

Original Article



Comparing the effects of ropivacaine and lidocaine associated with epinephrine on the heart rate, blood pressure, and amount of bleeding in patients candidate for cleft palate repair: A randomized clinical trial

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Abstract

Background and aims: This study was conducted to compare the effects of two compounds ropivacaine and lidocaine associated with epinephrine on the heart rate, blood pressure, and bleeding rate in children undergoing general anesthesia for the cleft palate repair surgery. **Methods:** In this study, 30 children candidates for cleft palate surgery who were referred to Mofid Children's Hospital, affiliated with Shahid Beheshti University of Medical Sciences in 2021, were included by using the convenience sampling method. The patients were randomly divided into two groups. Group 1 was treated with ropivacaine and group 2 was treated with lidocaine along with epinephrine. The data were analyzed by the SPSS, version 22.

Results: In total, no statistically significant difference was found between the two groups in terms of vital signs of blood pressure and heart rate in the 10 stages studied ($P < 0.05$). There was no difference between the two groups in the trend of the changes in blood pressure ($P = 0.381$) and heart rate ($P = 0.940$). However, the trend of blood pressure and heart rate had significantly changed during the study in both groups individually ($P < 0.001$). The bleeding rate (suction) ($P < 0.001$) and the weight of gases used ($P = 0.003$) in the second group were significantly higher than in the first group.

Conclusion: No difference was found between the effects of ropivacaine and lidocaine combined with epinephrine on the heart rate and blood pressure in patients who were candidates for the cleft palate surgery, but the rate of bleeding (suction) in the second group was more than the first group.

Keywords: Ropivacaine, Lidocaine, Epinephrine, Cleft palate, Heart rate, Blood pressure

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Introduction

Cleft palate is the second leading cause of birth defects, and cleft palate repair surgery is known as one of the most important reasons for referring to pediatric and ear, nose, and throat doctor (ENT) surgical centers, as well as plastic surgery centers in Iran and the world (1,2). This complication depends on several factors such as genetics, gender, economic status, and the living environment (3,4). Children with a cleft palate may have other genetic abnormalities (5), and this probability includes other abnormalities such as heart abnormalities, the most common of which is atrial septal defect abnormality (6). Thus, it seems important to manage and evaluate hemodynamic parameters in these patients before performing the surgeries (7). In cleft palate surgery, which is performed under general anesthesia, the surgeon uses lidocaine, along with epinephrine to control local bleeding and manage the postoperative pain. The use of lidocaine and epinephrine is also common in centers where the surgery is performed by local anesthesia (8-10). The combination of lidocaine with epinephrine is associated

with cardiovascular and neurological complications (11,12). Ropivacaine is an amide local anesthetic agent that has far fewer cardiac and neurological side effects compared to lidocaine, which also benefits from a strong vasoconstrictor effect (13,14). In addition, the safety of ropivacaine is approved by the Food and Drug Administration in pediatric and neonatal anesthesia and has been introduced as the drug of choice in children and infants (15). According to reports, ropivacaine appears to be a highly suitable agent for local anesthesia with its low cardiac toxicity and neurotoxicity, differential sensorimotor inhibition, and vasoconstrictor properties at low concentrations (16,17). Nonetheless, some studies revealed that ropivacaine may not be the local anesthetic of choice for spinal anesthesia in patients with longer duration (18). To the best of our knowledge, no study has so far compared the combination of lidocaine with epinephrine with ropivacaine; thus, this study was designed to compare the effect of these two compounds on the heart rate, blood pressure, and bleeding rate in children undergoing cleft palate surgery under general

anesthesia.

Materials and Methods

The present study was a single-blind clinical trial, which was conducted on children candidates for cleft palate surgery who were referred to Mofid Children’s Hospital affiliated with Shahid Beheshti University of Medical Sciences in 2021. In this study, the convenience sampling method was used, and the sample size was determined based on a similar previous study. The sample size was calculated using the following formula:

$$n = \frac{S1^2 \pm S2^2}{(\mu2 - \mu1)^2} f(\alpha, \beta)$$

$$\alpha = 0.05, \beta = 0.1, S1 = 5, S2 = 6, M1 = 18, M2 = 25, N = 25 + 36 / 49 * 10.5 = 13$$

The sample size in each group was determined to be 13 people, and considering the possible loss of samples, 15 people entered each group (19).

The method of blinding was such that the patient and the surgeon were unaware of the type of the applied drug, but the researcher knew the type of the treatment.

