



Research article

Comparative study of lidocaine- saline versus saline as washout for lumpectomy cavity on acute postoperative pain

Payman Rezagholi^a, Karim Nasser^{b,c}, Arvin Barzanji^{d,e}, Khaled Rahmani^f,
Asra foroughi^g, Hassan Moayeri^{h,*}

^a Department of Operating Room, School of Nursing and Midwifery, Besat Hospital, Kurdistan University of Medical Sciences, Sanandaj, Iran

^b Department of Anesthesiology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

^c Social Determinants of Health Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

^d Student Research Committee, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

^e Department of Anesthesiology, Faculty of Paramedical Sciences, Kurdistan University of Medical Sciences, Sanandaj, Iran

^f Liver and Digestive Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

^g Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

^h Department of Surgery, School of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

ARTICLE INFO

Keywords:

Lumpectomy
Lidocaine
Saline solution
Postoperative pain
Breast surgery

ABSTRACT

Purpose: This study aimed to evaluate the impact of lidocaine-saline solution compared to saline alone for washing out the lumpectomy cavity, focusing on its effect on acute postoperative pain—a prevalent and significant concern among patients undergoing breast surgery.

Methods: In this comparative study, 72 patients scheduled for lumpectomy surgery were randomly assigned to either the lidocaine-saline or saline group. The lidocaine-saline group was administered a washout of the lumpectomy cavity with 2 % lidocaine at a dosage of 1.75 mg/kg in 0.9 % normal saline, whereas the saline group received a washout with an equivalent volume of 0.9 % normal saline. We recorded the participants' basic characteristics, heart rate, blood pressure, the incidence and intensity of pain (measured by the visual analogue scale), and the usage of post-operative analgesics.

Results: The two study groups did not differ significantly in their basic characteristics, heart rate and blood pressure. The saline group had significantly higher pain intensity than the lidocaine-saline group at 30 min after surgery (4.61 vs. 2.88, $P < 0.0001$) and at all other time points ($P < 0.001$). The saline group also took the first dose of analgesics earlier than the lidocaine-saline (46.66 Vs. 170.55 min, $P < 0.001$) and used a significantly higher mean dose of meperidine (77.50 mg vs 33.47 mg, $P < 0.001$).

Conclusion: The use of a lidocaine-saline wash during lumpectomy procedures can significantly reduce postoperative pain and lower the necessity for analgesics in patients who have undergone breast surgery.

* Corresponding author.

E-mail address: moaiery@gmail.com (H. Moayeri).

<https://doi.org/10.1016/j.heliyon.2024.e39265>

Received 7 March 2024; Received in revised form 8 October 2024; Accepted 10 October 2024

Available online 11 October 2024

2405-8440/© 2024 Published by Elsevier Ltd.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Breast cancer is the most prevalent cancer among women, affecting both developing and developed nations. A WHO report indicates that in 2022, breast cancer was responsible for the deaths of 670,000 women, with 2.3 million new diagnoses [1]. Additionally, breast cancer has the highest rate among women, and represents includes 25 % of all cancers in Iran [2]. Over the past decade, the incidence of breast cancer has seen a rapid increase in most developing countries. In Iran, while the occurrence of breast cancer is surpassed by stomach and esophageal cancers, it is nonetheless recognized as the most common cancer across the entire population, according to the national cancer registry statistics [1].

Lumpectomy is a surgical technique where only the cancerous tissue is excised from the breast. Through a minimal incision, surgeons' access and remove the tumor. This method is considered relatively safe as it maintains the breast's shape and conserves most of its tissue, hence it is also referred to as breast-conserving surgery or partial mastectomy [2]. However, postoperative pain is a frequent complication of lumpectomy surgery, often resulting from bruising, stretching, or nerve damage incurred during the procedure [3].

