Original Article Assessing pediatric anesthesia outcomes and prognostic factors: a comparative study of ketamine vs. ketamine + propofol

Wei Wang¹, Weiwei Cai², Huiying Shao¹, Huanhuan Ni²

¹Department of Anaesthesiology, Children's Hospital of Fudan University, Shanghai 201102, China; ²Department of Anaesthesiology, Children's Hospital of Nanjing Medical University, Nanjing 210008, Jiangsu, China

Received May 27, 2023; Accepted September 6, 2023; Epub October 15, 2023; Published October 30, 2023

Abstract: Objective: To investigate the anesthesia outcomes of ketamine and propofol in pediatric anesthesia and analyze associated prognostic factors. Methods: A retrospective study was conducted on 160 children who underwent anesthesia and operation in Children's Hospital of Nanjing Medical University from 2020 to 2022. The anesthesia outcomes was analyzed by comparing the blood oxygen saturation (SpO₂), heart rate (HR), mean arterial pressure (MAP) at before (T_1) , during (T_2) and after (T_3) operations, recovery time after anesthesia, post-anesthesia care unit (PACU) stay, adverse reactions, as well as the Steward and FLACC scores between the control and research groups. Univariate analysis and logistic regression analysis were used to identify the prognostic factors in pediatric anesthesia. Results: The changes in SpO₂, HR, and MAP were different between the two groups at different time points (P < 0.05). There were significant differences in anesthesia recovery time, PACU stay, Steward and FLACC scores, and incidence of adverse reactions between the two groups (P < 0.05). Logistic regression analysis revealed that operation time \geq 49.5 minutes (P = 0.001, OR = 3.828, 95% CI: 1.715-8.544) and single use of ketamine for anesthesia (P = 0.048, OR = 2.257, 95% CI: 1.006-5.063) were independent risk factors for postoperative delirium. Conclusion: Combining propofol with ketamine for pediatric anesthesia yields superior clinical outcome compared to using ketamine alone. This combined approach can effectively maintain stable circulation during operation, lead to shorter anesthesia recovery time, ensure high recovery quality, reduce postoperative pain, adverse reaction rate, and risk of post-anesthesia delirium in children, thereby improving the prognosis.

Keywords: Ketamine, propofol, pediatric anesthesia, anesthesia outcomes, prognostic factors

Introduction

The progress in anesthesiology and pediatric surgery has notably advanced, leading to a heightened focus on the field of pediatric anesthesia [1]. Due to the particularity of child physiology and anatomy, the operations for children can not be performed according to anesthesia methods used for adults. Instead, tailored and scientifically informed approaches to pediatric anesthesia should be selected [2]. Ketamine is widely used in pediatric anesthesia, but the use of ketamine only as an anesthetic can increase the content of catecholamines, cause excessive cardiovascular excitation, and increase heart rate (HR) and blood pressure, resulting in a series of adverse reactions, such as nausea and vomiting [3]. Studies have

shown that ketamine can increase the incidence of adverse events, such as postoperative nausea and vomiting, and overdose of this anesthetic can even cause significant respiratory depression [4]. Propofol is a short-acting anesthetic that is often used in combination with other anesthetics. Its single use in anesthesia can lead to slow HR and low blood pressure, but it can shorten the anesthesia recovery time and significantly reduce adverse reactions [5]. Therefore, the combined application of propofol and ketamine can offset each other's side effects [6]. Specifically, propofol can reduce the incidence of adverse reactions such as postoperative nausea and vomiting that may be caused by ketamine, and ketamine can offset the circulatory inhibition caused by propofol.

Ketamine and propofol in pediatric anesthesia



Thus, the combined application of the two can help patients to maintain a more stable HR and blood pressure during operations [7]. The occurrence of delirium after anesthesia is common and related to poor prognosis [8]. When pediatric anesthesia is well recovered, and there is no occurrence of postoperative delirium following an evaluation using the Pediatric Anesthesia Emergence Delirium (PAED) scale, the overall prognosis for children after anesthesia and surgery is generally favorable [9]. At present, there are a number of studies on the anesthesia outcomes of ketamine and propofol alone or in combination [10], but few of them were conducted in the field of pediatric anesthesia. Therefore, we retrospectively analyzed data of children undergoing anesthesia in our hospital, compared the anesthesia outcomes of ketamine and propofol in pediatric anesthesia, analyzed the prognostic factors, and discussed whether the use of ketamine or ketamine-propofol affected the prognosis of the children. This study aimed at providing a theoretical basis and reference for healthcare practitioners to make informed decisions regarding suitable anesthesia methods for clinical management.

