown in Table 1. All the forty patients in Group A (ketamine-fentanyl group) completed the study, while 39 patients in Group B (Propofol-fentanyl group) completed the study; the only excluded patient in Group B regurgitated after LMA insertion and was dropped from the study. LMA insertion was successful at first attempt in all the patients in both groups. Both groups baseline (before LMA insertions) HRs, systolic, diastolic and mean arterial blood pressures were comparable and no significant differences in both groups: $108.4 \pm 24.8 \text{ bpm}$ versus $110.3 \pm 13.9 \text{ bpm}$ respectively ($P = 0.672$), $108.5 \pm 13.1 \text{ mmHg}$ versus $104.5 \pm 16.2 \text{ mmHg}$, respectively ($P = 0.229$), $64.2 \pm 12.1 \text{ mmHg}$ versus $62.8 \pm 14.4 \text{ mmHg}$, respectively ($P = 0.634$) and $80.7 \pm 10.8 \text{ mmHg}$ and $76.6 \pm 14.0 \text{ mmHg}$, respectively, ($P = 0.149$), [Tables 2-5]. However, the mean HRs in Group A were significantly higher when compared with Group B at 1, 3, 5, 10, 15 and 20 min after LMA insertion, $P < 0.05$. From the 25th min after LMA insertion till the end of surgery, there was no significant difference in the HRs between the patients in the two groups, $P > 0.05$, [Table 2].

Similarly, the mean SBP was significantly lower amongst patients in Group B compared with Group A at 1, 3, 5, 10, 15, 20, 25 and 30 min after LMA insertion ($P < 0.05$), but there was no significant difference in the mean SBP from 35th min after LMA insertion till the surgery was over ($P > 0.05$), [Table 3].

The mean DBP was significantly lower in Group B compared with Group A at 1, 3, 5, 10, 15 and 20 min ($P < 0.05$) after LMA insertion, but there was no significant difference ($P > 0.05$) in the mean DBP in both groups from the 25th min after LMA insertion till the surgery was concluded [Table 4]. The mean MAP at 1, 3, 5, 10, 15, 20, 25 and 30 min was significantly lower in Group B when compared with Group A after LMA insertion, $P < 0.05$ but the observed difference in the two groups from the 35th min after LMA insertion till the end of surgery was statistically insignificant ($P > 0.05$), [Table 5]. The trends in the haemodynamic parameters throughout the duration of the surgery are shown in Figure 1.

The RR at baseline, 1, 3 and 5 min after LMA insertion were similar in both groups with no significant difference, $P = 0.089$, $P = 0.190$, $P = 0.187$ and $P = 0.14$ respectively. However, the RR was significantly higher in Group A than Group B patients at 10, 15, 20, 25, 30 and 35 min after induction of anaesthesia, $P < 0.05$. There was no significant difference at 40 min after LMA insertion till the surgery was

Table 1: Demographic and anthropometric parameters of the patients

Variable	Group A (n=40), n (%)	Group B (n=39), n (%)	Total (n=80), n (%)	χ^2/t	P
Mean age $\pm$ SD	4.90 $\pm$ 3.23	3.78 $\pm$ 1.97		1.883 ^t	0.063
Age group (years)					
≤5	28 (70.0)	29 (74.4)	57 (72.2)	0.187	0.667
>5	12 (30.0)	10 (25.6)	22 (27.8)		
Sex					
Male	38 (95.0)	38 (97.4)	76 (96.2)	0.321	1.000 ^F
Female	2 (5.0)	1 (2.6)	3 (3.8)		
Weight					
Mean $\pm$ SD	18.04 $\pm$ 6.59	16.36 $\pm$ 5.31		1.251 ^t	0.215
Height					
Mean $\pm$ SD	1.08 $\pm$ 0.18	1.02 $\pm$ 1.15		1.528 ^t	0.131
ASA classification					
Class 1	38 (95.0)	39 (100.0)		2.001	0.494 ^F
Class 2	2 (5.0)	0			

Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl combination, χ^2 : Chi square test, T: Independent samples t-test, F: Fisher's exact P value, SD: Standard deviation, ASA: American Society of Anesthesiologists

Table 2: Mean heart rates of patients in the two groups before and during surgery