Postoperative pain, an acute condition, is associated with the extent and location of the surgery, the patient's psychological and physiological profile, as well as the manipulation and damage to tissues. It constituting an adverse sensory and emotional experience that stems from actual or possible tissue damage [4]. Damage to peripheral tissue and nerves leads to a local inflammatory reaction, which increases the level of pro-inflammatory cytokines and sensitizes the central and peripheral nervous systems, leading to severe pain [5]. Post-operative pain, remains a common issue for patients. Despite the availability of potent analgesics, 30–70 % of patients still report experiencing pain after surgery. Consequently, the utilization of local anesthetics is regarded as a cost-effective, lower-risk, and easy approach [6]. Without proper management, postoperative pain can lead to various physiological complications. These include delayed gastrointestinal function, resulting in issues such as nausea and vomiting [7] and the initiation of stress responses that compromise the immune system and delay wound healing [8]. Surgeries involving the chest or upper abdomen are linked to respiratory complications, which may reduce vital capacity and contribute to conditions like atelectasis and pneumonia [9]. Pain can also intermittently affect the cardiovascular system, increasing heart rate and vascular resistance, potentially leading to ischemic heart events [7]. Surgeons prioritize the management of postoperative pain to speed up patient recovery, shorten hospital stays, and reduce post-surgical morbidity [10]. The infiltration of local anesthetics into the surgical site is a cost-effective analgesic technique that is both safe and associated with minimal side effects. Theoretically, local application diminishes pain signal transmission from the wound, attenuates the inflammatory response, and prevents nociceptor sensitization [11]. Variations in the effectiveness of local anesthetics can be attributed to the volume and concentration, factors affecting absorption and tissue diffusion, and the site of medication injection [12]. For instance, the administration of 0.5 % bupivacaine and 2 % lidocaine was not effective in reducing postoperative pain in one study [13], whereas injections of 0.125 % bupivacaine and 0.3 % ropivacaine have shown efficacy in controlled clinical trials [14,15]. Lidocaine, an amino amide local anesthetic, induces a conduction nerve block, preventing stimulation and thereby reducing pain transmission [16]. Surgeons have constantly attempted to control postoperative pain in patients for faster recovery to reduce the length of hospital stay [17]. The use of local anesthetics for pain relief not only lessens the dependence on narcotics but also improves pain tolerance and decreases the incidence of nausea and vomiting in patients [18].

Considering the variation in surgical practices, where some surgeons prefer using normal saline while others opt for a combination of normal saline and local anesthetics for cleaning the surgical site, and recognizing the importance of effective postoperative pain management and reducing opioid analgesic use, this study aims to evaluate the comparative efficacy of lidocaine-saline versus normal saline washing of the lumpectomy cavity in reducing acute postoperative pain.

2. Materials and methods

2.1. Design

This was a comparative study approved by Institutional Clinical Research Ethics Committee (Kurdistan University of Medical Sciences, ethics code IR.MUK.REC.1398.289), and all the patients provided written informed consent to participate in the study. To compare the effectiveness of the two methods in this study, we used a specific formula to determine the sample size. The alpha and beta values were set at 0.05 and 0.2, respectively, with an anticipated difference of 40 %. To enhance the study's precision, 36 individuals were included in each group, resulting in a total sample size of 72 participants.

2.2. Participants

A total of 72 patients scheduled for lumpectomy surgery at Besat and Kowsar hospitals in Sanandaj, Iran, who met the inclusion criteria, were enrolled in the study. The inclusion criteria included patients with an American Society of Anesthesiologists (ASA) classification of 1–2, aged over 18 years, and without a history of anxiety, cognitive disorders, depression, or psychotic disorders. The exclusion criteria encompassed patients who were chronically treated with analgesics such as narcotics, non-steroidal or steroidal anti-inflammatory drugs, those with a known sensitivity to lidocaine, and those with cardiovascular diseases.

Patients were randomly allocated to either the lidocaine-saline or saline group using a double-blind block randomization method. In each block, two patients were randomly assigned 'A' or 'B' codes. Based on these codes, they received either the normal saline-lidocaine wash or the normal saline wash during surgery. To preserve the study's blinding, patients were not informed of their group assignment. Furthermore, the solutions for each group were prepared in identical volumes by a scrub nurse who was not

involved in the study. The nurse responsible for evaluating the patients and recording the data was also unaware of the group assignments.

2.3. Comparison

Upon patient admission to the operating room and the establishment of an IV cannula, a Ringer solution (10 ml/kg) was administered before the initiation of anesthesia. General anesthesia was induced using same intravenous medications, including sodium thiopental (5 mg/kg), atracurium (0.6 mg/kg), and fentanyl (2 µg/kg), and maintained with 1.3 MAC isoflurane and fentanyl. Vital signs, including systolic and diastolic blood pressure, mean arterial pressure, heart rate, and blood oxygen saturation (SpO₂), were monitored upon patient admission and while resting on the bed.

