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Comparing the effects of Total Intravenous Anesthesia and Sevoflurane on Respiratory Adverse Events in under-7 Children with Upper Respiratory Tract Infection

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Abstract

Background: Controlling the respiratory complications of anesthesia in children is one of the most challenging situations. The present study aimed to compare intravenous and inhalation anesthesia in respiratory adverse events in children under 7 with upper respiratory tract infection (URTI).

Method: All children with URTI referring to Labbafinejad hospital in Tehran for emergency surgery were randomly divided into two groups. The first group received Total Intra-Venous Anesthesia (TIVA) inducer and maintenance, and the second group received inhalation (Sevoflurane). The two groups were compared in terms of respiratory events at different times Laryngeal Mask Airway (LMA) implantation time, interoperation, LMA removal, and recovery).

Results: There were significant differences between the groups (p-value < 0.05) (1) before induction in terms of using respiratory sub-muscles, (2) during LMA implantation in terms of oxygen saturation percentage, stridor, cyanosis, laryngospasm, bronchospasm, and the presence of breath hold, (3) during LMA removal in terms of oxygen saturation percentage, cyanosis, laryngospasm, and bronchospasm, (4) after LMA removal in terms of stridor, cyanosis, the use of respiratory sub-muscles, persistent cough, and breath hold, and (5) in the Post-Anesthesia Care Unit (PACU) in terms of stridor and persistent cough.

Conclusion: in children with URTI, who have undergone emergency surgery, due to less PRAE in the intravenous method with Propofol, the use of TIVA method can reduce the risk of related adverse events.

Key Words: Persistent Cough, Propofol, Respiratory noise, Sevoflurane, Stridor.

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1- INTRODUCTION

Upper Respiratory Tract Infections (URTIs) are inflammatory infections of the upper airways, including ears, throat, nose, throat, larynx, sinuses and trachea. According to studies, about 50 million people worldwide die each year from URTI (1, 2). Children are one of the most vulnerable groups to URTI due to social interaction type they have with each other and weak immune system (3).

Children with URTI are associated with symptoms such as body aches, fatigue, anorexia, runny nose, sore throat, and cough. Although most URTI infections are mild, in some cases they can cause serious health problems by causing severe complications. In mild cases infection resolves after about two weeks without any treatments. In severe cases, it can cause death. Risk factors for URTI include immunodeficiency, air pollution, cigarette smoking and underlying diseases (4, 5).

Anesthesia induction is one of the most important pillars of general anesthesia, in which goals such as stability of hemodynamic status, intubation, and finally passing through different phases of anesthesia and reaching the surgical phase should be pursued. Since maintaining a safe and secure airway is a very serious responsibility for anesthesiologists, and given that children have significant anatomical and physiological differences compared to adults, these differences affect the techniques and tools used by anesthesiologists for safe airway control (6).

Induction methods in children include inhalation induction, muscle induction, venous induction and rectal induction. Each of these methods has advantages and disadvantages; nevertheless, the inhalation method has more proponents.

Given the side effects of Halothane, Sevoflurane is the drug of choice in pediatric and neonatal anesthesia today, but due to lack of access to Sevoflurane in Iran, Halothane was used more in the past (7, 8).

Total Intra-Venous Anesthesia (TIVA) is based on the use of Propofol along with Remifentanil, as an ultra-short-acting opioid, and are attractive for pediatric surgeries due to their synergic effects and properties (9, 10). Previous studies have shown that in Sevoflurane technique, the Volatile Induction and Maintenance of Anesthesia (VIMA) provides greater hemodynamic control and a better cardiac profile compared to Propofol (11). Also, the bolus injection of Propofol has often been associated with apnea (12).

On the other hand, the use of an intravenous drug as a maintenance drug of anesthesia has shown no significant difference regarding postoperative pulmonary tests (13). Also, intravenous maintenance has fewer short-term side effects, but this method has little effect on patient's spirometric tests, reflecting a long-term pulmonary pattern. Based on these findings, although VIMA Sevoflurane provides better hemodynamic profiles and stable breathing, but these two techniques have not been compared in terms of subsequent complications in children with cold; so, in this study, we compared the two anesthesia methods of TIVA and Sevoflurane in respiratory adverse events in children under 7 with Upper Respiratory Tract Infection (URTI).

2- MATERIALS AND METHODS

2-1. Participants

All URTI children eligible for emergency surgeries, who had referred to Labbafinejad hospital, were included in the experiment. They were 60 children, divided into two groups of 30 individuals (completely intravenous TIVA as group I, and inhaled Sevoflurane as group II) (**Fig. 1**).