Methods

Subjects

The data of 204 children who underwent anesthesia and operation in Children's Hospital of Nanjing Medical University from 2020 to 2022 were collected. Among them, 44 children were excluded because they did not meet the inclusion criteria, and finally 160 children were included for this retrospective study (**Figure 1**). This study was approved by the Ethics Committee of Children's Hospital of Nanjing Medical University.

Inclusion criteria: (1) children who were diagnosed in our hospital and received anesthesia and operation; (2) children whose family members were informed and agreed to participate in the study and signed informed documents; (3) children with ASA grade I; (4) children with complete medical records; (5) children underwent outcome assessment after surgery. Exclusion criteria: (1) children with mental disorders; (2) children with severe organ dysfunction or congenital diseases; (3) children with incomplete medical records; (4) children with endlergic to ketamine or propofol.

Data collection

The general data were preoperatively collected in children, including gender, age, American society of Anesthesiologists (ASA) grade, past history, and other data. Clinical vital signs were collected in children before (T_1) , during (T_2) and after (T_3) operation, including oxygen saturation (SpO_2) , HR, and mean arterial pressure (MAP). The operation time, recovery time after operation, post-anesthesia care unit (PACU) stay, and adverse reactions were compared between the two groups. Postoperative Steward, PAED, as well as Face, Legs, Activity, Cry, Consolability (FLACC) scale scores were evaluated by two experienced physicians.

Standard of scoring

Steward score was used to assess the quality of recovery after anesthesia in children [11]. The scale includes three aspects: sobriety, unobstructed breathing, and physical activity. Each aspect was assigned a score ranging from 0-2 points, with a maximum score of 6 points. Only patients with a score \geq 4 points were allowed to leave the PACU.

FLACC rating scale was used for assessment of pain after surgery in children [12]. The scale has five criteria, facial expression, leg movement, position, crying, and consolability. The score of each item ranges from 0 to 2 points, with a maximum score of 10 points. A final score of 1 to 3 indicates slight pain, a score of 4 to 6 suggests moderate pain, and a score of 7 to 10 indicates severe pain. Higher scores indicated more obvious discomfort and pain after surgery.

PAED scale was used to evaluate whether delirium occurred 24 hours after the anesthesia [13]. Delirium was scored from five aspects: eye contact with caregivers, purposeful behaviors, awareness of the surrounding environment, restlessness, and consolability. Each aspect was scored from 0 to 4 points, and a score \geq 12 points was defined as delirium.

Outcome indicators

The 160 patients were divided into a control group (ketamine group) and a research group (ketamine-propofol group) according to the different anesthesia methods. The specific anes-

thesia methods were as follows. In the control group, ketamine was used for preoperative intravenous induction anesthesia, with a dose of 1-2 mg/kg. Intermittent ketamine 1-2 mg/kg was given to maintain anesthesia according to the actual situation of the children during the operation. In the research group, ketamine and propofol were used for anesthesia. Ketamine was used to induce anesthesia before surgery, with a dose of 1-2 mg/kg. During the operation, propofol was used to maintain anesthesia with a dose of 5-8 mg/(kg.h) by intravenous injection using a micro pump.

Using PAED score at 12 points as the cut-off value, the children were split into a good prognosis group (< 12 points) and a poor prognosis group (\geq 12 points). The prognostic factors of pediatric anesthesia were analyzed using the clinical data of the two groups. Primary outcome: The primary outcome measures were SpO₂, HR, MAP, anesthesia recovery time and PACU stay of children at before (T₁), during (T₂) and after (T₃) operation. The prognosis was evaluated by using the PAED scale to assess the occurrence of delirium within 24 hours after anesthesia. Secondary outcome measures were Steward score, FLACC score, and the incidence of adverse reactions after anesthesia.

Statistical analysis

SPSS 26.0 was used for statistical analysis of the data. The data of age, SpO₂, HR, MAP at before (T_1) , during (T_2) and after (\overline{T}_2) operations, operation time, recovery time after anesthesia, PACU stay. Steward score, and FLACC score were not normally distributed. They were expressed as median and interquartile range. Counted data including gender, anesthetic methods, and adverse reactions were expressed as %. In the comparison of anesthesia outcomes, SpO₂, HR, MAP at before (T_1) , during (T_2) and after (T_3) operation were analyzed by generalized estimating equation. Kruskal-Wallis test was used for paired comparison between groups, and Friedman test was used for paired comparison within groups. The recovery time, PACU stay, Steward score, and FLACC score were analyzed by Wilcoxon rank sum test. Univariate analysis and logistic regression analysis were used to analyze the prognostic factors. P < 0.05 was considered to indicate significance.