The lidocaine-saline group received washing the lumpectomy cavity with a solution of 2 % lidocaine (LIGNODIC®, Caspian Tamin pharmaceutical company) at a concentration of 1.75 mg/kg mixed with 0.9 % normal saline (2 ml/kg). The saline group received a wash with an equivalent volume of 0.9 % normal saline. Blood pressure and heart rate were measured before and after the washout with saline and lidocaine, and the results were documented in the questionnaire.

2.4. Outcomes

The primary outcome of interest was pain intensity, assessed using the Visual Analog Scale (VAS), a 10-cm ruler that rates pain on a scale from 0 (no pain) to 10 (worst pain imaginable). Prior to the study, patients received training on how to use the VAS for pain reporting. Pain intensity was recorded in the questionnaire immediately after tracheal tube removal and patient transfer to the recovery room (time zero), and then at intervals of 15-, 30-, and 60-min post-admission to the recovery unit. Following transfer to the ward, pain intensity was measured at 2, 4-, 8-, 12-, and 24-h post-surgery using the VAS. If a patient’s VAS score exceeded 4, intravenous meperidine (0.4 mg/kg) was administered, and the initial administration was noted. Secondary outcomes, including the hemodynamic changes, anesthesia time, the requirement for analgesics (meperidine), and other potential side effects, were recorded

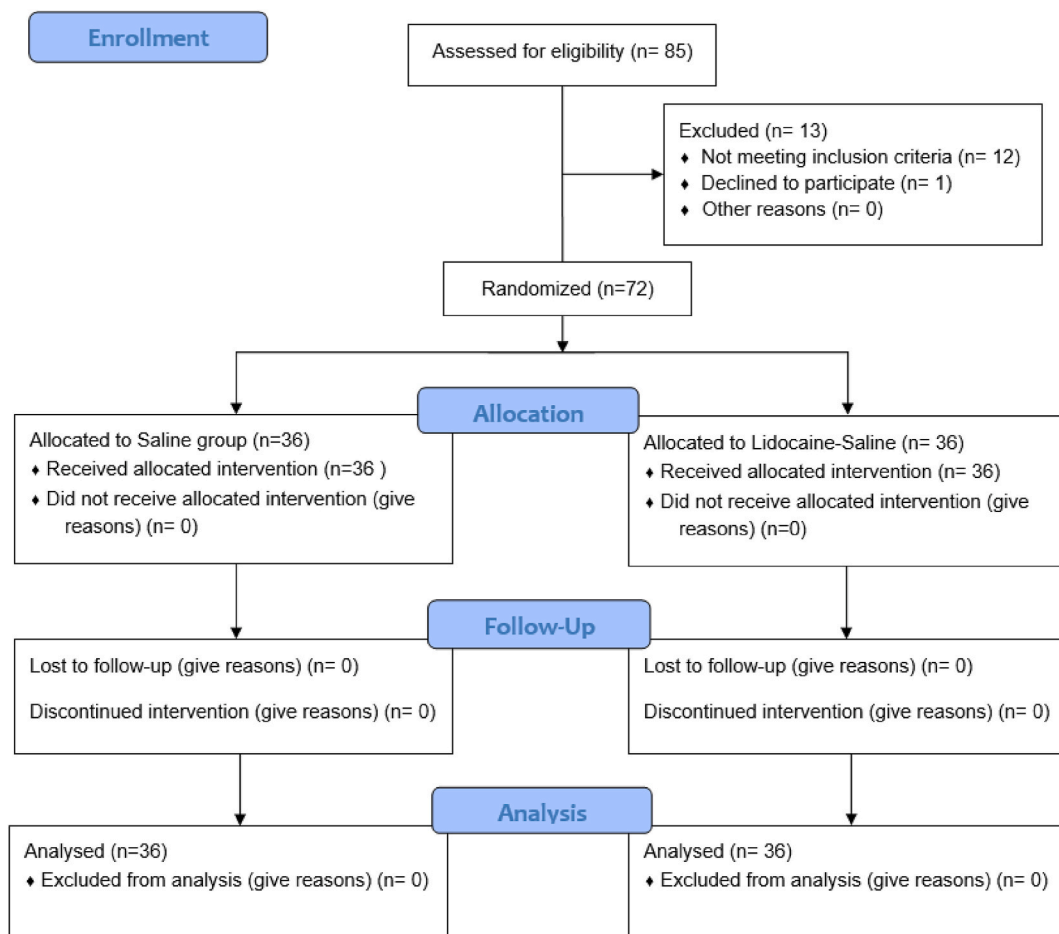


Fig. 1. Group randomization according to CONSORT 2010(17).

