Clinical Trial/Experimental Study

Medicine®

OPEN

The effects of target-controlled infusion of lidocaine undergoing vocal cord polypectomy

A randomized controlled trial (CONSORT compliant)

LongYuan Zhou, MB[a,*], RuiLan Wu, MB[a], Chang Cai, MM[a], Yong Qi, MM[a], XingHua Bi, MB[a], Qi Hang, MM[b]

Abstract

Background: The present study aimed to assess the efficacy and safety of general anesthesia-assisted target-controlled plasma infusion of lidocaine in patients with vocal cord polypectomy using a supporting laryngoscope.

Methods: In total, 80 patients undergoing vocal cord polypectomy using a supporting laryngoscope were randomly divided into an intervention group and a control group; each group contained 40 subjects: both groups received general anesthesia; subjects in the intervention also received an additional 3 mg/L of lidocaine by target-controlled plasma infusion during induction and maintenance of anesthesia; heart rate (HR) mean arterial pressure (MAP), propofol and urapidil consumption (Uradil, which is a blood pressure drug that blocks alpha-1, is called Urapidi Hydrochloride Injection. It is produced by Germany, the enterprise name is Nycomed Deutschland GmbH, the import drug registration number is H20090715, and it is widely used in China), recovery time, and cough score (measured by Minogue et al's 5-grade scoring method) during extubation, and throat pain score (measured by visual analogue scale,[VAS]) after extubation and adverse events were recorded.

Results: Significant differences were observed in HR ($P < .05$) and MAP ($P < .05$) immediately after intubation (T2), immediately after the operation starting to support laryngoscope exposure (T3), immediately after operation field adrenergic tampon hemostasis (T4), and 5 minutes after hemostasis (T5) between the 2 groups, and significant differences were also observed in HR ($P < .05$) before intubation (T1). Moreover, significant differences were observed in propofol consumption ($P < .05$), urapidil consumption ($P < .05$), cough score during extubation ($P < .05$), and throat pain score after extubation ($P < .05$). However, no significant difference was observed in the recovery time ($P > .05$). Furthermore, no adverse events were detected in either group.

Conclusion: The results of this study showed that target-controlled plasma infusion of lidocaine can reduce propofol consumption in patients undergoing vocal cord polypectomy by supporting laryngoscopy, and the hemodynamics are more stable and reduce the coughing reaction in the wake period and throat pain after extubation without adverse events.

Abbreviations: AEs = adverse events, ASA = American Society of Anesthesiologists, HR = heart rate, MAP = mean arterial pressure, VAS = visual analogue scale.

Keywords: analgesia, clinical trial, lidocaine, propofol, target-controlled infusion, vocal cord polypectomy

1. Introduction

The duration of vocal cord polypectomy using a supporting laryngoscope is relatively short, and is usually performed under general anesthesia. It requires stable hemodynamics, rapid recovery, and sufficient postoperative analgesia. Traditional general anesthesia requires deep anesthesia to reduce the stress response caused by supportive laryngoscope exposure or intraoperative nodal adrenalin, leading to prolonged recovery

Editor: Ahmet Eroglu.

This work was supported partly by the Medical Science and Technology Project of Ningbo (2017A03).

This study was registered in the Chinese Clinical Trial registry (ChiCTR2100042623).

All relevant data are within the paper and its Supporting Information files.

The authors report no conflicts of interest.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. All data generated or analyzed during this study are included in this published article [and its supplementary information files];

[a] Department of Anesthesia, [b] Department of otolaryngology, Ningbo Medical Center Lihuili Hospital.

[*] Correspondence: LongYuan Zhou, Department of Anesthesia, Ningbo Medical Center Lihuili Hospital, No.1111 Jiangnan Road, Yinzhou District, Ningbo City, Zhejiang Province315000, China (e-mail: 396919647@qq.com).

How to cite this article: Zhou L, Wu R, Cai C, Qi Y, Bi X, Hang Q. The effects of target-controlled infusion of lidocaine undergoing vocal cord polypectomy: a randomized controlled trial (CONSORT compliant). Medicine 2022;101:6(e27642).

