RESEARCH ARTICLE

Role of lidocaine and its effect on postoperative outcomes in abdominal cholecystectomy

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Abstract

Objectives: To investigate the role of pre- and intra-operative lidocaine infusion on post-operative pain management.

Method: The interventional, prospective study was conducted from September 2019 to June 2020 at the Pakistan Ordnance Factories Hospital, Wah Cantt, Pakistan, and comprised patients aged 18-60 years undergoing elective cholecystectomy who were randomised into intervention group A and control group B. Group A was given a bolus dose of lidocaine hydrochloride 2 mg/kg in addition to the standard anaesthesia protocol, while group B was given continuous intravenous infusion of 0.9% normal saline along with the standard protocol. Blood samples for interleukins 6 and 8 were taken at baseline, and then at 2, 6 and 8 hours Post-operatively. Data was analysed using SPSS 23.

Results: Of the 40 patients, 20(50%) were in each of the two groups. There was a marked decrease in interleukins 6 and 8 levels group A compared to group B ($p<0.05$). Interleukin 8 level showed a marked decline compared to that of interleukin 6 ($p<0.05$).

Conclusion: A decrease in interleukins 6 and 8 levels highlighted the anti-inflammatory role of lidocaine and resulted in a decrease in post-operative opioid consumption.

Keywords: Anaesthetic adjuvants, IL-6, IL-8, Opioid-free analgesia, Lidocaine. (JPMA 72: 1048; 2022)

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Introduction

Management of pain is one of medicine's greatest challenges. Pain is subjective, and the clinician must rely on the patient's description of pain and its intensity. Pain generally indicates some underlying inflammatory issues, but post-surgery pain occurs because of the release of inflammatory cytokines in response to surgical trauma. Pain can also affect the autonomic and behavioural responses of the individual.[1]

Opioids were the sole analgesic used for severe pain.[2] Till the 19th century, pain management was not proper, and it was due to the advances in management strategies that this field got modified.[3] Alternative analgesic methods have been used in place of opioids for analgesia, amongst which one is the use of systemic infusion of lidocaine, a local anaesthetic, pre-, intra-, and post-operatively.[4]

Lidocaine, an aminoethylamide anaesthetic, blocks conduction by blocking the influx of sodium ions (Na+) from the voltage-gated Na+ channels, inhibiting the generation of an action potential.

Any injury leads to inflammatory cytokines, like tumour necrosis factor-alpha (TNF-α) interleukin 6 (IL-6) and IL-8 which are associated with the promotion of immune evasion.[5] These factors stimulate the nociception in the sensory nerve endings, leading to hyperalgesia. Lidocaine, by blocking the sodium channels in these sensory nerve endings, helps to induce an inhibitory response on the propagation of action potential. Additionally, it also inhibits the release of pro-inflammatory cytokines. Collectively, all these factors help decrease post-operative pain.[6] Abdominal surgeries are associated with increased levels of these inflammatory mediators. Intravenous (IV) lidocaine can reduce post-operative pain by its analgesic and anti-inflammatory properties. When used as an anaesthetic adjuvant, IV lidocaine enhances effects on post-operative pain and bowel function.[5,7] The current study was planned to determine the anti-inflammatory role of lidocaine and its effect on post-operative outcomes in patients undergoing abdominal cholecystectomy.

Patients and Methods

The interventional, prospective study through convenient sampling was conducted at the Pakistan Ordnance Factories (POF) Hospital, Wah Cantt, Pakistan after taking the approval from institutional ethical committee. The sample size was calculated using online sample size calculator for genetic studies with MAF (minor allele

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frequency) of 0.24.[8] Those included were patients aged 20-60 years without any co-morbidity scheduled for elective abdominal cholecystectomy.[9] Those with co-morbidities and those who refused to volunteer were excluded.