within 24 h post-operation. All patients received uniform postoperative care.

2.5. Statistical analysis

Data analysis was conducted using STATA 14 software. The normality of distribution was evaluated using the Kolmogorov–Smirnov test, and ordinal variables were treated as non-normally distributed. Descriptive statistics such as mean, standard deviation, frequency, relative frequency, and corresponding graphs were used to summarize the data. Depending on the variable type, statistical tests including the Mann-Whitney *U* test, Chi-square test, and Fisher's exact test were applied. Given the multiple time points for pain intensity measurements, a repeated measures ANOVA was utilized. A *p*-value of less than 0.05 was deemed statistically significant.

3. Results

In this study, the data of 72 patients were analyzed (Fig. 1).

There was no significant difference according to the age, body mass index (BMI), duration of anesthesia and duration of surgery (Table 1).

The highest level of postoperative pain in the saline group was observed 30 min after surgery, which was significantly higher than the lidocaine-saline group (4.61 vs. 2.88, $P < 0.05$). The intensity of pain at all times had a significant difference between the two groups ($P < 0.05$) (Table 2).

Based on data analysis, the heart rate, systolic and diastolic blood pressure before and after washing were significantly different between lidocaine-saline and saline groups ($P < 0.05$). However, at other times, there was no significant difference in vital signs between the two groups ($P > 0.05$). Furthermore, there was no statistically significant difference between the two groups in SpO₂ at different times ($P > 0.05$) (Table 3).

According to results of statistical analysis, average analgesic consumption in the lidocaine-saline group was significantly lower than the saline group ($P < 0.05$). In addition, the first dose of meperidine (0.4 mg/kg) was taken sooner in the saline group ($P < 0.05$) (Table 4).

4. Discussion

The immediate postoperative period following general anesthesia is often complicated by issues such as pain, nausea, vomiting, and delirium. The administration of opioids for pain management can further complicate recovery due to associated side effects like nausea and constipation. Both patients and physicians are keen on reducing or preventing these adverse effects to facilitate a swift recovery and enable early hospital discharge. One alternative for post-surgical pain relief is the injection of lidocaine at the surgical site [16,17].

Lidocaine acts by blocking sodium channels in nerve cell membranes, playing a pivotal role in halting the onset and propagation of inflammatory and neuropathic pain [19,20]. Its anti-inflammatory properties are well-documented, including the inhibition of neutrophil aggregation at the injury site and the reduction of inflammatory mediator release [21]. Demonstrating antinociceptive effects in both peripheral and central nervous systems, lidocaine's application before surgical incision has been shown to reduce nerve conduction from damaged nerves, thus preventing the initiation of pain and the development of secondary hypersensitivity through both peripheral and central pathways. Its successful use in managing central and peripheral neuropathic pain, complex regional pain syndromes, and fibromyalgia is notable [22].

Our findings indicate a significant difference in postoperative pain intensity at various time points between the saline group and the lidocaine-saline group, with the latter experiencing less pain. Additionally, the lidocaine-saline group required a lower dosage of meperidine. The first dose of meperidine for pain relief was administered later in the lidocaine-saline group, indicating a delayed need for postoperative analgesics.

In the study of Xia et al. [23] which investigated the impact of perioperative intravenous lidocaine infusion on chronic postoperative pain in breast cancer patients, results showed a reduction in chronic pain incidence and an improvement in acute postoperative pain and intraoperative opioid requirements. These findings align with our study regarding the diminished use of narcotics and reduced postoperative pain.