Received: 7 April 2021 / Received in final form: 26 August 2021 / Accepted: 6 October 2021

http://dx.doi.org/10.1097/MD.0000000000027642

time. Numerous studies have shown that lidocaine can reduce the pain sensation and cardiovascular response caused by the stress response during surgery, and reduce the need for perioperative pain and analgesia.[1–3] Therefore, it could therefore be an ideal adjuvant to traditional general anesthesia; however, previous studies were designed for continuous infusion of lidocaine at varying rates based on body weight, and plasma concentrations are not known, and target-controlled infusion can quickly reach and stabilize the target concentration. It is simple, accurate, and controllable. This study is intended to evaluate the efficacy of general anesthesia assisted target-controlled plasma infusion of lidocaine undergoing vocal cord polypectomy by supporting laryngoscope. The primary outcome for analysis were the intraoperative hemodynamic changes, including heart rate (HR) and mean arterial pressure (MAP). The data were chosen as the primary outcome based on previous experience of the hemodynamic fluctuations of different operating nodes were obvious. Secondary outcomes included propofol consumption during anesthesia, urapidi hydrochloride injection consumption, recovery time, cough score during extubation, throat pain score after extubation, and adverse events.

2. Methods

This randomized controlled trial was approved by the medical ethics committee of Ningbo Medical Center Li Huili Hospital. This study was registered in the Chinese Clinical Trial registry (ChiCTR2100042623) and was conducted at this hospital from February 1, 2021, to March 31, 2021. Eighty patients were randomly allocated to an intervention group or a control group at a 1:1 ratio; all patients met the inclusion and exclusion criteria and provided written informed consent.

This study included the patients under American Society of Anesthesiologists (ASA) physical status I-II aged from 18 to 70 years, weight range from 50 to 80 kg. All patients were scheduled for vocal cord polypectomy by bracing laryngoscope. Patients were excluded if they were with a history of hypertension, diabetes, severe arrhythmia, hepatorenal insufficiency, or lidocaine allergy.

This randomization was performed using a SAS 8.1 (SAS Institute, Inc., Cary, NC) computerized number generator, and the assignments were masked to the participants, investigators, outcome assessors, and data analysts in this study; all researchers and investors were trained before this study.

All participants in both groups received general anesthesia. Specific methods: before intravenous rapid induction, the intervention group was injected with 3 mg/L of lidocaine by target-controlled plasma infusion, and the control group was injected with normal saline of the same volume. After routine injection, 0.02 mg/kg midazolam, 0.2 μg/kg sufentanil, propofol by closed loop target-controlled infusion (BIS50 ± 5) were injected. When BIS stabilized at 50 ± 5, endotracheal intubation was facilitated with 0.6 mg/kg rocuronium. Anesthesia maintenance: propofol closed-loop target-controlled infusion (BIS50 ± 5) was performed in both groups, and the intervention group received target-controlled plasma infusion of 3 mg/L lidocaine until the end of surgery; the control group was pumped with normal saline at the same volumetric rate; when intraoperative MAP exceeded 20% of baseline value, urapidil was administered to lower MAP.

HR and MAP were measured during surgery before induction (T0), before intubation (T1), immediately after intubation (T2), immediately after the operation starting to support laryngoscope exposure (T3), immediately after the operation field adrenergic tampon hemostasis (T4), and 5 minutes after hemostasis (T5). In addition, the duration of operation, consumption of propofol and urapidi hydrochloride injection, recovery time, cough score[4] [Level 1 was no cough; Grade 2 was mild cough (1–2 times) and the tracheal catheter was removed smoothly; Grade 3, moderate cough (3–4 times); Grade 4, severe cough (5–10 times); Level 5, agitation and the tracheal tube cannot be removed], throat pain score [using the visual analogue scale (VAS)] after extubation were recorded, and the possible toxic effects of lidocaine, such as arrhythmia, circulatory inhibition, convulsions, delayed recovery, unconsciousness, paresthesia during recovery, and other signs were considered as adverse events.

On the basis of the results of the pre-test, we assumed that there was a statistical difference in HR between the 2 groups at T1, $\alpha = 0.05$ and power = 0.8. The minimum sample size was calculated using PASS software with at least 24 patients in each group, and considering the dropout rate and the acquisition of more experimental data, we finally took 40 patients in each group as the sample size.

In this experiment, (SPSS 20.0) was used for statistical analysis. Continuous variables were expressed as the mean ± standard deviation and analyzed using the *t* test. Analysis of variance (ANOVA) and Wilcoxon rank tests with relative risks and 95% confidence intervals were used for data analysis. $P < .05$ was considered significant.

