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Hemodynamic Differences between Propofol-Remifentanil and Isoflurane-Remifentanil Anesthesia for Repair of Cleft Palate in Children

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ABSTRACT

Background: Cleft palate repair is associated with hemorrhage and hemodynamic changes in children. This study aimed to compare hemodynamic changes during cleft palate repair in patients anesthetized with isoflurane-remifentanil versus propofol-remifentanil.
Methods: In this randomized, double blind clinical trial, 100 cleft palate repair candidates who aged under three years were allocated to two groups of 50 to receive either isoflurane-remifentanil or propofol-remifentanil for maintaining anesthesia.
Results: The mean systolic and diastolic blood pressure and the mean arterial pressure were significantly lower in the propofol-remifentanil group (P<0.001). The mean extubation time (P<0.001), time to first analgesic administration (P: 0.04), and recovery time (P<0.001) were significantly longer in the isoflurane-remifentanil group.
Conclusion: Propofol-remifentanil-based anesthesia caused more stable hemodynamic state in patients undergoing cleft palate repair. The mean systolic and diastolic blood pressure, as well as the mean arterial pressure, was lower with propofol-remifentanil administration. Therefore, this combination can lower the risk of intraoperative hemorrhage.

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Introduction

Cleft palate is a common birth defect characterized by the opening of the roof of the mouth into the nose. Occurring either alone or in combination with a cleft lip, a cleft palate can cause breastfeeding and hearing problems, frequent ear infections, and impaired speech. The best time for cleft palate repair surgery is between nine and 18 months of age (1).

Cleft palate repair is a long procedure associated with a high risk of bleeding. Moreover, considering the patients' age, it is of paramount importance to maintain hemodynamic stability (1, 2) and minimize bleeding through various methods such as controlled hypotension using remifentanil (3, 4). Remifentanil is a potent, short-acting narcotic (twice as potent as fentanyl) metabolized by esterase. The drug is administered at a dosage of 0.1-1.0 μg/kg/min in combination with an anesthetic (3).

Isoflurane and propofol are anesthetic agents used to maintain anesthesia. Isoflurane is a halogenated inhalation anesthetic metabolized by the liver. It exerts its effects by interfering with the physiological activities of neuronal membranes in the brain (5). Propofol is an intravenous anesthetic metabolized by the liver. It acts by

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Table 1. Baseline patient's characteristics.

Variables	Isoflurane-remifentanil group Mean±SD	Propofol-remifentanil group Mean±SD	P
Age (Months)	16.8±5.7	17.2±5.9	0.77
Weight (Kg)	10.5±1.6	10.47±1.8	0.95
Sex, Male/female, N(%)	20/20 (50)	24/16 (40/60)	0.37

stimulating gamma-aminobutyric acid (GABA) receptors and blocking sodium channels (6, 7).

Numerous studies have evaluated various methods of maintaining hemodynamic stability, e.g. anesthesia induction using agents such as sevoflurane and propofol, using different narcotics during anesthesia, or using tranexamic acid to reduce intraoperative bleeding, in patients undergoing cleft palate repair (5-8).

Meanwhile, postoperative pain management and nausea/vomiting reduction are major challenges in pediatric surgery (9-11). Since no previous studies have compared hemodynamic changes during cleft palate repair in patients anesthetized with isoflurane-remifentanil and propofol-remifentanil, this research examined hemodynamic changes during anesthesia with the above-mentioned combinations in children undergoing cleft palate repair.

Methods

This study was a randomized, double blind comparative study without a control group. All procedures were conducted at Imam Hossein Children's Hospital (Isfahan, Iran) during 2016-2017. It was approved by the Ethics Committee of Isfahan University of Medical Sciences. Written informed consent was obtained from all the patients, according to the Declaration of Helsinki.

A total of 100 eligible cleft palate repair candidates whose parents consented for their participation were recruited. The inclusion criteria were age below three years and American Society of Anesthesiologists (ASA) Class I physical status (A normal healthy patient). The exclusion criteria were prolonged surgery (over three hours) and the incidence of any surgical or anesthetic complications such as: severe bleeding, shock state, brain damage, etc.

The participants were randomly allocated to two groups of 50 individuals using a list of random numbers. After premedication with midazolam (0.1 mg/kg) and ketamine (1.0 mg/kg), the patients were moved to the operating room and anesthesia was induced with atropine (0.02 mg/kg), fentanyl (2 µg/kg), thiopental sodium (5.0 mg/kg), and atracurium (0.05 mg/kg). Anesthesia was maintained using isoflurane 1% plus remifentanil (0.5 µg/kg/min) in the first group and using propofol plus remifentanil (0.5 µg/kg/min) in the second.

