RESEARCH





Midazolam premedication facilitates mask ventilation in children during propofol induction of anesthesia: a randomized clinical trial

Rafet Yarimoglu^{1*}, Betul Basaran², Tayfun Et², Aysegul Bilge² and Muhammet Korkusuz²

Abstract

Purpose Mask ventilation is the most widely used method to provide ventilation during anesthesia induction. Appropriate head and neck positions, exaggerated jaw lifts, two-hand and two-person ventilation, and the use of oral or nasal airways can facilitate mask ventilation. Neuromuscular blockers and premedication drugs such as midazolam and dexmedetomidine have also been proposed to facilitate mask ventilation. The hypothesis of this study was that midazolam premedication would facilitate mask ventilation in children.

Methods Children aged 2–10 years were randomized into two groups. The midazolam group (Group M) received an intravenous dose of midazolam premedication (0.1 mg/kg, maximum dose 3 mg), and the control group received an intravenous dose of saline of the same volume (Group C). The primary outcome of the study was to examine the effect of midazolam premedication on mask ventilation in children, using the Han mask grading scale.

Results The data of 120 children were analyzed (n = 60 in Group M, n = 60 in Group C). According to the Han mask grading scale, the scores of the patients in the midazolam group were significantly lower than those of the control group. The distribution of Han scores was significantly different between the groups (p < 0.001). In the midazolam group, 93.3% of the children had a Han score of 1 and 6.7% had 2, and in the control group, 60% had a score of 1, and 40% had 2. In the subgroup analysis of overweight children, a Han score of 1 was determined in 91.7% of the midazolam group and 61.1% of the control group (p = 0.03).

Conclusion In conclusion, the results of this clinical research demonstrated that midazolam premedication improves mask ventilation in children during general anesthesia induction. The findings also showed that the effect of midazolam in facilitating mask ventilation was similar in overweight children.

Clinical trial registration The study was registered in clinicaltrials.gov (trial ID: NCT05368441 on 10/05/2022). **Keywords** Pediatrics, Premedication, Midazolam, Anesthesia, general, Ventilation, Airway management

*Correspondence: Rafet Yarimoglu drrafety@gmail.com ¹Department of Anesthesiology and Reanimation, Karaman Training and Research Hospital, Universite District. 1984 Street, Number:1, Karaman, Turkey

²Department of Anesthesiology and Reanimation, Karaman Training and Research Hospital, Karamanoglu Mehmetbey University, Karaman, Turkey



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creative.commons.org/licenses/by-nc-nd/4.0/.

Introduction

Mask ventilation (MV) is often used to maintain patient breathing during anesthesia until airways are secured with an endotracheal tube or other devices. Patients with abnormal anatomy (e.g. craniofacial malformation) may pose challenges for mask ventilation [1, 2]. Mask ventilation difficulties can also be seen in children with normal anatomy. Although some studies state the opposite, obesity, a history of obstructive sleep apnea (OSA), and male gender are possible risk factors for difficult mask ventilation in children [3, 4]. Proper positioning (e.g. sniffing position), appropriately sized equipment, and continuous positive airway pressure (CPAP) improve mask ventilation.

The importance of mask ventilation is increased as it is a mandatory method at the beginning of general anesthesia. The early administration of neuromuscular blockers makes it easier to perform mask ventilation in adults. However, despite reports of efficacy in adults, there are few studies and conflicting data related to children. A recent study found that neuromuscular blockers improved mask ventilation for most patients but worsened it for a small proportion [2]. Inadequate mask ventilation may cause rapid desaturation and irreversible catastrophic conditions, particularly in pediatric patients who are not breathing spontaneously [5, 6]. Therefore, knowing the applications and methods that may facilitate mask ventilation is crucial.

Midazolam, a benzodiazepine derivative, is commonly used in premedication due to its rapid onset, short duration, anxiolytic effects, and amnesia-inducing properties. It creates an inhibitory effect by binding to Gamma-Aminobutyric Acid A (GABA_A) receptors [7]. This mechanism exhibits sedative, anxiolytic, anticonvulsant, muscle relaxant, and amnestic effects. Previous research has suggested that midazolam acts on $\alpha 2$ GABA_A receptor subunits, resulting in muscle relaxation in the upper respiratory tract [8, 9]. The effects of midazolam premedication facilitating mask ventilation in adults have been demonstrated [9]. However, there is no study examining this effect in the pediatric population.