Ghimire et al [24] evaluated the effectiveness of lidocaine infusion on postoperative pain outcomes in patients undergoing totally extraperitoneal (TEP) laparoscopic inguinal hernioplasty. Their study concluded that the lidocaine group had significantly lower median cumulative postoperative morphine consumption and reduced pain intensity, which is consistent with our findings, differing

Table 1

Comparison of basic characteristics of participants in the study groups.

Variable	Lidocaine- saline group	Saline Group	<i>P</i> Value
Age (mean ± SD)	37.63 ± 3.35	38.69 ± 3.15	0.173
BMI (mean ± SD)	27.68 ± 2.19	27.42 ± 1.81	0.598
Duration of anesthesia (mean ± SD)	102.22 ± 9.44	100.69 ± 9.86	0.524
Duration of surgery (mean ± SD)	92.08 ± 8.05	91.38 ± 8.91	0.730

BMI: Body Mass Index, $P < 0.05$.

Table 2
Comparison of pain levels at various intervals within the study groups.

Time	Pain (mean \pm SD)		P Value
	Lidocaine-saline group	Saline Group	
0 min	3.41 \pm 0.58	4.81 \pm 0.69	<0.0001
15 min	3.13 \pm 0.63	4.33 \pm 0.71	<0.0001
30 min	2.81 \pm 0.52	4.61 \pm 0.83	<0.0001
60 min	2.61 \pm 0.49	4.30 \pm 0.52	<0.0001
2 h	2.36 \pm 0.54	3.44 \pm 0.55	<0.0001
4 h	2 \pm 4.72	3.08 \pm 0.36	<0.0001
8 h	1.94 \pm 0.23	3.44 \pm 0.50	<0.0001
12 h	2.36 \pm 0.59	3.33 \pm 0.58	<0.0001
24 h	1.75 \pm 0.80	2.96 \pm 0.66	<0.0001

Pain measured by Visual Analogue Scale (VAS), min: minutes, $P < 0.05$.

Table 3
Comparison of the hemodynamic parameters between the study groups pre- and post-washing.

Variable (mean \pm SD)	Lidocaine- saline group	Saline group	P Value
SBP before washing	105.41 \pm 4.72	107.50 \pm 6.34	0.773
SBP after washing	112.50 \pm 5.52	115.44 \pm 6.22	0.037
DBP before washing	67.27 \pm 3.56	66.47 \pm 3.41	0.331
DBP after washing	61.66 \pm 2.79	66.30 \pm 2.94	0.001
HR before washing	76.52 \pm 6.26	76.16 \pm 4.08	0.774
HR after washing	71.66 \pm 5.78	77.22 \pm 4.12	0.001

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HR: Heart Rate, $P < 0.05$.

Table 4
Comparison of the dosage and time of initial administration of meperidine between study groups.

Variable (mean \pm SD)	Lidocaine - saline group	Saline group	P Value
Prescribed meperidine (mg)	33.47 \pm 11.20	77.50 \pm 15.56	< 0.0001
Time to receive the first dose (min)	170.55 \pm 38.98	46.66 \pm 15.44	< 0.0001

Mg: milligrams, Min: minutes, $P < 0.05$.

only in the method of lidocaine administration. Hassan et al. [25] assessed the influence of intravenous lidocaine infusion on early postoperative pain control after complex spine surgeries. They found that the lidocaine group had significantly lower pain scores and reduced intraoperative fentanyl use, with a longer duration before requesting rescue analgesia. These results corroborate our study's outcomes in terms of pain reduction and decreased narcotic use.

Nalbani et al. [26], investigated the effect of intravenous lidocaine on pain following knee arthroplasty and limb fracture surgeries. Their findings of reduced pain rates, delayed pain onset, and lower analgesic consumption are in agreement with our study.

In the research conducted by Pogorelic et al. [27] to assess the effect of intraperitoneal lidocaine injection as well as its injection into the surgical site on pain after laparoscopic varicocele surgery, it was concluded that the intensity of postoperative pain was lower in the group receiving lidocaine, and this result was consistent with our study. The similar precise injection method in the surgical site can be the reason for reaching comparable findings.

5. Conclusion

The use of lidocaine-saline washout at the surgical site in lumpectomy patients significantly reduces the need for opiates in the immediate postoperative period. This positive impact on reported pain levels supports the inclusion of lidocaine in the standard treatment protocols for lumpectomy in breast cancer patients. Our findings advocate for clinicians to consider adopting similar approaches in other surgical contexts.