In this study, 30 children with an age range from 6 months to two years who were candidates for cleft palate surgery for the first time were included in the trial. According to the table of random numbers, patients were randomly divided into control and intervention groups. Groups 1 and 2 were treated with ropivacaine and lidocaine plus epinephrine, respectively (Figure 1).

The exclusion criteria were having an allergy to local anesthetics, bleeding disorders, cardiovascular and cerebral problems, and parental non-consent with the participation of their child in the study. On the other hand, the inclusion criteria included two components; a written consent form by the parents, and the patient should be of the ASA1 class (A normal healthy patient). The children were kept “Nothing by mouth” for 6 hours before surgery, and their blood pressure and heart rate were recorded upon entering the operating room. The anesthesia was performed with fentanyl, propofol, and atracurium with the injection of fentanyl at 2 µg/kg, propofol at 2.5 µg/kg, and atracurium at 0.5 µg/kg. All patients were then incubated with a suitable size spiral endotracheal tube, and the anesthesia was continued with 50% N₂O, 50% O₂, and 1.2% isoflurane. In the first group, following the above-mentioned measures, carpool lidocaine 2 µg/kg associated with 1:80000 epinephrine was locally injected at the incision site, while the second group received 2 µg/kg of ropivacaine from a 0.5% solution as local infiltration. The throat of all patients was gas-packed. At the end of the surgery, all patients were reversed with atropine 0.02 µg/kg and neostigmine 0.04 µg/kg. The blood pressure and heart rate were measured every three minutes during surgery. At the end of the operation, the weight of the used gases was taken into account. Ultimately, all these items were recorded in the relevant checklist specifically designed for this purpose. The checklist included the patients’ personal information and type of medication, heart rate, blood pressure, bleeding rate (Suction), and

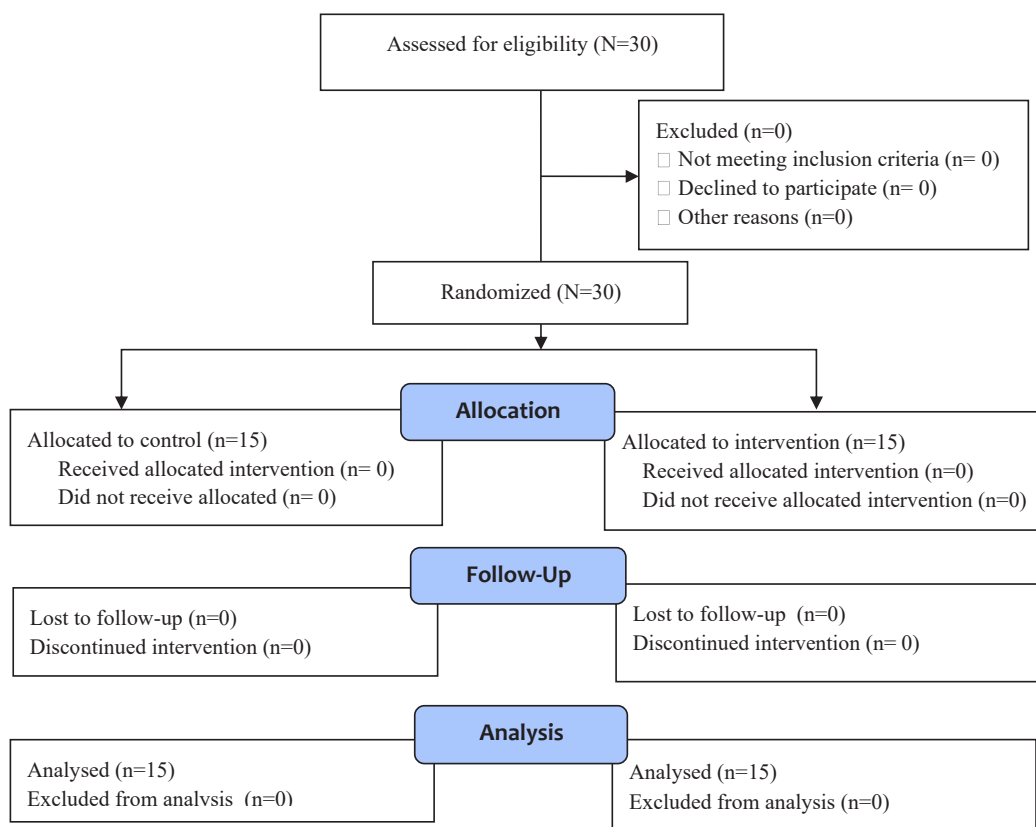


Figure 1. CONSORT flow diagram of the study population.

the weight of the applied gases. The collected data were entered into the SPSS software, version 22. The values of mean and standard deviation were reported for the existing variables. The independent t-test and analysis of variance with repeated observations were used to compare the heart rate and blood pressure before, during, and after the surgery and at regular recording intervals and to compare the variables between the two groups. The $P < 0.05$ was considered the significance level.