This randomized controlled trial aimed to assess the effect of midazolam premedication on mask ventilation in pediatric patients. The study hypothesis was that midazolam premedication would ease mask ventilation in pediatric patients.

Materials and methods Study design

The institutional review board of Karamanoglu Mehmetbey University Faculty of Medicine approved this singlecenter, blinded, randomized controlled trial. All study procedures were in line with the Helsinki declaration and its amendments. Parents provided a written consent. In addition, the trial was registered prior to patient enrollment at clinicaltrials.gov (number of registration: NCT05368441, date of registration: 10/05/2022, link of trial registry: https://clinicaltrials.gov/ct2/show/NCT053 68441?term=NCT05368441%26;draw=2%26;rank=1).

Patients

Pediatric patients undergoing elective surgery requiring general anesthesia at Karaman Training and Research Hospital were included in the study.

Inclusion criteria were;

- children aged 2–10 years,
- American Society of Anesthesiologists Classification (ASA) I-II,
- patients whose vascular access was performed in the wards before coming to the operating room (OR),
- patients who were scheduled for general anesthesia for any elective surgery,
- patients with a fasting period of six hours for solid foods and two hours for clear liquids.

Exclusion criteria were:

- allergic reaction to midazolam,
- respiratory tract infection or chronic respiratory disease,
- the presence of muscle disease,
- mechanical airway obstruction (children with mild or moderate OSA, history of snoring or witnessed apnea, tonsil size grade 3 or higher) or craniofacial anomaly,
- chronic use of sedative or anticonvulsant treatments,
- patients with ASA scores of III-IV,
- emergency surgery.

Group allocation and randomisation

Once recruited, participants were randomly assigned to either the intervention (intravenous midazolam premedication- group M) or the comparison group (intravenous normal saline premedication- group C). Computergenerated random numbers were used to ensure concealment, and participants were assigned using a closed envelope method by a blinded nurse. Group M consisted of patients who received midazolam for premedication, and Group C consisted of patients who received saline instead of premedication. An anesthesiologist, unaware of the groups to which the patients belonged, prepared the syringes according to the study procedure. To maintain blinding, syringes were designated as A (for midazolam) or B (for saline), and syringe contents were not clearly stated. Same anesthesiologist labeled the syringes A and B and then handed them to the medication nurse.

Finally, another blind nurse administered medications to patients in the preoperative room according to allocation.

Blinding

None of the nurses knew about the study protocol, and the four anesthesiologists were unaware of which patients were in which groups. One anesthesiologist prepared the syringes, another assessed anxiety and sedation levels, the third was in charge of induction and mask ventilation, and the fourth evaluated the difficulty of mask ventilation using a grading scale. Each anesthesiologist was only responsible for their part of the study protocol until the data collection phase was completed.

Intervention

The age, height, weight, Mallampati score, inter-incisor gap value, thyromental distance, sternomental distance, and neck circumference values of all the patients were recorded in the preoperative waiting room (PR) by an anesthesiologist who was blinded to the patient groups. Intravenous (i.v.) midazolam premedication (0.1 mg/kg of midazolam in 3 ml of normal saline; maximum total dose is 3 mg) was administered to the patients in Group M three minutes before being taken to the OR, and those in Group C were administered 3 ml of normal saline intravenously by a blinded nurse. The baseline values of the patient's anxiety and sedation levels were determined one minute before the premedication with the modified Yale Preoperative Anxiety Scale (mYPAS, range, 23–100, with higher scores show more anxiety, Supplemental file, Table 1) and the Modified Observer's Assessment of Alertness/Sedation scale (MOAA/S, range, 0-5 points, with a score of 5 indicates the patient is awake, while 0 means general anesthesia, Supplemental file, Table 2). The patients were admitted to the OR after the third minute following the premedication accompanied by one of their parents, and ECG and pulse oximetry monitoring were performed. Before anesthesia induction, the patients were evaluated with the mYPAS and MOAA/S scales for a second time by the same anesthesiologist who was blinded to the patient groups. After two minutes of preoxygenation with a fresh gas flow of 5 L/minute (L/ min), 0.5 mg/kg propofol was administered through the i.v. cannula at 30-second intervals until the patients lost

Description/Definition	Grade
Did not attempt	0
Easy mask	1
Difficult mask requiring an oral airway or other adjuvant	2
Very difficult mask ventilation (inadequate, unstable, or requir-	3
ing two providers)	
Unable to mask ventilate	4

consciousness and eye-lash reflex. The total propofol dose was recorded.