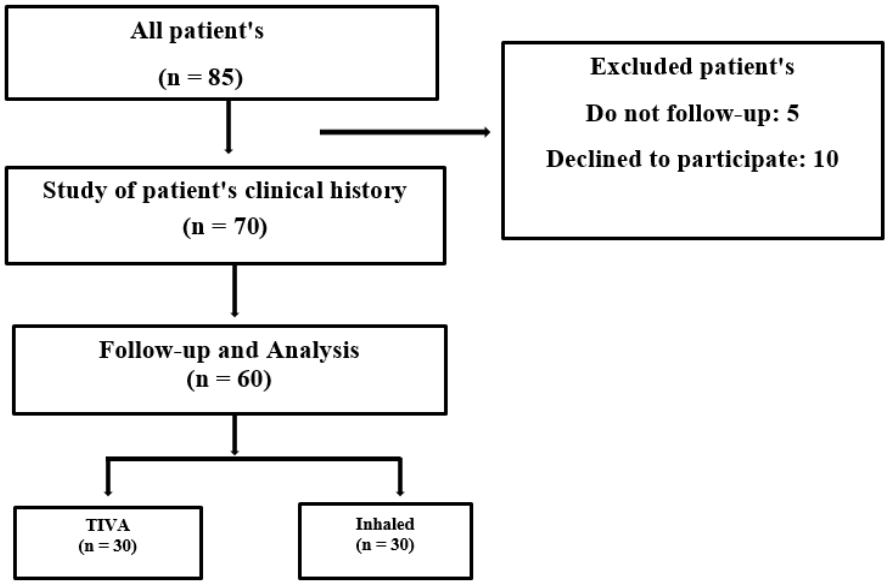

Fig. 1: Flow diagram showing patient selection, Exclusion, and follow-up

2-1-1. Inclusion and exclusion criteria

Inclusion criteria according to American Society of Anesthesiologists Classification (ASA CLASS 1,2) encompassed all children (between 2-7 years old) with URTI undergoing ureteral emergency surgery referring to Labbafinejad hospital, who had a lack of cardiopulmonary problems, lack of asthma, no history of airway problems, and lack of lower respiratory tract infection (LRTI) symptoms. The exclusion criteria were changing the surgical plan by the surgical team and increasing the surgery time by more than 1-1.5 hours.

2-1-2. Sample size

Based on statistical calculations and the study by Safaeian and Al-Nabi, in 2007, the following equation was used to determine the sample size (14):

$$n = \frac{(1.96)^2 \times (SD)^2}{d^2} \cong 60$$

SD=3.95

d^2=1

2-2. Anesthesia procedure

Group I: 2 µl/kg Fentanyl and 1 mg/kg Lidocaine, for induction of Propofol at the dose of 2-3 mg/kg after induction; laryngeal mask airway (LMA) was used to manage the airway, then the maintenance was considered with Propofol at the dose of 100 µg/kg/min and Remifentanil 1µg/kg/min during surgery.

Group II: at the beginning of surgery, Sevoflurane gas was induced only with a concentration of 8%, after deep anesthesia LMA was used; then Sevoflurane gas with a concentration of 3-5% without spontaneous respiration was considered for patient's maintenance. In both groups, 1 mg / kg Dexamethasone was prescribed before surgery for all patients.

2-2-1. Outcome

After induction of anesthesia in patients and surgery, the anesthetic drug complications were evaluated, including Spo2, tachycardia / bradycardia, stridor, cyanosis, tachycardia / bradycardia (number of breaths), respiratory distress (use of sub-muscle (The purpose is to use the secondary respiratory muscles, which are detected and recorded through observing.)), laryngospasm, bronchospasm, shortness of breath, persistent cough.

The Spo2, tachycardia and bradycardia are detected and recorded by a pulse oximeter device connected to the patient, and other variables such as stridor, cyanosis, tachypnea, bradypnea, respiratory distress, larynx spasm, bronchospasm, shortness of breath, and persistent cough were recorded by anesthesiologist's observation.

2-3. DataAnalysis

Data were analyzed using SPSS software version 23. Central frequency distribution and dispersion indices (mean, frequency, etc.) were studied and described. The two groups were compared and analyzed using the independent t-test. The significance level was considered as< 0.05.

3- RESULTS

3-1. Demographic information

The patients' demographic information is shown in **Table 1**. Both groups were almost similar in terms of age and gender. Previous records of tobacco use have also shown that the differences between the two groups were not statistically significant (**Table 1**).

