

Analgesic efficacy of Intraoperative lidocaine infusion in patients undergoing thyroidectomy

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SUMMARY

OBJECTIVE: A significant proportion of patients may experience moderate pain requiring treatment in the postoperative first 24 h following thyroidectomy. The aim of this study was to investigate the evaluation of postoperative patient-reported pain from intraoperative intravenous infusion of lidocaine in patients undergoing thyroidectomy surgery.

METHODS: A total of 40 patients with American Society of Anesthesiologists physical status classifications I and II, aged 18–65 years, who were scheduled for elective thyroidectomy with the same indications under general anesthesia at the Ataturk University Medical Faculty's Ear, Nose, and Throat Clinic between November 2019 and February 2020, were divided into two equal groups as randomized and double-blind. Before induction of anesthesia, patients in the lidocaine group were given 1.5 mg/kg lidocaine IV bolus infusion during the operation and until the end of the first postoperative hour, followed by a continuous infusion of 1.5 mg/kg/h. Patients in the control group were given 0.9% isotonic solution according to the same protocol. In the postoperative period, 50 mg of dexketoprofen trometamol was administered and repeated every 12 h. Postoperative pain scores, additional analgesia, and side effects were recorded.

RESULTS: Postoperative pain scores were significantly lower in the lidocaine group (n=20) compared to the control group (n=20) at 30 min and 1st, 2nd, 4th, 8th, and 12th h postoperatively ($p < 0.05$). Additional analgesia requirements were also significantly lower in the lidocaine group than in the control group ($p < 0.05$).

CONCLUSION: We recommended the use of intravenous lidocaine infusion intraoperatively in thyroidectomy surgery as it reduces pain scores.

KEYWORDS: Lidocaine. Thyroidectomy. Pain. Analgesics.

INTRODUCTION

Surgical treatment is of considerable importance in diseases of the thyroid gland, particularly thyroid gland malignancies¹. The principal causes of post-thyroidectomy pain include skin incisions to the neck region, cervical hyperextension, damage associated with orotracheal intubation, and drains inserted into the surgical area. Studies have reported that 90% require opioids in the first 24 h after thyroid surgery².

The multimodal analgesia technique, in which analgesics with different effect mechanisms are combined, is becoming increasingly used in the management of postoperative pain. With this technique, analgesia dosages are reduced through the additive and synergistic effects of the analgesic agents, fewer side effects occur, and more effective analgesia is provided³.

Lidocaine, one of the most commonly used anesthetic drugs, was first synthesized in 1942 under the name Xylocaine[®] and

was later approved for use in Sweden in 1948⁴. Lidocaine can be used clinically in different ways and by different routes of administration (epidural, subarachnoid, intrapleural, intravenous, intramuscular, intraarticular, and topical). It is also used in central and peripheral nerve blocks, in regional intravenous anesthesia applications, in the treatment and prophylaxis of life-threatening ventricular arrhythmias, in the treatment of chronic and neuropathic pain, and recently for postoperative pain control with IV infusion^{5,6}.

Lidocaine has analgesic, antihyperalgesic, and anti-inflammatory properties and thus has many beneficial effects in many surgeries^{7,8}. Several studies have shown that intravenous IV lidocaine use in the intraoperative period reduces postoperative pain⁹⁻¹³.

The aim of this study was to investigate the effect of intraoperative IV infusion of lidocaine on pain scores in patients undergoing thyroidectomy.

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Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.

Received on May 09, 2022. Accepted on September 30, 2022.

METHODS

This study was carried out after obtaining approval numbered B.30.2.ATA.0.01.00/552 from the Ethics Committee of Ataturk University Faculty of Medicine, which convened on November 07, 2019, at Ataturk University Faculty of Medicine, Department of Otorhinolaryngology. The study included patients with American Society of Anesthesiologists (ASA) physical status classifications I and II, aged 18–65 years, and who were scheduled for elective thyroidectomy surgery with the same indications under general anesthesia at the Ataturk University Medical Faculty's Ear, Nose, and Throat Clinic in Turkey between November 2019 and February 2020. All advantages and disadvantages were explained to all patients both verbally and in writing one day before surgery, after which informed consent was obtained. Patients with an ASA score of 3 and above, patients allergic to lidocaine, patients with severe hepatic and renal impairment, patients with a long history of opioid and non-opioid analgesic use, history of gastrointestinal bleeding, peptic ulcer and inflammatory patients, body weight less than 50 kg, patients who had to discontinue drug therapy for any reason during the study, did not volunteer to participate in the study, could not cooperate, and were inadequate in evaluating the postoperative pain score were excluded from the study.

