# Effect of intraoperative lidocaine infusion on postoperative analgesia: A randomized controlled trial.

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**ABSTRACT**

**Objective:** To evaluate the effect of intravenous lidocaine infusion on postoperative pain scores and narcotic consumption in patients undergoing abdominal surgery under general anesthesia.
**Study Design:** Randomized, double blinded controlled trial.
**Place and Duration:** Department of Anesthesia, Combined Military Hospital, Khuzdar from 15th November 2018 to 20th May 2019.
**Methodology:** A total of 80 adult patients were randomly assigned into two groups of 40 each to receive IV lidocaine bolus, 1 mg/kg followed by IV infusion, 2mg/kg/h (group L) or similar volume/kg of saline (group S). Each patient's level of pain was measured with a visual analogue scale (VAS) on arrival in post anesthesia care unit, at 2, 4, 8, 12, and 24 hours after surgery. Total postoperative morphine consumption and the incidence of side effects were also recorded.
**Results:** Intraoperative lidocaine infusion resulted in effective analgesia in first 12 h postoperatively, seen by low pain scores (P=<0.05). The total morphine consumption was also reduced in the lidocaine group (P=<0.05). No signs of systemic lidocaine toxicity were observed.
**Conclusion:** Intraoperative lidocaine infusion should be considered as an adjunct to opioids for postoperative pain management.
**Keywords:** Abdominal surgery, postoperative pain, postoperative analgesia, lidocaine, morphine, narcotic consumption, systemic lidocaine toxicity.

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## INTRODUCTION

Effective pain relief during surgery and postoperatively is very important for providing ideal patient care[1,2]. It is not only a part of balanced anesthesia technique, it also helps in reducing the surgical stress response. Surgical pain can initiate complex metabolic and hormonal response which can have undesirable effects on the outcome of the surgery[3,4]. Opioids have been traditionally used to provide balanced anesthesia and postoperative analgesia, but the use of narcotics comes with a certain price. Side effects like sedation, respiratory depression, nausea and vomiting are associated with the use of opioids[5] while the use of high doses can also lead to acute tolerance as well. In addition to that, for developing countries like Pakistan availability of narcotics at times may also be an issue. Furthermore, because of the recent concerns regarding opioid crisis[6] there has been change in strategy of managing the postoperative pain with other options. Regional anesthesia, multimodal analgesia, ketamine, dexmedetomidine, pregabalin and gabapentin are some of the unique alternative approaches in this regard[7].

Intravenous Lidocaine has been shown to have analgesic, anti-hyperalgesic and anti-inflammatory characteristics[8]. Systemic lidocaine stimulates secretion of anti-inflammatory cytokines, reduces secretion of inflammatory mediators, blocks voltage gated sodium channels as well it acts as N-methyl d-aspartate (NDMA) receptor antagonist[9,10]. Since studies have shown that NMDA receptors have a role in processing of pain at the level of central nervous system, therefore the lidocaine can be employed as a part of multimodal analgesia. Multimodal analgesia by targeting various pain mechanisms improves pain relief and reduces the opioid usage[11,12].

We hypothesized that lidocaine infusion given intraoperatively

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will reduce the postoperative pain scores and consumption of morphine. Although studies have been carried out all over the world to assess the effectiveness of intraoperative intravenous lidocaine infusion on postoperative pain scores but studies on local population are deficient in this regard. Therefore, objective of this study was to evaluate the effect of intravenous lidocaine infusion on postoperative pain scores and narcotic consumption in patients undergoing abdominal surgery under general anesthesia in local population.

## METHODOLOGY

This prospective, double blinded, randomized, placebo-controlled trial study was conducted from 15th November 2018 to 20th May 2019 at Combined Military Hospital, Khuzdar. The approval of the study was taken from hospital ethical committee of Combined Military Hospital Khuzdar. Written informed consent was taken from the patients enrolled in the study. A total of 80 patients between 18 to 65 years of age, both male and female fitting into physical status I and II of American Society of Anesthesiologists (ASA), scheduled to undergo variety of abdominal surgeries (open cholecystectomy, laparotomy, hysterectomy, pyelolithotomy, nephrectomy) under general anesthesia were included in the study. Patients with abnormal liver and renal functions, ischemic heart disease, cardiac arrhythmias and allergy to lidocaine were excluded from study. During preanesthesia assessment, patients were explained about the visual analogue scale (VAS) of 0-10 with 0 being "no pain" and 10 being "worst possible pain".

