

Effects of intravenous infusion of lidocaine and dexmedetomidine on inhibiting cough during the tracheal extubation period after thyroid surgery

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Research Article

Keywords: Lidocaine, Dexmedetomidine, Cough, Thyroid surgery

Posted Date: January 15th, 2019

DOI: <https://doi.org/10.21203/rs.2.216/v1>

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Version of Record: A version of this preprint was published on May 4th, 2019. See the published version at <https://doi.org/10.1186/s12871-019-0739-1>.

Abstract

Background: Intravenous lidocaine and dexmedetomidine treatments have been proposed as methods for inhibiting cough. We compared the efficacy of intravenous lidocaine and dexmedetomidine treatments on inhibiting cough during the tracheal extubation period after thyroid surgery.

Methods: One hundred eighty patients undergoing thyroid surgeries were randomly allocated to the LIDO group (received lidocaine 1.5 mg/kg loading, 1.5 mg/kg/h infusion), the DEX group (received dexmedetomidine 0.5 µg/kg loading, 0.4 µg/kg/h infusion) and the CON group (received saline), with 60 cases in each group. The incidences and severities of cough were recorded within 2 minutes after the extubations. Hemodynamic variables were measured at T0 (before the induction of anesthesia), T1 (immediately after the extubation) and T2 (5 minutes after extubation). The volume of drainage was recorded within 24 hours after the surgeries.

Results: The incidences of cough were significantly lower in the LIDO group (28.3%) and the DEX group (31.7%) than in the CON group (66.7%) ($P=0.000$). Additionally, both moderate and severe cough were significantly lower in the LIDO group (13.3%) and the DEX group (13.4%) than in the CON group (43.4%) ($P<0.05$). Compared with the two treatment groups, both mean arterial blood pressure and heart rate were significantly increased in the CON group at T1 and T2 ($P<0.05$). Compared with the CON group, the volume of drainage was significantly reduced in the two treatment groups within 24 hours after surgery ($P<0.05$).

Conclusion: Both intravenous infusions of lidocaine and dexmedetomidine had equal effectiveness in attenuating cough, hypertension, and tachycardia during the tracheal extubation period in patients undergoing thyroid surgery. Additionally, there was no significant difference in the reduction of postoperative drainage between the two treatments.

Trial registration: Chinese Clinical Trial Registry, ChiCTR1800017482 (date of registration August 2018).

Keywords: Lidocaine, Dexmedetomidine, Cough, Thyroid surgery.

Background

The reduction of complications, such as cough, delirium and hemodynamic disorder, during anesthetic emergence is a major concern for anesthesiologists. However, it is widely believed that approximately 82.5% of patients experience a cough upon emergence from general anesthesia [1], with causes possibly including the presence of an endotracheal tube, uncleared secretions and anesthetic gas [2]. Cough during the tracheal extubation period may lead to several complications, such as hypertension, tachycardia and postoperative hemorrhage [3-5]. These complications may negatively impact the quality of recovery. Furthermore, a cervical hematoma is a rare but fatal complication after thyroid surgery [6]. Therefore, the inhibition of cough is considered to be more important for thyroid surgery than any other

surgical factor. Various strategies aimed at inhibiting cough, including the administration of lidocaine and dexmedetomidine, have been studied [7,8].

Dexmedetomidine is a potent, alpha-2-selective adrenoceptor agonist, and the most characteristic features include sympatholysis, sedation, analgesia and a lack of respiratory depression [9]. Two studies showed that the administration of single-dose 0.5 mg/kg dexmedetomidine before the end of surgery effectively reduced cough during anesthetic emergence[10,11]. Additionally, a previous report showed that an intravenous administration of lidocaine can inhibit cough during extubation [12]. Even though both of these treatments have been reported to effectively inhibit the emergence of cough, the differences between intravenous lidocaine and dexmedetomidine in inhibiting cough during the tracheal extubation period are unclear.

Therefore, we conducted a study to compare the effects of intravenous infusions of lidocaine and dexmedetomidine in inhibiting cough during the tracheal extubation period after thyroid surgery.