The patients' systolic and diastolic blood pressure (SBP and DBP), mean arterial pressure (MAP), end-tidal carbon dioxide ($ETCO_2$), and partial pressure of arterial oxygen (PaO_2) were recorded before and every 15 minutes during the surgery. In the post-anesthesia care unit (PACU), the patients' SBP, DBP, MAP, PaO_2, and pain intensity were recorded every 15 minutes up to 1 hour. The pain was measured using the Wong Baker Faces Pain Rating Scale (13). The duration of PACU stay, determined by the Modified Aldrete Scoring System (14), was also recorded.

An anti-nausea agent (0.1 mg/kg of ondansetron) was used when necessary. An analgesic (acetaminophen suppository) was also used in the PACU if needed. The time to first anti-nausea and analgesic administration, along with the prescribed dosages, were recorded.

All of the data were logged into the SPSS software (version 24). Chi-square, independent t-test and Mann Whitney tests were used for evaluating the differences between both groups and ANOVA test with repeated measures was used for comparing the changes in the results of each group. Also the number (percent) and mean ± standard deviation for both groups were presented and the level of significance was set at $p < 0.05$.

Results

The analysis showed no significant differences between the mean age (P: 0.77) and weight (P: 0.95) of the two groups. Moreover, according to chi-square test, the two groups were matched in terms of sex distribution (P: 0.37; Table 1).

Analysis results indicated that the two groups had no significant differences in the mean SBP before the induction of anesthesia (P: 0.17), at the beginning of the operation (P: 0.22), and in minutes of 15 (P: 0.66) and 30 (P: 0.13) of the surgery. At other times during surgery, the isoflurane-remifentanil group had significantly higher mean SBP compared to the propofol-remifentanil group ($P < 0.001$). There were no significant differences in mean SBP between two groups upon entrance to the PACU (P: 0.41) and at the 15th minute in the PACU (P: 0.09). The mean SBP was significantly higher in the propofol-

Table 2. Comparison of the mean arterial blood pressure and heart rate between groups.

	Time	Mean Arterial blood pressure		P	Heart Rate		P
		Isoflurane-remifentanil group	Propofol-remifentanil group		Isoflurane-remifentanil group	Propofol-remifentanil group	
		Mean±SD	Mean±SD		Mean±SD	Mean±SD	
During the operation	Before anesthesia induction	70±4.9	6.3±69.9	0.78	154.3±11.5	155.5±14.1	0.10
	At the beginning of the surgery	67.2±4.4	4.9±66.7	0.57	151.2±11.2	150.8±15.2	<0.001
	15 min	66.5±4.1	4.7±64.7	0.06	162.8±11.1	147.2±14.4	<0.001
	30 min	66.3±4.5	4.1±62.6	<0.001	163.6±10.8	145.5±14.1	<0.001
	45 min	65.8±4.7	3.9±60.9	<0.001	165.2±11.3	144.7±14.5	<0.001
	60 min	65.2±4.8	3.8±59.8	<0.001	165.9±11.6	144.3±14.1	<0.001
	75 min	64.9±4.6	4.1±58.7	<0.001	167.6±11.4	141.8±13.9	<0.001
	90 min	64.6±4.7	4±58.04	<0.001	168.3±11.04	140.5±14	<0.001
	105 min	64.2±4.8	3.9±57.7	<0.001	168.7±10.9	139.6±13.5	<0.001
	120 min	64.1±5.04	3.6±57.1	<0.001	169.4±11	138.8±13.6	<0.001
In the post-anesthesia care unit	0 min	66.9±4.8	4.7±64.9	0.08	154.6±13.1	133.6±12.1	<0.001
	15 min	66.8±4.3	4±65.6	0.2	153.7±13.6	132.2±12.7	<0.001
	30 min	66.4±4.6	4.3±65.8	0.53	152.3±13.5	131.1±11.2	<0.001
	45 min	66.5±4.7	4.4±66.2	0.83	151.2±13.2	129.4±11.8	<0.001
	60 min	66.2±5.1	4.8±66.7	0.65	149.5±14.5	128.9±11.9	<0.001

Min: minutes, SD: standard deviation

remifentanil group than in the isoflurane-remifentanil group at minutes of 30 (P: 0.01), 45 (P: 0.008), and 60 (P: 0.006) in the PACU.

There were no significant differences between two groups in the mean DBP before the induction of anesthesia, at the beginning of the surgery, and minutes 45 and 60 in the PACU. However, the two groups had a significant difference in the mean DBP in minutes 15-120 of the surgery and minutes 0, 15, and 30 in the PACU.

The mean peripheral capillary oxygen saturation (SpO_2) and $ETCO_2$ of the two groups were not significantly different at any point of time (Figures 1 and 2).