Time (min)	Group A		Group B		T	P
	n	Mean $\pm$ SD	n	Mean $\pm$ SD		
Baseline	40	108.40 $\pm$ 24.80	39	110.33 $\pm$ 13.94	-0.426	0.672
1	40	135.33 $\pm$ 17.78	39	105.67 $\pm$ 21.34	6.717	<0.001*
3	40	127.80 $\pm$ 16.21	39	104.59 $\pm$ 15.86	6.431	<0.001*
5	40	124.43 $\pm$ 19.08	39	106.00 $\pm$ 14.86	4.765	<0.001*
10	40	121.88 $\pm$ 18.57	39	106.49 $\pm$ 13.96	4.156	<0.001*
15	40	118.55 $\pm$ 17.67	39	109.05 $\pm$ 15.17	2.561	0.012*
20	40	118.60 $\pm$ 15.87	38	109.05 $\pm$ 15.54	2.682	0.009*
25	36	116.47 $\pm$ 17.73	36	108.92 $\pm$ 15.36	1.932	0.057
30	25	116.48 $\pm$ 12.99	22	114.32 $\pm$ 17.57	0.483	0.631
35	17	110.35 $\pm$ 7.99	9	114.89 $\pm$ 12.28	-1.142	0.265
40	9	106.56 $\pm$ 8.02	4	108.50 $\pm$ 8.35	-0.399	0.697

*P<0.05. Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl combination, T: Independent samples t-test, n: Number of patients, SD: Standard deviation

concluded ($P > 0.05$) [Table 6].

The incidence of apnoea after LMA insertion was significantly higher in patients who received IV propofol-fentanyl combination compared with patients who had ketamine-fentanyl combination, 33 (84.6%) patients versus 26 (65%) patients, $P = 0.045$. However, the mean duration of apnoea was similar in both groups, 62.3 ± 23.9 s versus 68.2 ± 32.1 s, respectively, for Groups A and B, $P = 0.439$. Apnoea was observed only after the administration of the study drugs for induction of anaesthesia and before LMA insertion. Moreover, no incidence of prolonged apnoea (>120 s) was observed in both groups throughout the surgery. The incidence of apnoea amongst patients in this study is presented in Table 7.

DISCUSSION

This study shows that ketamine-fentanyl combination causes

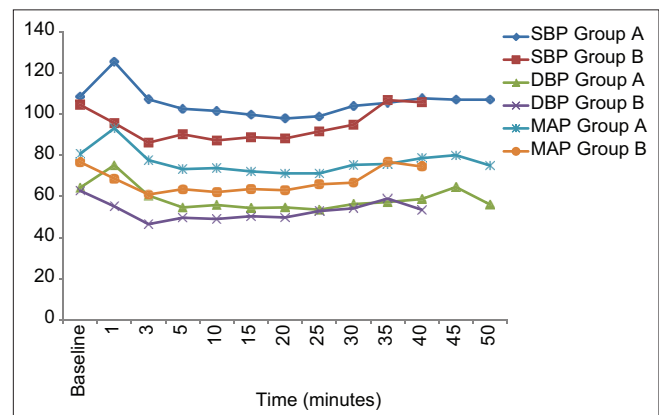


Figure 1: Trend of mean systolic blood pressure, diastolic blood pressure and mean arterial pressure of the patients over 50 min post laryngeal mask airway insertion

more significant increase in mean HR, SBP, DBP and MAP amongst patients in ketamine-fentanyl group (Group A), than patients in the propofol-fentanyl admixture group (Group B) that had propofol-fentanyl combination. The higher HR observed in the ketamine-fentanyl group in the present study agrees with the results of Singh *et al.*^[17] and Ghatak *et al.*^[18] While the duration of the tachycardia was not stated by the Singh *et al.*,^[17] Ghatak *et al.*^[18] only reported increase in HR within the first 3 min after LMA insertion in their study and this is much shorter than the observed 20 min duration of the tachycardia in our study. The shorter duration of tachycardia reported by Ghatak *et al.*^[18] might be due to the counteracting cardiovascular depressant effect of propofol on the ketamine which was the anaesthetic agent used for LMA insertions in their subjects. However, Bahk *et al.*^[19] failed to show any significant difference in the HR of patients in the various sub-groups of ketamine after LMA insertion compared with the propofol-only group. It should be noted that the vocal cords of all the patients in the Bahk *et al.*^[19] study were treated with

Table 3: Mean systolic blood pressure of patients in the two groups before and during surgery

Time (min)	Group A		Group B		T	P
	n	Mean±SD	n	Mean±SD		
Baseline	40	108.50±13.06	39	104.49±16.22	1.213	0.229
1	40	125.33±19.90	39	95.59±19.31	6.738	<0.001*
3	40	107.15±17.35	39	86.10±10.64	6.480	<0.001*
5	40	102.58±15.72	39	90.15±12.67	3.860	<0.001*
10	40	101.50±11.83	39	87.15±10.81	5.623	<0.001*
15	40	99.68±10.99	39	88.72±10.76	4.477	<0.001*
20	40	97.83±11.46	38	88.18±12.58	3.541	0.001*
25	36	98.92±13.39	36	91.56±12.23	2.435	0.017*
30	25	103.92±10.58	22	94.82±10.46	2.959	0.005*
35	17	105.41±8.27	9	106.78±11.50	-0.350	0.729
40	9	107.67±8.54	4	105.75±0.50	0.437	0.670

