

## **Propofol versus lidocaine on prevention of laryngospasm in tonsillectomy: A randomized clinical trial**

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### **Abstract**

Laryngospasm is an important complication of tonsillectomies. This study aimed to compare the effects of propofol versus lidocaine on prevention of laryngospasm in tonsillectomy. This randomized clinical trial included 102 patients who met the inclusion criteria. Patients were randomly divided into two groups treated with 0.5 mg/kg propofol (group P) or 1 mg/kg lidocaine 2% (group L). The frequencies of laryngospasm (within 10 min after extubation), agitation, nausea, vomiting, mean heart rate and mean arterial pressure (MAP) were assessed in both groups. Data were analyzed using SPSS software version 16 at a 95% confidence level. There were no significant differences between the two groups in terms of sex, age or weight. In the P group, the frequency of laryngospasm was significantly lower than L within 10 minutes after extubation (4.1% versus 16.3%). Furthermore, the frequencies of agitation ( $p = 0.003$ ), nausea and vomiting ( $p = 0.002$ ) and mean heart rate ( $p = 0.026$ ) were significantly higher in the L group than the P group. However, there were no differences between the two groups in terms of mean systolic and diastolic blood pressure, MAP, SPO<sub>2</sub>, awakening time, length of stay in recovery and frequency of shivering. Propofol can reduce the incidence of laryngospasm, agitation, nausea and vomiting but it has no effect on the patient's awakening time and length of stay in recovery.

**Key Words:** Laryngospasm; lidocaine; propofol; tonsillectomy.

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Tonsillectomy is one of the most common surgeries in children.<sup>1</sup> Laryngospasm is a dangerous complication of tonsillectomy that occurs following tracheal extubation.<sup>2,3</sup> It is characterized by a strong, involuntary contraction of the laryngeal muscles that manifests as apnea, cyanosis, acute respiratory distress, hypoxia, and hypercarbia.<sup>4,5</sup> If not treated immediately, it can lead to negative pressure pulmonary edema, insufficient oxygenation, brain damage, and even cardiac arrest and death.<sup>6-8</sup> The incidence of laryngospasm following general anesthesia is inversely related to the age of the patients.<sup>9,10</sup> The presence of factors such as secretions, blood and foreign bodies in the oropharynx, manipulation of the airways, and upper respiratory tract infection influence its occurrence.<sup>11</sup> There are several ways to prevent this complication, including complete haemostasis during surgery, gentle suctioning of the oropharynx before extubation, awake tracheal extubation and the use of drugs.<sup>12</sup> Specifically, Lidocaine is used

topically or intravenously to prevent laryngospasm. Regarding the neurological and cardiac side effects of lidocaine in children, other drugs have been considered in recent years.<sup>13-15</sup> Propofol is a high clearance anaesthetic. Considering the effects of propofol, it seems that it can be effective in the prevention or treatment of laryngospasm, but only a few studies have been done about this.<sup>16,17</sup> Therefore, the aim of this study is to compare the effect of intravenous injection of lidocaine 2% and propofol on prevention of laryngospasm in tonsillectomy.

### **Materials and Methods**

#### *Study Design*

This prospective, randomized, double blind, clinical trial was conducted in Besat Hospital in Hamadan, Iran, between 2018 and 2019. The protocol study was reviewed and approved by the Ethics Committees of Hamadan University of Medical Sciences