Patients were allocated in two different groups (Group L and Group S) of 40 each by sealed envelope procedure. Patients in Group L were given a bolus of intravenous lidocaine of 1 mg/kg followed by an infusion of lidocaine at a rate of 2 mg/kg/h. Whereas patients in Group S were administered a normal saline bolus and infusion at the same volume and rate. The administration of bolus dose followed by infusion of both lidocaine and saline was started before the skin incision. The infusion (Mindray SK-500, Germany) was continued intraoperatively and was stopped 1 hour after the skin closure in the postoperative period in the Recovery room.

In order to avoid bias the medical staff who was not involved in anesthetizing the patients prepared the study drugs. The drugs were prepared in 20 mL syringe (concentration of lidocaine was 20 mg/ml), the saline syringes were also labelled like lidocaine syringes. The anesthesiologist administering anesthesia was not aware of the group to which the patients belonged. The individual involved in gathering of pain scores data was not aware of the group to which the patient belonged. Similarly, the staff who provided the postoperative care in the hospital were unaware of the patient group.

Once the patients were shifted to the post anesthesia care unit (PACU) at the end of surgery pain scores using VAS were noted on arrival, 2 h, 4h, 8h, 12h and 24 h postoperatively. The patients remained in the post anesthesia care unit for 3 h after which they were shifted to the ward and given IV ketorolac 30 mg 12 hourly. All the patients who complained of pain score of VAS 4 or above were provided rescue analgesia of IV morphine bolus 0.07 mg/kg. The total quantity of morphine given in twenty-four hours was documented for both the groups.

**Data Analysis:** The results were analyzed using SPSS version 23.0.0 software (IBM). In order to detect a change of 30 % in morphine consumption between groups with power 80% and $\alpha = 0.05$ a sample size of 30 individuals in each group was required. Results are presented as mean ± standard deviation or as number of patients. Statistical significance of comparison of gender between two groups was analyzed with Chi-square test. Statistical significance of age, weight, duration of surgery, VAS and morphine consumption between two groups was tested with independent sample t-test. A $P<0.05$ was considered as statistically significant.

## RESULTS

A total of 80 patients were included and randomly allocated into two groups of 40 each and there were no dropouts. The demographics and duration of surgery were analogous between the two groups. We did not find statistically significant difference among age, gender and weight of the patients and in the duration of surgery between the two groups.

The comparison of VAS pain scores between group L and group S was statistically significant ($P <0.05$) at arrival in PACU, 2 h, 4 h, 8 h and 12 h intervals. However, the difference of pain score at 24 h between two groups was not significant ($P=0.2$) as shown in Table-I.

**Table-I: Pain assessment (VAS) in postoperative period (N=80)**

| Time (hours) | Groups L (n=40) | Group S (n=40) | P |
|---|---|---|---|
| On arrival in the post anesthesia care unit | 1.75±1.23 | 3.45±1.59 | 0.001 |
| 2h | 2.79±1.15 | 4.23±1.61 | 0.001 |
| 4h | 2.17±1.64 | 3.81±1.9 | 0.001 |
| 8h | 2.44±1.74 | 3.98±2.27 | 0.01 |
| 12h | 2.64±1.97 | 4.19±2.74 | 0.02 |
| 24h | 3.95±2.51 | 4.54±2.96 | 0.2 |

Data is presented as mean ± standard deviation.
n: number of patients, Group L: lidocaine group, Group S: saline/placebo group, VAS: visual analogue scale

**Table-II: Postoperative cumulative Morphine consumption (N=80)**

| | Groups L (n=40) | Group S (n=40) | P |
|---|---|---|---|
| **Cumulative Morphine consumption in 24 h (mg)** | 5.09±1.53 | 12.13±2.2 | 0.001 |

Data are presented as mean ± standard deviation or number of patients.
n: number of patients in each group, Group L: lidocaine group, Group S: saline/placebo group

The mean consumption of morphine in group L was 5.09 mg (SD 1.53) and in the group S was 12.13 mg (SD 2.2). This

difference was statically significant (Table-II).
There was no incidence of perioral numbness, metallic taste or other serious signs of systemic lidocaine toxicity.

