Local Airway Anesthesia Attenuates Hemodynamic Responses to Intubation and Extubation in Hypertensive Surgical Patients

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Background: The aim of this study was to evaluate the effects of topical ropivacaine anesthesia on hemodynamic responses during intubation and extubation of hypertensive patients.

Material/Methods: One hundred fifty patients with hypertension ASA II-III were scheduled for noncardiac operations. Patients were divided into 3 groups: a control group receiving 5 ml saline, and 2 groups receiving topical anesthesia with 100 mg lidocaine or 37.5 mg ropivacaine. Hemodynamic responses, including blood pressure and heart rate (HR), were recorded at baseline (T0), before intubation (T1), during tracheal intubation (T2), 2 min after intubation (T3), upon eye opening on verbal commands (T4), during tracheal extubation (T5), and 2 min after extubation (T6). Patients were injected with urapidil 5 mg during intubation and extubation if their systolic blood pressure (SBP) was \(\geq 160\) mmHg or diastolic blood pressure (DBP) was \(\geq 90\) mmHg, and esmolol 10 mg when HR was \(\geq 90\) bpm.

Results: During extubation, the total dosages of urapidil and esmolol were significantly higher in the saline than in the lidocaine or ropivacaine groups, and were significantly lower in the ropivacaine than in the lidocaine group. At T2, SBP, SBP, MAP, and HR were lower in the lidocaine and ropivacaine groups than in the saline group, but the differences were not significant. From T4 to T6, SBP, DBP, MAP, and HR were significantly lower in the ropivacaine group than in the other 2 groups (P<0.05 each).

Conclusions: Topical lidocaine and ropivacaine anesthesia can effectively reduce hemodynamic responses during intubation, with ropivacaine better at inhibiting hemodynamic changes at emergence in hypertensive patients.

MeSH Keywords: Adolescent Medicine • Anesthesia • Anesthesia and Analgesia

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Background

Both intubation and extubation can increase the concentration of catecholamine in the blood by stimulating the sympathetic nervous system, resulting in severe hemodynamic changes [1,2]. However, during intubation, agents such as opioids and propofol can effectively inhibit airway stimulation by endotracheal tubes. During extubation, the withdrawal of anesthetics and the emergence of patients from anesthesia stimulate the sympathetic nervous system, increasing the release of catecholamine and resulting in cough and hemodynamic responses [3–7], including hypertension and tachycardia. Although hemodynamic changes in laryngeal and tracheal tissues during this period are normally well tolerated by healthy individuals, they may be detrimental in hypertensive patients, leading to life-threatening complications such as myocardial ischemia, cardiac arrhythmias, and cerebrovascular hemorrhage [8–11].

The topical anesthetic lidocaine is widely used to inhibit intubation and extubation responses [13–17]. During long operations, however, preoperatively administered lidocaine will no longer be present at the time of extubation. Ropivacaine is a long-acting local anesthetic, and topical anesthesia with ropivacaine has been reported to significantly attenuate histamine-induced bronchospasm [22]. We hypothesized that topical ropivacaine anesthesia can inhibit hemodynamic responses during intubation and extubation in hypertensive patients. The aim of this prospective double-blinded study was to test this hypothesis.

Material and Methods

Study design and patients

This study was approved by the Ethics Committee of Harbin Medical University (HMUIRB20130011) and registered in the Chinese Clinical Trial Registry (ChiCTR-TRC-13003525). All patients provided written informed consent. We enrolled a total of 150 patients aged 20–60 years, ASA II–III, with hypertension according to World Health Organization criteria (systolic blood pressure (SBP) ≥160 mmHg or diastolic blood pressure (DBP) ≥90 mmHg) [23], undergoing noncardiac surgery.

The 150 patients were randomly assigned to receive saline (n=50), lidocaine (n=50), or ropivacaine (n=50) using a random number table. The assignments were recorded and sealed within envelopes, with the anesthesiologists blinded to assignments. Topical anesthesia was administered by one anesthesiologist, and hemodynamic changes were recorded by a second anesthesiologist. The drugs for topical anesthesia were prepared by a third anesthesiologist not blinded to randomization. Patients were excluded if they had ASA grade IV or higher; gastro-esophageal reflux; obesity (body mass index >30 kg/m²); anticipated difficulty maintaining airways on the face mask or more than 1 attempt at intubation; myocardial infarction within 6 months; heart function grade III or higher; or congestive cardiac failure. Patients with a cardiac pacemaker, congenital heart disease, or heart block on ECG were also excluded.

