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Evaluation of ketamine versus midazolam as co-induction agents with propofol for laryngeal mask airway insertion in children

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ABSTRACT

Background: The ideal combination of adjuncts with induction agents for Laryngeal mask airway (LMA) insertion is a matter of debate, particularly in children.

Objective: To comparatively evaluate LMA insertion using ketamine-propofol versus midazolam-propofol in children.

Methods: A total of 60 children of both sexes, aged 2–12 years with grade I and grade II ASA, were included in this study and randomly assigned to three groups (n = 20 each); group P received propofol alone, group PK received ketamine-propofol, and group PM received midazolam-propofol. Hemodynamic parameters, LMA insertion conditions, incidence of injection pain and apnea, recovery time and complications were assessed.

Results: Ketamine-propofol group achieved better hemodynamic stability compared to the other two groups. The overall LMA insertion conditions were significantly better in PK and PM groups compared to group P. The incidence of injection pain was significantly lower in PK and PM groups compared to group P ($P < 0.001$). Apnea occurred in 55% of patients in group P and in 35% of patients in group PM but did not occur in group PK. Total dose of propofol consumed and the number of patients required additional boluses of propofol were significantly higher in group P compared to the other two groups. Recovery time was significantly longer in group PM compared to group PK and group P (PM >PK >P).

Conclusion: Both midazolam-propofol and ketamine-propofol provide suitable insertion conditions of LMA in children but, the ketamine-propofol combination was advantageous in maintaining hemodynamic stability, decreasing incidence of apnea and less recovery time.

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1. Introduction

The management of the airway remains a vital and essential anesthetists' aptitude. The laryngeal mask airway (LMA) has demonstrated to be an acknowledged addition to the airway management equipments. It is fairly straightforward and safe to utilize over a wide range of surgical specialties [1]. The insertion of LMA requires adequate anesthetic depth for relaxing the jaw muscles and the inserted LMA to be tolerated without unwanted coughing, gagging, breath-holding or involuntary movement and there are many induction agents were attempted to promote smooth insertion of LMA [2].

Propofol is the induction agent of choice for LMA insertion when compared with other induction agents and it is commonly used for general anesthesia in children. It is a non-opioid, sedative-hypnotic, non-barbiturate agent with antiemetic effects and quick induction [3]. It permits soft insertion of LMA by discouraging airway reflexes, while depression of cardio-respiratory system, pain on injection and lack of analgesic properties are its adverse effects [4].

Utilization of adjuvants like ketamine, midazolam, opioids, low-dose muscle relaxants, and sevoflurane could improve LMA insertion conditions [5]. Ketamine is an N-methyl d-aspartate (NMDA) receptor antagonist, has some characteristics which are favorable in pediatric anesthesia such as airway-maintaining activity, increasing heart rate, and cardiac output in addition, it did not cause cardio-respiratory depression and it has analgesic effects "unlike propofol" [6]. Still, using Ketamine alone as an induction agent is restricted by some factors such as emergence hallucinations and elevation of both blood pressure and heart rate [7].

The combination of propofol and ketamine (ketofol) has been well-studied and may present an attractive induction agent that has good hemodynamics and little adverse effects caused by either drug [8]. Midazolam is a short-acting benzodiazepine, it is an effectual sedative pre-medicant in children and when it is combined with propofol, it could reduce the dose required for LMA insertion [9]. The objective of this study was to compare between ketamine and midazolam as co-induction agents with propofol for LMA insertion in children, considering hemodynamic stability, insertion conditions, local pain at injection, incidence of apnea and recovery time.

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2. Patients and methods

This is a randomized, prospective, double-blind study which was conducted in El-Minia University Hospital, Egypt after the approval of the University Ethical Committee in the period from February to December, 2016. A total of 60 children of both sexes with grade I and II physical status of American Society of Anesthesiologists (ASA) and aged 2–12 years, scheduled to undergo short elective surgeries under general anesthesia were included in this study. Patients with suspected difficult airway, increased risk of gastric regurge, cardiac or pulmonary abnormalities, neuromuscular disease or with known allergy to any of the study drugs were excluded. Allergy to the study drugs were suspected from parents' history, if the child had previous anesthetic and developed any complications due to anesthesia. After obtaining informed parental consent, patients were randomly divided according to computer-generated table numbers into three equal groups (20 patients per each): group P included patients who received 5 ml normal saline, followed by propofol 3.5 mg/kg IV, group PK received ketamine 0.5 mg/kg, diluted with NS to a total volume of 5 ml, followed by propofol 3 mg/kg IV and group PM included patients who received midazolam 0.1 mg/kg diluted with NS to a total volume of 5 ml, followed by propofol 3 mg/kg IV (Figure 1). A dose of 3 mg/kg propofol was used in the groups that received midazolam and ketamine as co-induction agents due to the synergistic action of midazolam when used with propofol [10] and the additive effect of ketamine when used with propofol [11].