	Before operation (T_1)	During operation (T_2)	After operation (T ₃)	
Sp0 ₂ (%)				
Control group	99 (98, 99)	97 (96, 98)	99 (98, 99)	
Research group	99 (98, 99)	98 (97, 99)	99 (98, 99)	
Wald χ^2	Wald $\chi^{2}_{Time} = 147.2$	40; Wald $\chi^2_{\text{Time*Group}} = 13.094;$	Wald $\chi^2_{Group} = 4.185$	
Р	P _{Time} < 0	$0.001; P_{\text{Time}*Group} = 0.001; P_{Group}$	= 0.041	
HR (bpm)				
Control group	106 (97, 116)	115 (106, 121)	106 (99, 113)	
Research group	105 (97, 114)	108 (103, 117)	105 (99, 112)	
Wald χ^2	Wald $\chi^2_{\text{Time}} = 46.9$	016; Wald $\chi^2_{\text{Time}*\text{Group}} = 7.384; V$	Vald $\chi^2_{Group} = 2.151$	
Р	P _{Tim}	$P_{\text{Time*Group}}; P_{\text{Group}} = 0$.142	
MAP (mmHg)				
Control group	76 (71, 82)	83 (77, 89)	76 (69, 83)	
Research group	77 (72, 83)	79 (75, 83)	78 (71, 82)	
Wald χ^2	Wald $\chi^2_{\text{Time}} = 42.82$	21; Wald $\chi^2_{\text{Time}*Group} = 11.404; $	Wald $\chi^2_{Group} = 0.142$	
Р	$P_{\text{Time}} < 0.001; P_{\text{Time*Group}} = 0.003; P_{Group} = 0.707$			

 Table 1. Generalized estimating equation

Note: SpO₂, blood oxygen saturation; HR, heart rate; MAP, mean arterial pressure.

 Table 2. Pairwise comparisons between groups

	Gi	roup	Р
SpO ₂			
Before operation (T_1)	Control group	Research group	0.420
During operation (T_2)	Control group	Research group	0.003
After operation (T_3)	Control group	Research group	0.222
HR			
Before operation (T_1)	Control group	Research group	0.832
During operation (T_2)	Control group	Research group	0.012
After operation (T_3)	Control group	Research group	0.655
MAP			
Before operation (T_1)	Control group	Research group	0.296
During operation (T_2)	Control group	Research group	0.002
After operation (T_3)	Control group	Research group	0.577

Note: $\mathrm{SpO}_{2^{\mathrm{t}}}$ blood oxygen saturation; HR, heart rate; MAP, mean arterial pressure.

Results

Comparison of SpO₂, HR and MAP at each time point

Among the 160 children in the study, 74 children were in the control group and 86 in the research group. Generalized estimating equation revealed that the main effect of groups was significant in SpO₂ (Wald χ^2 = 4.185, *P* = 0.041), and there was a significant difference in SpO₂ between the two groups. The main effect of time was also significant (Wald χ^2 =

147.240, P < 0.001). There were significant differences in SpO₂ between the two groups at different time points. There was a significant interaction effect between time and group (Wald χ^2 = 13.094, P = 0.001). This shows that the changes in SpO₂ in the two groups were different under the 2 anesthesia methods at different time points. In terms of HR, the main effect of group was not significant (Wald $\chi^2 = 2.151$, *P* = 0.142), and there was no difference in HR between the two groups. However, the main effect of time was significant (Wald χ^2 = 46.916, *P* < 0.001). There were significant differences in HR between the two groups at different time points. There was a significant interaction effect of time and group (Wald χ^2 = 7.384, P = 0.025). This shows that the changes in HR in the two groups were different under the 2 anesthesia methods at different time points. In terms of MAP, the main effect of group was not significant (Wald χ^2 = 0.088, P = 0.767). There was no significant difference in MAP between the two groups. However, the main effect of time was significant (Wald χ^2 = 40.853, P < 0.001). There were significant differences in MAP between the two groups at different time points. There was a significant interaction effect between time and group (Wald χ^2 = 12.203, P = 0.002). This shows that