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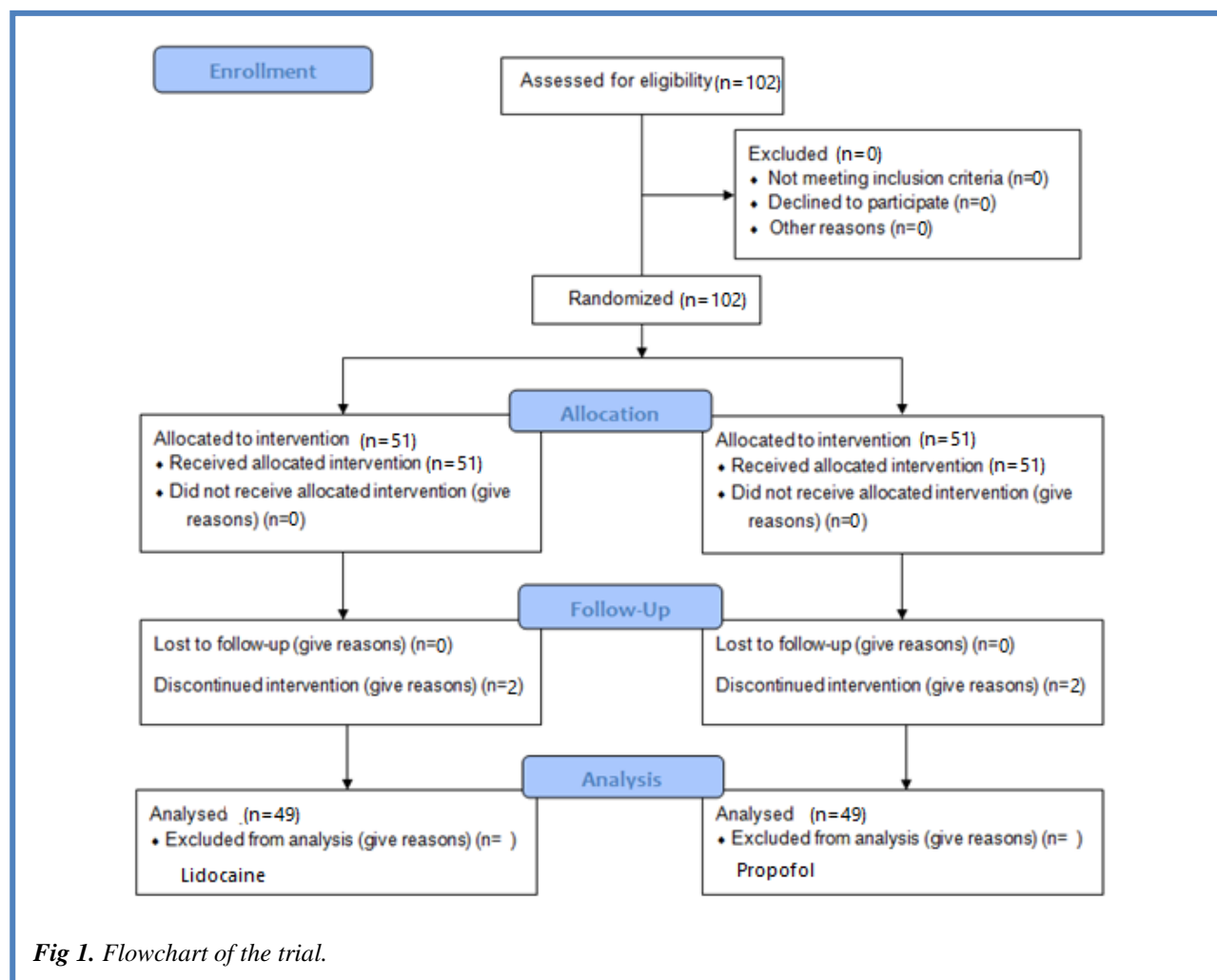


Fig 1. Flowchart of the trial.

(IR.UMSHA.REC.1397.628). Also registered at Iranian Registry of Clinical Trials (IRCT 20120915010841N16). Children 3 to 14 years and American Society of Anesthesiologists (ASA) physical status Class I & II who presented for tonsillectomy under general anesthesia were included in this study. Exclusion criteria were patients who refused to participate in this study, cardiac and respiratory diseases, upper respiratory tract infection, taking corticosteroids and history of allergies to eggs, soy, lidocaine and propofol.