After loss of consciousness, the patients were ventilated with a mask by an anesthesiologist, who was blinded to the groups. Mask ventilation was performed using a single-handed technique with a face mask of a size appropriate to the age and face of the patient (Altech[®] Anesthesia Mask, Meditera Medical Co., Izmir, Turkey). Surgical pillows were not used during the mask ventilations of the patients to ensure standardization among patients of different ages. The mask ventilation difficulty of the patients was evaluated for 30 s using the Han scale (1: easy mask ventilation, 4: impossible) (Table-1) by another anesthesiologist, who was blinded to the patient groups and the study protocol [10]. Easy mask ventilation means effective and fitted (leakage-free) mask ventilation with minimal resistance and ensuring an uninterrupted ingress and egress of gas. It does not require an extra airway device or a second person to assist in providing this. Continuous capnography monitoring was performed during and after mask ventilation. The tidal volumes provided during mask ventilation was monitored on the ventilator screen of the anesthesia machine (Drager Primus, Lübeck Germany).

Initially, according to the Waters ventilation scale criteria (Supplemental file, Table 3), the peak inspiratory pressure was increased to a maximum of 20 cmH2O to achieve a target volume of 5 ml/kg [11]. Patients who reached the target volume under these conditions were classified as grade one according to the Han scale. If the target volume could not be reached under these conditions, it was planned to use the airway, apply peak inspiratory pressure above 20 cmH₂O, and apply the mask ventilation technique with two people, respectively. The patients who underwent these procedures were graded according to the Han mask scale; patients needing the first two procedures were graded as Han 2, and those who needed the third procedure as Han 3. After evaluating mask ventilation difficulty, opioid and/or neuromuscular blockers were given to the patients in usual doses according to the surgical procedure, and intubation/ laryngeal mask airway (LMA) application was initiated, and the procedure was completed. Heart rate and pulse oximetry values were recorded before the induction and administration of the opioids or neuromuscular blockers. All the anesthetists who participated in the study were selected from those with at least five years of experience in pediatric anesthesia.

This manuscript complies with the current Consolidated Standards for Reporting of Trials (CONSORT) guidelines.
 Table 2
 Characteristics of patients in the intervention and control groups

control groups		Midazolam (n=60)	Control (n=60)	SD	P values
Age (y)		5.5 ± 2.24	6.18±1.62	-0.683 (-1.39 & 0.024)	0.06 ^c
Sex	Male Female	50 (83.3%) 10 (16.7%)	45 (75%) 15 (25%)	-	0.26 ^a
BMI (kg/m2)		17.04±2.82	16.51±3.42	0.53 (-0.6 & 1.66)	0.35 ^c
BMI for age	Under- weight (< 5 p)	8 (13.3%)	9 (15%)	-	0.66 ^a
	Healthy weight (5≤ -	28 (46.7%)	33 (55%)		
	<85 p) Over- weight (85≤ - <95 p)	10 (16.7%)	9 (15%)		
	Obese (95 p ≤)	14 (23.3%)	9 (15%)		
Ratio of height to thyromen- tal distance		3.565 (1.92–6.75) (3.75±1.01)	3.76 (1.85-8.9) (4.05±1.31)	-0.29 (-0.71 & 0.13)	0.30 ^d
Mallampati class (I/II/III/IV)	Easy Me- dium	43 (71.7%) 16 (26.7%)	40 (66.7%) 20 (33.3%)	-	0.55 ^b
	Dif- ficult/ dif- ficult/ very difficult	1 (1.7%)	0 (0%)		
Inter-incisor Gap (cm)		3.65±0.55	3.82±0.58	-0.17 (-0.37 & 0.04)	0.11 ^c
Thyromental distance (cm)		5.16±1.21	5.48±0.93	-0.32 (-0.71 & 0.06)	0.11 ^c
Sternomental distance (cm)		10.08±2.11	10.41 ± 1.47	-0.33 (-0.98 &	0.33 ^c
Neck Circum- ference (cm)		24.32±2.12	25.05±1.85	0.33) -0.73 (-1.45 & -0.01)	0.05 ^c

^aChi-Square test with n (%)

^bFisher exact test with n (%)

 c Student's t-test with mean \pm standard deviation (SD)

^dMann Whitney U test with median (Q1-Q3)