Methods

Study protocol

The Ethics Committee of the Anqing Affiliated Hospital of Anhui Medical University approved the study (Document No. 2018-06-09). Each patient signed an informed consent before surgery. This study was registered at ClinicalTrials.gov (Registration No. ChiCTR1800017482) before any patients were enrolled.

Subjects

180 patients were enrolled from August 2018 to December 2018. All of the patients in this study were classified as either American Society of Anesthesiologists (ASA) class I or II, were aged between 18-and 65-years-old from both sexes and were scheduled to undergo thyroid surgery. The exclusion criteria in this study included incidences of asthma, chronic cough, perioperative upper respiratory infection symptoms, a current smoking status, medication involving angiotensin-converting-enzyme inhibitors (ACE-I), bronchodilators or steroid medications, sinus bradycardia or an atrioventricular conduction block, hepatic insufficiency, renal insufficiency, a local anesthetic allergy and a refusal to participate in the study. Patients were randomized and allocated into three groups, including the LIDO group, the DEX group and the CON group (60 patients for each group), by using a random number table generated by a computer. The group assignments and the drugs were prepared by another person who was blind to the study. All of the patients were NPO since approximately 6 hours before surgery (Fig. 1).

Anesthesia

All surgeries were performed by three experienced surgeons. All patients received intramuscular hyoscine (0.3 mg) 30 minutes before the induction of anesthesia. Mean arterial blood pressure (MAP), heart rate (HR), electrocardiogram (ECG) and peripheral pulse oximeter (SPO₂) values were monitored by using a

multiparameter monitor (Philips MIX500, Boeblingen, Germany). In the LIDO group, the patients were given an intravenous administration of 1.5 mg/kg loading lidocaine over the 10 minutes before the induction of anesthesia, followed by a continuous intravenous administration of 1.5 mg/kg/h lidocaine until 30 minutes before the end of surgery. In the DEX group, patients were given an intravenous administration of 0.5 µg/kg loading dexmedetomidine over the 10 minutes before the induction of anesthesia, followed by a continuous intravenous administration of 0.4 µg/kg/h dexmedetomidine until 30 minutes before the end of surgery. In the CON group, the patients were given an intravenous infusion of an equal volume of normal saline until 30 minutes before the end of surgery. General anesthesia was induced with midazolam (0.05 mg/kg), propofol (2 mg/kg), sufentanil (0.5 µg/kg) and vecuronium (0.1 mg/kg), and anesthesia was maintained with propofol (50-80 µg/kg/min) and remifentanil (0.15-0.2 µg/kg/min). After an immediate intubation after adequate muscle relaxation, all of the patients were ventilated with an Aspire view anesthetic machine (GE Healthcare, Madison, WI, USA). In the three groups, the tidal volume (VT) was maintained at 8 ml/kg, the respiratory rate (RR) was fixed at 12 breaths/min, the inspiratory to expiratory time ratio (I: E) was 1:2 and the inspired oxygen fraction (FiO₂) was 0.5 (balanced with air) throughout the anesthesia period. To maintain a controlled ventilation, vecuronium was intermittently used for muscle relaxation. The depth of anesthesia was maintained with an infusion rate of propofol and remifentanil, according to the Bispectral Index values (BIS) and the hemodynamic parameters within 20% of the baseline. To prevent the occurrence of intraoperative awareness, the BIS values were kept between 45 and 60 in the three groups during surgery. Neuromuscular blocks were reversed with atropine (0.5 mg) and neostigmine (1 mg) before the tracheal extubation. After the tracheal extubation, all of the patients were transferred to the post anesthesia care unit (PACU).

Data collection

Demographic and clinical characteristics, including age, height, weight, ASA grade, gender, the duration of anesthesia and the duration of the operation were recorded. The incidence and severity of cough within 2 minutes after the extubations were recorded by another blinded person who did not know what drug had been administered to each patient; the coughs were graded according to the following criteria [13]:

- Grade 0: no cough;
- Grade 1: mild, 1 cough;
- Grade 2: moderate, >1 cough lasting for <5 seconds; and
- Grade 3: severe, sustained cough for >5 seconds).