Anesthesia and treatment

All patients received their usual antihypertensive drugs but were not otherwise preoperatively medicated. After transfer to the operating room, blood pressure, heart rate (HR), electrocardiography (ECG), and saturation of blood oxygen (SpO₂) were continuously monitored. The radial artery was cannulated with a 22-g catheter under local anesthesia (1% lidocaine 1 ml) to monitor real-time mean arterial pressure (MAP). All patients received 5 ml/kg⁻¹ Ringer lactate solution over a 10-min period before induction of anesthesia. Patients were preoxygenated for 5 min, followed by intravenous injection of 1 mg penehydricline hydrochloride. Anesthesia was induced with midazolam 0.5 mg/kg⁻¹, fentanyl 4 µg/kg⁻¹, rocuronium 0.6 mg/kg⁻¹ and propofol 1.5 mg/kg⁻¹. Two min after induction, the patients were topically anesthetized with saline (5 ml) 1%, 2% lidocaine (100 mg), or ropivacaine (37.5 mg) using a laryngotracheal topical anesthesia kit (Tuoren Group, Xinxiang, Henan, China). One-third of the total dose of local anesthetic was sprayed onto the larynx, the epiglottic area, and the trachea.

Four min after topical anesthesia, endotracheal intubation was performed by the first anesthesiologist. Patients who required more than 1 attempt to intubate were withdrawn from the study. Successful endotracheal intubation was confirmed by auscultation and end-tidal capnography. Anesthesia was maintained with remifentanil 10 µg/h⁻¹/kg⁻¹ and sevoflurane 1.5–2%. Tidal volume was controlled at 7 ml/kg⁻¹, the respiratory rate was set at 12 per minute, and the expiration/inspiration ratio was set at 1:2. During surgery, ephedrine or atropine was injected if MAP or HR decreased by 30% from baseline. TOF was continuously monitored with TOF-Watch S (Organon, Dublin, Ireland). After surgery and the withdrawal of anesthetics, 0.05 mg/kg⁻¹ of neostigmine and 0.3 mg of atropine were administered to reverse neuromuscular blockade. Exubation was performed when the TOF ratio (T4/T1) was >70%. During intubation and extubation, urapidil 5 mg was intravenously injected if SBP was ≥160 mmHg or diastolic blood pressure (DBP) was ≥90 mmHg, and 10 mg esmolol was intravenously injected if HR was ≥90 bpm. After confirmation of the absence of respiratory failure, hemorrhage, or hypertensive crisis, the patients were transferred to the ward.

Evaluation

The primary outcome measures were the dosages of urapidil and esmolol during emergence. Secondary outcomes included...
MAP and HR recorded by the second anesthesiologist at baseline (T0), at laryngoscopy before intubation (T1), at tracheal intubation (T2), 2 min after intubation (T3), upon eye opening in response to verbal commands (T4), at tracheal extubation (T5), and 2 min after extubation (T6).

The volume of bleeding and infusion were recorded. Five minutes after extubation, patients were transferred to the post-anesthesia care unit, and possible adverse events, including respiratory depression, hypoxemia, hypertension crisis, and nausea/vomiting, were evaluated.

**Statistical analysis**

Data were analyzed with SPSS 11.5 for Windows (Chicago, Illinois, USA). All data are expressed as mean (SD) or number (proportion,%). MAP and HR were analyzed using repeated measures analysis and compared at different time-points using the t-test. Categorical data were analyzed using the chi-square test or Fisher’s exact test, where appropriate. *P* values <0.05 were considered statistically significant.

A power analysis of number of patients who needed urapidil during extubation in a pilot study of 10 patients indicated that a sample size of 42 patients per group would reach approximately 80% power to reject the null hypothesis. To allow for lack of eligibility and attrition, 150 patients were enrolled in this study.