A careful medical history was taken from the parents. Then, general examination including (heart rate, blood pressure and respiratory rate), physical examination including (chest, heart and abdomen) and airway examination were done and complete blood picture was checked preoperatively. All children were fasted for 6 hours without solid food and for 2 hours without liquids.

On arrival into the operating theatre, one of the parents accompanied the child till induction of anesthesia. Standard ECG monitoring, oxygen saturation, and non-invasive blood pressure (NIBP) were attached and the baseline values of heart rate (HR), mean arterial blood pressure (MAP), and oxygen saturation (SaO_2) were recorded. An IV 22 G cannula was then inserted and atropine 0.01 mg/kg was given.

2.1. Anesthetic technique

The included patients were pre-oxygenated for 3 minutes before induction of anesthesia. Anesthesia was induced with propofol premixed with lidocaine 0.5 mg/kg [12] to alleviate the pain on injection, given over 15 seconds, 2 minutes after the study

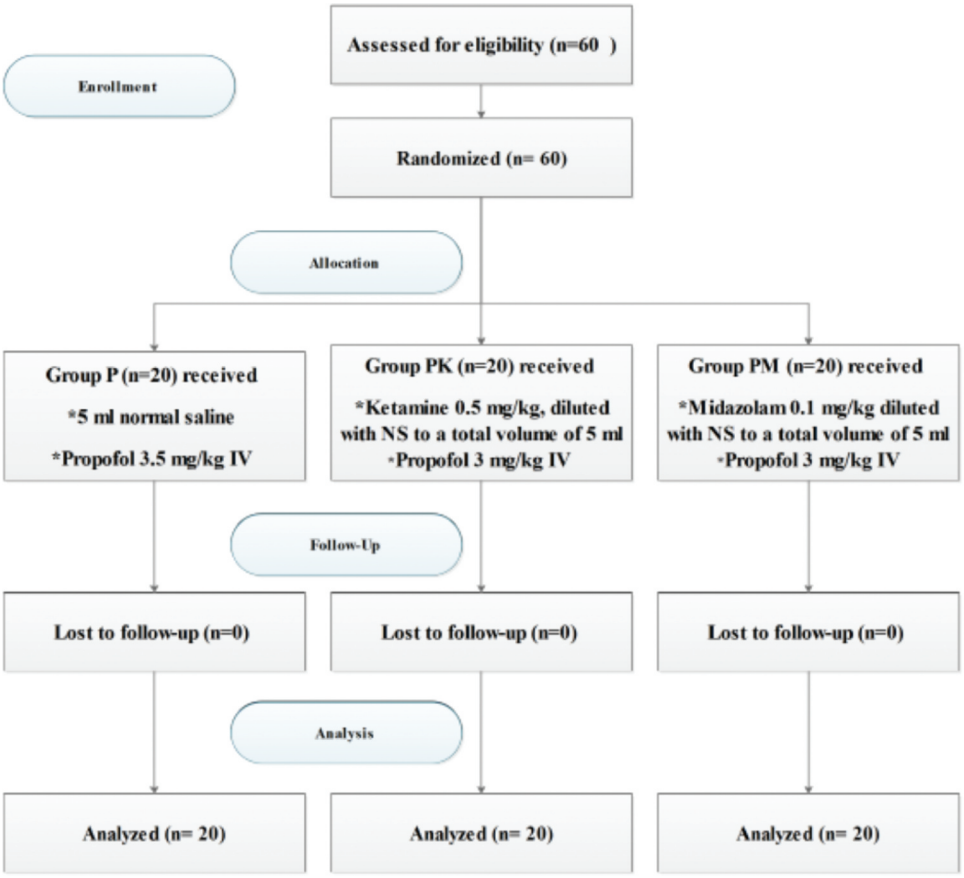

Figure 1. Consort flow chart of the patients included in the study.

drug. The induction agents were prepared and administered to the patients by an anesthetist who was not involved in the study. Pain on injection was graded using a four-point scale [13]: 0: no pain, 1: mild pain (grimace), 2: moderate pain (grimace + cry) and 3: severe pain (cry + withdrawal). Ninety seconds after induction of anesthesia, the insertion of the appropriate size LMA classic (sizes 2 or 2.5) was performed using the standard Brain method [14] by an experienced anesthetist who was blinded to the given medications.