Hemodynamic variables, including MAP and HR, were measured and recorded at T0 (the time before the induction of anesthesia), T1 (the time immediately after the extubation) and T2 (5 minutes after the extubation). The volume of drainage was recorded within 24 hours after surgery by another blinded person who did not know what drug had been administered to each patient.

Statistical analysis

A pilot study was performed prior to patient recruitment to estimate an appropriate sample size. The study encompassed 180 subjects (60 in each group). Data analysis was performed by using SPSS for Windows V.16.0 (SPSS Inc, Chicago, IL). Data were expressed as numbers, percentages or means±standard deviations. The comparison of the hemodynamic variables among the three time points within each group was performed by using a repeated measures analysis of variance. Intergroup differences of the parameters at each time point were determined by using a one-way analysis of variance with a post hoc analysis. The proportions of sex, ASA grades and incidences and grades of cough were performed by using a χ^2 analysis. The continuous data, such as age, height, weight, duration of anesthesia, duration of the surgery and the volume of drainage were performed by using an independent *t* test. *P* values of less than 0.05 were considered to be statistically significant.

Results

A total of 192 patients were assessed for eligibility for the study, and 180 subjects were enrolled in the study (Fig. 1). 12 patients were excluded (reasons for exclusion are listed in Fig. 1). There were no significant differences among the three groups with respect to age, weight, height, ASA class, sex, duration of anesthesia and duration of the surgery (Table 1). The incidences of cough were significantly lower in the LIDO group (28.3%) and the DEX group (31.7%) than in the CON group (66.7%) ($P=0.000$). Additionally, both moderate and severe cough were significantly lower in the LIDO group (13.3%) and the DEX group (13.4%) than in the CON group (43.4%) ($P<0.05$). There were no differences in the incidence and severity of cough between the two treatment groups (Table 2). Compared with the LIDO group and the DEX group, both MAP and HR were significantly increased in the CON group at T1 and T2 ($P<0.05$). There were no differences in MAP or HR between the two treatment groups (Fig. 2). Compared with the CON group, the volume of drainage was significantly reduced in both the LIDO group and the DEX group within 24 hours after surgery ($P<0.05$). There was no difference in the volume of drainage between the two treatment groups (Fig. 3).

Discussion

This study demonstrated that intravenous infusions of lidocaine and dexmedetomidine were effective in attenuating cough, hypertension and tachycardia during the tracheal extubation period in patients undergoing thyroid surgery, when compared with patients who were treated with normal saline. Additionally, both of these treatments were able to reduce postoperative drainage when compared with patients who were treated with normal saline.

Lidocaine has several beneficial effects, such as analgesia, anti-hyperalgesia and anti-inflammation [14,15]. Moreover, lidocaine can depress spike activity, amplitude and conduction time in both myelinated A and unmyelinated C nerve fibers [16]. Several studies have shown that lidocaine can reduce the incidence and severity of cough during anesthetic emergence through different methods, including intracuff, tube lubrication, intratracheal instillation and intravenous bolus infusions before an induction [17-20]. Shabnum et al [12]. found that both IV and intratracheal lidocaine are effective in the attenuation

of cough. In our study, the incidence and severity of cough was 28.3% in the LIDO group, and the rate of cough was significantly lower than the rate in a previous study (72.1%) [8]. We speculate that the methods of intravenous infusion of lidocaine might contribute to the difference. The effective serum concentration of lidocaine for the attenuation of cough is between 2.3 µg/ml and 3.0 µg/ml [21], and it is difficult to achieve this concentration in a timely manner via bolus infusion administration; however, the target concentration can likely be obtained by extending the intravenous infusion time. The present study demonstrated that the intravenous infusion of lidocaine can effectively suppress cough during the tracheal extubation period.

