# Low Dose Perioperative Lidocaine Infusion for Post-Operative Pain in Open Cholecystectomy

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# Abstract

**Background** : To compare low dose peri-operative lidocaine infusion and placebo for post-operative mean pain score and mean analgesic requirement in open cholecystectomy.

Methods: In this prospective randomized comparative study 120 patients, undergoing open cholecystectomy in general anaesthesia, were included. Patients were randomly allocated to either lidocaine infusion (L) or saline group (S) using systematic randomized sampling with 60 patients in each group. Patients in the lidocaine infusion group were given bolus injection of lidocaine 30 minutes before the skin incision followed by a continuous intraveonous via infusion pump whereas the patients in the saline group received 0.9% normal saline in equal volume and in the same manner. The infusion was continued throughout the surgery and was terminated 60 min after the skin closure.

**Results:** Out of the 120 patients 34 (28.3%) were male while 86 (71.7%) were female. Mean age was 41.32±11.512 years. Both mean VAS pain score and mean analgesic requirement were found to be significantly lower in the lidocaine Group (p-values 0.04 and 0.29 respectively), as compared to controls.

**Conclusion**: Peri-operative low dose systemic lidocaine appears to reduce pain in the immediate post-operative period.

Key words: Lidocaine, Post-operative Pain, Open Cholecystectomy.

# Introduction

Post-operative pain has unpleasant nature and physiological consequences. Search for safe and effective modalities for post-operative pain relief has been of great interest for perioperative physicians. Optimal post-operative pain relief not only increases patient's comfort but also intensifies his satisfaction towards surgery. Provision of effective analgesia in post-operative periods also facilitates early mobilization and rehabilitation of patients. Optimal post-operative pain control is associated with less post-operative cognitive impairment, enhanced quality of life and less risk of chronic post-surgical pain. Effective post-operative pain relief leads to shortened hospital stay, reduces hospital costs and increased patient's satisfaction.NSAIDS are commonly used for post-operative pain relief, they are easy to use but only ketorolac is available in injectable form. These drugs have potential deleterious effects on gastric and renal functions.Opioids are the most commonly used drugs for post-operative pain relief. They provide excellent pain relief but they can cause delay in recovery time, respiratorv nausea and vomiting and depression.Regional techniques may also be used for effective post-operative pain control. 1,2

Lidocaine , is amino amide type local anesthetic and class 1B antiarrhythmic drug. It has rapid onset of action and intermediate duration of action. Its use in chronic neuropathic pain is well established.<sup>3</sup> Now peri-operative use of lidocaine for post-operative pain relief is a topic of interest.<sup>4</sup> Peri operative systemic lidocaine has beneficial post-operative analgesic effects.<sup>5</sup> It also reduces post-operative analgesic requirement.<sup>3, 6,7</sup>

Baral BK et al and colleagues conducted a study in 60 patients undergoing upper abdominal surgery. Thirty patients received 2%lidocaine infusion and 30 patients received normal saline according to randomization. Post-operative requirement analgesic were significantly reduced (142.50±37.80mg Vs185.00±41.31mg p<0.001) in lidocaine Group as compared to control group.6 One study shows that post-operative pain intensity is less in lidocaine group (visual analogue scale score 3.1±2.04 vs 4.5±2.9; p = 0.043).8 Another study showed that there is no significant beneficial effect of peri-operative lidocaine infusion on post-operative pain relief VAS  $(3.5 \pm 1.7)$  in control group vs. (3.4 ±1.6) in lidocaine group. Perioperative lidocaine administration has no influence on postoperative analgesic consumption.9 Postoperative pain is a major issue after every surgical

Postoperative pain is a major issue after every surgical procedure and is a burden on hospitals because different modalities are used for postoperative pain relief.Lidocaine infusion is not used for postoperative pain relief locally and no local study is available on lidocaine for postoperative pain relief although it is an effective modality to control postoperative pain while there are international studies showing controversy in its effectiveness as an analgesic.