**Results**

Of the 150 patients enrolled in this study, 11 (2 in the saline group, 4 in the lidocaine group, and 5 in the ropivacaine group) were excluded because they needed 2 attempts to intubate (Figure 1). There were no significant differences among the 3 groups in demographic data, duration of anesthesia and surgery, or volume of bleeding and infusion (*P*>0.05 each; Table 1). Moreover, there were no significant differences in preoperative dosages of antihypertensive drugs or perioperative ephedrine among the 3 groups (*P*>0.05; Table 2).

During emergence, 25 patients in saline group required urapidil to decrease blood pressure, with 5 patients each requiring 2 doses. In comparison, only 15 patients in the lidocaine group and only 7 in the ropivacaine group required urapidil to decrease blood pressure, with 4 and zero patients, respectively, requiring 2 doses. The total dosage of urapidil was significantly higher in the saline group (150 mg) than in either the lidocaine (95 mg) or ropivacaine (35 mg) group and was significantly higher in the lidocaine group than in the ropivacaine group (*P*<0.05 each; Table 3). Esmolol was required by 18 patients in the saline group, 12 in the lidocaine group, and 4 in the ropivacaine group. The total dosage of esmolol was significantly higher in the saline group than in either the lidocaine or ropivacaine group and was significantly higher in the lidocaine group than in the ropivacaine group (*P*<0.05 each; Table 3).

At T2, SBP, DBP, MAP, and HR were lower in the lidocaine and ropivacaine groups than in the saline group, but blood pressure and HR did not differ significantly between the lidocaine and ropivacaine groups. No patient required urapidil or esmolol during intubation. From T4 to T6, SBP, DBP, MAP, and HR were significantly higher in the saline group than in the lidocaine and ropivacaine groups and were significantly higher in the lidocaine than in the ropivacaine group (*P*<0.05 each) (Figure 2).
We found that both ropivacaine and lidocaine, when used for topical anesthesia before intubation, can inhibit hemodynamic responses during intubation. Compared with lidocaine, however, ropivacaine more effectively inhibited hemodynamic responses during extubation.

Insertion and withdrawal of a laryngoscope and endotracheal tube during intubation and extubation can irritate the sympathetic nervous system, leading to severe tachycardia, hypertension, or arrhythmia [26]. Although the hemodynamic changes induced by general anesthesia are transitory and not harmful for healthy individuals, in hypertensive patients they can lead to life-threatening complications, including myocardial ischemia and cardiac arrhythmias, and may even be fatal.

Opioids, α-blockers, β-blockers, and α2 agonists have been used to stabilize hemodynamic responses during intubation or extubation [36–38,43–50]. Care should be taken when using these agents, however, because of delays in postoperative awakening and the occurrence of complications associated with a decline in cardiac function. Lidocaine as an airway topical anesthetic is widely used to attenuate hemodynamic reflexes [3,17,18,25,27–31]. Godzieba et al. indicated that use high dose or high concentration of lidocaine (≤ 4 ampules) with epinephrine seems to be relatively safe for cardiovascularly compromised patients [51]. Due to its short half-life,

| Table 1. Demographic data of the 2 groups. |
|------------------------------------------|
| **Saline group** (n=48) | **Lidocaine group** (n=46) | **Ropivacaine group** (n=45) | **P** |
| Sex (M) n (%) | 24.0 (50.0) | 26.0 (56.5) | 24.0 (53.3) | >0.05 |
| Age (year) | 60.3 (10.4) | 59.2 (10.8) | 61.4 (11.5) | >0.05 |
| Weight (kg) | 68.5 (7.4) | 67.2 (8.7) | 69.0 (5.8) | >0.05 |
| Duration of surgery (min) | 171.6 (19.1) | 169.0 (18.8) | 173.2 (18.5) | >0.05 |
| Duration of anesthesia (min) | 195.7 (22.1) | 196.3 (21.0) | 199.2 (21.8) | >0.05 |
| Volume of bleeding (ml) | 141.4 (27.5) | 133.9 (28.4) | 143.1 (26.7) | >0.05 |
| Volume of infusion (ml) | 659.8 (51.3) | 648.8 (49.1) | 665.2 (50.6) | >0.05 |

| Table 2. Antihypertensive medication in the 3 groups. |
|---------------------------------------------------|
| **Saline group** (n=48) | **Lidocaine group** (n=46) | **Ropivacaine group** (n=45) |
| Diuretic | 3 | 2 | 4 |
| Beta blocker | 4 | 5 | 3 |
| ACE inhibitor | 9 | 8 | 7 |
| Calcium channel blocker | 11 | 10 | 13 |
| Combination therapy | 21 | 21 | 18 |

