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Original Research Article

Lidocaine in Decreasing the Perioperative Opioid Analgesic Requirements After Ambulatory Surgery

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Abstract: *Infusions of lidocaine at low doses have an excellent safety record. It has been proposed that intravenous lidocaine infusion improved overall surgical outcomes and reduced postoperative discomfort.* ***Objective:*** *To compare the mean opioid analgesic requirements in patients undergoing ambulatory surgery receiving lidocaine versus placebo.* ***Methods:*** *This randomized control trial was conducted from January 2024 to June 2024 at the Anaesthesia Department of Liaquat National Hospital. A total of 80 patients were included and divided equally into the 1.5 mg/kg lidocaine group and the Placebo group. A visual analog scale (VAS) was used to measure pain while at rest. At the time of discharge from the anesthesia care unit (PACU), 2 hours and 4 hours in a hospital stay. The data was compiled and analyzed using SPSS.* ***Results:*** *The placebo group consisted of 45% males, while the lidocaine group comprised 50% male patients. The mean VAS in PACU at 2 and 4 hours for the lidocaine group was 1.50±2.01 and 1.70±1.69 respectively, while the mean VAS for the placebo group was 1.75±1.94 and 3.52±3.04. Overall, 20% of patients in the lidocaine group required nalbuphine, compared to 50% of placebo. The study groups and the need for nalbuphine were significantly associated (p = 0.005). There was a significant mean difference in nalbuphine dose by study group for patients whose surgeries lasted longer than 60 minutes (p = 0.038).* ***Conclusion:*** *Lidocaine infusion reduces the incidence of PONV, the total need for opioids, and the severity of postoperative pain.*

Keywords: Opioid Analgesics, Ambulatory Surgery, Lidocaine, Placebo

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Introduction

The primary reasons why patients are uncomfortable and dissatisfied after general anesthesia are postoperative pain and nausea or vomiting. Following ambulatory surgery, one of the most frequently mentioned causes of release delays and prolonged hospital stays is (1,2). Opioids' strong analgesic effects make them popular during the perioperative phase(3). Undesirable side effects include respiratory depression, hypotension, drowsiness, nausea, vomiting, urine retention, and postoperative ileus may be linked to them (4, 5). In surgical patients, analgesia-related side effects can be troublesome and result in higher institutional expenses, more extended hospital stays, and generally higher patient discontent (6, 7).

One drug that has demonstrated the potential to produce an analgesic effect is lidocaine. The mechanism of action of this amide local anesthetic involves blocking sodium channels in the neural cascade (8,9). Intravenous lidocaine is now utilized as a perioperative analgesic in a variety of settings, such as the intensive care unit (ICU), surgical ward, recovery room, and operating room (10). Instead of a direct local anesthetic effect, lidocaine exhibits anti-nociceptive, anti-hyperalgesic, and anti-inflammatory properties, which account for its apparent lasting effect hours after infusion has been completed (10-12). When given by low-dose infusion, lidocaine has an excellent safety record (13,14). An intravenous lidocaine infusion has been shown to reduce postoperative discomfort and enhance overall surgical results (15).

According to Wang T. et al., increasing the use of lidocaine in clinical settings is worthwhile because it may safely and effectively prevent postoperative nausea and vomiting in patients undergoing laparoscopic gynecological surgery and could accelerate the patients' early recovery (16).

According to McKay, systemic lidocaine, when administered perioperative, dramatically lowers the need for opioids in an ambulatory context without influencing the time to discharge. et al. Morphine IV equivalent doses (MEQ), or intraoperative opioid use, were decreased by about Thirty percent (30%) in patients belonging to groups who received lidocaine (mean dose 20.52±10.55 vs. mean dose 30.15±16.59), by about 50% in the PACU (mean dose 8.72±9.54 vs. mean dose 15.93±10.95), and by about 40% throughout the entire study period, including the operating room, PACU, and up to 24 hours after discharge (36.08±17.13 vs. 59.53±18.59). Patients in the lidocaine group reported reduced discomfort in the PACU. It provides a viable therapeutic method for perioperative analgesia in the outpatient context because it is safe, affordable, and doesn't require further monitoring beyond what is typically offered in the PACU setting (17).