## **Patients and Methods**

This prospective randomized comparative study was conducted by the Department of Anaesthesia at Benazir Bhutto Hospital, Rawalpindi, for 6 months from March, 2014 to August, 2014. Patients of elective cholecystectomy, patients of age 18- 60 years and patients of ASA I and ASA II physical status were included . Patients with emergency surgery, with known hepatic or renal dysfunction, with cardiac dysrhythmias /atrioventricular block, having and anticipated duration of surgery more than 3 hours and with a known hypersensitivity/allergy to the study medication were excluded. Patients were randomly allocated to either lidocaine infusion (L) or saline group (S) using systematic randomized sampling. Patients in the lidocaine infusion group were given bolus injection of lidocaine (1.5 mg/kg slowly over 10 min) 30 minutes before the skin incision followed by a continuous IV infusion at the rate of 1.5 mg/kg/h via infusion pump whereas the patients in the saline group received 0.9% normal saline in equal volume and in the same manner. The infusion was continued throughout the surgery and was terminated 60 min after the skin closure. Patients were pre-medicated with inj midazolam 1mg IV 2 hours prior to surgery. In all the patients, anesthesia was induced with inj.propofol 2.0 mg/kg, nalbuphine 0.1 mg/kg, followed by atracurium 0.5 mg/kg intravenously to facilitate the laryngoscopy and orotracheal intubation. After tracheal intubation, anesthesia was maintained with sevoflurane and 50% oxygen+50% N2O with intermittent intravenous boluses of atracurium 10 mg after every 20 min. After completion of surgery, inhalational anesthetics were stopped and the residual neuromuscular blockade was antagonized with the mixture of inj. neostigmine 0.05mg/kg and atropine 0.02mg/kg IV. Infusion was continued for further 1 hour.Severity of pain was monitored at 0 min, 30 min and 60 min in the immediate post-operative period. The severity of pain was assessed by asking the patient to indicate on the 10 cm line at the point that corresponded to the level of pain intensity they felt. The distance in Centimeter from no pain end of visual analogue scale (VAS) to the patient's mark was used as a numerical index of the severity of pain. Any patient complaining of pain immediately after extubation was

considered to have a pain VAS more than 4 and was managed accordingly. A patient with VAS score of more than four was treated with inj. Diclofenac sodium 75 mg IM. If the patient's VAS remained more than four even after 30 minutes of inj. diclofenac sodium then inj. tramadol 100mg IV was given as rescue analgesic. Further and subsequent doses of diclofenac were allowed after an interval of 6 hours without exceeding a total dose of 225mg in 24 hours.After one hour of observation, the patient was shifted to the surgical ward from the PACU where the severity of pain was again measured at 8, 16 and 24 hours post-op. The number of cumulative doses of Injection diclofenac and tramadol given during study period were recorded. If any signs of systemic toxicity or hypersensitivity reaction of the drugs were encountered, they were treated accordingly and patient was excluded from the study.

## Results

One hundred and twenty patients were randomized into two groups by the lottery method. Sixty patients were allocated to the Lidocaine group while 60 patients were allocated to the Control group. Mean age of the patients in the study was 41.32±11.512 years. Mean VAS scale pain score was 3.5±1.604 and the mean analgesia requirement was 78.75±62.9 mg.There were 34 male patients while 86 patients were female. In the Control Group the mean age of the patients was 41.43±11.238 years, mean VAS pain score was 3.8±1.802 and mean Analgesia requirement was 91.25±64.903 mg (Table 1).

Table 1 Comparison of mean VAS pain scores between patients belonging to Lidocaine group and Control Group (n=120)

	Mean VAS Pain	
	Score	p-Value
Lidocaine Group	3.2±1.325	
Control Group	3.8±1.802	0.04

## Table 2 Comparison of mean Analgesia requirement between patients belonging to Lidocaine group and Control Group (n=120)

	Mean Analgesia requirement in mg	p-Value
Lidocaine Group	66.25±58.734	0.029
Control Group	91.25±64.903	

There were 18 male patients (30%) and 42 female patients (70%) in this group.Mean VAS pain score was

3.2±1.325 and mean analgesia requirement was 66.25±58.734 mg. The mean VAS pain score and the mean analgesia requirement were compared between the two groups using independent sample t-test (Table 2).