Following insertion, the cuff was inflated with the recommended volume of air for each size. Then, the position of LMA and airway patency was confirmed by sufficient tidal ventilation, O_2 saturation > 95% and capnography values between 35 and 45 mm Hg. After that a nasopharygeal temperature probe was applied to monitor core temperature. Normothermia was maintained by warming IV fluids and operating theater temperature set at 24°C. Thereafter, the patients were allowed to breathe spontaneously and anesthesia was maintained with isoflurane 1.5–2.0 % in 100% O_2. Intra-operative analgesia was provided by fentanyl 1–2 µg /kg which was given before skin incision. If apnea occurred and exceeded 30 seconds, manual ventilation was provided to maintain SaO_2 > 95% and the incidence of apnea was reported but the duration of which was not recorded. The patient had a subsequent bolus dose of propofol 1 mg/kg and ventilated with a face mask if the first attempt of LMA insertion was unsuccessful. A maximum of three attempts were allowed for the insertion of the LMA and insertion condition assessment was done only for the first attempt. In addition, incremental bolus dose of propofol was given if the patients had laryngeal responses such as swallowing, coughing/gagging, or laryngospasm, after LMA insertion. Increasing the depth of anesthesia would be beneficial as removal of the LMA and reinserting it would be more stimulating to the patient. Also, the numbers of insertion attempts, the total dose of propofol given and the number of patients who required additional boluses of propofol were recorded.

Mean arterial blood pressure, HR, and SpO_2 were monitored continuously throughout the surgery and were recorded at the following time intervals: before induction (baseline values), immediately after induction, at 1 minute, 3 minute, 5 minute, and 10 minute after LMA insertion. LMA insertion conditions were assessed using six variables on a 3-point scale as follows [15]:

1) Resistance to mouth opening "1: no/ 2: significant/ 3: force required".

2) Resistance to insertion "1: easy/ 2: difficult/ 3: impossible".

3) Swallowing "1: nil/ 2: slight/ 3: gross".

4) Coughing/gagging "1: nil/ 2: slight /3: gross".

5) Limb/head movements "1:nil/ 2: slight /3: gross".

6) Laryngospasm "1: nil/ 2: partial/ 3: total".

We summed all the six scores to give a LMA insertion condition summed score which ranged from 6 to 18, a lower summed score indicating more favorable LMA insertion conditions. Modified Aldrete score (Table 1) [16] was evaluated and adopted as the discharge criteria according to which a score ≥9 is needed for discharge from PACU. The time from anesthetic discontinuation to attainment of this score was recorded.

Adverse events such as: excessive secretions, lacrimation, hallucination, breath-holding, postoperative nausea and vomiting (PONV), laryngospasm or bradycardia were recorded.

2.2. Statistical analysis

Prior to the study, the number of patients required in each group was determined after a power calculation according to data obtained from pilot study. The pilot study reported a mean LMA insertion score of 7.83 in group P, and a mean LMA insertion score of 6.5 in group PK and a mean LMA insertion score of 6.33 in group PM. A sample size of 20 patients in each group was determined to provide 95% power for one-way ANOVA test at the level of 5% significance using G Power 3.1 9.2 software. Statistical analysis was performed using SPSS (version 20) for Windows. Quantitative data were expressed as mean ± SD, however, qualitative data were presented as number (N) and percentage (%). Kolmogorov–Smirnov for normality test was used to differentiate between parametric data and non-parametric data. T-test was used to compare between two groups for quantitative variables and Chi-square (x^2) test was used for qualitative data. ANOVA test was used for the comparison of more than

Table 1. Modified Aldrete scoring system [16].

