INPLASY PROTOCOL

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None declared.

Efficacy of perioperative lidocaine infusion in pain management and quality of recovery following thyroid surgery

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Review question / Objective: **To figure out if intravenous infusion of lidocaine can relieve pain and facilitate recovery in patients underwent thyroid surgery.**
Eligibility criteria: **Inclusion criteria: (1)Population: patients underwent elective thyroid surgery under general anaesthesia; (2)Intervention: intervention group received infusion of lidocaine perioperatively; (3)Comparisions: control group received the same amount of saline or remained untreated; (4)Outcomes: pain scores, quality of recovery after surgery, opioids consumption during and after operation, propofol consumption, perioperative hemodynamics, emergence variables(emergence and extubation time), cough during extubation, time to first analgesic request, volume of drainage, length of PACU and hospital stay, the number of patients receiving rescue antiemetic agents in PACU and surgical wards, PONV(postoperative nausea and vomiting), POST(postoperative sore throat), and adverse effects (hypotention, bradycardia, lidocaine toxicity,etc.); (5)Study design:RCTs. Exclusion criteria:(1)patients involved were aged<18yr; (2)lidocaine was not given intravenously; (3)no comparison between lidocaine and placebo; (4)abstracts, letters, retrospective studies, conference articles, editorials, reviews, case reports, repeated studies, and biochemical trials are also excluded; (5)without sufficient data in outcomes mentioned above. We only include published literature, placing no limitation on time and language. Any non-English studies will be translated by an online translator.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 April 2022 and was last updated on 17 April 2022 (registration number INPLASY202240101).

INTRODUCTION

Review question / Objective: **To figure out if intravenous infusion of lidocaine can relieve pain and facilitate recovery in patients underwent thyroid surgery.**

Condition being studied: **Thyroid surgery, frequently performed in patients who developed thyroid diseases, is usually considered a minor surgery. However, many people still complained about**

moderate to severe pain after thyroid surgery, especially on the first postoperative day. Skin incision, pharyngolaryngeal discomfort after intubation, neck hyperextension, surgical manipulation and inflammation may serve as reasons for postoperative pain. Patients who feel pain after surgery suffered from the unpleasant experience, feared to move and had a bad recovery. Besides, persistent or severe postoperative pain could cause changes of psychological and mental status, such as anxiety and depression. It is reported that bilateral superficial cervical plexus block(BSCPB) could reduce postoperative pain after thyroid surgery, but it is invasive and may induce many complications, such as phrenic nerve and recurrent laryngeal nerve block. Opioids are still the most effective drugs for treating postoperative pain, while they are associated with a series of adverse effects such as respiratory depression, nausea, vomiting and pruritis, which could even be more intolerable than the pain itself. The application of Non-steroidal anti-inflammatory drugs is also limited, for it may induce postoperative bleeding inside the wound, which can sometimes be fatal to patients. Consequently, medications with definite analgesic effects but little side effects are urgent needed for patients underwent thyroid surgery. Lidocaine is a commonly used amide-type local anesthetic with analgesic and anti-inflammatory properties. The mechanism maybe that lidocaine is associated with sodium channel blockade of peripheral afferent pain fibres, attenuation of central excitability in the dorsal horns of the spinal cord, inhibition of neutrophil activation and reduction of cytokines production when used intravenously. The perioperative administration of intravenous lidocaine has been proved to be effective in pain management and recovery promotion in cholecystectomy, spinal surgery and colorectal surgery. However, benefits concerning infusion of lidocaine during thyroid operations are controversial. Some researchers argued that intravenous lidocaine effectively reduced postoperative pain following thyroid surgery as well as improved the quality of recovery, while the others suggest the opposite, namely intravenous lidocaine failed to reduce postsurgical pain or improved the quality of recovery. Furthermore, no meta-analysis has been conducted to explore the effects of lidocaine infusion in thyroid surgery. As a result, we design this system review and meta analysis, aiming to reach a conclusive result about efficacy of lidocaine infusion in thyroid surgery.

METHODS

Search strategy: We conducted a systematic search in the following eight databases: the Cochrane Library, PUBMED, Web of science, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang, VIP, and China Biomedical Literature Database(CBM). Search terms in PUBMED are as follows: ("Infusions, Intravenous"[Mesh] OR "Administration, Intravenous"[Mesh] OR “intravenous”[All fields] OR “intravenously”[All fields] OR “infusion”[All fields] OR “infusions”[All fields] OR “systemic”[All fields]) AND ("Lidocaine"[Mesh]) OR “lidocaine”[All fields] OR “lignocaine”[All fields] OR “xylocaine”[All fields]) AND ("Thyroid (USP)"[Mesh] OR "Thyroid Gland"[Mesh] OR "Thyroidectomy"[Mesh] OR “thyroidectomy”[All fields] OR “thyroidectomies”[All fields] OR “thyroid surgery”[All fields] OR “thyroid operation” [All fields]).