The data are presented with number. There was no significant difference of use of antihypertensive medication in the 3 groups.

| Table 3. Comparison of dosage of urapidil and esmolol in the 3 groups. |
|---------------------------------------------------|
| **Saline group** (n=48) | **Lidocaine group** (n=46) | **Ropivacaine group** (n=45) |
| Urapidil (mg) | 195 | 95* | 35*,# |
| Esmolol (mg) | 180 | 120* | 40*,# |

* P<0.05 compared with saline group. * P<0.05 compared with lidocaine group.

**Discussion**

We found that both ropivacaine and lidocaine, when used for topical anesthesia before intubation, can inhibit hemodynamic responses during intubation. Compared with lidocaine, however, ropivacaine more effectively inhibited hemodynamic responses during extubation.

Opioids, α-blockers, β-blockers, and α2 agonists have been used to stabilize hemodynamic responses during intubation or extubation [36–38,43–50]. Care should be taken when using these agents, however, because of delays in postoperative awakening and the occurrence of complications associated with a decline in cardiac function. Lidocaine as an airway topical anesthetic is widely used to attenuate hemodynamic reflexes [3,17,18,25,27–31]. Godzieba et al. indicated that use high dose or high concentration of lidocaine (≤ 4 ampules) with epinephrine seems to be relatively safe for cardiovascularly compromised patients [51].
however, lidocaine given prior to intubation cannot inhibit hemodynamic responses during extubation following a long operation. Moreover, endotracheal tube cuff lidocaine was not superior to intravenous lidocaine [19]. Laryngotracheal instillation of lidocaine for topical anesthesia during extubation may increase the risk of postoperative aspiration and costs to patients [16]. We therefore evaluated the effects of topical ropivacaine anesthesia on hemodynamic responses during intubation and extubation.

In this study, 13 patients underwent craniotomies for aneurysms. The stability of perioperative hemodynamics is very important for these hypertensive patients. An increase or decrease in blood pressure may cause bleeding or edema, or predispose the patient to cerebral ischemia. Tachycardia caused by irritation of sympathetic nervous system can result in increased oxygen consumption by the myocardium, and may even result in myocardial ischemia. To stabilize hemodynamics, intravenous urapidil and esmolol may be administered to decrease blood pressure and HR, respectively. However, administration of α- or β-blockers may lead to hypotension or bradycardia. In this study, we compared the dosages of urapidil and esmolol in 3 groups to determine whether topical ropivacaine could reduce the consumption of urapidil and esmolol, and stabilize hemodynamic changes.

We found that, compared with saline or lidocaine, topical ropivacaine significantly reduced the consumption of urapidil and esmolol during emergence from anesthesia and extubation by stabilizing hemodynamic responses. Ropivacaine significantly reduced SBP, DBP, MAP, and HR when compared with patients in the saline and lidocaine groups.

The effect of ropivacaine is due in large part to its blockade of sympathetic nerves distributed in the upper parts of the airway. Insertion of a laryngoscope and/or intake tube into the upper airways may directly produce pressure stimulation on laryngeal tissue. This causes marked cardiovascular responses by irritating the deep sensory receptors of the larynx. Topical anesthesia applied to the larynx or trachea is effective in suppressing intubation-induced increases in blood pressure [39,40], as well as blocking cardiovascular responses to airway irritation [41,42]. Topical ropivacaine was found to significantly attenuate the reactivity of the airways and to block the conduction of sympathetic nerves [22].

In conclusion, topical ropivacaine before intubation can effectively inhibit the intubation response, as well as decreasing the incidence and grade of cough and attenuating hemodynamic changes during the extubation period in hypertensive patients.

Conclusions

Topical ropivacaine before intubation can effectively inhibit the intubation response, as well as decreasing the incidence and grade of cough and attenuating hemodynamic changes during the extubation period in hypertensive patients.
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