## Discussion

The mean age in our study was 41.32±11.512 years while female patients were 86 (71.7%) in number. This is in line with the so called famous 5 F's of Cholelithiasis which include Female and Forty. <sup>10</sup> The presentation of patients in our study demonstrates that the international epidemiological data presented on cholelithiasis also holds true in our region, which shows the same epidemiology as the rest of the world. The mean VAS pain score of patients treated with lidocaine infusion peri-operatively in our study was found to be 3.2±1.325, which is significantly less as compared to the mean score of patients treated with placebo, 3.8±1.802. This finding can be compared with the results of McKay et al. whose study also showed a significant difference between the two groups<sup>7</sup>. These findings can also be correlated to some other studies which have shown similar results.<sup>3, 5, 11</sup>

The mean dose of Analgesic required by the patients in the Lidocaine group, 66.25±58.734, was also significantly lower than the mean dose required by patients in the placebo group, 91.25±64.903. This also validates the results of McKay et al. and Baral BK et al.<sup>7, 8</sup> These results can also be compared with other studies which demonstrated the efficacy of Lidocaine infusion peri-operatively in reducing post-op pain.<sup>2,</sup> 3,12, 13

The results of our study are in contrast to the study done by Wuethrich PY et al. whose study did not show any benefit of lidocaine infusion. This may be due to the difference in the outcome variable, the small sample size of Wuethrich PY et al. and the nature of the procedure. As compared to 120 patients in our study Wuethrich PY et al. had only 64 patients with the outcome variable of length of hospital stay. The patients in the study done by Wuethrich PY et al. underwent Laparoscopic Renal surgery conferring the benefit of Laparoscopy in the form of reduced post-op pain and early ambulation.<sup>9</sup>

There is a growing body of data suggesting the role of lidocaine in pain management in the immediate postoperative period but data also suggests that although lidocaine reduces post-operative pain and analgesic requirement, it does not affect the length of hospital stay and discharge timing of the patient.<sup>8, 9</sup>Intravenous lidocaine should not be used in patients with arrhythmias, heart failure, coronary artery disease, Adams-Strokes or heart block and may be used with caution in patients with liver failure, sinusoidal bradycardia and incomplete branch block.<sup>14-17</sup>

Most common side-effects are in general mild and relate to central nervous system. Patients may present with: sleepiness, dizziness, metal taste, headache, blurred vision, paresthesia, dysarthria, euphoria and nausea.<sup>18-20</sup> Higher doses rapidly administered may cause tinnitus, shivering and agitation.<sup>21,22</sup> Cardiovascular changes are in general minimal with usual doses.<sup>23,24</sup> A meta-analysis on the use of intravenous lidocaine in abdominal surgeries reports that with regard to infusion dose beginning and duration there is still not a consensus.<sup>25</sup>

## Conclusion

Lidocaine reduces mean VAS pain score and mean analgesic requirement in patients undergoing Open Cholecystectomy.