## DISCUSSION

The results of our study showed that intraoperative infusion of intravenous lidocaine reduced the postoperative pain scores significantly up to 12 hours. Our results are comparable to number of studies conducted internationally.
Several lidocaine infusion regimens with varying duration have been used in these researches. We used lidocaine infusion intraoperatively and until 1 hour after end of surgery in the postoperative period. Song et al[13] and Ahn et al[14] administered the lidocaine infusion only in the intraoperative period and the infusion was not continued in postoperative period. Whereas, Ram et al[15] gave lidocaine infusion from intraoperative period up to 1 hour into the postoperative period just like we did in our study and Farag et al[16] continued the lidocaine infusion until the patient remained in the PACU with a maximum of 8 hours postoperative infusion. In some studies, like Jendoubi et al[17] and Tauzin-Fin et al[18], the infusion was started at induction and continued even 24 hours postoperatively. The dosages of these lidocaine infusion have also differed slightly among studies. Song et al[13] and Ahn et al[14] gave a bolus of 1.5 mg/kg followed by 2 mg/kg/h infusion whereas Jendoubi et al[17] administered 1.5 mg/kg bolus following which an infusion of 1 mg/kg/hour was continued. Saleh et al[19] used a bolus of 1 mg/kg after which an infusion was carried out at 2mg/kg/hour just like our study. However, in some studies no bolus was given, and an infusion up to 2 mg/kg/hour was started on induction as the works done by Farag et al[16], Tauzin-Fin et al[18] and El Shal et al[20].
In terms of reduced visual analogue scores with lidocaine infusion we observed that there were statistically significant less pain scores up to 12 hours after surgery in lidocaine group as compared to the saline(placebo) group. Song et al[13] observed reduced VAS up to 6 hours postoperatively. Whereas research work by Ahn et al[14], Ram et al[15], El Shal et al[20] and Ventham et al[21] revealed reduced VAS up to 24 hours after surgery. This variance in the duration of reduced VAS maybe due to the differences in dosage and duration of lidocaine infusions employed in these studies. Furthermore, the dynamics of local population may have played a role as well due to possible differences in pharmacokinetics and pharmacodynamics. Therefore, the statistically significant reduced VAS up to 48 hours postoperatively in the studies by Jendoubi et al[17] and Tauzin-Fin et al[18] maybe since the lidocaine infusion was continued as long as 24 hours postoperatively.
Since lidocaine infusion has been associated with low VAS, the cumulative opioid consumption is also reduced in the postoperative period. Our result of reduced Morphine consumption was also comparable to other studies which have shown statistically significant reduction in cumulative opioid consumption for postoperative analgesia[13,14,21].
Another important factor obvious from literature review is that the lidocaine infusions are most effective in reducing VAS and cumulative opioid use for analgesia when given during abdominal surgeries[22,23]. Furthermore studies have also produced very promising results on various benefits of lidocaine infusion like inhibiting tumor growth which maybe useful for cancer surgeries[10,23]. Antithrombotic and antibacterial properties may also improve the surgical outcomes in many patients. Therefore, lidocaine infusion has some very encouraging results which can not only improve patient satisfaction but also improve the quality of surgery.

## CONCLUSION

Intraoperative lidocaine infusion should be considered as an adjunct to opioids for postoperative pain management.

## AUTHOR'S CONTRIBUTION

**Atif M:** Designed research methodology, Literature search, Data collection, Literature review, Data interpretation, Statistical analysis, Manuscript writing.
**Saeed U:** Literature review, Data interpretation, Manuscript final reading, Manuscript approval
**Khurshid T:** Literature review, Data interpretation, Manuscript final reading, Manuscript approval.
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**Khokhar MR:** Data collection, Data interpretation, Statistical analysis
**Syed FT:** Literature search, Data collection, Statistical analysis.

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## REFERENCES

1. Subramanian P, Ramasamy S, Ng KH, Chinna K, Rosli R. Pain experience and satisfaction with postoperative pain control among surgical patients. Int J Nurs Pract 2016;22(3):232-238.
2. Ahmed A, Yasir M. Role of acute pain service in optimizing postoperative pain relief in a tertiary care teaching hospital. J Pak Med Assoc 2015;65(11):1164-1168.
3. Fenton BW, Shih E, Zolton J. The neurobiology of pain perception in normal and persistent pain. Pain Manag 2015;5(4):297-317.
4. Timmers I, Kaas AL, Quaedflieg CWEM, Biggs EE, Smeets T, de Jong JR. Fear of pain and cortisol reactivity predict the strength of stress-induced hypoalgesia. Eur J Pain 2018;22(7):1291-1303.
5. Ismail S, Siddiqui AS, Rehman A. Postoperative pain management practices and their effectiveness after major gynecological surgery: An observational study in a tertiary care hospital. J Anaesthesiol Clin Pharmacol 2018;34(4):478-484.
6. Rummans TA, Burton MC, Dawson NL. How Good Intentions Contributed to Bad Outcomes: The Opioid