Ketamine and propofol in pediatric anesthesia

		0 1		
Indicators	Group	Time	epoint	Р
SpO ₂	Control group	Before operation (T_1)	During operation (T_2)	< 0.001
		Before operation (T_1)	After operation (T_3)	0.222
		During operation (T_2)	After operation (T_3)	< 0.001
	Research group	Before operation (T_1)	During operation (T_2)	< 0.001
		Before operation (T_1)	After operation (T_3)	0.742
		During operation (T_2)	After operation (T_3)	< 0.001
HR	Control group	Before operation (T_1)	During operation (T_2)	0.036
		Before operation (T_1)	After operation (T_3)	0.970
		During operation (T_2)	After operation (T_3)	0.033
	Research group	Before operation (T_1)	During operation (T_2)	< 0.001
		Before operation (T_1)	After operation (T_3)	0.565
		During operation (T_2)	After operation (T_3)	< 0.001
MAP	Control group	Before operation (T_1)	During operation (T_2)	0.033
		Before operation (T_1)	After operation (T_3)	0.594
		During operation (T_2)	After operation (T_3)	0.008
	Research group	Before operation (T_1)	During operation (T_2)	< 0.001
		Before operation (T_1)	After operation (T_3)	0.651
		During operation (T_2)	After operation (T_3)	< 0.001

 Table 3. Pairwise comparisons within groups

Note: SpO₂, blood oxygen saturation; HR, heart rate; MAP, mean arterial pressure.



Figure 2. Blood oxygen saturation of the two groups at each time point. Note: * compared to the research group, P < 0.05; # compared to T₁, P < 0.05.

the changes in MAP in the two groups were different under the 2 anesthesia methods at different time points (**Table 1**).

The results of pairwise comparison within the group showed that there was no significant difference in SpO₂, HR, or MAP between the control and research groups at T₁ and T₃ timepoints (P > 0.05), but there was a significant difference when comparing T₂ with T₁ and T₃ (P <

0.05). The results of pairwise comparison between groups showed that at T_1 and T_3 , there was no significant difference in SpO₂, HR, or MAP between the control and research groups (*P* > 0.05). There was a significant difference in SpO₂, HR, and MAP between the control and research group at T_2 (*P* < 0.05) (**Tables 2, 3**; **Figures 2-4**).

Comparison of PACU stay and anesthesia recovery time

The anesthesia recovery time and PACU stay in the research group were significantly shorter than in the control group (P = 0.001, P = 0.019) (**Figure 5**).

Compared of Steward scores

The scores of physical activity and total Steward score in the research group were significantly higher than those in the control group (P = 0.026, P = 0.007) (**Table 4**).

Compared of FLACC scores

The scores of facial expression, leg activity, crying, and the total FLACC score in the research group were significantly lower than those in the control group (P = 0.027, P = 0.021, P = 0.017, P < 0.001, respectively) (**Table 5**).



Figure 3. Heart rate of the two groups at each time point. Note: * compared to the research group, P < 0.05; # compared to T₁, P < 0.05.



Figure 4. Mean arterial pressure of the two groups at each time point. Note: * compared to the research group, P < 0.05; # compared to T₁, P < 0.05.

Compared of postoperative adverse reactions

The incidence of adverse reactions was significantly lower in the research group than the control group (P < 0.001) (**Table 6**).

Univariate analysis of factors affecting the prognosis of pediatric anesthesia

The 160 children were divided into a good prognosis group (without delirium, n = 120) and a poor prognosis group (with delirium, n = 40) according to the PAED score. The continuous variables including SpO_2 (T₂), HR (T₂), MAP (T₂), anesthesia recovery time, PACU stay, Steward



Figure 5. Comparison of the anesthesia recovery time and PACU stay in the two groups.*: P < 0.05. PACU, post-anesthesia care unit.

score, FLACC score, and operation time were treated as dichotomous variables according to the optimal cut-off value for univariate analysis. Univariate analysis showed that there were significant differences between the good prognosis group and the poor prognosis group in HR (T_2), Steward score, operation time, and anesthesia methods (P = 0.012, P = 0.043, P < 0.001, P = 0.11) (Table 7).

Logistic regression analysis of factors affecting prognosis of pediatric anesthesia

The prognosis after pediatric anesthesia (good prognosis = 0, poor prognosis = 1) was used as the dependent variable, and statistically significant variables in univariate analysis (HR (T_2), Steward score, operation time, and anesthesia method) were used as independent variables. The assignment is shown in **Table 8**. The results of logistic regression showed that operation time \ge 49.5 minutes (P = 0.001, OR = 3.828, 95% CI: 1.715-8.544) and using ketamine alone for anesthesia (P = 0.048, OR = 2.257, 95% CI: 1.006-5.063) were the risk factors for delirium after pediatric anesthesia (**Table 9**).

