

Lidocaine and Dexamethasone, Ketamine and Dexamethasone, and Dexamethasone Alone in Tonsillectomy Complications

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Abstract

Background: Common complications including stridor, laryngospasm, and bronchospasm are important in patients undergoing general anesthesia. Dexamethasone, lidocaine, and ketamine could have significant roles in reducing these complications. Here we aimed to compare the use of these drugs during tonsillectomy.

Materials and Methods: This study was performed on 100 children that were candidates of tonsillectomy. Patients were divided into 4 groups receiving dexamethasone 0.1 mg/kg and lidocaine 1 mg/kg, ketamine 0.5 mg/kg and dexamethasone 0.1 mg/kg, dexamethasone 0.1 mg/kg, and normal saline after surgical procedures. We evaluated and compared data regarding the duration of anesthesia, oxygenation saturation, blood pressure (systolic and diastolic (SBP and DBP)), re-intubation, laryngospasm, bronchospasm, requiring analgesics after surgeries, recovery stay duration, and nausea and vomiting.

Results: Administration of ketamine and dexamethasone was associated with the lowest pain and lowest need for postoperative analgesic administrations in patients ($P = 0.02$). Patients that received lidocaine and dexamethasone had the lowest frequencies of airway stimulations ($P < 0.001$). Evaluations of complications in patients revealed that stridor was significantly lower in patients that received ketamine and dexamethasone ($P = 0.01$).

Conclusion: Usage of ketamine and dexamethasone was associated with the lowest pain severities and lowest complications. On the other hand, patients that received lidocaine and dexamethasone had the least airway stimulations.

Keywords: Complication, dexamethasone, ketamine, lidocaine, tonsillectomy

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INTRODUCTION

Tonsillectomy is the second most common pediatric surgery performed on an average of more than 500,000 cases annually in the American community.^[1,2] The main reasons for this surgery are recurrent throat infections and obstructive sleep apnea. Common complications after tonsillectomy include bleeding, pain, laryngospasm and bronchospasm, nausea, vomiting, and dehydration.^[3]

Postoperative complications in adenotonsillectomy surgery can vary between 1.4% and 5%. Minor complications include

hypoxemia, hypercapnia, and apnea exacerbation events.^[4] One of these complications is laryngospasm. Its frequency in tonsillectomy and adenotonsillectomy has been reported to be 21–26%.^[5] In addition, a history of airway infections and anomalies and asthma is effective in increasing the risk of complications. Stridor is also a relatively common respiratory complication that is reported in 24% of cases after tonsillectomy and usually occurs before laryngospasm.^[6]

A variety of techniques have been used to reduce complications and cough during extubation, including extubation under

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deep anesthesia and the use of drugs such as narcotics, dexmedetomidine, calcium channel blockers, and lidocaine.^[7,8] Various drugs such as lidocaine, magnesium sulfate, tranexamic acid, remifentanyl, hydralazine, dexamethasone, etc., have been studied to prevent complications.^[8] Lidocaine is a class B anti-arrhythmic drug that inhibits the stimulatory effect and activity of the upper laryngeal nerve and reduces long-term obstruction of the glottis.^[9] Various surgeries have shown the benefits of lidocaine in reducing complications, including cleft palate surgery, which reduces the risk of complications such as cough and laryngospasm.^[10-12] In addition, taking this drug topically and by inhalation has reduced complications.

Ketamine relaxes the muscles of the bronchi and prevents the effect of histamine on smooth muscle, thus preventing tracheal spasms but increasing secretion.^[13,14] Dexamethasone belongs to the group of glucocorticoids that have anti-nausea, vomiting, and anti-inflammatory effects that reduce inflammation and edema of the airways and even accelerate recovery.^[15]

It has been reported that dexamethasone could relieve complications, especially in patients with histories of pulmonary diseases including asthma.^[16] Considering that the mentioned complications are preventable after tonsillectomy and of course, we still have problems in controlling and managing these complications, we decided to compare the effectiveness of the combination of intravenous dexamethasone and lidocaine, dexamethasone and intravenous ketamine, and dexamethasone alone in controlling the complications after tonsillectomy.