Several studies have shown that dexmedetomidine can effectively reduce cough during anesthetic emergence [8,10], but the exact mechanism is unclear. A previous study has shown that a peripheral alpha-2 receptor may be involved in cough inhibition [22]. In addition, a previous study showed that the sedative characteristics of dexmedetomidine can suppress the sensitivity of tracheal stimulation, which then results in cough inhibition [23]. However, several studies have shown that a dexmedetomidine infusion, at a rate of 0.4 µg/kg/h during the operation period, did not inhibit cough [24,25]. Park et al [26] compared the effect of a single dose of 0.5µg/kg dexmedetomidine with remifentanyl by the use of a target-controlled infusion in reducing cough during anesthetic emergence. The results of this study showed that the effect of dexmedetomidine was lower than that of remifentanyl. In addition to the administration of a loading dose of infusion before the induction of anesthesia, a continuous infusion administration was also given until 30 minutes before the end of surgery in the DEX group. In our study, the incidence of cough decreased by 35% in the DEX group, which thus contributed to the sedative effect of dexmedetomidine.

Cough during the tracheal extubation period in patients undergoing thyroid surgery may increase the incidence of postoperative bleeding, which can lead to cervical hematoma and reoperation [5]. Furthermore, severe cervical hematoma is a fatal complication after thyroid surgery [6]. Additionally, coughing can be accompanied by increased venous pressure, which may then cause a ligature to slip or cause nonligated small vessels to bleed profusely [27]. A recent study showed that incision drainage is closely correlated with inflammation, while dexmedetomidine and lidocaine both have anti-inflammation effects [28-30]. Postoperative hematomas usually occur within 12 hours, and especially occur within 6 hours after surgery [31]. In our study, the volume of drainage within 24 hours after surgery was lower in the two treatment groups than in the control group. The authors attribute these results to the reduction of cough, as well as the anti-inflammatory effects of dexmedetomidine and lidocaine.

The stimulation of the respiratory tract by an endotracheal tube during an endotracheal extubation causes transient sympathetic activity, which can lead to hypertension and tachycardia [32]. Various attempts have been made to attenuate the pressor response via intravenous administrations of lidocaine and dexmedetomidine. A previous study reported that intravenous lidocaine can blunt increases in HR and MAP during the tracheal extubation period [33]. Luthra et al [34] demonstrated that intravenous dexmedetomidine can alleviate stress responses to tracheal extubation. In our study, both MAP and HR were decreased in the LIDO group and the DEX group at the time of immediate extubation and 5 minutes

after extubation, compared to the CON group. These findings may be explained by the analgesic properties of both lidocaine and dexmedetomidine.

Although the abovementioned drugs, including both lidocaine and dexmedetomidine, can reduce the incidence of cough, some unexpected side effects, such as sinus bradycardia, hypotension, hypertension, and lidocaine-induced neurotoxicity, may occur during drug administration [34,35]. However, there were no adverse effects observed in our study.

There were several limitations in this study. First, the consumption of anesthetic agents and the incidence of postoperative pain were not evaluated; however, both lidocaine and dexmedetomidine have analgesic properties [9,36]. Second, this study was a single-center clinical study, and the conclusions still need to be further supported by large sample and multicenter studies.

Conclusion

This study demonstrated that intravenous lidocaine and dexmedetomidine infusions had equal effectiveness in attenuating cough, hypertension, and tachycardia during the tracheal extubation period in patients undergoing thyroid surgery. Furthermore, there was no significant difference in reduction postoperative drainage between the two treatments.

Abbreviations

ASA: American Society of Anesthesiologists; ACE-I: Angiotensin-converting-enzyme inhibitors, MAP: Mean arterial blood pressure; HR: Heart rate; ECG: Electrocardiogram; SPO₂: Peripheral pulse oximeter values; VT: Tidal volume; RR: Respiratory rate; FiO₂: Inspired oxygen fraction BIS: Bispectral index; PACU: post anesthesia care unit; LIDO: Lidocaine; DEX: Dexmedetomidine; CON: Control; T0:time before the induction of anesthesia; T1:time immediately after the extubation; T2:5 minutes after the extubation

Declarations

Acknowledgments

Not applicable.

Funding

Our own money and The Anqing Affiliated Hospital of Anhui Medical University resources.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest

The authors certify that there is no conflict of interest.