Limited studies have been published to evaluate the effectiveness of lidocaine in pain management. This study aims to determine the local statistics regarding the effectiveness of lidocaine versus placebo in patients undergoing ambulatory surgery for pain management in our clinical setting. The findings of our study will help us to know if lidocaine infusion is an effective alternative to minimize pain and decrease postoperative opioid consumption. Therefore, the compelling findings of our study will guide clinicians to a more effective regimen for pain management, which can reduce hospital stays after ambulatory surgery.

Methodology

We conducted our randomized controlled trial from January 2024 to June 2024 at the Department of Anaesthesia, Liaquat National Hospital & Medical College, Karachi. We conducted this trial after obtaining permission from both the institutional research committee and the ethics review committee. The sample size of the current study was calculated based on the mean and standard deviation of opioid doses reduced by 40% at PACU, i.e., 36.08±17.13 (17) in the lidocaine group and 59.53±18.59 (17) in the placebo group, using a power (1-β) of 80% and a 95% confidence level. The total calculated sample size was 80, with 40 patients in each group. This calculation was performed using the OpenEpi software for determining sample size. We include 80 patients, i.e., 40 in each group, to achieve the assumption of normality. Participants of either

gender, aged between 18 and 65 years, with an ASA class of I or II who were undergoing ambulatory surgery, were included in this study. Pregnant women, Patients who were allergic to lidocaine, and Patients with fever who had received antibiotics and steroids within the last month were excluded from the current research study.

This study was conducted after obtaining approval for a synopsis from the Ethical Review Committee and the College of Physicians and Surgeons of Pakistan. Patients who will be admitted for ambulatory surgery and visit the Department of Anaesthesia at the Hospital in Karachi and meet the following inclusion criteria will be included in the study. All patients will be enrolled in our study after obtaining informed consent. All the demographic and clinical details of the patients will be noted. All participants will be randomly assigned to either Group A, which receives lidocaine, or Group B, which gets a placebo. At induction, patients in group A will receive a slow IV push with the lidocaine dose of 1.5 mg/kg, while patients in group B will receive Normal Saline of equal volume. Immediately following the induction of anesthesia, the lidocaine infusion of dose 2 mg/kg/h or the identical volume of saline was initiated as a placebo. This was stopped before the patient was shifted out of the operating theatre. Standardized anesthetic therapy during surgery included prophylactic treatment, i.e., dexamethasone up to 0.1 mg/kg, opioid usage, and ketorolac (up to 30 mg IV if not contraindicated) for nausea and/or vomiting episodes, was administered when occurred postoperatively. Additionally, a visual analog scale was used to measure pain at rest at the time of PACU discharge, as well as at two and four hours into the hospital stay. When pain exceeded a score of four on the visual analog scale, nalbuphine 0.1 mg/kg was administered. Nausea and vomiting will also be observed and noted. All data will be entered into a predesigned pro forma. Confounding and bias will be controlled through stratification.

Patient data were compiled and analyzed using the Statistical Package for the Social Sciences (SPSS) Version 25. Frequency and percentage were calculated for qualitative variables, including gender, residence, hypertension, diabetes mellitus, asthma, nausea, and vomiting, between the two groups. The normality of the data was checked using the Shapiro-Wilk test. The mean ± SD was calculated for quantitative variables between the two groups, including duration of surgery, BMI, age, weight, height, length of PACU stay, nalbuphine doses, and VAS score. The median (IQR) was reported if the data were non-normal. Stratification was performed based on age, body mass index, gender, residence, hypertension, diabetes mellitus, nausea, vomiting, duration of surgery, length of PACU stay, and VAS score. Post-stratification chi-square or/and Fisher exact test was applied on age, body mass index, gender, residence, hypertension, diabetic mellitus, nausea, vomiting, duration of surgery, length of PACU stay, and VAS score to see the effect of these modifiers, on the outcome. P-value ≤0.05 was considered statistically significant.