3. Results

Eighty patients with polyps of vocal cord polyps who underwent vocal cord polypectomy using a supporting laryngoscope were initially recruited. No one were excluded. They were randomly divided into an intervention or a control group; each group included 40 patients, and all participants completed the trial.

The baseline characteristics of all the included patients in both groups are summarized in Table 1. No significant baseline differences in patient characteristics such as sex ratio, age, body mass index, race, ASA status, or time of operation were detected between the 2 groups (Table 1).

No significant differences in HR and MAP values were found between the 2 groups at T0. However, there were significant differences in HR at T1-5 between the 2 groups ($P < .05$, Table 2). Moreover, there were significant differences in MAP at T2-5 between the 2 groups ($P < .05$, Table 2).

There were no significant differences in the recovery time between the 2 groups ($P > .05$, Table 3). However, there were significant differences in propofol consumption, urapidil consumption, cough score during extubation, and throat pain score after extubation ($P < .05$, Table 3). In addition, no treatment-related complications were observed in either group.

4. Discussion

Lidocaine is a local anesthetic commonly used in clinical practice, its price is low, and it belongs to amide type local anesthetic, which has good effect on prevention and treatment of ventricular arrhythmia, and has obvious excitatory and inhibitory biphasic effect on central nervous system. When blood drug concentration is low, analgesia and pain threshold are increased.[5,6] As the dose increases the effect or toxicity increases, the subtoxic blood drug concentration has an anticonvulsive effect, and convulsions can occur when the blood drug concentration exceeds 5 mg/L.[7] Therefore, in this study, the plasma target-controlled

Table 1

Patients characteristics at baseline.

Characteristics	Intervention group (n = 40)	Control group (n = 40)	P
Age, yr	45.7 (10.8)	44.5 (9.6)	.61
Gender(male/female)	19/21	23/17	.37
Body mass index, kg/m^2	22.3 (1.2)	22.3 (1.1)	.37
Race			
Han ethnicity	40 (100.0)	40 (100.0)	1.00
ASA status (I/II)	17/23	14/26	.50
operation time, min	8.9 (1.3)	8.4 (1.4)	.09

Note: Date are presented as mean ± standard deviation or number (%).
ASA = American Society of Anesthesiologists.

concentration of lidocaine (3 mg/L) was used as a safe low-dose concentration.

The results of this study indicated that continuous intravenous target-controlled plasma infusion of lidocaine could reduce the intraoperative dosage of propofol and is beneficial to hemodynamic stability; exposure of the pharyngeal cavity by supporting laryngoscope can result in severe stimulation, poor anesthesia depth control or poor application of vasoactive drugs can lead to significant fluctuations in blood pressure and HR, and the application of intraoperative nodule adrenalin, which can promote the occurrence of cardiovascular and cerebrovascular events.[8,9] In this study, the stress response induced by surgery was not countered at the cost of deepening the depth of anesthesia. BIS value in both groups was set between 45 and 55, which was a more appropriate anesthesia depth,[10,11] which could not only avoid intraoperative awareness, but also avoid the delay of awakening caused by explosive suppression of brain waves. In this study, target-controlled plasma infusion of lidocaine reduced the dosage of propofol compared with the control group, and urapidil supplementation was also reduced, so the blood pressure and HR became more stable, which was consistent with the research results of Forster et al[12] during the application of lidocaine in colonoscopy, suggesting that 3 mg/L plasma concentration could inhibit the central nervous system and resist injury.

Table 2

Outcome measurements in HR, MAP during the period of the surgery.

Time	Outcome measurements	Intervention group (n = 40)	Control group (n = 40)	P
T0				
	HR	81.9 ± 6.4	82.4 ± 6.1	.71
	MAP	93.6 ± 6.4	94.0 ± 6.0	.75
T1				
	HR	81.4 ± 7.1	89.0 ± 7.8	<.001
	MAP	78.5 ± 7.6	81.0 ± 5.4	.10
T2				
	HR	74.0 ± 6.7	92.1 ± 7.5	<.001
	MAP	76.1 ± 7.8	93.0 ± 7.9	<.001
T3				
	HR	80.0 ± 7.1	98.8 ± 7.7	<.001
	MAP	78.1 ± 8.0	104.2 ± 5.9	<.001
T4				
	HR	80.5 ± 6.5	101.8 ± 7.3	<.001
	MAP	79.0 ± 7.4	110.9 ± 7.0	<.001
T5				
	HR	77.6 ± 7.5	96.3 ± 8.0	<.001
	MAP	79.1 ± 6.9	108.7 ± 4.9	<.001

Date are presented as mean ± standard deviation.
HR = heart rate, MAP = mean arterial pressure.