Discussion

In this study, the data of 160 children who underwent anesthesia and operation in our hospital were retrospectively analyzed. The vital signs at T_1 , T_2 , and T_3 anesthesia recovery times, PACU stay, Steward score, FLACC score,

	Sobriety Degree	Unobstructed Breathing Degree	Physical Activity Degree	Total Score
Control group	2 (1, 2)	2 (1, 2)	2 (1, 2)	4 (4, 6)
Research Group	2 (1, 2)	2 (1, 2)	2 (2, 2)	6 (4, 6)
Ρ	0.513	0.073	0.026	0.007
Z	-0.654	-1.796	-2.225	-2.682

Table 4. Comparison of Steward scores (point)

Table 5. Comparison of FLACC scores (point)

Facial Expression	Leg Movement	Position	Crying	Consolability	Total Score
1(1,1)	1(1,1)	1(1,1)	1 (1, 1)	1(1,1)	5 (4, 6)
0(0,1)	0(0,1)	0 (0, 1)	0.5 (0, 1)	0(0,1)	2 (1, 3)
0.027	0.021	0.608	0.017	0.727	< 0.001
-2.212	-2.310	-0.513	-2.394	-0.349	-3.522
	Facial Expression 1 (1, 1) 0 (0, 1) 0.027 -2.212	Facial Expression Leg Movement 1 (1, 1) 1 (1, 1) 0 (0, 1) 0 (0, 1) 0.027 0.021 -2.212 -2.310	Facial ExpressionLeg MovementPosition1 (1, 1)1 (1, 1)1 (1, 1)0 (0, 1)0 (0, 1)0 (0, 1)0.0270.0210.608-2.212-2.310-0.513	Facial ExpressionLeg MovementPositionCrying1 (1, 1)1 (1, 1)1 (1, 1)1 (1, 1)0 (0, 1)0 (0, 1)0 (0, 1)0.5 (0, 1)0.0270.0210.6080.017-2.212-2.310-0.513-2.394	Facial ExpressionLeg MovementPositionCryingConsolability1 (1, 1)1 (1, 1)1 (1, 1)1 (1, 1)1 (1, 1)0 (0, 1)0 (0, 1)0 (0, 1)0 (0, 1)0 (0, 1)0.0270.0210.6080.0170.727-2.212-2.310-0.513-2.394-0.349

Note: FLACC, Face, Legs, Activity, Cry, Consolability.

Table 6. Comparison of postoperative adverse reactions [n (%)]

	n	Drowsiness	Nausea	Vomiting	Dizziness	Headache	Fatigue	Incidence of adverse reactions
Control group	74	5 (6.76)	7 (9.46)	4 (5.41)	9 (12.16)	2 (2.70)	3 (4.05)	30 (40.54)
Research Group	86	2 (2.33)	3 (3.49)	2 (2.33)	4 (4.66)	1 (1.16)	1 (1.16)	13 (15.12)
X ²	13.083							
Р		< 0.001						

and incidence of adverse reactions were compared between the ketamine group and the ketamine-propofol group. The anesthesia outcomes of ketamine and propofol were compared by generalized estimating equation, nonparametric test, and χ^2 test. Univariate analysis and logistic regression were used to analyze the prognostic factors in pediatric anesthesia.

We found that the changes in SpO₂, HR, and MAP in the two groups were different under the 2 anesthesia methods at different time points. At T_1 and T_3 , there were no significant differences in SpO₂, HR, or MAP between the control group and the research group. At T_2 , there were significant differences in SpO₂, HR, and MAP between the control and research groups. The anesthesia recovery time, PACU stay, FLACC score, and adverse reaction rate in the research group were significantly lower than those in the control group, and the Steward score was significantly higher in the control group. These results indicate that the anesthesia outcome of ketamine combined with propofol in pediatric patients was better than that of ketamine alone. The combination could reduce the fluctuations of SpO₂, HR, and MAP during operation, and the use of ketamine combined with propofol for pediatric anesthesia was safer than that of ketamine alone. Children could wake up faster after anesthesia and get better postoperative recovery, shorter PACU stay, and lower incidence of postoperative pain and adverse reactions. Previous studies had shown that ketamine combined with propofol for anesthesia had a better effect on maintaining hemodynamics and cardiovascular stability during surgery [14, 15]. Moreover, similar to the results, a previous study also reported a shorter recovery time after anesthesia with ketamine and propofol, which is conducive to the prognosis of children [16]. It was previously shown that single use of ketamine for anesthesia could cause an increase in MAP and HR [17], and increase the incidence of nausea, fatigue, dizziness, vomiting and other adverse reactions [18]. Ketamine combined with propofol for anesthesia could reduce the incidence of nausea, vomiting and other adverse reactions [19] because of the anti-empathetic properties of propofol. Therefore, combing propofol with ketamine could reduce the incidence of nausea, fatigue, dizziness, vomiting and other