### Sample size

The sample size of this study was calculated based on previous studies (Iqbal et al. (18), according to the formula for difference in proportions between two groups, and concerning the type one error 5% and power of 80% ( $\beta=20\%$ ). A sample size of 102 patients, 51 in each group, was considered.

$$n = \frac{(sd1^2 + sd2^2) + (Z_\alpha + Z_\beta)^2}{(\mu1 - \mu2)^2}$$

### Randomization and blinding

Patients were randomly assigned to the group P (propofol) and group L (lidocaine) based on block

randomization. At the end of the surgery, two minutes before endotracheal extubation, group P, 0.5 received intravenously mg/kg propofol while group L received intravenously 1 mg/kg of lidocaine 2%. An anesthesia nurse prepared the drugs in syringes of similar shape and size and covered them by aluminum foil and injected according on block randomization. The anesthesiologist who recorded data, was blinded to the patient group.

### Data collection

After obtaining written consent, a form was completed for each patient, which included demographic characteristics, age, weight, sex, and so on. Then 3 ml/kg saline was administered and standard monitoring including electrocardiography, pulse oximetry and non-invasive blood pressure (NIBP) monitoring was performed for each patient by monitoring device (Saadat, Novin S1800 model, Iran) for all of the patients.

Induction of anesthesia was performed with midazolam 0.05 mg/kg, fentanyl 1  $\mu$ g/kg, propofol 2 mg/kg and atracurium 0.5 mg/kg and patients were intubated with endotracheal tube of appropriate size. Then anesthesia was maintained with  $\text{NO}_2/\text{O}_2$  50% and IMAC (1.2%) of isoflurane. At the end of the surgery, neuromuscular

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**Table 1** Comparison of frequency of laryngospasm, shivering, agitation, nausea and vomiting after extubation in propofol (P) and lidocaine (L) groups.

Variable	Groups		p-value
	L N (%)	P N (%)	
Laryngospasm	8 (16.3)	2 (4.1)	0.048*
Agitation	21 (42.9)	7 (14.3)	0.003*
Nausea & Vomiting	19 (38.8)	5 (10.4)	0.002*
Shivering	2 (4.1)	0 (0)	0.495

block was reversed and two minutes before endotracheal extubation, 0.5 mg/kg propofol (Ultrafol 1%, Italy) in the group P and 1 mg/kg of lidocaine 2% (Lidocaine 2%, IranHormon Co, Iran) in the group L were injected intravenously. Then the patients were extubated and evaluated for laryngospasm and inspiratory stridor. Systolic, diastolic and mean arterial pressure (MAP), heart rate (HR) and SPO<sub>2</sub> were measured using an X162 monitor (Saadat Co., Iran) at intervals of 1, 3, 5, 10 and 15 minutes after extubation. The anesthesiologist who recorded the study outcome, was blinded to the group allocated of patients. If laryngospasm occurred, 100% oxygen, jaw thrust maneuver, positive pressure ventilation and succinylcholine were used.

In case of nausea and vomiting, metoclopramide was administered intravenously and was recorded in a questionnaire. Also, awakening time, agitation and length of stay in recovery were recorded.

### Statistical analysis

All data were analyzed with SPSS software version 16 (SPSS Inc., Chicago, IL, USA). Descriptive information of qualitative data was expressed in the form of ratios and percentages. Chi-square and Fisher's exact tests were used to compare the incidence of laryngospasm, nausea and vomiting. Student's T-test and Mann-Whitney nonparametric test were used to compare systolic and diastolic blood pressure changes, MAP, PR, RR and other quantitative variables. In all analyses, p-values less than 0.05 were considered significant.

### Results

In this study, 102 patients were eligible for inclusion in the study, but finally 98 patients were included in two groups of L (n = 49) and P (n = 49). Two patients from each group were excluded from the study because they

regretted their cooperation. The enrollment flow chart of patients is presented in Figure 1.

In the lidocaine group, 18 patients were females (36.7%) and 31 patients were males (63.3%), and in the propofol group, 21 patients were females (42.9%) and 28 patients were males (57.1%). The mean age was  $6.86 \pm 2.96$  in the lidocaine group and  $7.11 \pm 2.9$  years in the propofol group. The mean weight was  $25.14 \pm 10.91$  kg in the lidocaine group and  $23.8 \pm 10.71$  in the propofol group. According to the results, there were no significant differences between the two groups in terms of sex ( $p = 0.68$ ), age ( $p = 0.631$ ) or weight ( $p = 0.547$ ).