Results

A total of 30 children undergoing cleft palate surgery under general anesthesia (15 in each group) participated

in the study. The mean age of patients in the first (ropivacaine) and second (lidocaine with epinephrine) groups was 9.73 ± 2.12 and 10.26 ± 2.05 years with an age range of 7-14 years, respectively. The two groups had no significant differences in terms of age ($P = 0.49$) and weight ($P = 0.825$) based on the findings of the independent *t* test (Table 1). Further, the weight of the applied gases in the lidocaine group associated with epinephrine was reported significantly higher than that of the ropivacaine group ($P = 0.003$, Table 1).

The vital signs of patients, including blood pressure and heart rate in 10 stages of the study are provided in Tables 2 and 3 and Figures 2 and 3. The 10 stages of the

Table 1. The mean and SD of age, weight, bleeding volume, and gas use in the patients of the first (ropivacaine) and second (lidocaine with epinephrine) groups

| Variables | Ropivacaine (group 1) | | | Lidocaine with epinephrine (group 2) | | | P value |
|-------------------------|-----------------------|------|------|--------------------------------------|------|------|------------|
| | Mean \pm SD | Min. | Max. | Mean \pm SD | Min. | Max. | |
| Age (y) | 9.21 \pm 1.73 | 7 | 14 | 10.20 \pm 1.82 | 7 | 14 | 0.49 |
| Weight | 9.11 \pm 2.70 | 8 | 10 | 9.10 \pm 5.26 | 7 | 11 | 0.82 |
| Bleeding rate (suction) | 19.60 \pm 3.06 | 15 | 25 | 28.00 \pm 6.46 | 18 | 45 | * <0.001 |
| Weight of used gases | 22.66 \pm 3.81 | 15 | 25 | 32.13 \pm 10.51 | 18 | 45 | *0.003 |

Note. SD: Standard deviation; Max.: Maximum; Min.: Minimum; * $P < 0.05$ is considered significant.

Table 2. The mean and SD of blood pressure in the patients of the first (ropivacaine) and second (lidocaine with epinephrine) groups

| Variable | Study groups | | P value ^a | |
|----------------|-----------------------------|-------------------|----------------------|-------|
| | First group | Second group | | |
| | Mean \pm SD | Mean \pm SD | | |
| Blood pressure | Before anesthesia | 59.73 \pm 7.28 | 61.8 \pm 11.11 | 0.552 |
| | 3 Minutes after anesthesia | 75.06 \pm 10.50 | 69.33 \pm 11.81 | 0.171 |
| | 5 Minutes after anesthesia | 75.46 \pm 11.62 | 76.06 \pm 13.69 | 0.898 |
| | 10 Minutes after anesthesia | 75.46 \pm 9.16 | 72.93 \pm 9.32 | 0.459 |
| | 20 Minutes after anesthesia | 72.86 \pm 8.85 | 69.00 \pm 7.54 | 0.209 |
| | 30 Minutes after anesthesia | 69.80 \pm 8.71 | 68.06 \pm 8.53 | 0.587 |
| | 40 Minutes after anesthesia | 67.13 \pm 6.42 | 66.73 \pm 7.72 | 0.879 |
| | 50 Minutes after anesthesia | 69.46 \pm 8.26 | 64.66 \pm 6.38 | 0.086 |
| | 60 Minutes after anesthesia | 64.93 \pm 8.06 | 62.40 \pm 6.06 | 0.339 |
| | 90 Minutes after anesthesia | 66.60 \pm 8.49 | 62.40 \pm 6.87 | 0.148 |

Note. SD: Standard deviation. ^a Independent *t* test.

Table 3. The mean and sd of the heart rate of patients in groups 1 (ropivacaine) and 2 (lidocaine with epinephrine)