Table-1: Demographic information of patients

Patients Characteristic		Group II	Group I	P-Value
Age (mean ± SD)		3.3±1.46	4.35±1.7	0.015
BMI		15.67±0.99	16.01±0.99	0.87
Gender	Male	15 (48.4)	16 (51.7)	0.9
	Female	15 (51.6)	14 (48.3)	
Asthma	NO	29(96.1)	24(80)	0.051
	YES	1(3.3)	6(20)	
Fever	NO	28(93.3)	28(93.3)	0.697
	YES	2(6.7)	2(6.7)	
Passmoker #	NO	24(80)	23(76.7)	0.5
	YES	6(20)	7(23.3)	
Sustained Cough	NO	26(86.7)	23(76.7)	0.253
	YES	4(13.3)	7(23.3)	

It means that the patients were exposed to cigarette smoke inhalation previously.

3-2. The evaluation of patients' status before induction

As the results show, there was no statistically significant difference between intravenous and inhalation before induction in oxygen saturation percentage, heart rate and respiration rate per minute, Stridor and pulmonary auscultation (P > 0.05), but a significant difference was found There was a statistically significant difference in respiratory factors between the two groups at this time (P<0.05) (**Table 2**).

3-3. Evaluation of LMA information

The condition of patients during LMA implantation was as follows: in the TIVA group, the mean oxygen saturation was 96.6%, and the mean heart rate was 96 beats per minute. It should also be noted that none of the patients in this group experienced stridor, cyanosis, laryngospasm, bronchospasm, and breath hold during LMA implantation (all 30 patients were 100% negative). In the Sevoflurane group, the mean oxygen saturation was 94.6% and the mean heart rate was 119 beats per minute (**Table 3**).

Table-2: Evaluation of patients' status before induction in TIVA and Sevoflurane groups

	Group/value	SpO2a		HRb		RRc		Stridor	Use of Respiratory Sub-Muscles	Lung Auscultation
		Mean	Range	Mean	Range	Mean	Range			
Patients' status before induction	TIVA	96.2%	104.3	26.13	20-41	75-161	94-98	-27(90%) +3(10%)	-26(86.7%) +4(13.3%)	21(70%) clear 9(30%) coarse
	Sevoflurane	96.5%	116.73	28.33	20-40	90-150	94-99	-28(93.3%) +2(6.7%)	-30(100%)	24(80%) clear 6(20%) coarse
	P-value*	0.314		0.216		0.403		0.358	0.000	0.080

[a]Oxygen saturation, [b]Heart rate, [c]Respiratory rate, * Significance level was calculated by independent t-test at 95% confidence level

Table-3: Evaluation of patients' status in TIVA and Sevoflurane groups during and after the LMA implementation and removal

		SpO2a		HRb		RRc		Stridor	Cyanosis	Laryngospasm	Bronchospasm	Breath Hold	Use of respiratory sub-muscles	Persistent cough
		Mean	Range	Mean	Range	Mean	Range							
Patients Status during LMA implantation	TIVA	96.6	95-99	96	73-153	-		-30 (100%)	-30 (100%)	-30 (100%)	-30 (100%)	30 (100%) clear	-	-
	Sevoflurane	94.6	79-98	118.83	70-168	-		-20 (66.7%) +10 (33.3%)	-29 (96.7%) +1 (3.3%)	-20 (66.7%) +10 (33.3%)	-27 (90%) +3 (10%)	18 (66%) clear 12 (40%) coarse	-	-
	P-value*	0.005		0.714		-		0.000	0.043	0.000	0.000	0.000	-	-
Patients Status during LMA removal	TIVA	94.9%	80-98	112.93	77-168	-		-	-29 (96.7%) +1 (3.3%)	-29 (96.7%) +1 (3.3%)	-29 (96.7%) +1 (3.3%)	-	-	-
	Sevoflurane	92.2%	56-97	118	36-175	-		-	-27 (90%) +3 (10%)	-23 (76.7%) +7 (23.3%)	-26 (86.7%) +4 (13.3%)	-	-	-
	P-value*	0.024		0.390		-		-	0.038	0.000	0.004	-	-	-
Patient status after LMA removal	TIVA	96.2%	84-99	106.83	75-159	24.96	19-35	-27 (90%) +3 (10%)	-29 (96.7%) +1 (3.3%)	-28 (93.3%) +2 (6.7%)	-28 (93.3%) +2 (6.7%)	-26 (86.7%) +4 (13.3%)	-26 (86.7%) +4 (13.3%)	-28 (93.3%) +2 (6.7%)
	Sevoflurane	95.3%	90-98	118.33	100-152	29.83	21-47	-20 (66.7%) +10 (13.3%)	-30 (100%)	-26 (86.7%) +4 (13.3%)	-26 (86.7%) +4 (13.3%)	-17 (56.7%) +13 (43.3%)	-19 (63.3%) +11 (36.7%)	-22 (73.3%) +8 (26.7%)
	P-value*	0.451		0.273		0.065		0.000	0.043	0.087	0.087	0.000	0.000	0.000