The MAP of two groups were not significantly different before the induction of anesthesia, at the beginning and minute 15 of the surgery, and at any points of time in the PACU. However, the isoflurane-remifentanil group had significantly higher MAP than the propofol-remifentanil group at minutes 30-120 of the surgery ($P < 0.001$; Table 2).

The mean heart rates of two groups were not significantly different before the induction of anesthesia (P: 0.01). At other times, however, the propofol-remifentanil group showed a significantly lower heart rate than the isoflurane-remifentanil group ($P < 0.001$; Table 2).

The mean duration of extubation ($P < 0.001$), the time at which an analgesic was needed in the PACU (P: 0.04), and the recovery duration ($P < 0.001$) were significantly higher in the isoflurane-remifentanil group than in the propofol-remifentanil group. The analysis suggested no significant differences in terms of the incidence of nausea and vomiting (P: 0.31) and the need for an anti-nausea agent (P: 0.18) between two groups. Moreover, the two

Table 3. Comparison of other study variables between groups.

Variables		Isoflurane-remifentanil group	Propofol-remifentanil group	P
		Mean±SD	Mean±SD	
Mean duration of extubation (minutes)		9.1±1.9	6.7±1.5	<0.001
The time of the first analgesic administration in the PACU (minutes)		24.3±12.9	14.6±5.4	0.04
PACU stay (minutes)		63±7.2	53.1±8.5	<0.001
Frequency of nausea and vomiting, N (%)		3 (7.5)	1 (2.5)	0.31
Frequency of anti-nausea administration, N (%)		4 (10)	1 (2.5)	0.18
Complications in the PACU, N (%)	Spasm	4 (33.3)	3 (33.3)	1
	Dropped oxygen saturation	3 (25)	2 (22.2)	0.92
	Cough	5 (41.7)	4 (44.4)	0.89

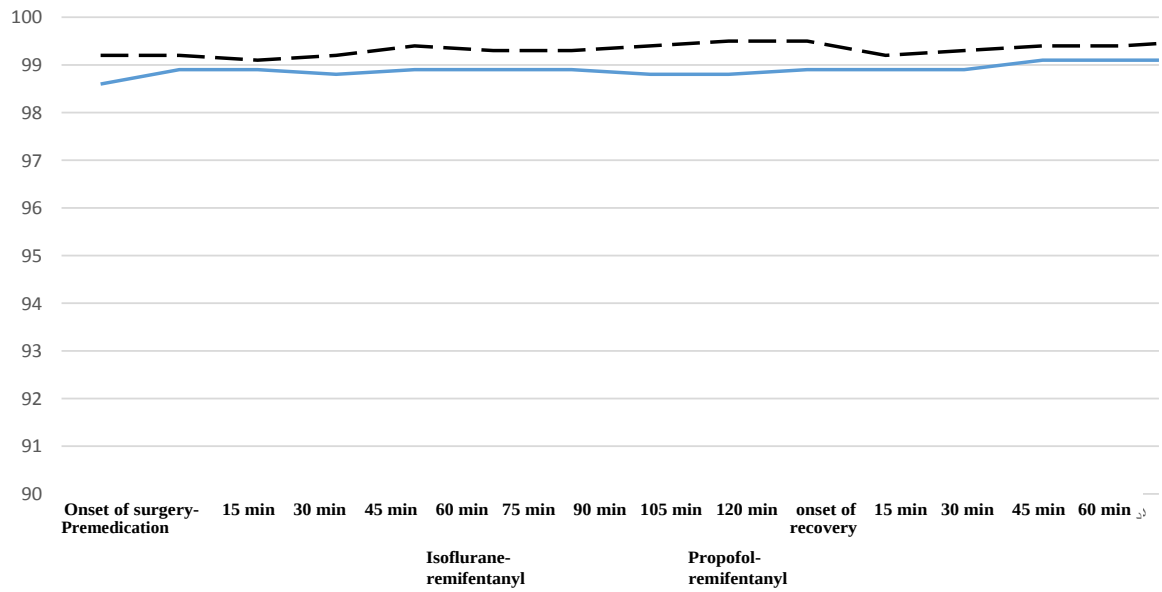

Figure 1. Comparison of mean peripheral capillary oxygen saturation (SpO2) at different times between groups.