After taking informed written consent, were randomised into intervention group A and control group B. Group A was given a bolus dose of lidocaine hydrochloride 2mg/kg in addition to the standard anaesthesia protocol, while group B was given continuous IV infusion of 0.9% normal saline along with the standard protocol. , Before the procedure, height (feet) and weight (kg) were noted for all the subjects. Two IV cannulas were placed, and every patient was preloaded with saline/dextrose infusion at a rate of 12-15ml/kg/hr during surgery.[10]

General anaesthesia standardised protocol included midazolam 0.04mg/kg, propofol 2mg/kg and rocuronium bromide 0.6mg/kg.[9,10] In group A, anaesthesia was maintained by using sevoflurane[11] and continuous IV infusion with lidocaine hydrochloride 1.5mg/kg/hr.[12]

Each procedure took about 2 hrs. The patient was immediately transferred to the post-anaesthesia care unit (PACU) and PACU hours were noted with no complaint of pain in the immediate post-operative period. No opioid analgesic was given to any patient.[13] They were given 1gm paracetamol as and when required. Blood samples were obtained 10 min before lidocaine infusion, at the end of the surgery, and after the operation at 2, 6 and 8 hrs. Plasma concentrations of IL-6 and IL-8 were measured with commercially quantitative sandwich enzyme-linked immunosorbent assay (ELISA) kits (Thermo Fisher Scientific).[14] All values are reported using the unit µg/ml.[15]

Data was analysed using SPSS 23. IL levels were compared using post-hoc Bonferroni test and one-way analysis of variance (ANOVA). Correlation analysis was also done and correlation coefficient between IL-6 and IL-8 also calculated.[16,17] Data was presented frequencies, percentages, mean ± standard deviation. Statistical significance was set at $p<0.05$.[18]

Results

Of the 80 patients, 40(50%) were in each of the two

Table-1: Clinical characteristics of the patients included in the study (n=80) (Control Group=40, Study Group=40).

		Age (years)	Weight (kg)	Height (feet)	Body Mass Index
N	Valid	800	80	80	80
	Missing	5	9	3	2
Mean		47.69	72.79	5.14	23.20
Std. Error of Mean		1.128	1.302	.040	.311
Median		50.00	75.00	5.00	23.00
Std. Deviation		11.285	13.018	.403	3.090
Skewness		-.346	-.358	1.073	.412
Std. Error of Skewness		.241	.241	.241	.243
Kurtosis		.208	-.207	1.807	-.479
Std. Error of Kurtosis		.478	.478	.478	.481
Minimum		18	38	4	18
Maximum		60	102	6	30

Table-2: Relationship of interleukin 6 (IL-6) and IL-8 levels (pg/ml) between study and control groups.

		Sum of Squares	Df	Mean Square	F	Sig.
IL6 & IL8 pg/ml at 0 hrs before surgery control group (n=40)	Between Groups	1.561	1	1.561	.045	.05*
	Within Groups	130.839	38	3.443		
	Total	132.400	39			
IL6 & IL8 pg/ml at 2hrs after surgery control group (n=40)	Between Groups	.252	1	.252	.042	.039*
	Within Groups	228.523	38	6.014		
	Total	228.775	39			
IL6 & IL8 pg/ml at 6 hrs after surgery control group (n=40)	Between Groups	366.352	1	366.352	.156	.018*
	Within Groups	2261.548	38	59.514		
	Total	2627.900	39			
IL6 & IL8 pg/ml at 8 hrs after surgery control group (n=40)	Between Groups	77.167	1	77.167	.751	.036*
	Within Groups	617.233	38	16.243		
	Total	694.400	39			
IL6 & IL8 pg/ml at 2hrs after surgery study group (n=40)	Between Groups	52.714	1	52.714	.900	.005*
	Within Groups	225.061	38	5.923		
	Total	277.775	39			
IL6 & IL8 pg/ml at 6hrs after surgery study group (n=40)	Between Groups	4.142	1	4.142	.552	.006*
	Within Groups	285.233	38	7.506		
	Total	289.375	39			
IL6 & IL8 pg/ml at 8 hrs after surgery study group (n=40)	Between Groups	1.633	1	1.633	.194	.002*
	Within Groups	319.742	38	8.414		
	Total	321.375	39			

P>0.05 = Not significant (Ns). P<0.05 = Significant (*).