Table 3

Outcome measurements in consumption of propofol, urapidil, recovery time, cough score, and post-extubation sore throat score during perioperative period.

Variables	Intervention group (n = 40)	Control group (n = 40)	P
Propofol consumption, mg	263.1 ± 32.4	317.2 ± 28.2	<.001
urapidil consumption, mg	0.8 ± 1.8	7.1 ± 5.3	<.001
recovery time	16.3 ± 2.9	16.7 ± 2.9	.57
cough score	1.9 ± 0.6	3.5 ± 0.6	<.001
post-extubation sore throat score	1.3 ± 0.6	2.2 ± 0.7	<.001

Note: Date are presented as mean ± standard deviation.

In this study, there was no significant difference in recovery time between the 2 groups of patients, which may be due to the short operation time, not exceeding the half-life of rocuronium, which affected the results to a certain extent. This is also the defect of this study. But the resurgence of the intervention group has better quality, show the awakening period choking cough score is lower, more stable hemodynamics, and sore throat score lower after extubation, prompt continuous pump injection of lidocaine partly inhibits the trachea cardiovascular reaction and cough reflex, both at the same time calm analgesic action, can improve and increase patient satisfaction. Harnaya Yoshihiro has shown that intravenous lidocaine can only partially block the airway response, and it is suspected that peak plasma lidocaine concentrations and the timing of their occurrence differ significantly depending on the airway site being applied[13]; However, in this study, this defect was avoided, and the plasma concentration was stable and continued until the end of surgery, so the effect of blocking airway response was theoretically better. In this study, the intervention group was also observed to significantly reduce intravenous pain. Clinical, the static note during propofol, and the interaction between rocuronium in patients with pain at the injection site make the patient produces bad feelings, even if consciousness disappeared after the pain is still there, characterized by hand and body dynamic stress response, and even affect the hemodynamic stability, this research through the pre injection of lidocaine have played an important role in prevention of injection pain, also can explain the induction period more stable hemodynamics. At present, the principle of lidocaine intravenous analgesia is still unclear. Considering the comprehensive effect of various factors, besides the effect on sodium channels,[14,15] it also involves the direct or indirect effects on different receptors and pain conduction pathways,[16,17] including Effect of muscarine antagonists; Glycine receptor inhibitors; Reduces the production of excitatory amino acids; Reduces the production of prothrombin A2; Promotes the release of endogenous opioid substances; Reduces the production of neurokinin; Promotes the release of adenosine triphosphate; Effects on central sensitization; and in physical pain, intravenous lidocaine has a peripheral analgesic effect. The production of laryngopharyngeal pain after vocal cord polyp is caused by the release of local inflammatory factors, resulting from surgical trauma, stress response caused by supporting laryngoscope, and throat insertion during endotracheal intubation. Studies have shown that systematic lidocaine therapy has anti-inflammatory

effects in many diseases and can effectively inhibit the inflammatory process.[18] In study by ZHENHAI LIU et al, it was found that plasma IL-6 increased after laryngoscopy insertion. We speculated that target-controlled plasma infusion of lidocaine at 3 mg/L could inhibit the laryngoscopy-mediated inflammatory response; patients with vocal cord polyp surgery, clinical need to wake up completely, in order to avoid inhalation of blood and oropharyngeal secretions, many authors have proved that lidocaine provides efficient analgesia without any serious side effects and complications, which can effectively avoid the traditional analgesia method of sedation, dizziness, respiratory depression, nausea, vomiting, and stomach discomfort.[4,5] In this study, the above adverse reactions and toxic reactions of related local anesthetics, such as arrhythmia, circulatory inhibition, convulsions, delayed recovery, unconsciousness, and paresthesia during recovery were still not found.