MATERIALS AND METHODS

This study was performed from September 2020 to September 2021 on children that were candidates of tonsillectomy with the ethics code of IR.MUI.MED.REC.1400.418 (Iranian Registry of Clinical Trials (IRCT) code: IRCT20210718051928N1).

The inclusion criteria were age between 2 and 8 years, being a candidate of tonsillectomy, grade 1 or 2 based on American Society of Anesthesiologists (ASA) physical classifications, and signing the written informed by the parents to participate in this study. The no-entry criteria were active upper respiratory tract infection within two weeks before surgery, active lower respiratory tract infection within 5 weeks before surgery, history of asthma, comorbid anomalies and Down syndrome, coagulation and blood disorders, high body mass index (BMI), history of lidocaine hypersensitivity, and history of dexamethasone and ketamine hypersensitivity. The exclusion criteria were prolongation of surgery for more than one and a half hours or a severe drop in blood pressure due to arterial bleeding to less than 75% of baseline.

The patients, their parents, the data collector, and the data analyzer were blinded to the groupings of patients. The study population was considered 100 patients based on the sample size calculation formula. All patients were divided into four groups using Random Allocation Software (201 Harbour House, Aberystwyth, Wales, SY23 1AS).

In this study, an anesthesiologist who was not a member of the research team prepared the injections (specifying the time of injection) and assessed possible complications in recovery. A nurse who was blind to grouping patients collected the data (duration of intubation, repeated attempts for intubation, blood pressure and heart rate during the study, duration of surgery and duration of anesthesia, possible complications in recovery, etc.).

Demographic data of patients including age, gender, and weight were collected using a checklist. Maintenance fluid was formulated for each patient according to the 4-2-1 formula of dextrose saline serum. All patients received 0.1 mg/kg midazolam as pre-medication half an hour before surgeries. They were then transferred to the operating room and after being placed on the bed, standard monitoring such as non-invasive measurement of arterial blood pressure, electrocardiography, and pulse oximetry was established for them. Each patient received 10 cc/kg of Ringer's lactate serum and was pre-oxygenated with 100% oxygen for 3 min. The mentioned amount of serum was injected over 30 min.

Before induction of anesthesia, systolic, diastolic, and mean arterial blood pressure (SBP, DBP, and MAP) were measured and recorded in a checklist.

In all patients, endotracheal intubation was performed after induction of anesthesia with a suitable laryngoscope blade and with an endotracheal tube appropriate to the patient's age and by one anesthesiologist. The duration of the intubation (the time to perform a laryngoscopy until successful intubation) was recorded. The patients were then connected to a ventilator with a tidal volume of 8 cc/kg. Capnography monitoring was available for all patients. Continued anesthesia with isoflurane equivalent to one MAC plus N₂O and 50% oxygen each and 0.1 mg/kg morphine was administered.

During the surgical procedures, the patients received 3 cc of normal saline fluid for each cc of bleeding. After the surgeries, the patient's anesthetics were discontinued and all patients received 100% oxygen. At the end of surgeries, the remnants of the muscle relaxant effect were reversed with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg and each patient received the study drugs that had already been prepared by a blinded anesthesiologist in a syringe with the same volume equal to 5 cc based on the groups of patients.

The first group of patients received dexamethasone 0.1 mg/kg and lidocaine 1 mg/kg, the second group received ketamine 0.5 mg/kg and dexamethasone 0.1 mg/kg, the third group received only dexamethasone 0.1 mg/kg, and the fourth group received normal saline with the same volume.

The duration of anesthesia (from the time of isoflurane closure until the patient woke up completely) and extubation and the length of stay in recovery were recorded in minutes. In recovery, 100% oxygen was given to the patients through a mask with a flow of 6 l per minute. Electrocardiographic monitoring, pulse oximetry, and non-invasive measurement of SBP and DBP were

performed for all patients in the recovery room every 10 min until 30 min. We also recorded complications and severity of airway stimulation such as cough, laryngospasm, stridor, decrease in arterial oxygen saturation, as well as, recovery time, arrhythmia, and nausea and vomiting. Other evaluated variables were re-intubation, laryngospasm, bronchospasm, and requiring analgesics after surgeries.