[a]Oxygen saturation, [b]Heart rate, [c]Respiratory rate, * Significance level was calculated by independent t-test at 95% confidence level

The condition of patients during LMA removal was as follows: in the TIVA group, the mean oxygen saturation was 94.96%, and the mean heart rate was 113 per minute; it should also be noted that cyanosis, laryngospasm and bronchospasm were observed in 1 patient (3.3%) of this group. In the inhaled group, the mean oxygen saturation was 92.2% and the mean heart rate was 118 beats per minute. In the TIVA group, 23.3% had laryngospasm and 4 patients (13.3%) had bronchospasm.

After LMA removal, mean oxygen saturation was 96.16%, mean heart rate was 107 and mean respiratory rate was 25 beats per minute. In 4 patients (3.3%) stopped breathing and persistent cough, laryngospasm and bronchospasm were reported in 2 patients (6.7%). In the inhaled group, the mean oxygen saturation was 95.33%, the mean heart rate was 118 and the mean respiratory rate was 30 per minute. 8 patients (26.7%) had persistent cough, 13 patients (43.3%) stopped breathing, and cyanosis was not found in any of the patients (**Table 3**).

3-4. Evaluation of PACU information

As can be seen in the above table, in PACU there was a statistically significant difference between intravenous and inhaled groups in terms of stridor and persistent cough ($P < 0.05$), but no statistically significant difference was observed in terms of oxygen saturation percentage and heart rate per minute ($P > 0.05$) (**Table 4**).

Table-4: Evaluation of patients' status in PACU, in TIVA and Sevoflurane groups

Patient status in PACU	SpO2a		HRb		Stridor	Persistent Cough
	Mean	Range	Mean	Range		
TIVA	96.9%	94-99	104.3	74-156	-28 (93.3%) +2 (6.7%)	-29 (96.7%) +1 (3.3%)
Sevoflurane	95.9%	93-99	118.8	90-148	-25 (83.3%) +5 (16.7%)	-19 (63.3%) +11 (36.7%)
P-value*	0.986		0.759		0.015	0.000

[a]Oxygen saturation, [b]Heart rate

* Significance level was calculated by independent t-test at 95% confidence level

4- DISCUSSION

Induction of anesthesia is very important in terms of stability of hemodynamic status, intubation and finally passing through different phases of anesthesia and reaching the surgical phase in children with URTI. Accordingly, various drugs and methods have been used to anesthetize these children. Considering the advantages of intravenous anesthesia (Propofol) over inhalation (Sevoflurane), the effects of these methods were compared in children under 7.

About 25% of children with cough experienced PRAE as a common complication. In the study by Ungern-Sternberg et al., intravenous injection of Propofol PRAE was lower than inhalation in children with URI, and endotracheal intubation in patients with bronchial hyperreactivity had higher PRAE than face mask and LMA implantation (15). In that study, a history of asthma, atopy, and

smoking also increased the risk of adverse respiratory events, as did in our study. In line with our results, they also found that the use of intravenous anesthesia has a lower risk of adverse respiratory events compared to inhaled gasses (15). In contrast, in the study by Safaeian et al., it was concluded that the use of intravenous drugs as a maintenance anesthetic did not differ significantly from postoperative pulmonary tests (13).

According to our findings, compared to Sevoflurane patients, no complications of stridor, cyanosis, laryngospasm and bronchospasm were observed during LMA implantation in any of the patients receiving TIVA; but the difference between the two groups in mean Spo2, stridor, cyanosis, laryngospasm, bronchospasm and apnea was significant ($p < 0.05$). However, a study by Saeed et al. showed that the use of Propofol during LMA implantation could be associated with reduced complications in patients (16). In Perera et al.'s study, morbidity associated with respiratory complications along with short episodes of hypoxia and laryngospasm was reported using TIVA in pediatric endoscopic procedures (15).