SD: Standardized difference, BMI: body mass index

		Mid- azolam (n=60)	Control (n=60)	P values
HAN Grading Score	1 (Ventilated by mask)	56 (93.3%)	36 (60%)	<0.001 ^a
(for all patients)	2 (Ventilated by airway)	4 (6.7%)	24 (40%)	
HAN Grading Score	J		11 (61.1%)	0.03 ^b
(only for over- weight and obese patients)	2 (Ventilated by airway)	2 (8.3%)	7 (38.9%)	

^aChi-Square test with n (%)

^bFisher exact test with n (%)

Study outcomes

Primary outcome

The primary outcome of this study was the evaluation of mask ventilation difficulty in the premedicated and nonpremedicated pediatric population using the Han mask grading scale and grading class as indicated in the study intervention.

Secondary outcomes

The effects of midazolam premedication on preoperative anxiety were evaluated with the mYPAS scale and sedation level with the MOAA/S scale. Changes in heart rate and pulse oximetry values were evaluated before the induction and before the opioids/neuromuscular blocker administration after sedation.

Statistical analysis

The primary purpose of this study was the examination the effect of midazolam premedication on mask ventilation in children using the Han mask grading scale. A pilot study of 20 patients (10 pairs; Group midazolam = 10, Group control = 10) undergoing general anesthesia was conducted to determine the number of participants required. According to the pilot study results, 9 patients in the midazolam group and 6 patients in the control group could be ventilated by mask according to the Han mask grading scale. It was calculated that 52 patients were required to be included in the study to reveal a significant difference between the two ratios of 0.6 and 0.9 with 95% power and 5% error. Assuming that some patients might drop out of the study, a 25% (52*0.25 = 13) patients) patient increase in each group (52 + 13 = 65) was considered, and thus it was decided to include 65 patients in each group.

Data obtained in the study were analyzed statistically using SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA). Conformity of the data to normal distribution was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests and some graphical approaches (Histogram and Q-Q plots). Descriptive statistics were reported as mean±standard deviation values for normally distributed numerical data and as median (minimum, maximum) values for non-normally distributed numerical data. Categorical data were stated as number (n) and percentage (%). The analyses of relationships and ratio comparisons between categorical variables were performed with either the Chi-square test or Fisher's Exact test, according to the sample sizes of the crosstab cells. The Levene test was applied to examine the homogeneity of variances between two independent groups. In comparing numerical data between two independent groups, the Student's t-test was used when parametric test assumptions were met, and the Mann Whitney U-test was used when they were not. The Paired Samples t-test was used to compare two related numerical data (pre-post) when parametric test assumptions were met, and in other cases, the Wilcoxon signed-rank test was used.

Results

A total of 130 patients between May 2022 and December 2022 were eligible in the present study. Of the 130 patients initially eligible for the study, 4 were excluded; two declined to participate, and two did not meet the inclusion criteria. Therefore, the remaining 126 patients were randomly divided into two groups, with 63 patients in each group. After assessing preoperative anxiety and administering medication/placebo, the parents of six patients refused to continue the study before the patients were transferred to the operating room. Finally, the data were analyzed of 120 patients who completed the study (n = 60 in Group M, n = 60 in Group C) (Fig. 1). The statistical findings of the comparisons of the clinical characteristics of the patients in the study groups are given in Table 2. No significant difference was determined between the two groups regarding these characteristics (Table 2). The doses of propofol needed to achieve loss of consciousness were similar in both groups: 2.57 mg/ kg (0.39 mg/kg) in the midazolam group and 2.66 mg/kg (0.19 mg/kg) in the control group (p = 0.117).

The distribution of Han scale results was significantly different between the groups (p < 0.001). A Han score of 1 was determined in 93.3% of the midazolam group and in 60% of the control group (Table 3). Based on the sub-group analysis of overweight and obese patients, there was a significant difference in the distribution of Han scale results between the groups (p = 0.03). In the sub-group of overweight and obese children, easy mask ventilation (Han score: 1) was determined in 91.7% of the midazolam group and in only 61.1% of the control group (Table 3).

The relationship between gender and difficult mask ventilation was evaluated and while no significant associations were found in the midazolam group (p = 0.53),

there was seen to be a significant relationship between gender and ease of mask ventilation in the control group. The rate of airway use was 31.1% in males and 66.7% in females (Han score two) (p = 0.02). No significant correlations were determined in the groups between age and difficulty in mask ventilation (p > 0.05). The age of patients with Han scores 1 and 2 or Han scores 2 and 3 did not differ significantly (p = 0.92, p = 0.29, respectively).