Authors' contributions

SHH, SBW, and YHL conceived the study design and drafted the study protocol. SHH, SBW, SQX, XJ, LM, and YHL all participated in the study design and coordination. SHH, SBW, XJ and SQX contributed to data collection. YHL was the principal investigator and has overall responsibility for this study. SHH performed the statistical analysis for the study protocol. SHH and SBW drafted and revised the manuscript. SHH, SBW and YHL critically revised the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

This study and its protocol were approved by the Institutional Medical Ethics Committee of The Anqing Affiliated Hospital of Anhui Medical University (2018-06-09). Written informed consent was obtained from all subjects.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1

Demographic and clinical characteristics

Variables	LIDO group [n=60]	DEX group [n=60]	CON group [n=60]	P value
Age (years)	48.4±8.8	47.6±7.8	49.3±7.2	0.661
Weight (kg)	58.8±6.9	57.6±5.7	60.1±6.4	0.320
Height (cm)	158.6±5.1	157.7±4.5	158.9±6.1	0.815
ASA class (I/II)	55/5	58/2	57/3	0.477
Gender, Female/Male	35/25	37/23	34/26	0.933
Duration of anesthesia (min)	82.1±19.4	92.2±25.5	81.8±20.4	0.242
Duration of surgery(min)	99.4±20.7	111.4±30.8	104.0±24.1	0.333

Categorical variables were expressed as the mean ± standard deviation (SD) or numbers. LIDO group, iv. lidocaine; DEX group, iv. dexmedetomidine; CON group, iv. equal volume normal saline.

Table 2

Incidence and grade of cough

Variables	LIDO group [n=60]	DEX group [n=60]	CON group [n=60]	<i>P</i> value
Incidence of cough, n (%)	17(28.3) *	19(31.7) *	40(66.7)	0.000
Grade 0	43(71.7) *	41(68.3) *	20(33.3)	0.000
Grade 1	9(15.0)	11(18.3)	14(23.3)	0.502
Grade 2	6(10.0) **	5(8.4) **	16(26.7)	0.008
Grade 3	2(3.3) **	3(5.0) **	10(16.7)	0.016

Categorical variables were expressed as numbers (proportions). LIDO group, iv. lidocaine; DEX group, iv. dexmedetomidine; CON group, iv. equal volume normal saline. Grade 0: no cough; Grade 1: mild, 1 cough; Grade 2: moderate, >1 cough lasting for<5 seconds; Grade 3: severe, sustained for>5 seconds). **P*=0.000 vs the CON group. ***P*<0.05 vs the CON group.