*P<0.05. Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl combination, T: Independent samples t-test, n: Number of patients, SD: Standard deviation

Table 4: Mean diastolic blood pressure of patients in the two groups before and during surgery

Time (min)	Group A		Group B		T	P
	n	Mean±SD	n	Mean±SD		
Baseline	40	64.20±12.12	39	62.77±14.43	0.478	0.634
1	40	75.13±17.23	39	55.15±15.65	5.388	<0.001*
3	40	60.35±12.83	39	46.46±10.12	5.334	<0.001*
5	40	54.60±7.17	39	49.62±13.27	2.084	0.040*
10	40	55.80±8.51	39	49.03±10.03	3.241	0.002*
15	40	54.35±5.74	39	50.33±10.26	2.156	0.034*
20	40	54.60±5.16	38	49.76±10.18	2.667	0.009*
25	36	53.47±6.05	36	52.86±11.15	0.289	0.773
30	25	56.24±4.30	22	54.18±10.32	0.912	0.367
35	17	57.18±6.26	9	58.89±15.69	-0.399	0.693
40	9	58.67±5.50	4	53.50±3.00	1.739	0.110

*P<0.05. Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl combination, T: Independent samples t-test, n: Number of patients, SD: Standard deviation

lidocaine spray and this might have blunted the hyperdynamic response of the larynx during LMA insertion thereby accounted for the no change in the HRs observed in any of the subgroups of ketamine and the propofol group.

Similarly, the significant rises in SBP, DBP and MAP observed in the ketamine-fentanyl group compared with the propofol-fentanyl group after LMA insertion in our study are in agreement with the findings reported by Gupta *et al.*^[20] and Bahk *et al.*^[19] The observed increases in the HR and blood pressure (SBP, DBP and MAP) in the ketamine-fentanyl group can be explained by the indirect sympathomimetic effect of ketamine. The fact that propofol induces hypotension by decreasing the peripheral vascular resistance and myocardial contractility and slowed HR due to its more vagotonic effect at larger doses could explain the better haemodynamic parameters observed in our study amongst patients in the

Table 5: Mean arterial pressure of patients in the two groups before and during surgery

Time	Group A		Group B		t	P
	n	Mean±SD	n	Mean±SD		
Baseline	40	80.68±10.80	39	76.59±13.95	1.458	0.149
1	40	93.10±17.01	39	68.64±15.81	6.616	<0.001*
3	40	77.58±13.94	39	60.90±8.70	6.359	<0.001*
5	40	73.23±10.51	39	63.46±12.97	3.682	<0.001*
10	40	73.75±9.46	39	62.05±9.21	5.568	<0.001*
15	40	72.13±7.25	39	63.54±9.45	4.540	<0.001*
20	40	71.13±7.05	38	62.95±9.50	4.331	<0.001*
25	36	71.19±8.41	36	66.86±10.81	2.336	0.022*
30	25	75.28±5.88	22	66.68±8.82	3.977	<0.001*
35	17	75.71±4.36	9	76.78±13.56	-0.302	0.765
40	9	78.56±4.72	4	74.50±3.00	1.562	0.146

*P<0.05. Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl combination, T: Independent samples t-test, n: Number of patients, SD: Standard deviation

Table 6: Respiratory rate of patients in both groups before and during surgery

Time	Group A		Group B		T	P
	n	Mean±SD	n	Mean±SD		
Baseline	40	22.46±2.52	39	21.33±3.28	-1.724	0.089
1	40	19.49±4.36	39	18.10±4.94	-1.322	0.190
3	40	21.92±2.66	39	21.00±3.44	-1.332	0.187
5	40	22.21±2.46	39	21.15±3.70	-1.489	0.141
10	40	22.67±2.39	39	21.15±3.48	-2.252	0.027*
15	40	22.74±2.37	39	21.03±3.23	-2.690	0.009*
20	40	22.61±1.94	38	21.23±3.30	-2.237	0.028*
25	36	23.00±2.50	36	21.72±3.00	-1.964	0.048*
30	25	23.45±1.87	22	20.96±3.17	-3.228	0.002*
35	17	23.33±1.00	9	20.71±2.82	-2.682	0.013*
40	9	23.50±1.00	4	19.78±3.38	-2.113	0.058

*P<0.05. Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl combination, T: Independent samples t-test, n: Number of patients, SD: Standard deviation

ketamine-fentanyl group than in the propofol-fentanyl group. In the same vein, Cheam and Chui^[21] reported that fentanyl enhances the depressant effects of propofol on blood pressure and HR.