The comparisons of the groups in respect of the anxiety (m-YPAS) and sedation (MOAA/S) scores and the changes between the preoperative room (PR) and the operating room (OR) are given in Table 4. The changes in the anxiety (m-YPAS) and sedation (MOAA/S) scores in the PR and OR were significantly different between the control and midazolam groups (p < 0.001, p < 0.001, Table 4). The MOAA/S and mYPAS scores recorded in the OR were lower in the midazolam group (Table 4).

The heart rate values of the groups were significantly different before and after anesthesia induction (104 (72–150) vs. 95 (65–130), p < 0.001, 109.5 (75–144) vs. 104 (72–150) vs. 109.5 (75–144), p < 0.001, respectively). A decrease in heart rate and an increase in oxygen saturation were observed in both groups after induction. No significant difference was determined between the groups in respect of the changes in these values (p = 0.72, p = 0.4, respectively).

Discussion

In this study, the effect of midazolam premedication on mask ventilation was evaluated in pediatric patients using the Han grading scale. The results showed that midazolam premedication improved mask ventilation by approximately 30% in all children, and similar results were found in the subgroup of overweight and obese patients.

Mask ventilation difficulties are rare in children when compared to adults [1]. However, it is not easy to predict the difficulty of MV in children. Various previous studies have reported the incidence of difficult MV in children to be 3%, 6.6%, and 9.5% [4, 12, 13]. Pediatric patients with low oxygen reserves and high metabolic requirements are more susceptible to hypoxia when they lose consciousness, and spontaneous breathing is suppressed, especially during anesthesia induction. This increases the importance of knowing the methods to facilitate MV in anesthesia induction.

The criteria used in the Han mask grading scale, such as oropharyngeal/nasopharyngeal airway use and ventilation with two people, are consistent with the Canadian Airway Focus Group (CAFG) consensus-based recommendations for difficult mask ventilation [13]. In addition, although the Han grading mask scale was initially defined for adults, its criteria match the Difficult Airway Society (DAS) difficult mask ventilation algorithm

CONSORT Flow Diagram

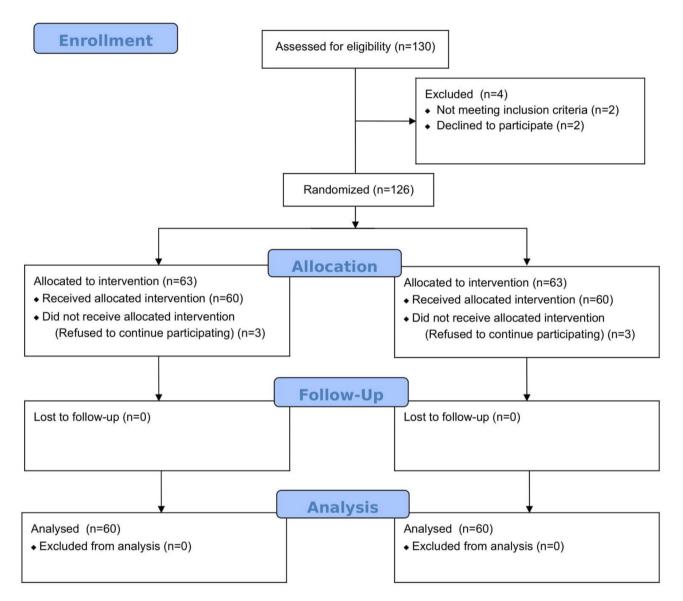


Fig. 1 Consolidated standards of reporting trials (CONSORT) diagram for the trial

adapted for children [14]. As a result of these features, the Han mask grading scale has been used in previous pediatric studies [12].