Assessment items	Condition	Grade
Activity, able to move voluntarily or on command	4 extremities	2
	2 extremities	1
	No	0
Breathing	Able to breathe deeply & cough freely	2
	Dyspnea, shallow or limited breathing	1
	Apnea	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Unresponsive	0
Circulation (BP)	± 20% of pre-anesthesia level	2
	±20% to 49% of pre-anesthesia level	1
	± 50% of pre-anesthesia level	0
SPO2	Maintain SpO2 > 92% in ambient air	2
	Maintain SpO2 > 90% with O2	1
	Maintain SpO2 < 90% with O2	0

two groups. The probability value of less than 0.05 was considered significant.

3. Results

Regarding the demographic data, the results showed that there were no statistically significant differences among the three groups with respect to age, weight, and sex distribution. Also, ASA class and both type and duration of surgery were similar in the three groups (Table 2).

The baseline values of mean arterial blood pressure, heart rate, and oxygen saturation were comparable in the three groups (Table 3), MAP decreased significantly in groups P and PM compared to baseline values throughout the study period (post-induction, at 1, 3, 5, and 10 minutes after LMA insertion). On the other hand, group PK showed better hemodynamic profile where blood pressure was maintained post-induction and throughout the measurement points compared to the baseline value. Compared to groups P and PM, group PK showed a significant increase in blood pressure shortly after induction.

Regarding heart rate changes (Table 3), group P showed significant decrease at all measurement points compared to baseline values. Compared to baseline readings, HR increased significantly in group PK and almost it did not change in group PM. Post-induction, HR was significantly higher in group PK compared to its value in P and PM groups.

Concerning oxygen saturation, there were no significant changes among the three groups or when compared to baseline values within each group during the study period (Table 3).

The incidence of injection pain was significantly lower in the PK and PM groups than in the P group ($P < 0.001$), with no significant difference between PM and PK groups (Figure 2). Regarding apnea, it occurred after LMA insertion in 55% (11/20) and 35% (7/20) of patients in groups P and PM respectively, while it was not observed in any patient in group PK. So, the incidence of apnea was significantly higher in group P than group PM and group PK (Figure 3).

Concerning the LMA insertion conditions (Table: 4), the incidence of complete jaw relaxation and full mouth opening was significantly higher in groups PK and PM (100% and 80% of patients respectively) as compared to group P (40%), ($P < 0.001$). Similarly, LMA insertion was easy in the majority of the patients in groups PK and PM (18 out of 20 and 16 out of 20 patients, respectively), with no significant difference between the two groups. When compared to group P, LMA insertion was significantly easier in groups PK and PM ($P < 0.01$). The incidence of swallowing, coughing/gagging, and head/limb movements was almost the same in the three groups. Partial laryngospasm occurred in one patient in group PK, while severe laryngospasm was not seen in any patient in the study groups. LMA insertion score was similar in both PK and PM groups (6.9 ± 0.94 and 6.7 ± 0.80, respectively) and was significantly better than the summed score for group P (8.6 ± 1.7).

Table 2. Patients characteristics and operative data.

Variable	Group P (n = 20)	Group PK (n = 20)	Group PM (n = 20)
Age (years)	7.8 ± 2.9	6.2 ± 3.3	6.3 ± 3.2
Sex: Male/ Female	13/7	13/7	14/6
Weight (kg)	23.2 ± 5.5	20.4 ± 5.4	20.7 ± 5.9
ASA: I/ II	17/3	17/3	15/5
Type of operation: Plastic/General Surgery/ Urology/Orthopedic	8/6/ 3/3	4/6/ 5/5	6/5/ 6/3
Duration of surgery (min)	36.4 ± 8.6	41.1 ± 9.3	39.5 ± 7.9

Data were expressed as mean ± SD or numbers.

Table 3. Hemodynamic data.