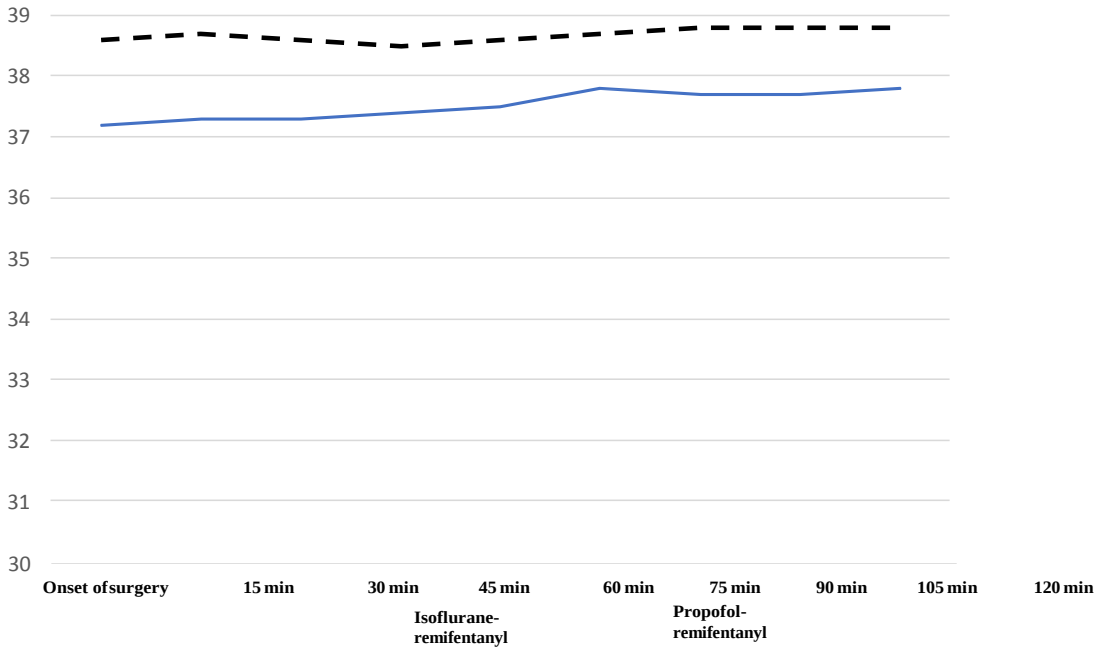

Figure 2. Comparison of mean end tidal carbon dioxide ($ETCO_2$) at different times between groups.

groups had no significant differences in distribution of oxygen saturation (P: 0.92) and frequency of cough (P: 0.89) in the PACU. Two groups were also similar in the distribution of spasm in the PACU (Table 3).

Discussion

The results showed that the use of propofol-remifentanil improved hemodynamic stability during surgery. In fact, as the mean SBP, DBP, and MAP were lower during anesthesia with propofol-remifentanil than during anesthesia with isoflurane-remifentanil, the propofol-remifentanil combination could decrease the risk of bleeding during surgery. Patients receiving propofol-remifentanil had lower heart rate than the isoflurane-remifentanil during anesthesia and at the PACU. The duration of PACU stay was also lower in the propofol-remifentanil group than in the isoflurane-remifentanil group.

Steinmetz et al., compared anesthesia with propofol-remifentanil and sevoflurane-fentanyl in patients undergoing cleft palate repair and observed lower mean heart rate, but higher blood pressure in the propofol-remifentanil group during anesthesia. The mean duration of PACU stay and the amount of opioid consumed after surgery were similar in the two groups (3). Gall et al., recommended the use of remifentanil as an appropriate opioid for pediatric cleft palate surgery (4).

In a study on transsphenoidal surgery, Cafiero et al., found sevoflurane-remifentanil to be associated with a faster recovery compared to propofol-remifentanil. Meanwhile, the two groups had no significant differences in terms of hemodynamic changes and bleeding during the surgery (7). In the present study, however, a combination of propofol and remifentanil led to a lower duration of PACU stay compared to isoflurane-remifentanil. This inconsistency can be justified by the longer metabolism of isoflurane compared to that of sevoflurane.

Topical epinephrine is used for localized infiltration and reduction of bleeding during cleft palate repair. This will, in turn, increase blood pressure and heart rate. Therefore, Gunnam et al., recommended the use of isoflurane instead of sevoflurane and showed that patients undergoing anesthesia with sevoflurane had higher blood pressure and heart rate during surgery (12). In our study, the patients receiving propofol had more stable heart rate and blood pressure than those receiving isoflurane.

In conclusion, propofol-remifentanil-based anesthesia provides more stable hemodynamic state in patients undergoing cleft palate repair. The mean systolic and diastolic blood pressure, as well as the mean arterial pressure, was lower with propofol-remifentanil administration. Therefore, this combination can lower the risk of intraoperative hemorrhage. Furthermore, because of the lower mean duration of extubation, and also the

recovery duration in the propofol-remifentanil group, this combination can be a better choice in anesthesia of cleft palate repair surgery.

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