Recovery stay duration was assessed and recorded based on the modified Aldrete score.^[17] The severity of nausea was assessed and recorded based on the Nausea and vomiting (NV) score^[18] as well as the number of vomits in recovery. Based on the NV score, the score of 0 was when the patient had no nausea and no vomiting, a score of 1 was the presence of nausea, a score of 2 was the presence of nausea and vomiting, and a score of 3 was vomits more than 2 times within 30 min. The patient's pain intensity at the end of recovery was assessed based on FLACC.^[19] The FLACC scale or Face, Legs, Activity, Cry, Consolability scale.

In case of vomiting as well as an NV score greater and equal to 2, ondansetron at a dose of 0.15 mg/kg was prescribed. Also, if there was a FLACC score equal to or more than 3, intravenous pethidine was injected at a dose of 0.5 mg/kg. In case of breath holding or decreased oxygen saturation, a mask and ampoule were used immediately to ventilate the patient, and in case of laryngospasm, re-intubation was conducted after injection of 1 mg/kg succinylcholine. All evaluations were done by one person.

The obtained data were analyzed with SPSS version 24 (Chicago, IL: SPSS Inc.) using one-way analysis of variance (ANOVA), Chi-square, and repeated measure tests.

RESULTS

In this study, 108 were evaluated for eligibility. Four cases did not enter the study due to lack of consent. Cases were divided into 4 groups each containing 26 patients. During the study, one patient in each group was excluded due to incomplete data. In the end, data from 100 cases were analyzed. The Consolidated Standards of Reporting Trials (CONSORT) flow chart of the study is shown in Figure 1.

Analysis of demographic data showed that there were no significant differences between the four groups regarding age ($P=0.70$), gender ($P=0.61$), ASA classification ($P=0.42$), and weight ($P=0.78$) [Table 1].

Also in terms of hemodynamic parameters including heart rate ($P=0.71$), SBP ($P=0.07$), and DBP ($P=0.63$), there was no significant difference between the four treatment groups over time. Over time, the pain was significantly different between the four treatment groups ($P=0.02$) and there was a significant difference between the control group and ketamine + dexamethasone ($P<0.05$). Pain severity was significantly lowest in ketamine + dexamethasone and lidocaine + dexamethasone groups, respectively, during the study. The prevalence of nausea and vomiting was also higher in the control group compared to others ($P=0.02$). Airway stimulation was significantly lower in the lidocaine + dexamethasone group and higher in the control group ($P<0.001$). None of the patients in this study required repeated attempts for intubation. These data are presented in Table 2.

Further assessments revealed that there were no significant differences between the four groups regarding the duration