CRedit authorship contribution statement

Payman Rezagholi: Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Karim Nasseri:** Writing – review & editing, Supervision, Conceptualization. **Arvin Barzanji:** Writing – original draft, Data curation, Conceptualization. **Khaled Rahmani:** Writing – review & editing, Formal analysis. **Asra foroughi:** Writing – review & editing, Data curation. **Hassan Moayeri:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization.

Data availability statement

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

This research was supported by the Deputy of Research and Technology of Kurdistan University of Medical Sciences. The authors extend their heartfelt gratitude to the directorate of Kowsar and Besat Hospitals in Sanandaj, as well as the dedicated operating room staff, for their invaluable support and assistance.

References

- [1] World Health Organization, Breast cancer [Internet] (2023) [cited 2024 Sep 13]. Available from: <https://www.who.int/news-room/fact-sheets/detail/breast-cancer>.
- [2] A. Sharifian, M.A. Pourhoseingholi, M. Emadedin, M.R. Nejad, S. Ashtari, N. Hajizadeh, et al., Burden of breast cancer in Iranian women is increasing, *Asian Pac. J. Cancer Prev. APJCP* 16 (12) (2015) 5049–5052.
- [3] J.S. Khan, K.S. Ladha, F. Abdallah, H. Clarke, Treating persistent pain after breast cancer surgery, *Drugs* 80 (1) (2020 Jan) 23–31.
- [4] S.A. Naghibi, D. Shojaizadeh, A. Montazeri, J.Y. Cherati, Sociocultural factors associated with breast self-examination among Iranian women, *Acta Med. Iran.* (2015) 62–68.
- [5] V.B. Sheppard, M. Figueiredo, J. Canar, M. Goodman, L. Caicedo, A. Kaufman, et al., Latina a LatinaSM: developing a breast cancer decision support intervention, *Psycho Oncol.: Journal of the Psychological, Social and Behavioral Dimensions of Cancer* 17 (4) (2008) 383–391.
- [6] V. Wylde, J. Rooker, L. Halliday, A. Blom, Acute postoperative pain at rest after hip and knee arthroplasty: severity, sensory qualities and impact on sleep, *J. Orthop. Traumatol.: Surgery & Research* 97 (2) (2011) 139–144.
- [7] M. Kjaergaard, S. Moïniche, K. Olsen, Wound infiltration with local anesthetics for post-operative pain relief in lumbar spine surgery: a systematic review, *Acta Anaesthesiol. Scand.* 56 (3) (2012) 282–290.
- [8] R. Rikalainen-Salmi, J. Förster, K. Mäkelä, P. Virolainen, K. Leino, M. Pitkänen, et al., Local infiltration analgesia with levobupivacaine compared with intrathecal morphine in total hip arthroplasty patients, *Acta Anaesthesiol. Scand.* 56 (6) (2012) 695–705.
- [9] Z-d Lu, P. Li, Analgesic effect of periarticular Ropivacaine infiltration and cyclooxygenase-2 inhibitor following total hip arthroplasty, *Chinese Journal of Tissue Engineering Research* 14 (43) (2010) 7991.
- [10] W. Liu, R. Cong, X. Li, Y. Wu, H. Wu, Reduced opioid consumption and improved early rehabilitation with local and intraarticular cocktail analgesic injection in total hip arthroplasty: a randomized controlled clinical trial, *Pain Med.* 12 (3) (2011) 387–393.
- [11] N. Byager, M.S. Hansen, O. Mathiesen, J.B. Dahl, The analgesic effect of wound infiltration with local anaesthetics after breast surgery: a qualitative systematic review, *Acta Anaesthesiol. Scand.* 58 (4) (2014 Apr) 402–410.
- [12] I.J. Koh, Y.G. Kang, C.B. Chang, S.-H. Do, S.C. Seong, T.K. Kim, Does periarticular injection have additional pain relieving effects during contemporary multimodal pain control protocols for TKA?: a randomised, controlled study, *Knee* 19 (4) (2012) 253–259.