Table-3: Correlation between interleukin 6 (IL-6) and IL-8 levels.

Time	IL6		IL8	
Before surgery 0 hrs	Correlation coefficient	0.54	Correlation coefficient	0.54
	Sig (2-tailed)	0.02*	Sig (2-tailed)	0.02*
2 hrs after surgery	Correlation coefficient	0.67	Correlation coefficient	0.6
	Sig (2-tailed)	0.004*	Sig (2-tailed)	0.002*
6hrs after surgery	Correlation coefficient	0.87	Correlation coefficient	0.78
	Sig (2-tailed)	0.005*	Sig (2-tailed)	0.001*
8 hrs after surgery	Correlation coefficient	0.39	Correlation coefficient	0.32
	Sig (2-tailed)	0.005*	Sig (2-tailed)	0.025*

P>0.05 = Not significant (Ns). P<0.05 = Significant (*).

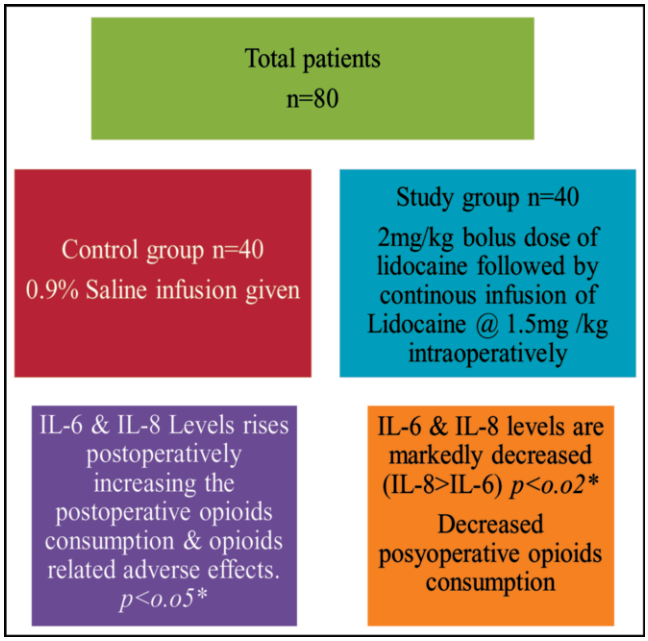

Figure-1: Study flowchart.