Figures

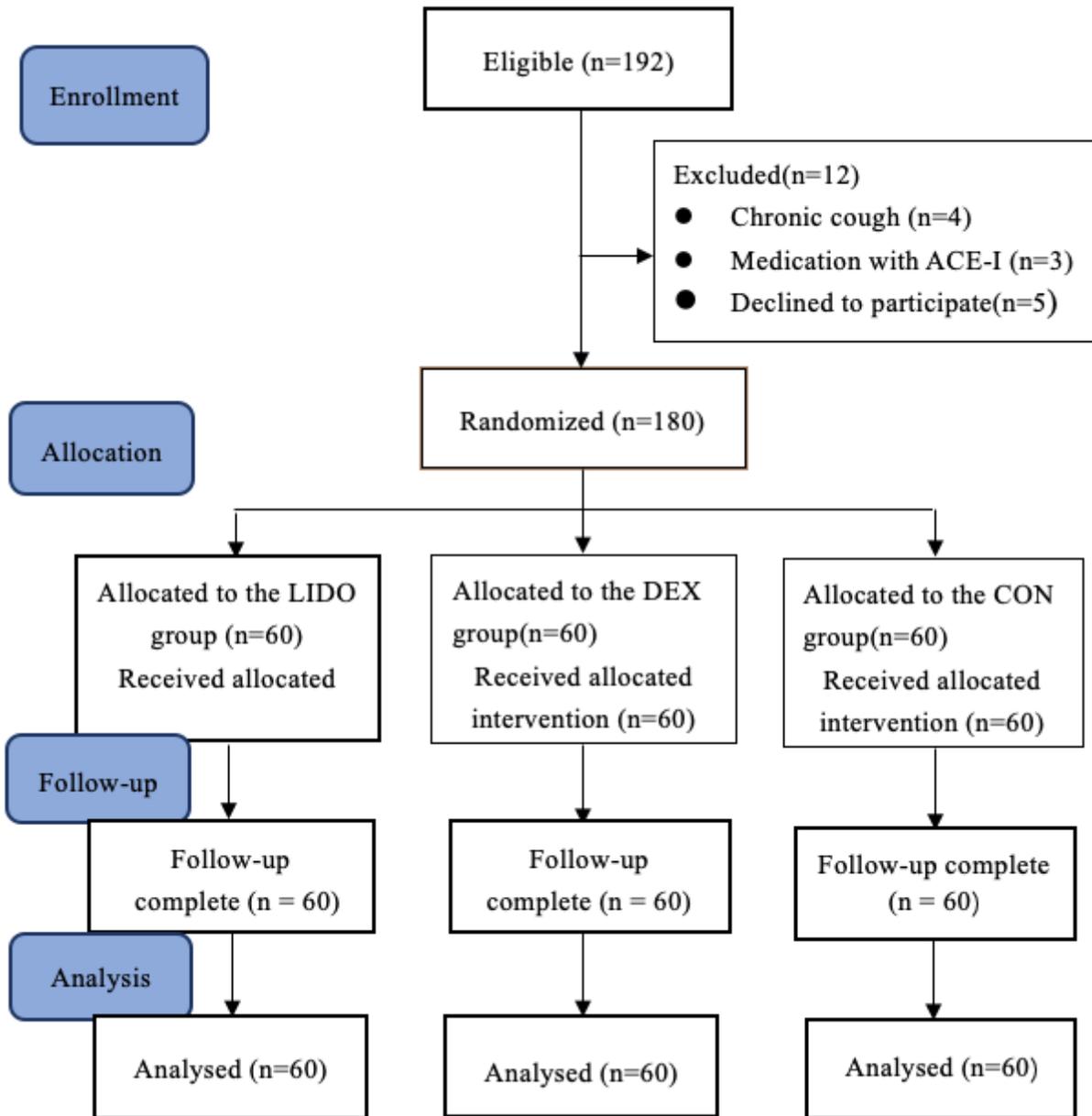


Figure 1

CONSORT flow diagram for the study.