| Variable | Study groups | | P value ^a | |
|------------|-----------------------------|--------------------|----------------------|-------|
| | First Group | Second Group | | |
| | Mean \pm SD | Mean \pm SD | | |
| Heart rate | Before anesthesia | 129.86 \pm 14.55 | 135.20 \pm 22.87 | 0.453 |
| | 3 Minutes after anesthesia | 147.93 \pm 19.47 | 140.06 \pm 24.47 | 0.338 |
| | 5 Minutes after anesthesia | 148.53 \pm 19.37 | 149.66 \pm 24.58 | 0.889 |
| | 10 Minutes after anesthesia | 151.20 \pm 18.11 | 147.93 \pm 24.51 | 0.681 |
| | 20 Minutes after anesthesia | 147.53 \pm 16.14 | 148.46 \pm 24.64 | 0.909 |
| | 30 Minutes after anesthesia | 143.06 \pm 18.17 | 146.60 \pm 24.14 | 0.654 |
| | 40 Minutes after anesthesia | 140.66 \pm 19.04 | 144.66 \pm 22.61 | 0.604 |
| | 50 Minutes after anesthesia | 140.33 \pm 17.59 | 141.26 \pm 22.58 | 0.900 |
| | 60 Minutes after anesthesia | 139.20 \pm 17.73 | 139.60 \pm 22.94 | 0.958 |
| | 90 Minutes after anesthesia | 138.06 \pm 15.65 | 138.60 \pm 23.82 | 0.943 |

Note. SD: Standard deviation. ^a Independent *t* test.

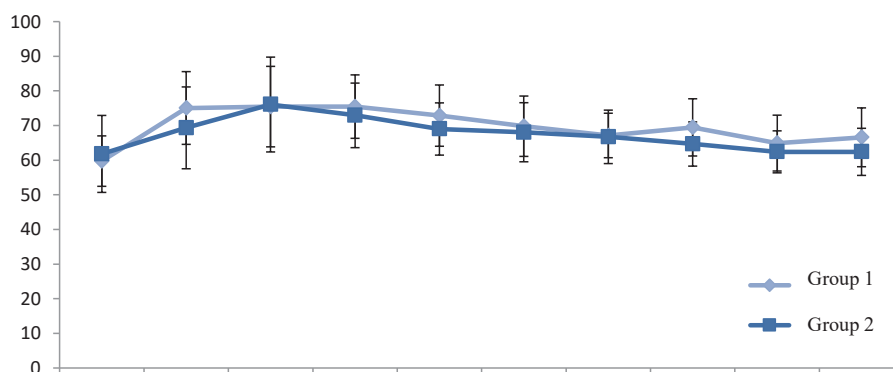


Figure 2. The blood pressure of patients during the study in groups 1 (ropivacaine) and 2 (lidocaine with epinephrine).

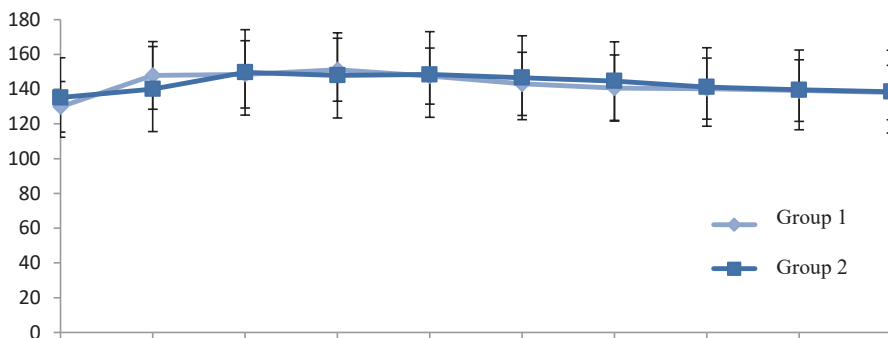


Figure 3. The heart rate of patients during the study in groups 1 (ropivacaine) and 2 (lidocaine with epinephrine).

study included before anesthesia, 3, 5, 10, 20, 30, 40, 50, 60, and 90 minutes after anesthesia, respectively. In general, no statistically significant differences were found between the two groups in terms of vital signs of blood pressure and heart rate in the 10 studied stages ($P < 0.05$).

Furthermore, the analysis of the variance test with repeated observations did not show any difference between the two groups in the trend of changes in blood pressure ($P = 0.381$). However, the trend of blood pressure significantly changed during the study in both groups individually ($P < 0.001$).

Based on the analysis of the variance test with repeated observations, no differences were observed between the two groups in the trend of heart rate changes ($P = 0.940$). However, the trend of heart rate changes during the study represented a significant reduction in both groups individually ($P < 0.001$).

A significant difference was found between the two groups regarding the amount of bleeding (suction) so that the rate of bleeding (suction) in the lidocaine with epinephrine group was significantly higher compared to the ropivacaine group ($P < 0.001$).

Discussion

This study was performed to compare the effects of two drugs (i.e., ropivacaine and lidocaine along with epinephrine) on the heart rate, blood pressure, and bleeding rate in patients who were candidates for cleft palate repair surgery. Ropivacaine is a local anesthetic that reversibly inhibits the sodium ion influx and thus, blocks the conduction of impulses in the nerve fibers.