Factors	Good prognosis group (n = 120)	Poor prognosis group (n = 40)	Z/χ^2	Р
Age (age)	5 (4, 6)	5 (4, 5)	-1.691	0.091
Gender [n (%)]			0.133	0.715
Male	61 (50.83)	19 (47.50)		
Female	59 (49.17)	21 (52.50)		
SpO ₂ (T ₂) (%) [n (%)]			0.859	0.354
≥ 98.5	30 (25.00)	13 (32.50)		
< 98.5	90 (75.00)	27 (67.50)		
HR (T ₂) (bpm) [n (%)]			6.296	0.012
≥ 114.5	42 (35.00)	23 (57.50)		
< 114.5	78 (65.00)	17 (42.50)		
MAP (T ₂) (mmHg) [n (%)]			0.077	0.781
≥ 79.5	69 (57.50)	24 (60.00)		
< 79.5	51 (42.50)	16 (40.00)		
Anesthesia recovery time (min) [n (%)]			2.060	0.151
≥ 16.5	97 (80.83)	28 (70.00)		
< 16.5	23 (19.17)	12 (30.00)		
PACU stay (min) [n (%)]			3.295	0.069
≥ 20.5	39 (32.50)	7 (17.50)		
< 20.5	81 (67.50)	33 (82.50)		
Steward (points) [n (%)]			4.097	0.043
≥ 5.5	58 (48.83)	12 (30.00)		
< 5.5	62 (51.67)	28 (70.00)		
FLACC (points) [n (%)]			1.283	0.257
≥ 2.5	85 (70.83)	32 (80.00)		
< 2.5	35 (29.17)	8 (20.00)		
Adverse reactions [n (%)]	29 (24.17)	14 (35.00)	1.792	0.181
Operation time (min) [n (%)]			13.640	< 0.001
≥ 49.5	41 (34.17)	27 (67.50)		
< 49.5	79 (65.83)	13 (32.50)		
Anesthesia method [n (%)]			6.406	0.011
Ketamine	47 (39.17)	27 (67.50)		
Ketamine-propofol	73 (60.83)	13 (32.50)		

Table 7. Univariate analysis

Note: SpO₂, blood oxygen saturation; HR, heart rate; MAP, mean arterial pressure; PACU, post-anesthesia care unit; FLACC, Face, Legs, Activity, Cry, Consolability.

Table 8.	. Assignment	and de	scription	of pro	ognostic	factors
----------	--------------	--------	-----------	--------	----------	---------

Factors	Assignment of value
HR (T ₂)	$1 = \ge 114.5$ bpm, $0 = < 114.5$ bpm
Steward	$1 = \geq 5.5$ points, $0 = < 5.5$ points
Anesthesia medication method	1 = Ketamine, 0 = Ketamine-propofol
Operation time	1 = ≥ 49.5, 0 = < 49.5

Note: HR, heart rate.

adverse reactions caused by ketamine, which is similar to the results obtained in our study [20, 21]. This study also found that ketamine combined with propofol for anesthesia could

Variable	β	S.E.	Р	OR	95% CI
HR (T ₂)	0.685	0.415	0.098	1.984	[0.880, 4.474]
Steward	-0.523	0.437	0.232	0.593	[0.252, 1.396]
Anesthesia medication method	0.814	0.412	0.048	2.257	[1.006, 5.063]
Operation time	1.342	0.410	0.001	3.828	[1.715, 8.544]

Table 9. Logistic regression analysis of factors affecting anesthesia prognosis

Note: HR, heart rate.

better manage the clinical indicators during surgery, provide more stable hemodynamic indicators, improve patients' comfort and safety, and enable patients to get better recovery after anesthesia, which is similar to previous findings [22, 23]. Therefore, the combined application of ketamine and propofol can exert the full advantages of the two anesthetics and make up for the shortcomings of each other. Compared with the single use of ketamine, the combination can better maintain the clinical indicators during the operation, improve the adverse reactions caused by ketamine, and improve recovery quality, reduce postoperative pain, and shorten PACU stay.

In the analysis of factors influencing the prognosis of pediatric anesthesia, operation time \geq 49.5 minutes and use of ketamine alone for anesthesia were found to be risk factors for delirium after pediatric anesthesia. Some studies have shown that the duration of surgery was a risk factor for delirium after anesthesia [24. 25], which is similar to our study. The use of ketamine in pediatric anesthesia was associated with a higher risk of delirium compared to combined use of ketamine and propofol. Studies have shown that the use of propofol could reduce the incidence and the severity of delirium in children [26, 27]. Intraoperative use of ketamine may not prevent delirium, and the use of ketamine alone may increase the risk of adverse psychotic experiences during the perioperative period [28], which is similar to the results of our study. By analyzing the prognostic factors of pediatric anesthesia, our findings suggest that reducing the operation time and choosing ketamine combined with propofol for anesthesia can reduce the risk of postoperative delirium in children. Selecting an appropriate anesthesia method can not only promote the anesthesia recovery of children, but also lead to a better prognosis, which is of great significance.