In conclusion, target-controlled plasma infusion of lidocaine can reduce the consumption of propofol in patients undergoing vocal cord polypectomy by supporting laryngoscopy, and the hemodynamics were more stable, and reduced the coughing reaction in the wake period and throat pain after extubation.

The plasma concentration of lidocaine set in this study was only 3 mg/L, with a single concentration. Whether a lower plasma concentration can achieve a stable anesthetic effect requires further study.

Author contributions

Conceptualization: Qi Hang.
Data curation: RuiLan Wu.
Formal analysis: LongYuan Zhou.
Funding acquisition: Chang Cai.
Investigation: Qi Hang.
Methodology: Chang Cai, XingHua Bi.
Project administration: Yong QI.
Supervision: Yong QI.
Validation: Yong QI.
Writing – original draft: LongYuan Zhou.

References

[1] Hans GA, Lauwick SM, Kaba A, et al. Intravenous lidocaine infusion reduces bispectral index-guided requirements of propofol only during surgical stimulation. Br J Anaesth 2010;105:471–9.
[2] Altermatt FR, Bugedo DA, Delfino AE, et al. Evaluation of the effect of intravenous lidocaine on propofol requirements during total intravenous anaesthesia as measured by bispectral index. Br J Anaesth 2012;108: 979–83.
[3] De Oliveira GSJr, Fitzgerald P, Streicher LF, et al. Systemic lidocaine to improve postoperative quality of recovery after ambulatory laparoscopic surgery. Anesth Analg 2012;115:262–7.
[4] Panti A, Cafrita IC, Clark L. Effect of intravenous lidocaine on cough response to endotracheal intubation in propofol anaesthetized dogs. Vet Anaesth Analg 2016;43:405–11.
[5] Tauzin-Fin P, Bernard O, Sesay M, et al. Benefits of intravenous lidocaine on post-operative pain and acute rehabilitation after laparoscopic nephrectomy. J Anaesthesiol Clin Pharmacol 2014;30:366–72.
[6] Couceiro TCM, Lima LC, Couceiro LM, Valenza MM. Intravenous lidocaine to treat postoperative pain. Rev Dor 2014;15:55–60.
[7] Koppert W, Ostermeier N, Sittl R, et al. Low-dose lidocaine reduces secondary hyperalgesia by a central mode of action. Pain 2000;85: 217–24.
[8] Ghause MS, Singh V, Kumar A, et al. A study of cardiovascular response during laryngoscopy fintubation and their attenuation by ultra short acting b-blocker esmolol. Indian J Anaesth 2002;46:104–6.
[9] Yumoto E. Laryngeal surgery-vocal cord polyp and anaesthesia [in Japanese]. Nihon Jibiinkoka Gakkai Kaiho 2013; 116:34-37.
[10] Wang D, Song Z, Zhang C, Chen P. Bispectral index monitoring of the clinical effects of propofol closed-loop target-controlled infusion systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) 2021;100:e23930.
[11] Yang N, Yang M, Peng W, et al. Comparison of anesthesia effects between closed-loop and open-loop target controlled infusion of propofol using the bispectral index in abdominal surgery. Zhong Nan Da Xue Bao Yi Xue Ban 2020;45:1419–24.
[12] Forster C, Vanhaudenhuyse A, Gast P, Joris J. Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: a randomised placebo-controlled study. Br J Anaesth 2018;121:1059–64.
[13] Hamaya Y, Dohi S. Differences in cardiovascular response to airway stimulation at different sites and blockade of the response by lidocaine. Anesthesiology 2000;93:95–103.
[14] Lan B. Trafficking regulates the subcellular distribution of voltage-gated sodium channels in primary sensory neurons. Mol Pain 2015;11:60–3.
[15] Baiping L, James E, Ira S. Neuroprotective effects of Low-dose lidocaine in a rat model of transient focal cerebral ischemia. Anesthesiology 2001;95:445–51.
[16] Ho MLJ, KeH SJ, Stevens J. Intravenous lidocaine infusions for 48 hours in open colorectal surgery: a prospective, randomized, double-blinded, placebo-controlled trial. Korean J Anesthesiol 2018;71:57–65.
[17] McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery a systematic review of randomized controlled trials. Drugs 2010;70: 1149–63.
[18] Masic D, Liang E, Long C, et al. Intravenous lidocaine for acute pain: a systematic review. Pharmacotherapy 2018;38:1250–9.