The present research was planned as a prospective, randomized, placebo-controlled, double-blinded clinical study. The patients were randomly divided into two groups using a computer program at a ratio of 1:1. Thus, lidocaine group (n=20) and control group (n=20) were formed. Practitioners, patients, and postoperative pain evaluators did not know which drug was administered to the group. The volumes of preoperative, intraoperative, and postoperative infusion solutions prepared for the lidocaine group were prepared with the same volume of 0.9% isotonic solution as those for the control group to ensure a double-blind study. All patients were taken to the operating room after administration of 6 mL/kg crystalloid and crystalloid infusion (8 mL/kg/h) was continued during the surgery. All personnel in the operating room were unaware of randomization. All patients underwent standard ECG, peripheral oxygen saturation (SpO₂), and noninvasive blood pressure monitoring, and all measurements were recorded at 5-min intervals during surgery. Anesthesia in both groups was established by a specialist anesthetist, with anesthesia induction being performed with a lidocaine 1.5 mg/kg iv bolus (lidocaine group) or 0.9% isotonic solution 1.5 mg/kg iv bolus (control group), 2–3 mg/kg propofol, 0.25–1 µg/kg/min remifentanyl, and 0.6 mg/kg rocuronium. Lidocaine infusion at 1.5 mg/kg/h was maintained during surgery and

in the first hour in the postanesthetic care unit. Postoperative pain scores were evaluated at postoperative 30 min and 1, 2, 4, 8, 12, and 24 h. All patients were given 50 mg iv dexketoprofen 30 min before the end of the surgery and was repeated every 12 h after the surgery. An anesthetist, unaware of the drugs used for analgesia and the grouping, made the postoperative evaluation of the patients. Postoperative analgesia was assessed using the visual analog scale (VAS) (VAS 0=no pain, VAS 10=the most severe pain that can be felt). Patients with a VAS score of 4 and above were administered 1 mg/kg tramadol iv as additional analgesics and recorded. Toxicity symptoms such as tongue numbness, arrhythmia, metallic taste, tinnitus, anaphylaxis, nausea, and vomiting were recorded during the 24-h follow-up.

Thyroidectomy was performed in all patients with the same technique, the same indication, and the same surgical team.

Age (years), sex, height (cm), weight (kg), BMI (kg/m²), VAS scores at rest (at 1, 2, 4, 8, 12, and 24 h), time of the first analgesia (min), side effects such as nausea, vomiting, arrhythmia, metallic taste, tinnitus, and anaphylaxis, total surgery time and duration of anesthesia (min), and total analgesic consumption were evaluated.

Statistical analysis

Data were analyzed using SPSS (Statistical Package for the Social Sciences) version 20.0 software. Categorical variables were recorded as number and percentage, and numerical variables as mean±standard deviation. The compatibility of normal distribution for numerical variables was evaluated using the Kolmogorov-Smirnov test, while z-values calculated for skewness and kurtosis were assessed using graphs. The Kruskal-Wallis and Friedman tests were applied to non-normally distributed numerical variables, while the Bonferroni-corrected Mann-Whitney U test and Bonferroni-corrected Wilcoxon test were employed in post-hoc analyses. The χ^2 test was applied in the analysis of categorical variables. Correlations between non-normally distributed constant variables were evaluated using Spearman's rho correlation analysis. P<0.05 were regarded as statistically significant.

RESULTS

A total of 40 patients undergoing thyroid surgery under general anesthesia completed this study. Patients were randomly divided into two equal groups (20 patients in each group).

Demographic data such as age (years), sex, height (cm), body weight (kg), and body mass index (BMI, kg/m²) are shown in Table 1.

Operation data of the groups (duration of surgery, duration of anesthesia, and the average gland weight) are shown in Table 2.

Time-dependent changes in VAS scores between the groups are shown in Table 3 and Figure 1. VAS scores at postoperative 30 min and 1, 2, 4, 8, and 12 h were statistically significantly lower in the lidocaine group than in the control group ($p < 0.05$). No significant difference was determined between the VAS scores in two groups at 24 h postoperatively ($p = 0.060$). The highest VAS scores were observed at the postoperative 30th minute in both groups, and the VAS scores decreased gradually in both groups except at the 4th hour in the lidocaine group.

Additional analgesic requirements (tramadol 1 mg/kg) were significantly lower in the lidocaine group compared to the control group ($p = 0.027$). Two of the 14 cases in the control group with additional analgesic requirements also needed a second dose of tramadol. No second tramadol requirement occurred in the lidocaine group.