During LMA removal, the difference between the two groups was significant in all cases except mean heart rate ($p < 0.05$). In the study by O'mara et al., as in the present study, the rate of agitation and laryngospasm in TIVA group was significantly lower ($p < 0.047$) compared to that in the Sevoflurane group, but the time of LMA removal in TIVA group with Propofol was significantly longer ($p<0.001$). It was concluded that in infants under cleft palate surgery, TIVA PRAE anesthesia is less effective (17). Similarly, in the study by Hajijafari et al., it was shown that there was no significant difference in the incidence of complications during LMA removal in patients receiving TIVA and Sevoflurane (18).

After LMA removal, in terms of stridor, cyanosis, use of respiratory sub-muscles, persistent cough, and cessation of respiration, the Propofol group was significantly better than the Sevoflurane ($p < 0.05$). However, in terms of oxygen saturation percentage, heart rate and respiration per minute, as well as laryngospasm and bronchospasm, although the difference between the study group was not significant, the condition of patients in the Propofol group was still better. Chai et al. also concluded that respiratory complications (cough, bronchospasm, and laryngospasm) were significantly more common in Propofol-Remifentanil group of anesthetized children than in Propofol-Sevoflurane group (19).

In another study by Chen et al., the emergence time in the TIVA group was slower than that in the Sevoflurane group, which appears to cause less agitation compared to inhaled gasses (19). Also, in the Ungern-Sternberg study similar to the present study, the rate of postoperative cough was higher in the inhaled group than in the intravenous group. Early emergence can be an important reason. On the other hand, in many studies similar to ours, evidence shows that TIVA reduces airway response, resulting in bronchospasm and laryngospasm in children, and restlessness, delirium, less nausea, and faster recovery are also observed more in this group than in inhalation anesthesia (20).

Comparison of the two groups in terms of respiratory complications in recovery demonstrated that although TIVA group showed less stable stridor and cough than inhalation group ($p < 0.05$), the difference between the two groups in terms of oxygen saturation and mean heart rate per minute was not significant ($p > 0.05$). Chen et al., evaluated children with upper respiratory tract infection; one of the studied cases had laryngospasm and two

of them had reduced O2 saturation, these cases were completely controlled and treated with no long-term side effects. It was concluded that in children with active upper respiratory tract infections, exposure to secondhand smoke is a major risk factor for adverse respiratory events (21).

Ortiz et al. in a systematic review of intravenous and inhaled drugs in surgery, in 2014, demonstrated that Propofol is better than inhaled in terms of risk and recovery (22). In a study on 52 children under Propofol-Remifentanil anesthesia and spontaneous respiration, Malherbe et al. reported cough in 14 patients (27%) and seborrhea below 90% in 10 patients (19%). The study showed no laryngospasm or stridor. It was concluded that TIVA and spontaneous respiration are effective techniques in children undergoing bronchoscopy for airway surgery (20). Contrary to the results obtained in our study, Liao et al. reported less frequent intravenous respiratory arrest and decreased oxygen saturation in the inhaled group compared to intravenous anesthesia, which could be due to airway intervention (rigid bronchoscopy). However, in their study, similar to ours, the heart rate per minute in Sevoflurane group was higher than that in Propofol group (23).

4-1. Limitations and future perspective

It is best to monitor the effect of anesthesia agents during treatment of patients in relation to response to treatment. Evaluation of anesthesia agents in relation to patient survival has not been studied.

5- CONCLUSION

According to the results of this study, induction of anesthesia and its maintenance intravenously led to a significant reduction in respiratory complications such as cough, respiratory arrest, laryngospasm, bronchospasm, stridor, cyanosis and hypoxia compared with inhaled anesthesia by Sevoflurane. Therefore, although according to some similar studies, duration of LMA recovery in the inhalation method can be somewhat shorter than in intravenous anesthesia method, but due to less PRAE in the intravenous method with Propofol, the use of TIVA method in children with URTI, who have undergone emergency surgery, can reduce the risk of related adverse events.

6- ETHICAL CONSIDERATIONS

This study was reviewed and accepted by the Research Committee of the Department of Anesthesiology and the Ethics Committee of Shahid Beheshti University of Medical Sciences and Health Services (IR.SBMU.REC.1399.816). All the procedures performed in the studies involving human participants were in accordance with ethical standards of the local ethics committee of Shahid Beheshti University of Medical Sciences, as well as 1964 Helsinki declaration. Written informed consent was obtained from all participants.

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