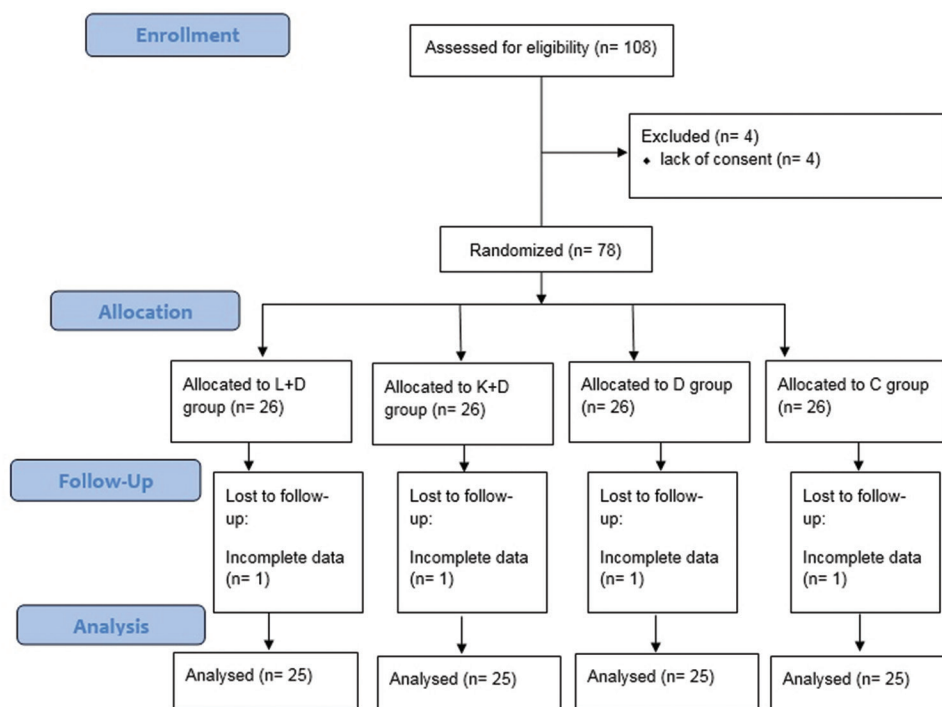


Figure 1: The CONSORT flow chart of the study

Table 1: Comparison of demographic data of patients

Variable		Lidocaine + dexamethasonee <i>n</i> =25	Ketamine + dexamethasonee <i>n</i> =25	Dexamethasonee <i>n</i> =25	Control <i>n</i> =25	<i>P</i>
Age (years) Mean±SD		5.64±1.80	5.24±2.12	5.68±1.88	5.20±1.58	0.70*
Weight (kg) Mean±SD		23.40±6.89	22.20±5.70	21.40±7.93	22.56±7.22	0.78*
ASA classification <i>n</i> (%)	1	20 (80%)	18 (72%)	19 (76%)	19 (76%)	0.42**
	2	5 (20%)	7 (28%)	6 (24%)	6 (24%)	
Gender <i>n</i> (%)	Girl	9 (36%)	14 (56%)	12 (48%)	12 (48%)	0.61**
	Boy	16 (64%)	11 (44%)	13 (52%)	13 (52%)	

*One-way ANOVA, **Chi-square

Table 2: Hemodynamic information, pain, airway stimulation, and nausea-vomiting by study group and time

Variable	Treatment group	T0	10 min after surgery	20 min after surgery	30 min after surgery	End of recovery	P1	P2	P3
HR (beats/min)	L+D	95.04±14.44	93.16±11.43	90.32±12.01	90.96±12.26	89.92±16.23	0.07	0.21	0.71
	K+D	92.04±14.21	90.32±14.45	88.72±16.31	85.92±11.67	85.60±14.74	0.03		
	D	93.68±10.71	89.76±9.67	90.40±10.88	91.68±10.55	85.72±10.51	0.01		
	C	92.01±12.84	89.08±12.50	89.20±14.95	88.60±13.44	86.32±13.54	0.003		
	P4	0.81	0.65	0.96	0.32	0.51			
SBP (mmHg)	L+D	106±5.36	107.36±5.37	103.88±8.39	99.96±7.78	101.32±4.95	0.004	0.50	0.07
	K+D	107±6.04	108.20±5.36	107.12±7.69	102.36±7.22	102.72±4.43	0.005		
	D	104.01±7.09	105.88±5.89	104.12±8.46	102.72±5.08	99.48±7.71	0.004		
	C	105.64±5.67	106.72±6.49	106.08±6.42	103.96±4.41	103.90±6.38	0.05		
	P4	0.25	0.54	0.39	0.15	0.06			
DBP (mmHg)	L+D	73.80±7.74	69.16±5.67	65.12±8.92	60.52±7.79	67.92±8.22	0.001	0.44	0.63
	K+D	72.72±6.42	70.40±4.98	66.52±7.01	61.56±11.32	68.44±8.45	0.004		
	D	68.32±7.15	67.36±6.71	67.72±7.79	63.92±7.90	65.16±7.63	0.14		
	C	72.32±10.81	68.48±5.74	67.80±7.42	63.04±7.97	64.80±6.91	0.001		
	P4	0.10	0.31	0.58	0.54	0.24			
Pain (VAS)	L+D	2.80±1.08	2.40±0.81	2.24±1.09	1.52±0.91	1.40±0.76	0.001	0.64	0.02
	K+D	2.60±0.57	2.32±0.55	1.84±0.47	1.12±0.66	1.04±1.73	0.001		
	D	2.72±1.36	2.56±1.15	2.12±1.23	1.56±1.76	1.48±0.82	0.002		
	C	3.04±1.05	3.20±1.25	2.36±1.15	1.72±0.84	1.60±0.50	<0.001		
	P4	0.51	0.009	0.32	0.06	0.04			
Nausea/Vomiting (times)	L+D	1.64±0.63	1.2±0.66	0.52±0.50	0.48±0.40	0.40±0.20	0.001	0.25	0.02
	K+D	1.28±0.45	1.04±0.67	0.72±0.72	0.58±0.52	0.48±0.36	0.001		
	D	1.44±0.76	0.84±0.76	0.48±0.50	0.47±0.32	0.47±0.32	0.001		
	C	1.80±0.57	1.20±0.57	0.84±0.62	0.68±0.62	0.52±0.50	<0.001		
	P4	0.22	0.26	0.12	0.17	0.07			
Airway Irritability (VAS)	L+D	2.21±0.97	1.60±0.86	1.08±0.86	0.76±0.69	0.72±0.56	<0.001	0.03	<0.001
	K+D	2.48±0.87	1.84±0.94	1.28±0.89	0.76±0.77	0.70±0.60	<0.001		
	D	2.56±0.51	2.60±0.50	1.76±0.43	1.36±0.81	1±0.64	<0.001		
	C	2.80±0.81	2.56±0.50	1.84±0.47	1.36±0.81	1.08±0.70	<0.001		
	P4	0.33	0.001	0.001	0.002	0.01			