Variable		Group P (n = 20)	Group PK (n = 20)	Group PM (n = 20)
MAP (mmHg)	Baseline	89.7 ± 9.7	85.3 ± 14.4	84.9 ± 12.4
	Post induction	74.2 ^{x*} ± 9.8	87.0 $^{*\#}$ ±13.1	74.5 $^{x\#}$ ±10.7
	1 min after LMA insertion	74.8 ^{x} ± 9.3	80.5 $^{\#}$ ± 13.6	73.3 $^{x\#}$ ± 9.9
	3 min	73.05 ^{x} ± 9.4	78.9 ± 13.9	71.9 ^{x} ± 9.41
	5 min	70.9 ^{x} ± 9.9	76.6 ± 14.6	72.1 ^{x} ± 8.29
	10 min	75.3 ^{x} ± 8.1	76.4 ± 15.8	75.1 ^{x} ± 8.23
HR (bpm)	Baseline	136.4 ± 13.1	121.6 ± 27.2	131.7 ± 20.4
	Post-induction	121.1 ^{x*} ± 13.8	134.7 $^{x*\#}$ ± 16.6	127.6 $^{\#}$ ± 17.9
	1 min after LMA insertion	117.8 ^{x} ± 31.9	133.1 ^{x} ± 19.4	130.2 ± 17.3
	3 min	124.1 ^{x} ± 18.1	133 ^{x} ± 20.1	134.5 ± 18.7
	5 min	123.1 ^{x} ± 17.3	134.2 ^{x} ± 20.1	129.9 ± 35.7
	10 min	127.2 ^{x} ± 16.3	132.9 ^{x} ± 17.7	134.8 ± 18.4
SPO_2	Baseline	99.3 ± 0.73	99.4 ± 0.60	99.5 ± 0.51
	Post-induction	99.8 ± 0.04	99.8 ± 0.41	100 ± 0
	1 min after LMA insertion	100 ± 0	99.8 ± 0.36	100 ± 0
	3 min	100 ± 0	99.8 ± 0.36	100 ± 0
	5 min	100 ± 0	99.8 ± 0.36	100 ± 0
	10 min	100 ± 0	99.8 ± 0.36	100 ± 0

Data were expressed as mean ± SD.
* $P < 0.05$ (P vs PK groups). + $P < 0.05$ (P vs PM groups). # $P < 0.05$ (PK vs PM groups).
x $P < 0.05$ compared to baseline values in the same group.

Table 4. LMA insertion conditions of the study groups.

Variable	Group P (n = 20)	Group PK (n = 20)	Group PM (n = 20)
Resistance to mouth opening: (no/ significant/ force required)	8/7/5 *+	20/0/0 *	16/4/0 +
Resistance to insertion: (easy/ difficult/impossible)	7/13/0 *+	18/2/0 *	16/4/0 +
Swallowing: (nil/slight/gross)	13/7/0	12/8/0	17/3/0
Coughing/gagging: (nil/slight/ gross)	17/3/0	15/5/0	19/1/0
Limb/head movements: (nil/slight/gross)	12/8/0	15/5/0	18/2/0
Laryngeospam: (nil/partial/total)	20/0/0	19/1/0	20/0/0
LMA insertion score	8.6 ± 1.7* +	6.9 ± 0.94*	6.7 ± 0.80 +

* P < 0.05 (P vs PK groups). + P < 0.05 (P vs PM groups). # P < 0.05 (PK vs PM groups).

The present results showed that the number of attempts for LMA insertion was comparable in the three groups where LMA insertion was successful in the first attempt in 90%, 95%, and 95% of patients in groups P, PK, and PM, respectively (Table 5). LMA was inserted in second attempt in two cases in group P and one case in both PK and PM groups, respectively, and no cases required more than two attempts to insert LMA.

More than half of patients in group P (55%) needed additional doses of propofol compared to five cases (25%) in group PK and three cases (15%) in group PM (p < 0.05), while group PK and PM did not differ significantly regarding the need for supplemental doses of propofol (Table 5). Total dose of propofol consumed for LMA insertion (mg/kg) was significantly higher in group P (5.6 ± 2.08) than in group PK and PM (3.6 ± 1.2 and 3.4 ± 1.09, respectively) (P < 0.001), with no significant difference between PK and PM groups (Table 5). The time to achieve Modified Aldrete Score ≥ 9 was significantly longer in group PM (14.9 ± 1.5 minute) than in group PK (12.8 ± 1.08 minute) and group P (8.9 ± 1.09 minute. Also, group PK showed more prolonged recovery as compared to group P (p < 0.001) (Table 5).

The complications after LMA removal were infrequent, three cases in group P suffered from laryngospasm relative to one patient in group PK with no statistically significant difference among the three groups. Laryngeal spasm was successfully managed by application of positive pressure ventilation with an anesthesia bag and mask using 100% O2 and suctioning of the secretions from the hypopharynx. No patient needed succinylcholine or tracheal intubation. NO one in the three groups suffered from increased secretions, hallucination, PONV, or bradycardia.