Midazolam premedication is frequently used in children because of the anxiolytic effects. The muscle relaxant effect of midazolam, which makes MV easier for adults [9], occurs because midazolam induces muscle relaxation in both the striated muscles of the upper airways and the smooth muscles of the lower airways [15, 16]. New-generation asthma medications being currently developed make use of this significant muscle relaxant effect of benzodiazepines [17]. The results of this study showed that midazolam premedication facilitated MV in approximately 30% of children, which was a similar finding to the results of a previous adult study [9]. The sub-group analyses also showed that midazolam premedication facilitated MV at similar rates in overweight (85-95% percentile) and obese (>95% percentile) children according to the BMI-for-age values [18]. Although previous articles have reported that obesity increases perioperative respiratory complications in children [19], a recent study stated that obesity was not a risk factor

Tab	le 4	The anxiety score	, sedation level	, and the cl	hange of anxiet [,]	y score between [.]	the preoperative room and	d the operating room

	Midazolam (n=60)				Control (<i>n</i> = 60)				
	Preoperative Room	Operating Room	Anxiety Change	P ^a	Preoperative Room	Operating Room	Anxiety Change	P ^a	P ^b
Anxiety (m-YPAS)	54.51±14.68	32.44±7.67	-22.07±11.79	< 0.001	43.82±10.13	53.48±17.46	9.66±11.83	< 0.001	< 0.001
Sedation (MOAA/S scale;5/4/3)	5 (5, 5)	4 (3, 5)	-1 (-2, 0)	<0.001	5 (5, 5)	5 (4, 5)	0 (-1, 0)	0.16	<0.001

Continuous values are shown as mean (standard deviation). Discrete variables are expressed as median (min, max)

Abbreviations: MOAA/S, Modified Observer's Assessment of Alertness/Sedation; m-YPAS: modified Yale Preoperative Anxiety Scale

^aComparisons of anxiety/sedation between the preoperative room and the operating room, within each group, using a paired t test and the Wilcoxon signed-rank test for the anxiety and sedation levels, respectively

^bA comparison of the anxiety/sedation change with premedication between the 2 groups, using Student t test and the Mann Whitney U test for the anxiety and sedation levels, respectively

for difficult MV [4]. However, the association of other comorbidities causes these patients to be more susceptible to hypoxia compared to the average population [20]. This increases the importance of the results of the current study despite the low number of obese patients preventing a definitive judgment on this issue.

Previous studies have reported that early administration of neuromuscular blockers facilitates MV in adults [11, 21]. However, there is insufficient data to be able to make any recommendations for children [22]. The lack of information about the effect of neuromuscular blockers on MV in children could be due to the lack of need for neuromuscular blockers for many pediatric surgical procedures. Therefore, with the use of midazolam premedication instead of neuromuscular blockers to facilitate MV, the possible side-effects of neuromuscular blockers in children can be avoided [23].

No significant relationships were detected between gender and difficulty in MV in either of the study groups, although in the control group, the Han scores of females were higher than those of males. In the literature, no relationships of gender and MV difficulty in children have been reported, unlike for adults [4]. The reason for these results in the current study was thought to be possibly due to the low number of female participants.

Midazolam is frequently used to prevent preoperative anxiety in children as it has been shown to have a positive effect on both separation anxiety and anxiety that may arise during anesthesia induction [24]. This was seen to be confirmed by the mYPAS scale scores in the current study. The use of midazolam at doses that cause profound sedation, especially in patients with airway obstruction, may cause desaturation because of the muscle relaxant effect. In the current study, all the patients in the midazolam group were conscious at a level to be able to respond to the questions asked, and no desaturation (<95%) or bradycardia were observed in any patient.

It has been considered that reducing anxiety could help in preventing children from producing additional secretions, which cause respiratory complications, thereby increasing MV difficulty [25]. According to the mYPAS and MOAA/S data, the midazolam dose used in this study prevented anxiety without causing deep sedation in children and contributed to easy MV.

Propofol and midazolam exert their effects through GABA_A receptors and have a synergistic effect when used together. Studies have reported that the dose of propofol required for the placement of LMA is higher in children who are non-premedicated [26]. Increasing the dose of propofol in non-premedicated patients may facilitate MV, but higher propofol doses will cause significant hemodynamic changes [27]. Conversely, midazolam premedication has minimal effects on hemodynamics [26]. The results of the current study also confirmed this as no differences were detected between the groups when the heart rate changes before and after induction were compared.

Midazolam premedication is primarily used orally in children. However, the agitation and hemodynamic changes that may occur during cannulation and inhalation anesthesia after oral premedication may impair the optimal evaluation of the ease of mask ventilation, which was the primary objective of this study. Therefore, intravenous induction was planned after intravenous premedication with the aim of excluding other factors that may affect mask ventilation. Also, a recent study showed that intravenous induction can cause more difficult mask ventilation in susceptible children due to rapid loss of airway tone and patency [2]. From another perspective, choosing the induction method with more frequent mask ventilation difficulties is more meaningful for examining the facilitating effect of premedication. Furthermore, after using the oral route of premedication, optimal conditions may not be created to evaluate the facilitating effect of midazolam on mask ventilation. Nevertheless, the results of this study can be extrapolated to patients premedicated with oral midazolam.