P1 (Time Effect), P2 (Interaction Effect), P3 (Intervention Effect) based on repeated measures, P4: One-way ANOVA, L: lidocaine, D: dexamethasone, K: ketamine, C: control

of extubation (*P* = 0.61), duration of anesthesia (*P* = 0.56), duration of surgery (*P* = 0.53), duration of recovery (*P* = 0.25), re-intubation (*P* = 0.66), repeated operation (*P* = .61), and laryngospasm (*P* = 0.50). But stridor (*P* = 0.01) and analgesic requirement (*P* = 0.003) were significantly lower in the ketamine + dexamethasone group. Bronchospasm was not observed in any of the groups [Table 3].

DISCUSSION

In this study, we observed that the administration of ketamine and dexamethasone was associated with the lowest pain and lowest need for postoperative analgesic administrations in patients. Patients that received lidocaine and dexamethasone had the lowest frequencies of airway stimulations. Furthermore, patients in the control group had the highest frequencies of

Table 3: Other surgery-related information including time, drug use, and symptoms by group therapy

Variable	Lidocaine + dexamethasone n=25	Ketamine + dexamethasone n=25	Dexamethasone n=25	Control n=25	P
Extubation duration (min) Mean±SD	18.61±10.54	16.80±4.97	20.27±12.18	17.25±8.18	0.61*
Anesthesia duration (min) Mean±SD	121.60±40.99	128.60±9.07	132.17±28.15	124.58±20.79	0.56*
Surgery duration (min) Mean±SD	99.60±31.81	108.12±6.72	104.40±20.78	101.25±18.54	0.53*
Recovery duration (min) Mean±SD	99.54±25.35	98.40±8.01	93.18±27.10	88.75±17.46	0.25*
Requiring analgesic n (%)	11 (44%)	7 (28%)	16 (64%)	18 (72%)	0.003**
Re-intubation n (%)	2 (8%)	0	1 (4%)	1 (4%)	0.66***
Laryngospasm n (%)	2 (8%)	0	2 (8%)	3 (12%)	0.50***
Bronchospasm n (%)	0	0	0	0	-
Stridor n (%)	6 (24%)	3 (12%)	11 (44%)	13 (52%)	0.01***

*One-way ANOVA, **Chi-square, ***Exact Fisher test

nausea and vomiting, and airway stimulations. Evaluations of complications in patients revealed that stridor was significantly lower in patients that received ketamine and dexamethasone.