Our study has some limitations. First, this is a small-sample and a single-center study, lacking comparison among children from multiple centers. In later in-depth studies, it will beadvisable to consider expanding both the sample size and geographic source regions to enhance the credibility of the findings [29]. Secondly, this study included only children with ASA grade I, sofurther corresponding research in children with grade I or higher needs to be conducted [30]. Finally, we evaluated the delirium of children only within 24 hours after surgery. It is possible that some children would develop delirium after this period of time, so the evaluation time of delirium could be extended to more accurately understand the prognosis of pediatric anesthesia.

In conclusion, the combination of ketamine and propofol has better anesthesia outcomes than the single use of ketamine in pediatric patients. This combined approach can effectively maintain stable circulation during operation, lead to shorter anesthesia recovery time, ensure high recovery quality, reduce postoperative pain and adverse reaction rates, as well as lower the risk of post-anesthesia delirium in children, thereby improving the prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Huiying Shao, Department of Anaesthesiology, Children's Hospital of Fudan University, Shanghai 201102, China. Tel: +86-021-64931870; E-mail: shao252903641@ 163.com; Huanhuan Ni, Department of Anaesthesiology, Children's Hospital of Nanjing Medical University, Nanjing 210008, Jiangsu, China. Tel: +86-025-83117500; E-mail: njnhh1984@163.com

References

[1] Davidson A. The future of pediatric anesthesia. Paediatr Anaesth 2012; 22: 570-572.

- [2] Kurth CD and Hyman D. Worldwide journey in pediatric anesthesia quality and safety. Paediatr Anaesth 2022; 32: 1181-1184.
- [3] Song JW, Shim JK, Song Y, Yang SY, Park SJ and Kwak YL. Effect of ketamine as an adjunct to intravenous patient-controlled analgesia, in patients at high risk of postoperative nausea and vomiting undergoing lumbar spinal surgery. Br J Anaesth 2013; 111: 630-635.
- [4] Amer AM, Youssef AM, El-Ozairy HS and El-Hennawy AM. Propofol-ketamine versus dexmedetomidine-ketamine for sedation during upper gastrointestinal endoscopy in pediatric patients: a randomized clinical trial. Braz J Anesthesiol 2020; 70: 620-626.
- [5] Irwin MG, Chung CKE, Ip KY and Wiles MD. Influence of propofol-based total intravenous anaesthesia on peri-operative outcome measures: a narrative review. Anaesthesia 2020; 75 Suppl 1: e90-e100.
- [6] Frey K, Sukhani R, Pawlowski J, Pappas AL, Mikat-Stevens M and Slogoff S. Propofol versus propofol-ketamine sedation for retrobulbar nerve block: comparison of sedation quality, intraocular pressure changes, and recovery profiles. Anesth Analg 1999; 89: 317-321.
- [7] Foo TY, Mohd Noor N, Yazid MB, Fauzi MH, Abdull Wahab SF and Ahmad MZ. Ketamine-propofol (ketofol) for procedural sedation and analgesia in children: a systematic review and meta-analysis. BMC Emerg Med 2020; 20: 81.
- [8] Quintão VC and Carmona MJC. A call for more pediatric anesthesia research. Braz J Anesthesiol 2021; 71: 1-3.
- [9] Janssen NJ, Tan EY, Staal M, Janssen EP, Leroy PL, Lousberg R, van Os J and Schieveld JN. On the utility of diagnostic instruments for pediatric delirium in critical illness: an evaluation of the pediatric anesthesia emergence delirium scale, the delirium rating scale 88, and the delirium rating scale-revised R-98. Intensive Care Med 2011; 37: 1331-1337.
- [10] Ghojazadeh M, Sanaie S, Paknezhad SP, Faghih SS and Soleimanpour H. Using ketamine and propofol for procedural sedation of adults in the emergency department: a systematic review and meta-analysis. Adv Pharm Bull 2019; 9: 5-11.
- [11] Wang XH, Zhang SY, Huang Y, Wang Q, Zou L, Zhao G and Wang TL. Multimodal analgesia with sevoflurane provides enhanced intraoperative analgesic effects in percutaneous nephrolithotomy: a randomized, blinded clinical trial. Pain Physician 2022; 25: 283-291.
- [12] Malviya S, Voepel-Lewis T, Burke C, Merkel S and Tait AR. The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. Paediatr Anaesth 2006; 16: 258-265.