Results

A total of 80 patients participated in the study, and they were split into two treatment groups of 40 each. One group received lidocaine treatment, while the other group received a placebo. The placebo group consisted of 45% male participants, while the lidocaine group comprised 50% males. The mean age of the patients in the Lidocaine group was 35.27±14.34 years, while the placebo group's patient's age was 33.40±9.26 years. In patients in the lidocaine group, the mean height, weight, and body mass index were 165.86±11.61 cm, 73.00±15.18 kg, and 26.65±5.81 kg/m², respectively. In patients in the placebo group, these values were 164.26±6.04 cm, 64.67±6.51 kg, and 23.93±1.75 kg/m², respectively. In the lidocaine group, 20% of the patients were Obese. Among the lidocaine group, eighty percent of patients belonged to Karachi, whereas ninety-two percent were in the placebo group. There were 85% of patients with NKCM in the Lidocaine group and 92.5% in the placebo group. Additionally, 15% of hypertensive patients were found in the Lidocaine group and 7.5% in the placebo group. The Lidocaine group patients experienced an average length of surgery and PACU stay of 75.75±39.05 minutes and 65.25±19.96 minutes, respectively, while the Placebo group patients experienced an average length of surgery and PACU stay of 59.0±43.63 minutes and 80.62±37.87 minutes. Table 1 provides comprehensive descriptive statistics.

As shown in Figure-1, the mean visual analog score at PACU at 2 and 4 hours for the lidocaine group was 1.50±2.01, 1.70±1.69, and 1.90±1.59, respectively, while the mean score for the placebo group was 1.75±1.94, 3.52±3.04, and 3.45±2.27.

In our study, 20% of patients in the lidocaine group require nalbuphine, compared to 50% of those receiving a placebo. Patients in the lidocaine group received an average dose of 5.25±0.88 mg of nalbuphine, whereas those in the placebo group received an average dose of 5.45±0.51 mg. The study group and the need for nalbuphine were significantly associated (p = 0.005).

Additionally, as shown in Table 2, we discovered a significant association between the study group and the need for nalbuphine for male patients (p=0.010), patients aged ≤45 years (p=0.002), patients whose surgeries lasted longer than 60 minutes (p<0.001), and patients with NKCM (p=0.011). We found no significant difference in nalbuphine dosage between study groups (p = 0.564). However, a substantial difference in nalbuphine dose was observed by the study group for patients whose surgeries lasted longer than 60 minutes (p = 0.038). Table 3 displays the comprehensive mean comparison results.

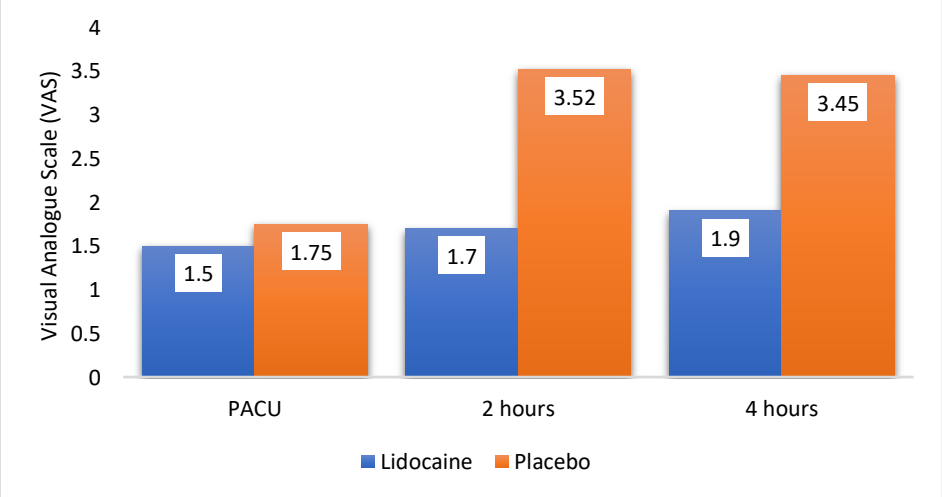

Figure-1: Mean visual analog score at PACU, at 2 hours and 4 hours

Table 1: Descriptive statistics of the study population (n=80)

