Original Article

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Effect of Lignocaine on Postoperative Serum Lactate Dehydrogenase and Lactate Levels in Patients Undergoing Bowel Surgery

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Author`s Contribution

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ABSTRACT

Objective: To evaluate effect of intraoperative lignocaine on postoperative serum LDH and lactate levels and to compare with placebo in patients undergoing bowel surgery.

Methodology: This randomized controlled trial was conducted at the Department of Biochemistry, Islam Medical, Sialkot, Pakistan from August 2023 to January 2024. Serum LDH and lactate levels were measured preoperatively on automatic biochemical analyzer (produced by Beckman Coulter, GRM, 2166) was used to analyze, before extubation, and at 6 and 24 hours postoperatively, between patients who received intraoperative lignocaine versus those who received saline during bowel surgery under general anesthesia.

Results: The study involved two groups: Group lignocaine (n = 20) where patients received 2% lignocaine at the rate of 1.5 mg/kg intravenous followed by maintenance infusion at the same rate until the end of surgery, and Group normal saline (n = 20) where patients received normal saline at the rate 1.5 mg/kg IV followed by infusion at the same rate until the end of surgery The average serum lactate postoperative, before extubation, 6 hours and 24 hours of lignocaine group was 2.68±0.32 mmol/l, 1.26±0.22 mmol/l, 1.09±0.28 mmol/l, and 1.15±0.13 mmol/l, respectively ($p<0.001$). Whereas the average serum lactates at postoperative, before extubation, 6 hours and 24 hours of normal saline group was 2.86±0.37 mmol/l, 2.64±0.65 mmol/l, 2.15±0.31 mmol/l, and 1.65±0.38 mmol/l, respectively ($p<0.001$).

Conclusion: Patients undergoing bowel surgery who received intraoperative IV lignocaine exhibited lower postoperative serum LDH and lactate levels compared to those who received normal saline. It was also concluded that indirectly intravenous lignocaine also improves postoperative outcomes by reducing pain and hospital stay.

Keywords: Intravenous Lignocaine, Serum lactate dehydrogenase, Lactate level, Bowel surgery, Pain

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Introduction

In abdominal surgeries adjuvant therapies and multimodal analgesia was recommended for management of pain relief in postoperative period of abdominal surgeries[1], with lignocaine intravenous (IV) being considered a suitable alternative for patients who are not suitable or hesitant for interventional peripheral and neuraxial nerve blocks.[2] Intravenous lignocaine in perioperative period offers various benefits, such as analgesic effects, facilitating earlier return of bowel function, reducing the incidence of

postoperative nausea and vomiting (PONV), and contributing to shorter hospital stays.[3]

Elevated lactate levels can result from increased aerobic glycolysis, where pyruvate production exceeds the capacity of pyruvate dehydrogenase enzymes. This phenomenon is often triggered by cytokine release, elevated circulating catecholamines, or the accumulation of leukocytes at sites of inflammation.[4] High serum levels of lactate dehydrogenase (LDH), a non-specific biomarker found in nearly all body tissues, indicate tissue damage[5], hypoxic conditions, and various specific diseases, serving as a prognostic indicator, particularly in critically ill patients, and correlating with the degree of cerebral damage in acute brain injury cases.[6]

Serum lactate levels serve as a marker indicating the equilibrium between oxygen demand and supply, influencing the immunoinflammatory response.[7] Following major elective abdominal surgery, heightened postoperative lactate levels can correlate with a higher risk of complications and mortality.[8] Additionally, pain can influence the levels of biochemical markers such as lactate dehydrogenase (LDH), with elevated LDH levels being associated with the release of tissue architecture damage, cell necrosis, tissue injury, and inflammatory markers.[9]

In the context of hyperlactatemia, it is crucial to consider alternative aerobic mechanisms and address underlying causes accordingly, particularly by recognizing signs of hepatic dysfunction, which significantly affect lactate clearance.[10]

This study may helpful in understanding the impact of lignocaine on postoperative serum lactate and LDH levels could lead to more effective pain management strategies and better postoperative recovery protocols for patients undergoing bowel surgery. Study might be helpful in fulfillment of research gap of this region that is lacking from couple of tears.

Methodology

This randomized controlled study was conducted at the Department of Biochemistry, Islam Medical College, Sialkot, Pakistan from August 2023 to January 2024, spanning six months, obtained ethical approval IMDC/Biochem/DERC/2023/10 from the hospital's ethics committee and secured informed consent from patients.

Sample size was calculated by using online software openepi.com with 95% confidence interval, 80 % power of study and statistics from previous study conducted by Ahuja et al, in his study mean VAS score at 6 hours serum LDH was 251.63 ± 91.9 in lignocaine group and 446.7 ± 257.8 in control groups. The study included 40 patients categorized as physical status ASAI–II. Patients with hepatic or renal deficit, neurological disorders, unable to describe VAS scale, hypersensitivity to study drugs, previous history of substance abuse, autoimmune disorder, chronic pain and use of analgesics, congestive heart failure and abnormal conduction of cardiac activity were excluded.

Baseline hemodynamic data were collected in the operating room using a multichannel monitor. Serum lactate levels were measured using a metabolite analyzer, while LDH levels were measured using an automated chemistry analyzer. Randomization of the patients was done in two groups Lignocaine or normal saline using a lottery method as lottery envelope chosen by the patients either in normal saline group or lignocaine group. Group lignocaine (n = 20) where patients received 2% lignocaine at the rate of 1.5 mg/kg intravenous followed by infusion at 1.5 mg/kg/h until the end of surgery, and Group normal saline (n = 20) where patients received normal saline at the rate 1.5 mg/kg IV followed by infusion at the same rate until the end of surgery.