According to the results of Table 1, the incidence of laryngospasm in the lidocaine group was significantly higher than the propofol group ( $p < 0.05$ ). The frequencies of agitation, nausea and vomiting in the lidocaine group was significantly higher than propofol group. But no significant difference was found in the both groups in terms of the frequency of shivering in recovery.

No significant difference was found between two groups in terms of the need to positive pressure ventilation. According to the Table 2, there were no significant differences between the groups in terms of mean systolic and diastolic blood pressure at 1, 3, 5, 10 and 15 minutes after extubation. According to the Table 3, there were no significant differences between the two groups in terms of mean arterial pressure (MAP) at 1, 3, 5, 10 and 15 minutes after extubation. The mean heart rate (HR) in the propofol group was significantly lower than the lidocaine group at 3 and 5 minutes after tracheal extubation ( $p = 0.045$  &  $0.026$ ). While the difference was not statistically significant in other times ( $p > 0.05$ ).

No significant differences were found between the lidocaine group and propofol group in terms of mean SPO<sub>2</sub> at 1, 3, 5, 10 and 15 minutes after extubation.

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**Table 2.** Comparison of mean systolic and diastolic blood pressure at 1, 3, 5, 10 and 15 minutes after extubation in propofol (P) and lidocaine (L) groups.

Time (Min)	Systolic Blood Pressure Mean ±SD		p-value	Diastolic Blood Pressure Mean ±SD		p-value
	L	P		L	P	
1	115.4 ± 6.35	115.66 ± 8.19	0.867	69.65±5.81	68.95±7.66	0.617
3	112 ± 5.78	113.51 ± 8.69	0.473	67.55±5.84	66.91±7.4	0.619
5	109.63 ± 5.93	110.57 ± 8.39	0.535	65.41±5.34	64.81±6.39	0.226
10	106.1 ± 4.63	107.47 ± 7.16	0.238	63.45±4.76	63.32±5.36	0.466
15	102.57 ± 3.85	105.42 ± 6.67	0.086	60.98±3.52	62.25±4.76	0.489

Mean awakening time in recovery was 29±26 minutes in lidocaine group and 41±29 minutes in propofol group that was not statistically significant (p = 0.713). The length of stay in recovery in the lidocaine group was lower than the propofol group (39 ±10 vs 51±15 minutes), but this difference was not statistically significant (p = 0.543).

### Discussion

This study aimed to compare the effects of intravenous injection of Lidocaine 2% or propofol in the prevention of laryngospasm. In the present study, patients undergoing tonsillectomy in two groups of lidocaine or propofol were assessed in terms of sex, age or weight. In the lidocaine group, the frequency of laryngospasm was

significantly higher than the propofol group. Also, the frequencies of agitation, nausea, vomiting and the mean heart rate (at 3 and 5 min after extubation) in the lidocaine group were significantly higher than the propofol group. However, there were no significant differences between the groups in terms of mean systolic and diastolic blood pressure, MAP, SPO<sub>2</sub>, awakening time, length of stay in recovery and frequency of shivering. An important complication following tonsillectomy and endotracheal intubation is laryngospasm.<sup>3</sup> In a study by Iqbal et al.<sup>18</sup> the effect of 1 mg/kg intravenous propofol on the incidence of laryngospasm was evaluated in 80 children between 4 to 12 years of age who were candidates for tonsillectomy. They showed that the incidence of laryngospasm after extubation of the trachea was 42% in

**Table 3.** Comparison of MAP and HR at 1, 3, 5, 10 and 15 minutes after extubation in propofol (P) and lidocaine (L) groups.