	Study groups	
	Lidocaine	Placebo
Gender n(%)		
Male	20(50.0)	18(45.0)
Female	20(50.0)	22(55.0)
Age		
Age (mean±SD)	35.27±14.34	33.40±9.26
≤45 years	32(80.0)	36(90.0)
>45 years	8(20.0)	4(10.0)
Obesity		
Height (cm) (mean±SD)	165.86±11.61	164.26±6.04
Weight (kg) (mean±SD)	73.00±15.18	64.67±6.51
Body mass index (kg/m^2) (mean±SD)	26.65±5.81	23.93±1.75
Obese	8(20.0)	0(0)
Non obese	32(80.0)	40(100.0)
Residence		
Karachi	32(80.0)	37(92.5)
Quetta	4(10.0)	3(7.5)
Khairpur	2(5.0)	0(0.0)
Lasbela	2(5.0)	0(0.0)
Co-morbid		
HTN	6(15.0)	3(7.5)
NKCM	34(85.0)	37(92.5)
Surgery time		
Duration of surgery (min) (mean±SD)	75.75±39.05	59.0±43.63
≤60 min	22(55)	28(70)
>60 min	18(45)	12(30)
Length of PACU stay (min) (mean±SD)	65.25±19.96	80.62±37.87

SD: Standard deviation

Table 2: Association of opioid analgesic requirements with study groups

Need of Nalbuphine	Study group		P-value
	Lidocaine	Placebo	
Overall	8(20.0)	20(50.0)	0.005*
Gender			
Male	4(20)	11(61.1)	0.010*
Female	4(20)	9(40.9)	0.143
Age group			
≤45 years	6(18.8)	20(55.6)	0.002*
>45 years	2(25)	0(0)	0.273
Surgery duration			
≤60 min	6(27.3)	9(32.1)	0.709
>60 min	2(11.1)	11(91.7)	<0.001*
Co-morbid			
Hypertensive	2(33.3)	3(100)	0.058
NKCM	6(17.6)	17(45.9)	0.011*

*The Chi-square/fisher exact test was applied. A P-value less than 0.05 is considered significant. *Significant at 0.05 level.*

Table 3: Mean comparisons of nalbuphine doses according to study groups

	Study group		P-value
	Lidocaine	Placebo	
Overall	5.25±0.88	5.45±0.51	0.564
Gender			
Male	5.50±0.57	5.63±0.50	0.662
Female	5.00±1.15	5.22±0.44	0.731
Age group			
≤45 years	5.00±0.89	5.45±0.51	0.126
>45 years	6.00±0.00	-	-
Co-morbid			

HTN	6.00±0.00	6.00±0.00	-
NKCM	5.00±0.89	5.35±0.49	0.239
Surgery duration			
≤60 min	5.33±1.03	5.55±0.52	0.642
>60 min	5.00±0.00	5.36±0.50	0.038*

*An Independent t-test was applied. A P-value less than 0.05 is considered significant. *Significant at 0.05 level.*

Discussion

When applied topically to block peripheral nerves, lidocaine is known to operate on voltage-gated sodium channels (18). However, systemic lidocaine alone cannot provide direct analgesia at lower concentrations by blocking the sodium channels in neurons (19).

While the exact mechanism by which intravenous lidocaine generates analgesia remains unclear, several plausible pathways have been clarified. Intravenous lidocaine increases the pain threshold by turning on both muscarinic and nicotinic receptors, which raises the amount of acetylcholine at the spinal level (20). Systemic lidocaine injection may be able to dramatically decrease pain by modulating the inflammatory process that is connected to perioperative discomfort. Another significant issue is how intraoperative IV lidocaine injections reduce opioid and pain ratings following infusion. It may exhibit antinociceptive, anti-hyperalgesic, and anti-inflammatory properties as it acts on a variety of receptors and signal cascades (21). Systemic lidocaine is a commonly researched adjuvant in the regimen of multimodal analgesia to minimize postoperative opioid intake and discomfort because of its impact on several pain pathways.

This study's primary goal was to determine if intravenous lidocaine was a better option than a placebo for managing perioperative pain in addition to routine care. In contrast to normal saline, a currently conducted study demonstrated that intraoperative infusion of low-dosage lidocaine reduced postoperative opioid demand and pain severity. Compared to patients receiving saline, those receiving lidocaine reported improved quality of recovery and greater satisfaction with postoperative pain treatment. Compared to the saline group, patients in the lidocaine group complained of discomfort later.

In 2018, an updated Cochrane study provided much-needed information about the analgesic properties of systemic lidocaine (22). According to the same review's random-effects meta-analysis, lidocaine was preferred over the placebo in terms of overall postoperative opioid intake (95% CI - 6.25 to 2.79, p <0.001).