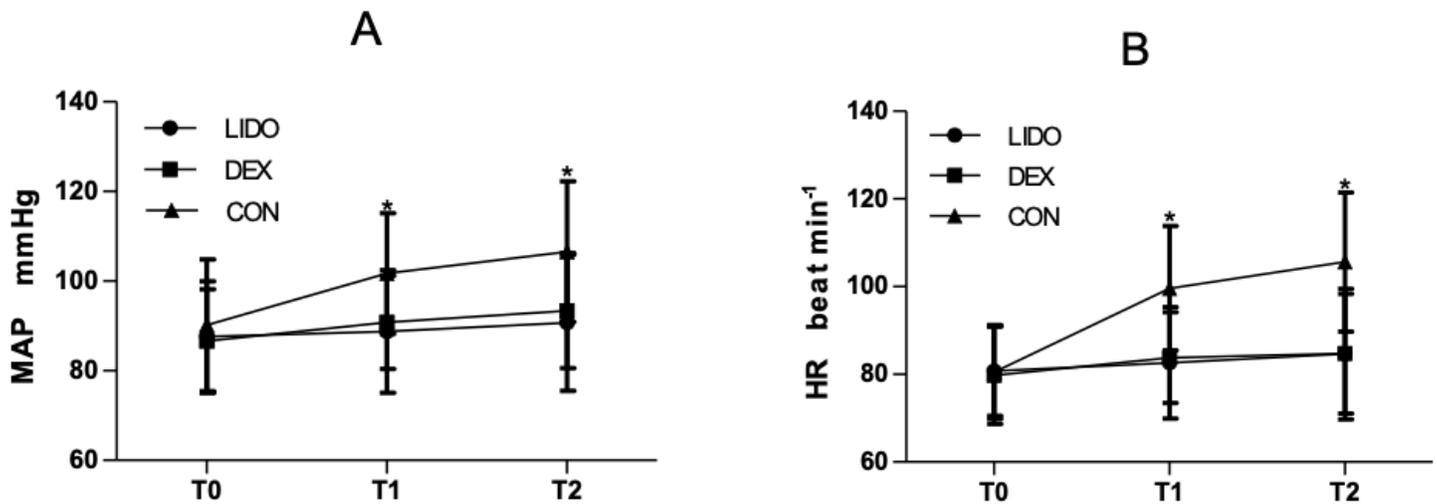


Figure 2

Changes in MAP (A) and HR (B) at different time points. Categorical variables were presented as the mean \pm standard deviation for all of the patients, with 60 cases in each group. LIDO group, iv. lidocaine; DEX group, iv. dexmedetomidine; CON group, iv. equal volume normal saline. MAP, mean arterial pressure; HR, heart rate. T0, time before the induction of anesthesia; T1, time immediately after the extubation; T2, 5 minutes after the extubation. Compared with the LIDO group and the DEX group, both MAP and HR were significantly increased in the CON group at T1 and T2 (* $P < 0.05$).

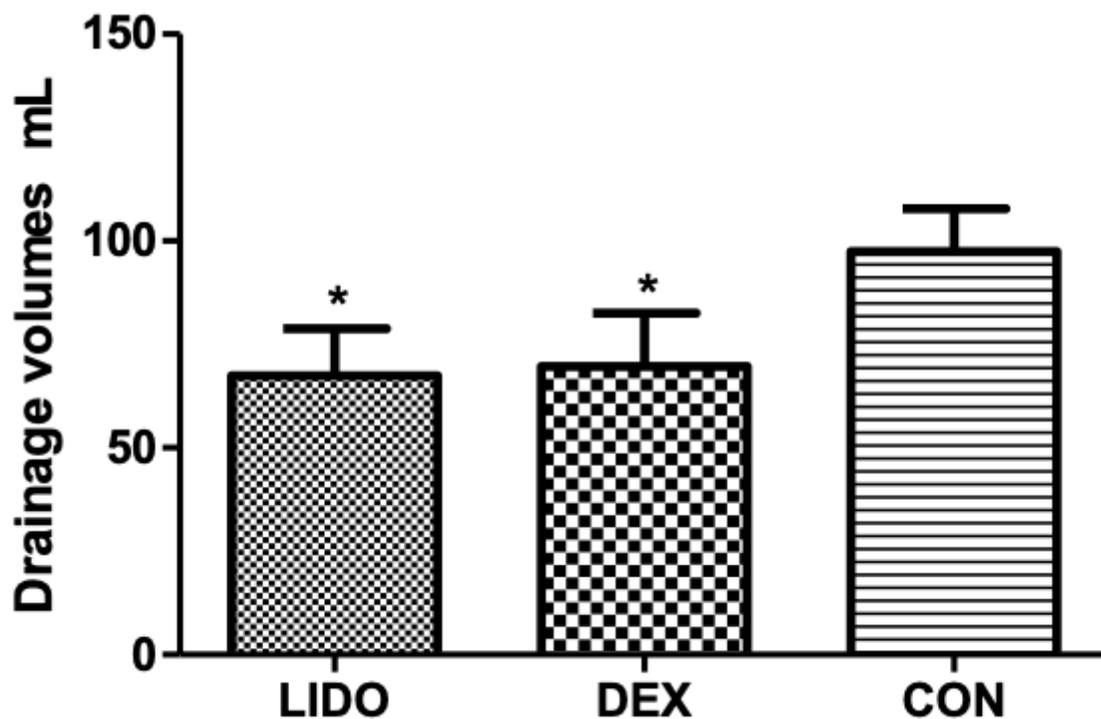


Figure 3

The volume of drainage was recorded within 24 hours after surgery. Categorical variables were presented as the mean \pm standard deviation for all of the patients, with 60 cases in each group. LIDO group, iv. lidocaine; DEX group, iv. dexmedetomidine; CON group, iv. equal volume normal saline. Compared with the CON group, the volume of drainage was significantly reduced in the LIDO group and the DEX group (*P<0.05).