4. Discussion

Co-induction is the term meaning combination of little doses of anesthetic agents to decrease the overall required dose of induction drugs, it could provide a balance between therapeutic effects and the unfavorable side effects [17]. Our study had been planned to compare between ketamine and midazolam as co-induction agents with propofol for LMA insertion in children, considering the hemodynamic response, insertion conditions, recovery time and complications with both drugs.

Allsop et al. [18] studied LMA insertion in children who received propofol doses of 2.5, 3, and 3.5 mg/kg with no premedication. They found that the majority of unpremedicated children (95%) who received 3.5 mg/

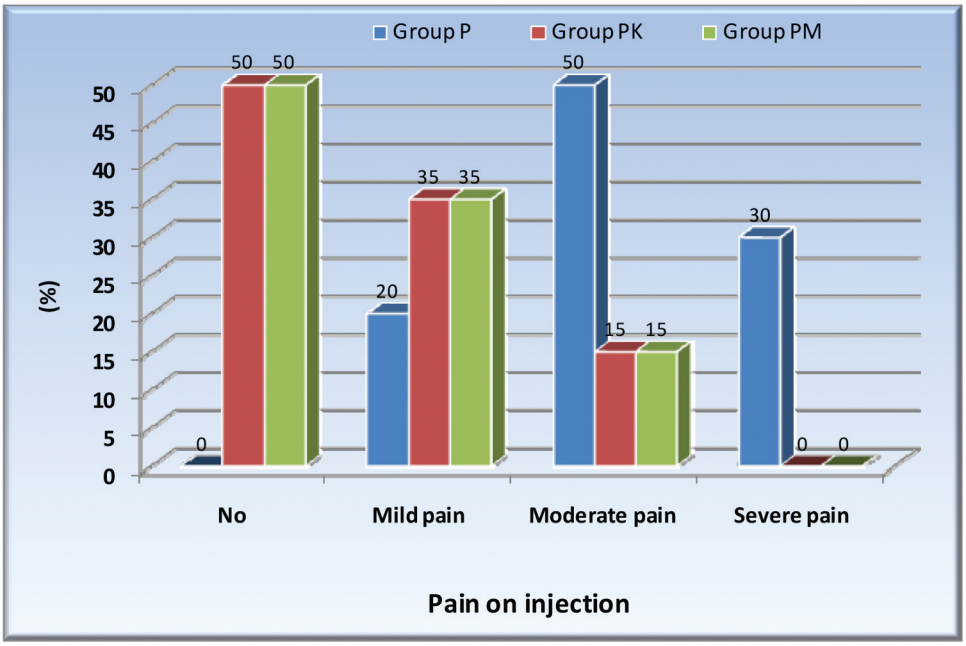

Figure 2. Incidence of pain on injection among the study groups.

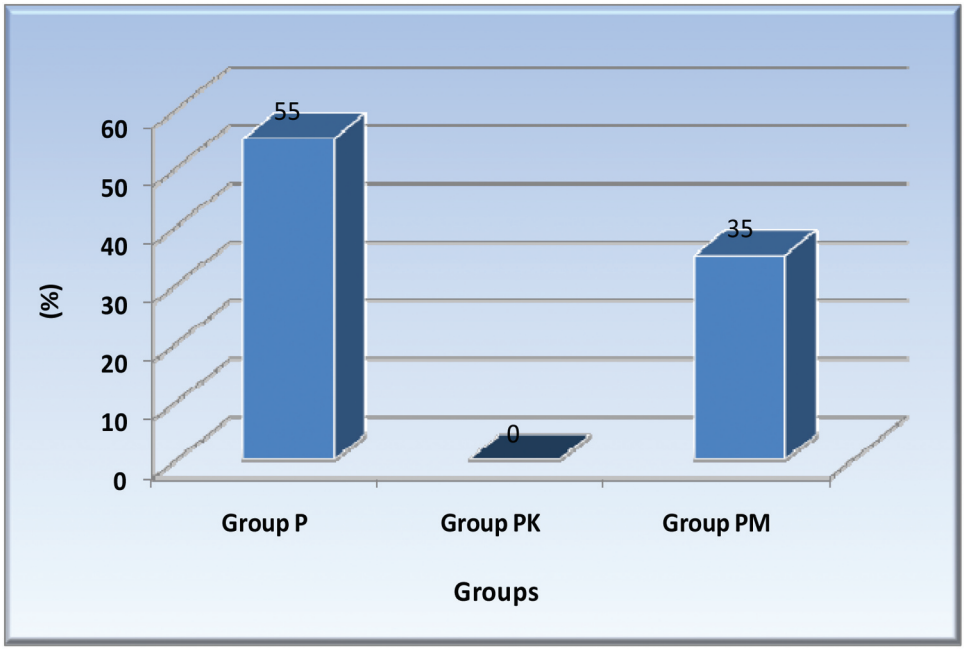

Figure 3. Incidence of apnea among the study groups.