This study had some limitations, primarily that the ease of MV was evaluated only according to the Han scale, which is a simple subjective scale [10], whereas the Warters scale is more complex and formed by scoring a set of criteria used to reach a certain volume [11]. Although the Han scale was combined with some criteria from the Warters scale in the current study, the scale used was not wholly objective. A second limitation was the timing of the administration of the opioids. The administration of opioids after the MV evaluation excluded MV difficulties that may occur due to opioids. However, as the main aim of the study was to determine whether midazolam premedication facilitates MV in children, the effects of opioids were deliberately excluded from consideration. Further studies are needed on the results of premedication on MV difficulties that may develop due to opioid use in children. Another limitation was that the study was conducted with an average pediatric patient population. Although it is difficult to predict, running similar research on children with expected difficult MV might benefit the literature. One another limitation is that this study did not assess whether propofol doses causing loss of consciousness would lead to apnea. Even though we did not observe this effect in this study, there is a risk that mask ventilation may become challenging in patients with spontaneous breathing. In addition, the depth of anesthesia was not evaluated using any monitoring technique, although the eyelash reflex was used as a clinical endpoint of depth of anesthesia.

Conclusions

In conclusion, the results of this study showed that midazolam premedication improves mask ventilation in the pediatric population during propofol induction for general anesthesia. Moreover, similar results were obtained in obese and overweight children. Mask ventilation is the most basic method used when problems arise in airway management, so knowing the procedures or practices that facilitate mask ventilation are as crucial as mask ventilation.

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12871-025-03002-4.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Acknowledgements

The authors thank all participants and their parents in this study. The authors thank Naile Yıldırım and Birtan Demirel for their assistance.

Author contributions

RY: This author helped design the study, analyze the statistical data, and write and prepare the manuscript for submissionBB: This author helped design the study, analyze the statistical data, and write and prepare the manuscript for submission.TE: This author helped design the study and prepare the draft.AB: This author helped collect the data and revise the manuscript.MK: This author helped develop the protocol and collect the data.

Funding

No funding from any source was received for this research.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted with the approval of the Clinical Research Ethics Committee of Karamanoglu Mehmetbey University Faculty of Medicine, Karaman, Turkey (ID: 08-2021/13), and written informed consent was obtained from the parents of all the patients. The study was conducted in line with the Declaration of Helsinki.

Consent for publication

Not Apllicable.

Competing interests

The authors declare no competing interests.

Received: 24 May 2023 / Accepted: 10 March 2025 Published online: 18 March 2025

References

- Sunder RA, Haile DT, Farrell PT, Sharma A. Pediatric airway management: current practices and future directions. Paediatr Anaesth. 2012;22(10):1008–15.
- Garcia-Marcinkiewicz AG, Lee LK, Haydar B, Fiadjoe JE, Matava CT, Kovatsis PG, et al. Difficult or impossible facemask ventilation in children with difficult tracheal intubation: a retrospective analysis of the pedi registry. Br J Anaesth. 2023;131(1):178–87.
- Crawley SM, Dalton AJ. Predicting the difficult airway. Contin Educ Anaesth Crit Care Pain. 2015;15(5):253–7.
- Valois-Gómez T, Oofuvong M, Auer G, Coffin D, Loetwiriyakul W, Correa JA. Incidence of difficult bag-mask ventilation in children: a prospective observational study. Paediatr Anaesth. 2013;23(10):920–6.
- Bhananker SM, Ramamoorthy C, Geiduschek JM, Posner KL, Domino KB, Haberkern CM, et al. Anesthesia-related cardiac arrest in children: update from the pediatric perioperative cardiac arrest registry. Anesth Analg. 2007;105(2):344–50.
- Hardman JG, Wills JS. The development of hypoxaemia during Apnoea in children: a computational modelling investigation. Br J Anaesth. 2006;97(4):564–70.
- Rudolph U, Crestani F, Benke D, Brünig I, Benson JA, Fritschy JM, et al. Benzodiazepine actions mediated by specific gamma-aminobutyric acid(A) receptor subtypes. Nature. 1999;401(6755):796–800.
- 8. Drummond GB. Comparison of sedation with Midazolam and ketamine: effects on airway muscle activity. Br J Anaesth. 1996;76(5):663–7.
- Park JW, Min BH, Park SJ, Kim BY, Bae SI, Han SH, et al. Midazolam premedication facilitates mask ventilation during induction of general anesthesia: A randomized clinical trial. Anesth Analg. 2019;129(2):500–6.
- Han R, Tremper KK, Kheterpal S, O'Reilly M. Grading scale for mask ventilation. Anesthesiology. 2004;101(1):267.
- Warters RD, Szabo TA, Spinale FG, DeSantis SM, Reves JG. The effect of neuromuscular Blockade on mask ventilation. Anaesthesia. 2011;66(3):163–7.
- Aggarwal A, Sharma KR, Verma UC. Evaluation of Difficult Airway Predictors in Pediatric Population as a Clinical Investigation. J Anesthe Clinic Res [Internet]. 2012 [cited 2022 Dec 22];03(11). Available from: https://www.omicsonline.org /evaluation-of-difficult-airway-predictors-in-pediatric-population-as-a-clinica l-investigation-2155-6148.1000256.php?aid=9442