- [13] P. Ali, B. Cotton, K. Williamson, G. Smith, Intraperitoneal bupivacaine or lidocaine does not provide analgesia after total abdominal hysterectomy, *British journal of anaesthesia* 80 (2) (1998) 245–247.
- [14] E. Zohar, A. Shapiro, A. Phillipov, D. Hoppenstein, Z. Klein, B. Fredman, The postoperative analgesic efficacy of wound instillation with ropivacaine 0.1% versus ropivacaine 0.2, *J. Clin. Anesth.* 16 (6) (2004 Sep 1) 399–404.
- [15] E. Zohar, B. Fredman, A. Phillipov, R. Jedeikin, A. Shapiro, The analgesic efficacy of patient-controlled bupivacaine wound instillation after total abdominal hysterectomy with bilateral salpingo-oophorectomy, *Anesth. Analg.* 93 (2) (2001 Aug 1) 482–487.
- [16] W. Shi, Y.F. Ren, J.F. Chen, X. Ye, Efficacy and safety of lidocaine patch in the management of acute postoperative wound pain: a comprehensive systematic review and meta-analysis of randomized controlled trials, *Adv. Wound Care* 12 (8) (2023 Aug 1) 453–466.
- [17] J. Gudín, S. Nalamachu, Utility of lidocaine as a topical analgesic and improvements in patch delivery systems, *PGM (Postgrad. Med.)* 132 (1) (2020 Jan 2) 28–36.
- [18] J.L. Levene, E.J. Weinstein, M.S. Cohen, D.A. Andraea, J.Y. Chao, M. Johnson, C.B. Hall, M.H. Andraea, Local anesthetics and regional anesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children: a Cochrane systematic review and meta-analysis update, *J. Clin. Anesth.* 55 (2019 Aug 1) 116–127.
- [19] M. Bailey, T. Corcoran, S. Schug, et al., Perioperative lidocaine infusions for the prevention of chronic postsurgical pain: a systematic review and meta-analysis of efficacy and safety, *Pain* 159 (2018) 1696–1704.
- [20] R. Karnina, S.K. Arif, M. Hatta, et al., Molecular mechanisms of lidocaine, *Ann Med Surg (Lond)* 69 (2021) 102733.
- [21] H. Hermanns, M.W. Hollmann, M.F. Stevens, et al., Molecular mechanisms of action of systemic lidocaine in acute and chronic pain: a narrative review, *Br. J. Anaesth.* 123 (2019) 335–349.
- [22] J. Tully, J.W. Jung, A. Patel, et al., Utilization of intravenous lidocaine infusion for the treatment of refractory chronic pain, *Anesth Pain Med* 10 (2021) e112290.
- [23] M. Xia, Q. Wei, Q. Zhang, H. Jiang, Effect of intravenous lidocaine on chronic postoperative pain in patients undergoing breast cancer surgery: a prospective, double-blind, randomized, placebo-controlled clinical trial, *Ann. Transl. Med.* 10 (14) (2022 Jul).
- [24] A. Ghimire, A. Subedi, B. Bhattarai, B.P. Sah, The effect of intraoperative lidocaine infusion on opioid consumption and pain after totally extraperitoneal laparoscopic inguinal hernioplasty: a randomized controlled trial, *BMC Anesthesiol.* 20 (2020 Dec) 1–8.
- [25] E.R. Hassan, A.A. Pawaz, S.S. Hefny, T.N. Abdelrahman, The impact of intraoperative intravenous lidocaine infusion on early postoperative pain after complex spine surgeries, *Ain-Shams Journal of Anesthesiology* 15 (1) (2023 Aug 16).
- [26] R.K.E. Nallbani, F. Sada, I.Q. Jusufi, A. Hasani, Ntravenous lidocaine for postoperative analgesia in 90 patients after total knee arthroplasty and limb fractures, *Med. Sci. Mon. Int. Med. J. Exp. Clin. Res.: International Medical Journal of Experimental and Clinical Research* 28 (2022) e935852.
- [27] Z. Pogorelič, T. Gaberc, M. Jukić, G. Tintor, A. Neveščanin Biliškov, I. Mrkljić, A. Jerončić, The effect of subcutaneous and intraperitoneal instillation of local anesthetics on postoperative pain after laparoscopic varicocelectomy: a randomized controlled trial, *Children* 8 (11) (2021 Nov 13) 1051.