Table 5. Number of attempts for LMA insertion, need for supplemental anaesthetic, total dose of propofol consumed and recovery time.

Variable	Group P (n = 20)	Group PK (n = 20)	Group PM (n = 20)
Number of attempts for LMA insertion: (1/2/3)	18/2/0	19/1/0	19/1/0
Number of patients needed supplemental propofol	11^{*+}	5*	3^{+}
Total dose of propofol used (mg/kg)	5.6 ± 2.08^{*+}	3.6 ± 1.2*	3.4 ± 1.09^{+}
Recovery time (min)	8.9 ± 1.09^{*+}	12.8 ± 1.08$^{*\#}$	14.9 ± 1.5$^{+\#}$

* P < 0.05 (P vs PK groups). + P < 0.05 (P vs PM groups). # P < 0.05 (PK vs PM groups).

kg of propofol had good LMA insertion conditions so, we used this dose (3.5 mg/kg of propofol) for induction in the control group. It was found that premedication with oral midazolam (0.5 mg/kg, 30–60 minute) before anesthetic induction, reduced significantly the required propofol dose by about 30% compared to unpremedicated children [10]. The peak effect of midazolam occurs between 2 and 5 minutes after a bolus dose. Therefore, the optimum time of propofol administration would be between 2 and 3 minutesfollowing midazolam [19]. The peak effect of intravenous ketamine occurs at 1 minute [20]. So, we used propofol in lower doses (3 mg/kg) in the study groups where ketamine (0.5 mg/kg) or midazolam (0.1 mg/kg) were given 2 minutes before propofol induction.

Our research revealed hemodynamic stability with group PK after induction and throughout the measurement points, compared to other groups. This favorable hemodynamic effect seen in the PK group may be due to ketamine's indirect sympathomimetic effect, as it inhibits the reuptake of catecholamines (CAs) [4].

Our findings are in line with the results of Goyagi et al. [21] who found a significant decrease in BP and HR from pre-induction values, after propofol induction with 1.95–2.6 mg/kg and before insertion of LMA. Also, this concurs with Ashwini and Kempachary [22], who studied 60 children allocated into two groups, group I received propofol (3.5 mg/kg) and group II received midazolam (0.05 mg/kg), 2 minutes before propofol induction (2.5 mg/kg). These results showed a significant decrease in systolic, diastolic, and mean BP and HR in both groups, compared to their baseline values. However, the reduction in hemodynamic variables was gradual and less marked in group II. On the other hand, Bhaskar et al. [1] found that the addition of midazolam achieved more hemodynamic stability than propofol alone (with different doses) during LMA placement. This differs from our findings where BP decreased significantly in PM group compared to baseline values. This may be due to the large dose of midazolam used in our study (0.1 mg/kg).

Regarding the desirable hemodynamic effect observed in PK group in our study, this was in agreement with various studies that used ketofol for anesthetic induction for LMA insertion in children [23,24] and adults [25,26]. Goel et al. [23] studied the effect of ketamine and midazolam as co-induction agents with propofol for LMA insertion in children. Although, they found that SBP decreased significantly compared to baseline readings in all groups, propofol group showed a larger reduction in SBP compared to PK and PM groups with no significant difference between PK and PM groups. Similar to our findings, HR decreased significantly at all times when compared to preinduction values in the propofol group. Similar findings were reported by other researches [6,27].

The incidence of injection pain in the present study was significantly lower in PK and PM groups than in propofol group. This matches with the study of Yousef and Elsayed [24], that showed the incidence of pain on injection was significantly lower in ketofol group (10%) than in propofol group (80%). Also, it was found that pre-treatment with a small dose of ketamine decreased the frequency and intensity of propofol injection pain [28].