The observed lack of significant difference in the HRs between the study groups in the Bahk *et al.*^[19] study despite the significantly higher blood pressure observed in the ketamine subgroups than propofol-only group could not be explained by any pharmacokinetic stand point because most studies reported significant increases in both HRs and blood pressure when ketamine was used for LMA insertion. The increases in the arterial blood pressure and HR following administration of ketamine occurs through central and peripheral mechanisms.^[22] Perhaps, the observed lack of significant differences in the HR reported by the researcher could be due to observer error.

The current study also revealed a significantly higher mean

Table 7: Incidence of apnoea in both groups before and during surgery

	Group A, n (%)	Group B, n (%)	Total, n (%)	RR (95% CI)	χ^2	P
Apnoea						
Yes	26 (65.0)	33 (84.6)	59 (74.7)	0.630 (0.419-0.945)	4.018	0.045*
No	14 (35.0)	6 (15.4)	20 (25.3)			
Total	40 (100.0)	39 (100.0)	79 (100.0)			
Duration of apnoea (s)						
Mean $\pm$ SD	62.31 $\pm$ 23.88	68.18 $\pm$ 32.06			-0.779 ^a	0.439

Group A: Received ketamine-fentanyl combination, Group B: Received propofol-fentanyl, χ^2 : Chi square test, RR: Relative risk, CI: Confidence interval, SD: Standard deviation, * $P < 0.05$

RR in patients that received ketamine-fentanyl combination from 10 to 35 min after LMA insertion compared with patients in the propofol-fentanyl group. This is similar to the findings of Singh *et al.*^[17] and Ghatak *et al.*,^[18] but the increase in mean RR in both studies was only observed during the first 5 min post LMA insertion and this corresponded to the study periods in the two studies. Our study shows increases in the RR in both groups (ketamine-fentanyl and propofol-fentanyl groups) up to 50-min post LMA insertion with significantly higher rate in the ketamine-fentanyl group from the 10th to the 35th min. The lowered RR observed in the propofol-fentanyl group could be partly explained by the ability of propofol to cause respiratory depression and provocation of apnoea even at induction doses^[18] and partly due to little or no respiratory depressant action of ketamine at induction doses.^[11]

The incidence of apnoea was significantly higher in the propofol-fentanyl group than ketamine-fentanyl group, (84.6% patients versus 65%) in the present study. This is comparable with the findings by Ghatak *et al.*^[18] (25% vs. 8.33%) and Gupta *et al.*^[20] (60% vs. 27%), respectively, in the propofol-fentanyl group and propofol-ketamine groups.

In another study, Cheam and Chui^[21] compared propofol-fentanyl, propofol-mivacurium and propofol-saline groups. They reported that the use of propofol-fentanyl and propofol-mivacurium was associated with significant increases in the duration of apnoea after LMA insertion. Similar statistically significant difference ($P = 0.002$) was also seen in the incidence of apnoea between the two groups studied by Singh *et al.*,^[17] as apnoea was seen in 40 (80%) out of 50 patients in the propofol-fentanyl group and 25 (50%) out of 50 patients in the propofol-ketamine group. Expectedly, the incidence of apnoea in the propofol-fentanyl groups should be higher than in the propofol-ketamine group because either of fentanyl or propofol is a potent cause of apnoea when used during anaesthesia without the appropriate precaution. Moreover, these drugs potentiate each other when combined, which may exert synergistic apnoeic effect.

Nevertheless, the findings of our study should be considered within the context of its limitations. First, the depth of anaesthesia before insertion of LMA could not be objectively ascertained, because bispectral index was not used to monitor patients in this study. There is possibility that its use might have affected the intraoperative haemodynamic status of the patients.

Finally, in the absence of a propofol-placebo group in the study, propofol-fentanyl combination could not be compared with propofol alone, which is commonly used induction agent by most anaesthetists for LMA insertion.

CONCLUSION

This comparative study shows that IV administration of pre-mixed ketamine (2 mg/kg) and fentanyl (2 μ g/kg) produces better and more stable haemodynamic parameters and lower incidence of apnoea after LMA insertions in children undergoing herniotomy than IV propofol 2.5 μ g/kg and fentanyl 2 μ g/kg.

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Conflicts of interest

There are no conflicts of interest.

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