The additional analgesic requirement occurred within the first 4 h postoperatively in all cases with such requirements. In terms of time of first analgesic requirement, first tramadol use occurred significantly later in the lidocaine group compared to the control group ($p = 0.042$). A comparison of the two groups in terms of total tramadol consumption in the first 24 h postoperatively revealed that the total analgesic requirement was significantly lower in the lidocaine group than in the control group ($p = 0.019$).

No nausea, vomiting, anaphylaxis, or arrhythmia occurred as lidocaine-related side effects in any case in the lidocaine group. No cases of lidocaine toxicity were also observed. No intraoperative excessive hemorrhage, postoperative hematoma, or vocal cord paralysis occurred in any case.

DISCUSSION

Although pain occurring following thyroidectomy is not as severe as that developing after major surgery, such postoperative pain must still not be overlooked¹⁴. Pain severity is subjective and highly variable, and it is important to ameliorate pain. The

Table 3. Pain scores.

	Lidocaine group (n=20, Mean±SD)	Control group (n=20, Mean±SD)	p-value
VAS 30. min	3.05±0.6	4.25±1.37	0.001
VAS 1. h	2.55±0.6	3.35±0.88	0.002
VAS 2. h	2.45±0.83	3.05±0.69	0.008
VAS 4. h	2.5±0.51	2.95±0.6	0.021
VAS 8. h	2.1±0.55	2.65±0.59	0.006
VAS 12. h	1.95±0.51	2.4±0.6	0.018
VAS 24. h	1.30±0.47	1.6±0.5	0.060

n: number of patients; min: minutes; $p < 0.05$: statistically significant; SD: standart deviation; VAS: visual analog scale.

Table 1. Patients demographic data (mean±std. deviation).

	Lidocaine group (n=20, Mean±SD)	Control group (n=20, Mean±SD)	p-value
Gender (F/M)	15/5	17/3	0.695
Age (year)	46.5±10.15	49.8±11	0.285
Height (cm)	164.7±6.53	163.05±5.34	0.4
Weight (kg)	75.2±7.52	73.4±7.24	0.724
BMI (kg/m ²)	27.79±3.17	27.7±3.39	0.818

n: number of patients; F: female; M: male; $p < 0.05$: statistically significant; SD: standart deviation; BMI: body mass index.

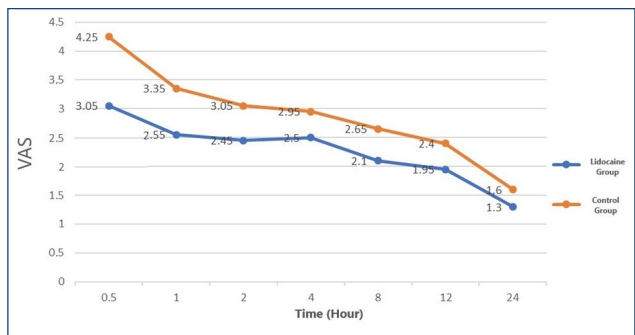


Figure 1. The relation between pain scores and time in the groups in postoperative period.

Table 2. Operation data (mean±std. deviation).

	Lidocaine group (n=20, Mean±SD)	Control group (n=20, Mean±SD)	p-value
Duration of surgery (min)	119.75±29.4	130.25±24.79	>0.05
Duration of anesthesia (min)	146±29.54	158.25±23.91	>0.05
The average gland weight (g)	43.2±1.361	43.05±1.495	>0.05
Recurrent laryngeal nerve injury	0	0	

n: number of patients; min: minutes; $p < 0.05$: statistically significant; g: gram.

aim of postoperative pain control is to reduce the pain felt by the patient, and various studies have been performed for the reduction of post-thyroidectomy pain^{2,10,15,16}.

The principal causes of post-thyroidectomy pain include the skin incision to the neck region, cervical hyperextension, damage associated with orotracheal intubation, and drains inserted in the surgical site².

“Multimodal analgesia” methods, in which more than one drug and technique are combined, have begun being employed in the management of postoperative pain. Analgesia dosages are thus restricted by making use of the additive and synergistic effects of the analgesic agents, and more effective analgesia is provided with fewer side effects^{3,17}. The present study investigated the effects of iv lidocaine administered intraoperatively and in the postoperative first hour on postoperative pain and analgesic consumption in patients undergoing thyroidectomy.