In the current study, apnea occurred after LMA insertion in 55% of patients in propofol group and in 35% of patients in PM group, while it did not happen in any patient in PK group. This was concordant with Mohamed et al. [26] who found that co-induction with midazolam produced a significantly longer duration of apnea compared to ketamine. They revealed that this suppression of breathing is due to the synergistic action between midazolam and propofol at the common GABA receptor sites. This also concurred with other studies [27,29] that found significantly less prolonged apnea with administration of ketamine with propofol.

Concerning the LMA insertion conditions, our study has shown better LMA insertion conditions in PK and PM groups compared to propofol group with no significant difference between PK and PM groups. Nevertheless, swallowing and coughing/gagging occurred more frequently in PK group (40% and 25%, respectively) than in propofol (35% and 15% respectively) or PM groups (15% and 5% respectively). These results may be explained by ketamine's ability to maintain the airway reflexes [30]. Laryngospasm was the least frequent patient response encountered in our study (occurred only in one patient in PK group), although it is usual for LMA to cause some transient cord closure. This may be due to the high propofol dose used in the control group and the ability of propofol [31] and benzodiazepines [26] to suppress the upper airway reflexes. Although we encountered resistance to mouth opening in 12 patients in the propofol group, apnea occurred in 11 patients in the same group. This was due to the additional doses of propofol given to increase the anesthetic depth and insert the LMA successfully.

The number of attempts required for LMA insertion was comparable in the three groups. However, more patients in propofol group (55%) needed additional boluses of propofol compared to 25% and 15% of patients in PK and PM groups, respectively ($P < 0.01$). So, the total dose of propofol (in mg/kg) consumed for successful LMA insertion was significantly greater in propofol group than that used in PK or PM groups.

Similar to our finding, it has been reported that co-induction using ketamine with propofol improved the LMA insertion conditions in children [6,24,29] and adults [25]. Also, Goel et al. [23] confirmed more acceptable insertion conditions in PK and PM groups compared to propofol alone group with no significant difference between PK and PM groups. They found that 22% of patients in propofol group required additional doses of propofol while none of the patients in other groups needed supplemental anesthetic.

Likewise, our results were in agreement with the findings of Mohamed et al. [26] in adults, where they found comparable overall insertion conditions in patients who received ketamine or midazolam as co-induction agents with propofol. However, the ketamine-propofol group had a significantly higher incidence of full mouth opening compared to the midazolam-propofol group. Contrary to that, Ashwini and Kempachary [22], studied the effectiveness of midazolam (0.05 mg/kg) with propofol (2.5 mg/kg) compared to propofol alone (3.5 mg/kg) for LMA insertion in children and they found comparable LMA insertion conditions in both groups. This difference may be due to the different doses of induction agents used in their study.

In our study, recovery (assessed by the time to reach Modified Aldrete score ≥ 9) was significantly more prolonged in group PM than PK or P groups, whereas it was significantly earlier in P than PK group (PM >PK >P). This was similar to other studies [23,32]. However, recovery time did not differ significantly between PK and PM groups in Goel et al. study. This may be due to using a higher dose of midazolam in our study (0.1 mg/kg).

We did not notice significant adverse events in our study such as increased airway secretions, desaturation, emergence hallucinations, nausea and vomiting, or bradycardia, after removal of LMA in the three groups. Ketamine is known to increase airway secretions, which is clinically important in pediatric population. The ketamine propofol combination has not been found to cause excessive secretions with the use of LMA or endotracheal tube in airway management [32]. It has been shown that propofol could be effective in eliminating the side effects of subanesthetic doses of ketamine [33]. Finally, the limitation in this study was the relatively lower sample size.

5. Conclusion

In conclusion, the addition of midazolam (0.1 mg/kg) to propofol (3 mg/kg) and ketamine (0.5 mg/kg) to propofol (3 mg/kg) provide suitable LMA insertion conditions in children, but the ketamine-propofol combination was advantageous in maintaining hemodynamic stability, decreasing incidence of apnea and lowering prolonged time of recovery. Using propofol alone (3.5 mg/kg) for

insertion of LMA has the disadvantage of hemodynamic instability, increased incidence of pain on injection and increased occurrence of apnea but with rapid recovery. Further studies are warranted to confirm our findings and determine the optimal dosing of induction agents used for LMA insertion.

Disclosure statement

No potential conflict of interest was reported by the authors.

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