- [13] Turkel S, Hanft A, Epstein D and Jacobson J. Review of delirium in the pediatric intensive care unit. J Pediatr Intensive Care 2013; 2: 169-176.
- [14] Smischney NJ, Seisa MO, Morrow AS, Ponce OJ, Wang Z, Alzuabi M, Heise KJ and Murad MH. Effect of ketamine/propofol admixture on peri-induction hemodynamics: a systematic review and meta-analysis. Anesthesiol Res Pract 2020; 2020: 9637412.
- [15] Damps M, Stołtny L, Siemek-Mitela J, Lekstan A, Krzych Ł and Kucewicz-Czech E. Comparison of propofol-ketamine versuspropofol-remifentanil in children anaesthetized for gastroscopy. Anaesthesiol Intensive Ther 2019; 51: 262-267.
- [16] Alletag MJ, Auerbach MA and Baum CR. Ketamine, propofol, and ketofol use for pediatric sedation. Pediatr Emerg Care 2012; 28: 1391-5; quiz 1396-8.
- [17] Fang H, Li HF, Yang M, Zhang FX, Liao R, Wang RR, Wang QY, Zheng PC and Zhang JP. Effect of ketamine combined with lidocaine in pediatric anesthesia. J Clin Lab Anal 2020; 34: e23115.
- [18] Gao M, Rejaei D and Liu H. Ketamine use in current clinical practice. Acta Pharmacol Sin 2016; 37: 865-872.
- [19] Hayes JA, Aljuhani T, De Oliveira K and Johnston BC. Safety and efficacy of the combination of propofol and ketamine for procedural sedation/anesthesia in the pediatric population: a systematic review and meta-analysis. Anesth Analg 2021; 132: 979-992.
- [20] Chidambaran V, Costandi A and D'Mello A. Propofol: a review of its role in pediatric anesthesia and sedation. CNS Drugs 2015; 29: 543-563.
- [21] Zaki HA, Shallik N, Shaban E, Bashir K, Iftikhar H, Mohamed Khair Y, Abdelrahim MG, Fayed M, Hendy M, Salem EE and Elmoheen A. An analytical comparison between ketamine alone and a combination of ketamine and propofol (ketofol) for procedural sedation and analgesia from an emergency perspective: a systematic review and meta-analysis. Cureus 2022; 14: e27318.
- [22] Nowroozi A, Kianipour H, Taleby H and Yazdi B. Comparison of ketamine-propofol and ketamine-thiopental on bispectral index values during monitored anesthesia care (MAC) in minor traumatic orthopedic surgery; a randomized, double-blind, clinical trial. Bull Emerg Trauma 2019; 7: 118-123.
- [23] Phillips W, Anderson A, Rosengreen M, Johnson J and Halpin J. Propofol versus propofol/ ketamine for brief painful procedures in the emergency department: clinical and bispectral index scale comparison. J Pain Palliat Care Pharmacother 2010; 24: 349-355.

- [24] Nazemi AK, Gowd AK, Carmouche JJ, Kates SL, Albert TJ and Behrend CJ. Prevention and management of postoperative delirium in elderly patients following elective spinal surgery. Clin Spine Surg 2017; 30: 112-119.
- [25] Baek W, Kim YM and Lee H. Risk factors of postoperative delirium in older adult spine surgery patients: a meta-analysis. AORN J 2020; 112: 650-661.
- [26] van Hoff SL, O'Neill ES, Cohen LC and Collins BA. Does a prophylactic dose of propofol reduce emergence agitation in children receiving anesthesia? A systematic review and metaanalysis. Paediatr Anaesth 2015; 25: 668-676.
- [27] Xiao Y, Jin X, Zhang Y, Huang T, Zhou L and Gao J. Efficacy of propofol for the prevention of emergence agitation after sevoflurane anaesthesia in children: a meta-analysis. Front Surg 2022; 9: 1031010.

- [28] Vlisides P and Avidan M. Recent advances in preventing and managing postoperative delirium. F1000Res 2019; 8: F1000.
- [29] Oh TK, Kim K, Jheon S, Lee J, Do SH, Hwang JW and Song IA. Long-term oncologic outcomes for patients undergoing volatile versus intravenous anesthesia for non-small cell lung cancer surgery: a retrospective propensity matching analysis. Cancer Control 2018; 25: 1073274818775360.
- [30] Wang XQ. Comparative study of postoperative rehabilitation of different anesthetic methods on patients with thoracotomy and lobectomy. Shandong University 2018.