This action is enhanced by the dose-dependent inhibition of potassium channels (20). The results of the present study demonstrated no statistically significant differences between the two groups in terms of the vital signs of blood pressure and heart rate in the studied 10 stages. Consistent with these results, the findings of a study showed that epidural anesthesia with 1.5% lidocaine and 0.5% ropivacaine has similar effects on the level of consciousness (LOC) time, propofol concentration, site effect, total propofol dose, and hemodynamic variables during the induction of general anesthesia (21). The findings of another clinical trial on the assessment of pain relief in different areas and the safety of ropivacaine-epinephrine flap injection in thyroidectomy revealed no significant differences between the control group and ropivacaine-epinephrine group concerning heart rate and blood pressure (22). Cheng et al found that the blood pressure level and heart rate in the group of women receiving levobupivacaine for anesthesia were lower than in the ropivacaine group. However, ropivacaine had a faster onset and less effect on maternal vital signs for anesthesia in delivery compared to levobupivacaine and was associated with a decrease in maternal the cesarean section rate among patients who did not initially choose a cesarean section. Therefore, it is useful in clinical practice (23). Evaluating ropivacaine and bupivacaine in cesarean section anesthesia, it was observed that ropivacaine had a little effect on hemodynamic indices (including blood pressure and heart rate) with a decreasing effect on the duration of sensory and motor block. Ropivacaine was also safe and harmless for patients (24). The results of

another study revealed that the use of 0.05% ropivacaine induced a significant reduction in blood pressure (systolic and diastolic) and the heart rate in patients undergoing craniotomy. Thus, it can be applied as a high-quality drug for local anesthesia. Therefore, it seems to be a suitable drug for neurological anesthesia due to hemodynamic stability (25). Other studies indicated that ropivacaine is effective in lowering blood pressure and heart rate in patients undergoing surgery and establishing stable hemodynamic conditions (26-28). However, animal studies suggested that the drug is dose-dependent and can cause tachycardia and T-wave stimulation at doses of 5 mmol/kg in laboratory animals (29,30). Accordingly, it causes cardiotoxicity and CNS toxicity in some cases (31). Contrarily, some studies reported that ropivacaine has a lower toxic effect on the cardiovascular system and the heart of patients compared to bupivacaine (32). This discrepancy in the reports may seem to be due to different doses of the applied ropivacaine.

In the present study, the rate of bleeding (suction) in the lidocaine with epinephrine group was significantly higher in comparison to the ropivacaine group. Based on the results of a study, ropivacaine also had a vasoconstrictive effect in addition to its anesthetic, analgesic, and anxiolytic properties; as a result, it could reduce the absorption of drugs into the plasma and lead to a long-term effect (33). Another study on the analgesic and anti-bleeding effects of lidocaine, bupivacaine, and ropivacaine revealed no statistically significant differences between the studied groups (the use of various anesthetics) in terms of postoperative bleeding (34). In the analysis of bleeding scores after the removal of the nasal pack, Gencer et al concluded that all three studied groups consuming ropivacaine, bupivacaine, and prilocaine had less bleeding compared to the saline control group. Bleeding was significantly lower in the lidocaine group than in the bupivacaine and prilocaine groups (35). However, in the current study, this rate was higher in the lidocaine group. Unlike other studies, Guinard et al found that ropivacaine did not reduce capillary blood flow in swine models (36). Another study on the human population also indicated that the mean bleeding volume during surgery in the lidocaine group was lower than in the ropivacaine group (37). Although the reason for this discrepancy in the results is unclear, it seems unlikely. However, differences in the population and personal factors of patients or differences in the methodology and dosage of the drug may cause such different results.

Conclusion

Overall, no differences were found between the two drugs of ropivacaine and lidocaine combined with epinephrine regarding the heart rate and blood pressure in patients who were candidates for the cleft palate surgery. However, the rate of bleeding (suction) was higher in the lidocaine group with epinephrine compared to the ropivacaine group. Due to different results of studies, it is

recommended to perform more studies in this regard to clarify the ambiguous aspects of the issue.

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Authors' contribution

AE contributed to conception and design, as well as data acquisition, analysis, and interpretation. In addition, BK collaborated in the drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, obtaining funding, administrative, technical, or material support, and supervision. Eventually, AE and BK approved the final draft.

Conflict of interests

The authors declared that there is no conflict of interests.

Ethical approval

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1400.055) and approved by the Iranian Registry of Clinical Trials (IRCT) with IRCT20210515051299N1.

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