Another study's findings (18) also showed that, even though both groups used multimodal analgesia, the lidocaine group consumed fewer opioids overall in the first 24 hours following surgery than the saline group (median difference of 4 mg morphine equivalents). Additionally, the previously reported meta-analysis showed that the lidocaine group experienced lower pain scores at rest ("early time points" in the PACU or 1 to 4 hours postoperatively) compared to the control group (P < 0.0001). This was comparable to the lidocaine group's average pain decrease on a VAS (22).

Additionally, we found a statistically significant difference in pain levels up to four hours after surgery, although a clinical difference was only observed at rest during the same period. The length of continuous infusions (ranging from 1 to 48 hours after surgery) and dose (ranging from 1.5 to 5 mg/kg/hour) vary significantly (23,24). In a newly released study, patients received systemic administration of lidocaine (1.5 mg/kg bolus, followed by a 2 mg/kg/hour infusion). However, there was no impact (25).

Although they only included a small number of patients, Slovack et al. discovered that intravenous lidocaine did not affect thoracic surgery. Furthermore, the authors did not mention the specific length of the lidocaine infusion or its local application; the degree of pain was not reported, and the control group's morphine consumption was less than expected (26).

According to a recently released meta-analysis, the duration of intravenous lidocaine infusion may affect its analgesic efficacy, with more favorable results occurring when the injection is administered for at least 24 hours (27). In a previous research, coughing pain levels were evaluated. Within the first twenty-four hours, participants in the lidocaine group reported over VAS 4, whereas those in the placebo group had over VAS 5. Although this 20% decrease in VAS is below the clinical relevance threshold, it is statistically significant and warrants reporting (28). The limited research size may be the primary reason why intravenous lidocaine did not affect any of the other secondary measures. For example, the improved time to defecation was one of the statistically insignificant trends that we found favoring intravenous lidocaine. With more significant sample populations, Guinot et al. showed that lidocaine reduced postoperative complications while reducing given opioids (29), while Zhang et al. merely reduced intraoperative opiate consumption (30). The frequency was significantly lower in the trial: after 14 days, 9 out of 52 patients (17%) reported mild discomfort (mean VAS score <2) during coughing. Only four out of the fifty-two participants in the study (eight percent) experienced coughing discomfort with a VAS severity level of three or below after 180 days. Thus, they conclude that intravenous lidocaine seems to help with acute pain that lasts longer than three months but not chronic pain (23,31).

Another study's findings indicate that intraoperative lidocaine infusion, when used to manage post-operative pain, has a modest impact 24 hours after ambulatory surgery and a moderate opioid-sparing effect in the post-anesthesia care unit. The combined outcomes of studies support its use in outpatient surgery as a component of a multimodal regimen. Nevertheless, it is unclear if lidocaine infusion will be used for postoperative pain management after the initial postoperative phase (32). Our results of a decrease in opioid usage in this cohort are consistent with a recent meta-analysis of eight RCTs that looked at systemic lidocaine use (33). Additionally, recent research showed that patients receiving lidocaine after major abdominal surgery have lower pain levels, less PONV, shorter ileus duration, and a shorter hospital stay (34). According to Farag and colleagues, patients who had a lidocaine infusion from the time of induction until eight hours following surgery saw a 25% decrease in opioid use at 48 hours (35).

In a different trial (32), systemic lidocaine did not reduce the incidence of nausea and vomiting at PACU when compared to control, nor did it discover a decrease in resting pain ratings at PACU or 24 hours post-surgery. This finding contrasts with the results of previous studies, which have shown a general decline in VAS values after surgery (33, 34).

Conclusion

Our findings imply that intravenous lidocaine treatment during surgery lowers pain ratings. When thoracic epidural analgesia and other kinds of local pain management are not practical or indicated, intravenous lidocaine may be a viable option as part of a multimodal pain treatment plan. Therefore, it may be concluded that intraoperative lidocaine infusion reduces the postoperative pain severity and total opioid demand. Additionally, it reduces the prevalence of PONV, enhances recovery quality, and increases patient satisfaction without having any sedative effects.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. ((IRBEC-NIKHR-58-24))
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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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Review of Literature, Data entry, Data analysis, and drafting article.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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