Time (Min)	Mean Arterial Pressure Mean ±SD		p-value	Heart Rate(Min) Mean ±SD		p-value
	L	P		L	P	
1	84.79±6.01	84.16±7.3	0.617	124.4±10.53	121.91±13.99	0.325
3	82.18±5.13	82.38±7.72	0.58	119.49±4.72	114.79±12.93	0.045*
5	79.83±5.18	79.77±7.43	0.226	113.47±10.76	108.36±11.36	0.026 *
10	77.22±4.39	77.73±6.13	0.797	107.9±11.7	104.64±11.88	0.179
15	74.54±3.41	76.31±4.9	0.167	104.57±12.7	100.55±12.1	0.116

the placebo group and 30% in the propofol group. The results showed that administration of intravenous propofol significantly prevented the occurrence of laryngospasm following extubation of the trachea in children.<sup>18</sup> The study by Mokhtar et al.<sup>19</sup> compared the effect of propofol (0.5 mg/kg) versus lidocaine (1.5 mg/kg) on treatment of laryngospasm in pregnant women undergoing cesarean section. The frequency of laryngospasm was 5% in lidocaine group and 4.7% in propofol group. They indicated that 65.6% in the lidocaine group and 82.8% in the propofol group responded to treatment. The researchers concluded that low-dose propofol was more effective than lidocaine in treating laryngospasm.<sup>19</sup> Despite the fact that children under 14 years of age underwent tonsillectomy instead of pregnant women under cesarean section, in line with the results of Mokhtar et al.,<sup>19</sup> the results of this study revealed that propofol was more effective than lidocaine in reducing the incidence of laryngospasm. This study was similar to Iqbal et al.'s study in terms of target group and age of patients, except that in this study lidocaine was used instead of placebo and propofol dose was lower than Iqbal et al.'s study.<sup>18</sup> But the results of the two studies are consistent. Malik et al.<sup>20</sup> conducted a study on 150 children aged 5 to 12 years who were candidates for tonsillectomy. They compared the intravenous injection of 1.5 mg/kg lidocaine and normal saline two minutes before extubation. The incidence of laryngospasm within 10 minutes after extubation was 8% and 20% in lidocaine and placebo groups, respectively. Lidocaine effectively reduced the incidence of laryngospasm after endotracheal extubation in children undergoing tonsillectomy.<sup>20</sup> In the present study, instead of lidocaine and placebo, lidocaine was tested with propofol. The maximum incidence of laryngospasm in this study in lidocaine group was determined 16.3% versus 4% in propofol group within 10 minutes after extubation, which is higher than Malik et al.'s study.<sup>20</sup> The inconsistency of the results may be that in this study, 1 mg/kg lidocaine 2% was used instead of 1.5 mg/kg lidocaine. In the study by Batra et al.,<sup>21</sup> the effect of a low dose of propofol compared to placebo on the prevention of laryngospasm was evaluated among 120 children aged 3-14 years who were candidates for tonsillectomy. They divided the patients into two groups of 60 patients. In one group, 0.5 mg / kg of propofol was injected intravenously when the patient began to swallow, and the same volume of the normal saline was added in the other group. Sixty seconds after drug administration, tracheal extubation was performed and patients were examined for laryngospasm for 2 minutes. They reported an incidence of 20% for laryngospasm in the control group and 6.6% in the propofol group.<sup>21</sup> In present study, the incidence of laryngospasm after extubation in the propofol group was almost consistent with the findings of Batra et al.<sup>21</sup> In the this study, a dose of 0.5 mg/kg propofol was injected two minutes before extubation instead of one minute before extubation. The sample size of this study was smaller than in Batra et al.<sup>21</sup>

study and lidocaine was used instead of normal saline. On the other hand, a limitation of the present study is that we do not have a control group.

In conclusion, this study showed that propofol can reduce the incidence of laryngospasm, agitation, nausea and vomiting but it has no effect on the patient's awakening time and length of stay in recovery. So, propofol is more effective than lidocaine in preventing laryngospasm, nausea and vomiting in children undergoing tonsillectomy.

### List of acronyms

ASA - American Society of Anesthesiologists

HR - heart rate

MAP - mean arterial pressure

NIBP - non-invasive blood pressure

### Contributions of Authors

Study concept and design NM, and FAM; Analysis and interpretation of data, NM, and NJ. Critical revision of the manuscript NM and FAM. Statistical analysis NJ. All authors reviewed and approved the final manuscript. .

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### Conflict of Interest

The authors declare no conflict of interests.

### Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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