Crisis. Mayo Clin Proc 2018;93(3):344-350.
7. Dunn LK, Durieux ME, Nemergut EC. Non-opioid analgesics: Novel approaches to perioperative analgesia for major spine surgery. Best Pract Res Clin Anaesthesiol 2016;30(1):79-89.
8. Estebe JP. Intravenous lidocaine. Best Pract Res Clin Anaesthesiol 2017;31(4):513-521.
9. Ortiz MP, Godoy MC, Schlosser RS, Ortiz RP, Godoy JP, Santiago ES et al. Effect of endovenous lidocaine on analgesia and serum cytokines: double-blinded and randomized trial. J Clin Anesth 2016; 35:70-77.
10. Weinberg L, Peake B, Tan C, Nikfarjam M. Pharmacokinetics and pharmacodynamics of lignocaine: a review. World J Anesthesiol 2015;4:17–29.
11. Jian W, Rejaei D, Shihab A, Alston TA, Wang J. The role of multimodal analgesia in preventing the development of chronic postsurgical pain and reducing postoperative opioid use. J Opioid Manag 2018;14(6):453-461
12. Helander EM, Webb MP, Bias M, Whang EE, Kaye AD, Urman RD. A Comparison of Multimodal Analgesic Approaches in Institutional Enhanced Recovery After Surgery Protocols for Colorectal Surgery: Pharmacological Agents. J Laparoendosc Adv Surg Tech A 2017 ;27(9):903-908.
13. Song X, Sun Y, Zhang X, Li T, Yang. Effect of perioperative intravenous lidocaine infusion on postoperative recovery following laparoscopic Cholecystectomy-A randomized controlled trial. Int J Surg 2017; 45:8-13.
14. Ahn E, Kang H, Choi GJ, Park YH, Yang SY, Kim BG at al. Intravenous lidocaine for effective pain relief after a laparoscopic colectomy: a prospective, randomized, double-blind, placebo-controlled study. Int Surg 2015; 100(3):394-401.
15. Ram D, Sistla SC, Karthikeyan VS, Ali SM, Badhe AS, Mahalakshmy T. Comparison of intravenous and intraperitoneal lignocaine for pain relief following laparoscopic cholecystectomy: a double-blind, randomized, clinical trial. Surg Endo 2014;28(4):1291-1297.
16. Farag E, Ghobrial M, Sessler DI, Dalton JE, Liu J, Lee JH et al. Effect of perioperative intravenous lidocaine administration on pain, opioid consumption, and quality of life after complex spine surgery. Anesthesiology 2013;119(4):932-940.
17. Jendoubi A, Naceur IB, Bouzouita A, Trifa M, Ghedira S, Chebil M et al. A comparison between intravenous lidocaine and ketamine on acute and chronic pain after open nephrectomy: A prospective, double-blind, randomized, placebo-controlled study. Saudi J Anaes 2017;11(2):177-184.
18. Tauzin-Fin P, Bernard O, Sesay M, Biais M, Richebe P, Quinart A et al. Benefits of intravenous lidocaine on post-operative pain and acute rehabilitation after laparoscopic nephrectomy. J Anaesthesiol Clin Pharmacol 2014;30(3):366-72.
19. Saleh E, El-Wafa HA, Abd El-Salam Ahmed MI. The effect of intraoperative lidocaine infusion on perioperative opioid consumption for laparoscopic cholecystectomy. Menoufia Med J 2018; 31:83-86.
20. El Shal, S. A Comparative Study of Effect of Intravenous Lidocaine Infusion, Gabapentin and Their Combination on Postoperative Analgesia after Thyroid Surgery. Open J of Anesthesiol 2017; 7:296-314.
21. Ventham NT, Kennedy ED, Brady RR, Paterson HM, Speake D, Foo I et al. Efficacy of Intravenous Lidocaine for Postoperative Analgesia Following Laparoscopic Surgery: A Meta-Analysis. World J Surg 2015;39(9):2220-2234.
22. Beaussier M, Delbos A, Maurice-Szamburski A, Ecoffey C, Mercadal. Perioperative Use of Intravenous Lidocaine. Drugs 2018; 78(12):1229-1246.
23. Dunn LK, Durieux ME. Perioperative Use of Intravenous Lidocaine. Anesthesiology 2017; 126(4):729-737.