Choi et al. investigated the clinical effect of perioperative lidocaine infusion by dividing 56 patients scheduled for thyroidectomy into two groups. The patients in the lidocaine group received 1.5 mg/kg lidocaine iv bolus infusion immediately prior to surgery, followed by continuous 2 mg/kg/h lidocaine infusion. The patients in the control group received saline solution by using the same method. Postoperative VAS scores were significantly lower in the first 4 h after surgery in the lidocaine group compared to the control group. The highest VAS scores in both groups were registered in the postoperative care unit, decreasing in a time-dependent manner in the lidocaine group with the exception of the 12th postoperative hour. Total fentanyl consumption and the total number of analgesia requirements were significantly higher in the control group than in the lidocaine group¹¹. Similarly, in the present study, the highest VAS scores in both groups were observed in the postoperative care unit. VAS scores in the lidocaine group were significantly lower than those in the control group, with the exception of the postoperative 24th hour.

Statistically significantly lower VAS scores have been reported in patients receiving lidocaine infusion compared to opioid analgesia in various types of surgery^{12,18}. Terkawi et al. showed that intraoperative lidocaine infusion in major abdominal surgery reduced postoperative pain and accelerated the return of bowel functions¹⁹. Wang et al. investigated the effects of postoperative pain of lidocaine infusion in gynecological surgeries, applying 2 mg/kg maintenance following a 1.5 mg/kg bolus dose, and observed significantly lower VAS scores with lidocaine infusion²⁰.

McCarthy et al. published a meta-analysis consisting of 16 studies comparing iv lidocaine infusion with placebo in abdominal surgery, cardiac surgery, orthopedic surgery, and

tonsillectomy cases. Decreases were determined in intraoperative anesthetic requirements, postoperative pain, and additional analgesia requirements in the groups receiving iv lidocaine infusion in the abdominal surgery cases. In contrast, no postoperative analgesic efficacy of lidocaine infusion was observed in the tonsillectomy, total knee arthroplasty, and coronary bypass surgery cases¹³.

Additionally, in a study of patients undergoing hysterectomy, De Oliveira et al. reported no significant difference between the patients in the lidocaine group (2 mg/kg/h lidocaine) and the control group (0.9% saline solution) in terms of pain severity of additional morphine consumption²¹.

The inconsistencies between these findings in the previous literature and the present study may be due to variations in the dosages of lidocaine infused or to lidocaine being administered at different times. In addition, different types of surgery and different areas capable of affecting peripheral and central sensitization patterns may also have resulted in these discrepancies. Another explanation for these inconsistencies may involve individual pain threshold variations and the different responses to analgesic drugs of different patient groups.

Thyroid surgery generally involves a high incidence of postoperative nausea and vomiting. The mechanisms involved in postoperative nausea and vomiting after thyroidectomy are still unclear, although they may be associated with surgical inflammatory responses caused by surgical injury to the structures of the neck and the stimulation of vagal afferents²². In the present study, the incidence of nausea and vomiting in the lidocaine group was significantly lower than in the control group. In one meta-analysis, Marret et al. evaluated 170 patients from five different randomized controlled studies and reported 20% less nausea and vomiting in patients receiving lidocaine infusions compared to the control (saline) groups²³.

Some previous studies have avoided administering non-steroid anti-inflammatory agents in the postoperative period since these increase the risk of postoperative hemorrhage and hematoma^{15,24,25}. Despite our use of dexketoprofen as an analgesic agent in the postoperative period in the present study, no postoperative hemorrhage or hematoma developed in any patient.

Examination of the data for patients receiving a 1.5 mg/kg bolus dose followed by a 1.5 mg/kg/h lidocaine infusion in this study revealed no toxicity findings in any case. There are a number of limitations to the present study. The most important limitation of our study was the small sample size. The fact that plasma lidocaine levels were not investigated may be a limitation of this research. However, the lidocaine dosage applied in this study was lower than that in previous studies in which

toxic lidocaine levels were not observed and in which no side effects were reported. In addition, patients were followed up until the postoperative 24th hour. A longer monitoring period might have revealed the duration of the decreases observed in VAS scores.

CONCLUSION

We conclude that intraoperative IV lidocaine infusion is an effective alternative method that can be used in thyroidectomy operations as a component of multimodal analgesia.

ACKNOWLEDGMENTS

We want to thank Mr. Carl Austin Nino Rossini for his precious contribution.

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AUTHORS' CONTRIBUTIONS

EA: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **MSG:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **AK:** Data curation, Formal Analysis, Methodology, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **AS:** Conceptualization, Data curation, Formal Analysis, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **IA:** Data curation, Formal Analysis, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing.

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