Participant or population: Patients underwent elective thyroid surgery.

Intervention: Received an intraoperative lidocaine infusion (1.0-2.0 mg/kg bolus followed by 1.0-3.0 mg/kg/h).

Comparator: Received the same amount of saline or were left untreated.

Study designs to be included: Randomised controlled trials only.

Eligibility criteria: Inclusion criteria: (1)Population: patients underwent elective thyroid surgery under general anaesthesia; (2)Intervention: intervention group received infusion of lidocaine perioperatively;

(3)Comparisions: control group received the same amount of saline or remained untreated; (4)Outcomes: pain scores, quality of recovery after surgery, opioids consumption during and after operation, propofol consumption, perioperative hemodynamics, emergence variables(emergence and extubation time), cough during extubation, time to first analgesic request, volume of drainage, length of PACU and hospital stay, the number of patients receiving rescue antiemetic agents in PACU and surgical wards, PONV(postoperative nausea and vomiting), POST(postoperative sore throat), and adverse effects (hypotention, bradycardia, lidocaine toxicity,etc.); (5)Study design:RCTs. Exclusion criteria: (1)patients involved were aged<18yr; (2)lidocaine was not given intravenously; (3)no comparison between lidocaine and placebo; (4)abstracts, letters, retrospective studies, conference articles, editorials, reviews, case reports, repeated studies, and biochemical trials are also excluded; (5)without sufficient data in outcomes mentioned above. We only include published literature, placing no limitation on time and language. Any non-English studies will be translated by an online translator.

Information sources: A systematic search will be conducted in the Cochrane Library, PUBMED,Web of science ,EMBASE,China National Knowledge Infrastructure (CNKI), Wanfang, VIP, and China Biomedical Literature Database(CBM). In addition, we will also search reference lists of relevant reviews and all RCTs.

Main outcome(s): (1)Postoperative pain levels up to 48 hours postoperatively as measured by the VAS or NRS score, split by static and dynamic pain; (2)quality of recovery after surgery(QoR-40 scores).

Additional outcome(s): (1)perioperative opioids and propofol consumption; (2)hemodynamic variables during operation; (3)emergence variables(time to recovery and extubation); (4)incidence of cough during extubaton; (5)time to first analgesic request; (6)volume of drainage; (7)length of PACU and hospital stay; (8)the number of patients receiving rescue antiemetic agents in PACU and surgical wards; (9)PONV(postoperative nausea and vomiting); (10)POST(postoperative sore throat); (11)adverse events(hypotention, bradycardia, lidocaine toxicity, etc.).

Data management: Pain scores(at rest or during movement), as assessed by the visual analogue scale(VAS) or numeric rating scale(NRS), are standardized to a 0-10 scale. The VAS and NRS for pain are treated as equivalent. Medians and interquartile ranges of relevant outcomes are converted to means and standard deviations using the method developed by Hozo SP. If data are presented in statistical plots, WebPlotDigitizer is used for extracting numerical data. Where opioid drugs other than morphine were provided by the study, a standard conversion table are used to standardise all opiates to intravenous morphine milligram equivalents.

Quality assessment / Risk of bias analysis: The methodological quality of the selected studies will be assessed by two blinded reviewer according to the revised Cochrane risk of bias tool for randomized trials (RoB 2.0). Any disagreements will be settled by a third person.

Strategy of data synthesis: Review Manager and Stata are going to be used for data management. For continuous variables, we will calculate the mean difference(MD) and 95% confidence intervals (CIs) by the method of inverse variance. For dichotomous variables, we will calculate the risk ratio (RR) and 95% CIs based on the method of Mantel-Haenszel. $\chi 2$ test and I2 statistics are used for evaluating the heterogeneity across studies for each analysis, with P-value on $\chi 2$ test 50% meaning significant heterogeneity. When the heterogeneity are statistically significant, a random-effects model is used. Otherwise, a fixed-effects model is used. We plan to assess the overall certainty of evidence for each outcome using the Grading of Recommendations Assessment,

Development, and Evaluation (GRADE) approach. Furthermore, we would like to carry out the trial sequential analysis (TSA) of main outcomes to see if the results are reliable. The Egger's regression test and funnel plots will be used to assess publication bias.

Subgroup analysis: Subgroup analysis will be conducted to evaluate pain scores at different time points postoperatively. If the necessary data are available, subgroup analysis of perioperative opioids consumption will also be performed among different combinations of loading and infusion doses.

Sensitivity analysis: Studies published in Chinese and defined as low quality are eliminated for sensitivity analysis respectively.

Language: No limitation.

Country(ies) involved: China.

Keywords: lidocaine infusion, thyroid surgery, postoperative pain, quality of recovery.

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