These data show that usage of ketamine and dexamethasone was associated with the lowest pain severities and lowest complications. On the other hand, patients that received lidocaine and dexamethasone had the least airway stimulations. Therefore, this information could have high clinical values because as explained earlier, complications including airway stimulation, laryngospasm, bronchospasm, and stridor are common in patients undergoing endotracheal intubation.

There have been previous reports on the use of various drugs including ketamine and lidocaine in decreasing complications following endotracheal intubation. A study was conducted by Rajkumar and colleagues in 2012 in India. In this study, 90 adult patients undergoing elective open cholecystectomy surgery were included. Based on this study, the administration of ketamine 40 mg led to decreased incidence of postoperative sore throat, hoarseness, and pain.^[20] In another study by Merelman and others in 2019 in the United States, the use of ketamine and possible complications during endotracheal intubation were assessed. It was shown that administrations of ketamine lead to significantly decreased stridor and laryngospasm during both regular and rapid sequence intubation (RSI).^[21]

Most previous studies have focused on the effects of ketamine on postoperation sore throats. Similarly, in 2015, Kang and colleagues assessed data from 40 patients undergoing elective laparoscopic cholecystectomy and reported that abdominal pain, sore throat, and respiration complications were significantly lower in patients treated with ketamine compared to controls.^[22] As de Moraes and colleagues showed in 2015, the use of ketamine alone or in combination with other drugs such as propofol could decrease postoperative, intubation-induced complications.^[23] These data are also consistent with the findings of our study. Another study by Marrugo Pardo and colleagues reported that the prevalence of

postoperative complications was 3.59% (6/167).^[4] In this study, we observed higher efficacy in patients that were treated with a combination of ketamine and dexamethasone.

Another point of this study was that we observed significantly lower pain intensity and analgesic requirements in patients receiving ketamine and dexamethasone. The prevalence of nausea and vomiting was also lower in cases receiving medications. Dexamethasone alone is also another effective agent for reducing intubation-induced complications.^[24,25] Studies have shown that injections of dexamethasone could decrease patient's pain and nausea and vomiting. Our data are in line with these findings. We showed that the patients that received dexamethasone had also lower pain and nausea and vomiting compared to controls.

The use of lidocaine and dexamethasone was associated with lower pain and airway stimulation compared to controls. Therefore, it is believed that lidocaine could have significant effects. Previously in 2018, Hashemian and others showed that intravenous administration of fentanyl and lidocaine could significantly decrease pain and sore throat.^[26] Panti and others also reported lower airway stimulation after the injection of lidocaine in patients.^[27]

It was also observed that all cases in the four therapeutic groups had similar surgery and intubation outcomes and there were no significant differences between them regarding the duration of extubation, duration of anesthesia, duration of surgery, duration of recovery, re-intubation, repeated operation, and laryngospasm.

An important point of our survey was that we used combinations of ketamine, lidocaine, and dexamethasone in this study while similar comparisons have not been conducted previously. In another report in 2021, Fathy and others evaluated the efficacy of adding lidocaine to ketamine during endotracheal intubation. By administering 1 mg/kg ketamine, they showed that patients had significantly lower pain and bronchospasm. It was indicated that these complications are lowest especially if

associated with 1 mg/kg lidocaine.^[28] This study also highlights the importance of further research in the search for the most effective combination of drugs to reduce these complications.

The limitations of our study were the restricted study population and evaluation of the medications with only one dosage while some previous studies have observed different effects with changes in the drug dosage. We suggest that anesthesiologists should pay more attention to the therapeutic properties of lidocaine, ketamine, and dexamethasone.

CONCLUSION

We conclude that the administration of ketamine and dexamethasone was associated with better outcomes in patients undergoing tonsillectomy. Stridor was significantly lower in patients that received ketamine and dexamethasone.

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Ethics approval and consent to participate

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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