## References

- 1. Rawal N. Epidural technique for postoperative pain: gold standard no more? Regional anesthesia and pain medicine. 2012;37(3):310-17.
- 2. Grimsby GM, Conley SP, Trentman TL, Castle EP. A doubleblind randomized controlled trial of continuous intravenous Ketorolac vs placebo for adjuvant pain control after renal surgery. Mayo Clinic Proceedings; 2012:
- 3. Grigoras A, Lee P, Sattar F, Shorten G. Perioperative intravenous lidocaine decreases the incidence of persistent pain after breast surgery. Clin J Pain. 2012;28(7):567-72.
- 4. Choi SJ, Kim MH, Jeong HY, Lee JJ. Effect of intraoperative lidocaine on anesthetic consumption, and bowel function, pain intensity, analgesic consumption and hospital stay after breast surgery. Korean J Anesthesiol. 2012;62(5):429-34.
- 5. Vigneault L, Turgeon AF, Côté D, Lauzier F. Perioperative intravenous lidocaine infusion for postoperative pain control: a meta-analysis o frandomized controlled trials. Can J Anaesth. 2011; 58(1):22-37.
- 6. De Oliveira Jr GS, Fitzgerald P, Streicher LF, Marcus R-J, McCarthy RJ. Systemic lidocaine to improve postoperative quality of recovery after ambulatory laparoscopic surgery. Anesthesia & Analgesia. 2012;115(2):262-67.
- Baral BK, Bhattarai BK, Rahman TR, Singh SN, Regmi R. Perioperative intravenous lidocaine infusion on postoperative pain relief in patients undergoing upper abdominal surgery. Nepal Med Coll J. 2010;12(4):215-20.
- 8. McKay A, Gottschalk A, Ploppa A, Durieux ME. Systemic lidocaine decreased the perioperative opioid analgesic requirements but failed to reduce discharge time after ambulatory surgery. Anesth Analg. 2009;109(6):1805-08.
- 9. Wuethrich PY, Romero J, Burkhard FC. No benefit from perioperative intravenous lidocaine in laparoscopic renal surgery. European Journal of Anaesthesiology (EJA). 2012;29(11):537-43.
- Schirmer BD, Winters KL, Edlich RF. Cholelithiasis and cholecystitis. J Long Term Eff Med Implants. 2005;15(3):329-38.
- 11. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery

from surgery: a systematic review of randomized controlled trials. Drugs. 2010;70(9):1149-63.

- Kranke P, Jokinen J, Pace NL, Schnabel A, Hollmann MW. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. Cochrane Database Syst Rev. 2015;7:CD009642.
- 13. Kim KT, Cho DC, Sung JK, Kim YB. Intraoperative systemic infusion of lidocaine reduces postoperative pain after lumbar surgery: a double-blinded, randomized, placebo-controlled clinical trial. Spine J. 2014;14(8):1559-66.
- 14. Moldovan M, Alvarez S, Romer Rosberg M, Krarup C. Axonal voltage-gated ion channels as pharmacological targets for pain. Eur J Pharmacol. 2013;708(1-3):105-12.
- 15. DeToledo JC. Lidocaine and seizures. Ther Drug Monit. 2000;22(3):320-22.
- 16. Kindler CH, Yost CS. Two-pore domain potassium channels: new sites of local anesthetic action and toxicity. Reg Anesth Pain Med. 2005;30(3):260-74.
- Clarke C, McConachie I, Banner R. Lidocaine infusion as a rescue analgesic in the perioperative setting. Pain Res Manag. 2008;13(5):421-23.
- Catterall WA, Mackie K. Local anesthetics. In: Brunton LL, Lazo JS, Parker KL, (editors). Goodman and Gilman's the Pharmacological Basis of Therapeutics. 11th ed.New York: McGraw-Hill; 2006. 369-85.

- 19. Olschewski A, Schnoebel-Ehehalt R, Li Y, Tang B, Bräu ME. Mexiletine and lidocaine suppress the excitability of dorsal horn neurons. Anesth Analg.2009;109(1):258-64.
- 20. Lui KC and Chow YF, Safe use of local anaesthetics: prevention and management of systemic toxicity. Hong Kong Med J. 2010;16(6):470-75.
- 21. Lauretti GR. Mechanisms of analgesia of intravenous lidocaine. Rev Bras Anestesiol. 2008;58(3):280-86.
- 22. Light AR, Trevino DL, Perl ER. Morphological features of functionally defined neuron in the marginal zone and substantia gelatinosa of the spinal dorsal horn. J Com Neurol. 1979;186(2):151-71.
- 23. Kindler CH and Yost CS. Two-pore domain potassium channels: new sites of local anesthetic action and toxicity. Reg Anesth Pain Med. 2005;30(3):260-74.
- 24. Sheets MF and Hanck DA. Molecular action of lidocaine on the voltage sensors of sodium channels. J Gen Physiol. 2003;121(2):163-75.
- 25. McCarthy GC, Megalla SA, Habib AS. Impact of Intravenous lidocaine Infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. Drugs. 2010;70(9):1149-63.

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