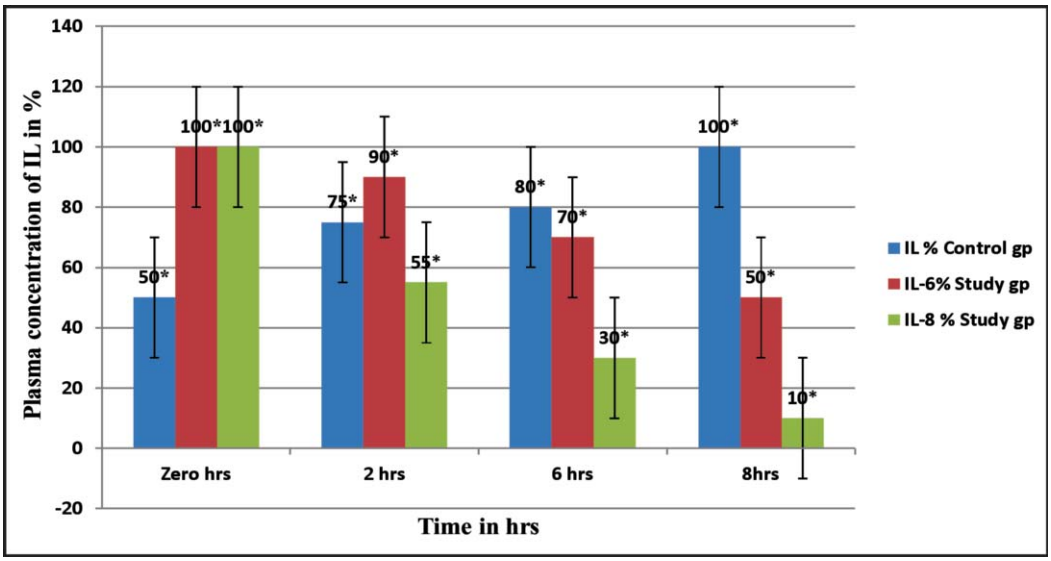

Figure-2: Mean values of interleukin 6 (IL-6) and IL-8 in control and study groups. Error bars showing the standard deviation.

groups (Figure-1). Age, weight, height and body mass index (BMI) were noted for all subjects (Table-1). There was a marked decrease in IL-6 and IL-8 levels in group A compared to group B (Tables-2, 3). IL-8 level showed a marked decline compared to that of IL-6 (Figure-2).

Discussion

Lidocaine infusion has an anti-inflammatory effect when used as an anaesthetic adjuvant and it remarkably changes post-operative pain management.[13] To evaluate its anti-inflammatory effects, plasma levels of IL-6 and IL-8 were observed in the current study, because after an injury, IL starts to appear in blood circulation within 60 min, and its level continues to rise and reach the maximum level in 4-6 hrs, and may last for as long as 10 days if no intervention is done.[17]

In the current study, IL-6 and IL-8 levels decreased after the operation, but a more marked decrease was observed in samples taken at 6 hrs post-surgery. Circulating cytokines levels appear to be proportionate to the extent of tissue injury during the operation. The sympathetic nervous system, through its autocrine and paracrine stimulation in response to surgical trauma, causes the release of IL-6 and IL-8, which, in turn, stimulates the pain pathways. The current results are supported by an earlier study.[19]

IL-8, when released in

response to surgical incision, causes the release of neutrophils and monocytes at the site of trauma, accelerating the inflammation. This, in turn, stimulates the sympathetic discharge, accelerating the release of IL-6 and intensifying the pain. Lidocaine, by blocking the release of these inflammatory mediators, inhibits the humoral link between tissue injury and sympathetic hyperalgesia.[8]

A study postulated that G protein-coupled receptors in response to inflammation get stimulated and result in the development of paralytic ileus. The inhibition of this anti-inflammatory action by IV lidocaine infusion proves to be beneficial in preventing the paralytic ileus.[20]

Another study demonstrated that lidocaine acts as a 'functional antagonist' of inflammatory mediators, reducing the acute response, inhibiting the release of mediators, and providing an anti-inflammatory effect.[21] The finding further strengthens the results of the current study.

A randomised, placebo-controlled study in China demonstrated that the use of IV lidocaine pre- and intra-operatively is associated with the inhibition of lymphocyte proliferative response, and decreases the production of nitrous oxide and cytokines that help in the inhibition of post-operative pain.[22] The Chinese study concluded that the main therapeutic effect of IV lidocaine after major surgeries with extensive tissue damage was attributed to analgesic effect mediated by mechano-sensitive nociceptors, and inhibition of pro-inflammatory cytokines, thus decreasing post-operative narcotic consumption. The finding supports the results of the current study.

Further research is required for comparing the effects of lidocaine given epidurally for post-operative pain.[22]

Conclusion

Lidocaine as an anaesthetic adjuvant is a gateway to opioid-free anaesthesia (OFA) and helps minimise narcotic-related complications without compromising on patient comfort.

Disclaimer: The text is based on an academic thesis.

Conflict of Interest: None.

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