- 14. Weiss M, Engelhardt T. Proposal for the management of the unexpected difficult pediatric airway. Paediatr Anaesth. 2010;20(5):454–64.
- 15. Crestani F, Löw K, Keist R, Mandelli M, Möhler H, Rudolph U. Molecular targets for the myorelaxant action of diazepam. Mol Pharmacol. 2001;59(3):442–5.
- 16. von Ungern-Sternberg BS, Erb TO, Habre W, Sly PD, Hantos Z. The impact of oral premedication with Midazolam on respiratory function in children. Anesth Analg. 2009;108(6):1771–6.
- Perez-Zoghbi JF, Sajorda DR, Webb DA, Arnold LA, Emala CW, Yocum GT. Imidazobenzodiazepine PI320 relaxes mouse peripheral airways by inhibiting calcium mobilization. Am J Respir Cell Mol Biol. 2022;67(4):482–90.
- Growth Charts -. Data Table of BMI-for-age Charts [Internet]. [cited 2023 Jan 3]. Available from: https://www.cdc.gov/growthcharts/html_charts/bmiagere v.htm
- 19. Tait AR, Voepel-Lewis T, Burke C, Kostrzewa A, Lewis I. Incidence and risk factors for perioperative adverse respiratory events in children who are obese. Anesthesiology. 2008;108(3):375–80.
- Nafiu OO, Reynolds PI, Bamgbade OA, Tremper KK, Welch K, Kasa-Vubu JZ. Childhood body mass index and perioperative complications. Paediatr Anaesth. 2007;17(5):426–30.
- Soltész S, Alm P, Mathes A, Hellmich M, Hinkelbein J. The effect of neuromuscular Blockade on the efficiency of facemask ventilation in patients difficult to facemask ventilate: a prospective trial. Anaesthesia. 2017;72(12):1484–90.

- 22. Plaud B, Baillard C, Bourgain JL, Bouroche G, Desplanque L, Devys JM, et al. Guidelines on muscle relaxants and reversal in anaesthesia. Anaesth Crit Care Pain Med. 2020;39(1):125–42.
- 23. Ammar AS, Mahmoud KM, Kasemy ZA. A comparison of Sugammadex and neostigmine for reversal of rocuronium-induced neuromuscular Blockade in children. Acta Anaesthesiol Scand. 2017;61(4):374–80.
- 24. Heikal S, Stuart G. Anxiolytic premedication for children. BJA Educ. 2020;20(7):220–5.
- Parnis SJ, Barker DS, Van Der Walt JH. Clinical predictors of anaesthetic complications in children with respiratory tract infections. Paediatr Anaesth. 2001;11(1):29–40.
- Bhaskar P, Malik A, Kapoor R, Kohli M, Agarwal J, Harjai M. Effect of Midazolam premedication on the dose of Propofol for laryngeal mask airway insertion in children. J Anaesthesiol Clin Pharmacol. 2010;26(4):503–6.
- Goel S, Bhardwaj N, Jain K. Efficacy of ketamine and Midazolam as co-induction agents with Propofol for laryngeal mask insertion in children. Paediatr Anaesth. 2008;18(7):628–34.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.