The study-maintained blinding for both the observer and the patient, with an independent anesthesia resident preparing the study drug and not being involved in subsequent patient analysis or management. A standard general anesthesia (GA) technique was used, including 1-2 µg/kg fentanyl intravenously, 2-3 mg/kg propofol, 0.1 mg/kg vecuronium, 1%-2%sevoflurane, and mixture of nitrous oxide with oxygen at a ratio of 60:40, for targeted minimum alveolar concentration (MAC) of 1.0. Hemodynamics stability was maintained was kept within 20% deviation from baseline using routine balanced anesthesia, fluid administration, and vasopressors as required. Fluid therapy was done as 10-12 ml/kg in the 1st hour and after that 1.5-2 ml/kg/h for maintenance fluid. Throughout the perioperative period urine output was maintained at 1 ml/kg/h.

In the postoperative period, patients who experienced a VAS >3 were administered rescue analgesia with IV tramadol at a dose of 2 mg/kg, with a maximum allowable dose of 400 mg within 24 hours. Additionally, all patients were given IV paracetamol (1g every 6 hours) and IV diclofenac (75 mg every 12 hours) for the first 24 hours after surgery.

Serum LDH and lactate levels were measured preoperatively on automatic biochemical analyzer (produced by Beckman Coulter, GRM, 2166) was used to analyze, before extubation (removal of endotracheal tube to wean off from mechanical ventilation), and at 6 and 24 hours postoperatively, between patients who received intraoperative lignocaine versus those who received saline during bowel surgery under general anesthesia. Other outcomes assessed included VAS scores at rest and on movement, measured at baseline, 1 hour in the postoperative anesthesia care unit (PACU), and at 6-, 12-, and 24-hours' post-surgery.

SPSS version 27 was used for data analysis. Mean ans standard deviation was calculated and presented for numerical values like age, VAS score, serum LDH, lactate level, BMI and time for 1st flatus. Frequency and percentages were calculated for categorical variables like gender. Student t test was applied on numerical values and chi square for categorical values. After test of significance p value less than or equal to 0.05 was taken as significant.

Results

Demographic profile of both the groups was shown in table I. The mean age and BMI of lignocaine group was 41.80±3.91 years and 25.65±5.09 kg/m^2, respectively. Mean age and BMI of normal saline groups was 43.45±3.85 years and 27.20±6.31 kg/m^2, respectively. Demographic profile was homogeneous in both the groups, (p>0.050). The mean time to flatus of lignocaine and normal saline group was 66.80±8.87 hours and 87.41±7.55 hours, respectively, (p<0.001). Whereas mean hospital stay of lignocaine and normal saline group was 2.61±1.39 days and 4.35±2.30 days, respectively. (p<0.001). (Table I).

The average serum LDH at postoperative, before extubation, 6 hours and 24 hours of lignocaine group was 381.14±33.51IU/l, 243.25±24.14 IU/l, 257.18±14.66 IU/l, and 337.96±16.93 IU/l, respectively. Whereas the average serum LDH at postoperative, before extubation, 6 hours and 24 hours of normal saline group was 306.62±32.15 IU/l, 426.29±47.83 IU/l, 443.66±20.46 IU/l, 398.79±16.13 IU/l, respectively (p<0.001). (Table II).

The average serum lactate postoperative, before extubation, 6 hours and 24 hours of lignocaine group was 2.68±0.32 mmol/l, 1.26±0.22 mmol/l, 1.09±0.28 mmol/l, and 1.15±0.13 mmol/l, respectively. Whereas the average serum lactates at postoperative, before extubation, 6 hours and 24 hours of normal saline group was 2.86±0.37 mmol/l, 2.64±0.65 mmol/l, 2.15±0.31 mmol/l, and 1.65±0.38 mmol/l, respectively. (p<0.001). (Table III).

Table I: Demographic profile of the groups.

Variable	Group		p-value
	Lignocaine n=20	**Normal saline n=20**	
	Mean±SD		
Age (years)	41.80±3.91	43.45±3.85	0.187
BMI (kg/m^2)	25.65±5.09	27.20±6.31	0.398
Gender N (%)			
Male	11 (55.0)	12 (60.0)	0.749
Female	9 (45.0)	8 (40.0)	
Time to 1st flatus (hours)	66.80±8.87	87.41±7.55	<0.001
Hospital Stay (days)	2.61±1.39	4.35±2.30	<0.001

Table II: Serum LDH (IU/l) levels at different time intervals among the groups.

Serum LDH (IU/l)	Group		p-value
	Lignocaine n=20	**Normal saline n=20**	
	Mean±SD		
Preoperative	381.14±33.51	306.62±32.15	<0.001
Before extubation	243.25±24.14	426.29±47.83	<0.001
6 hours	257.18±14.66	443.66±20.46	<0.001
24 hours	337.96±16.93	398.79±16.13	<0.001

Table III: Serum lactate (mmol/l) levels at different time intervals among the groups.

Serum lactate (mmol/l)	Group		p-value
	Lignocaine n=20	**Normal saline n=20**	
	Mean±SD		
Preoperative	2.68±0.32	2.86±0.37	<0.001
Before extubation	1.26±0.22	2.64±0.65	<0.001
6 hours	1.09±0.28	2.15±0.31	<0.001
24 hours	1.15±0.13	1.65±0.38	<0.001

The postoperative VAS score at rest and at movement over time of lignocaine group was lower than the normal saline group at each time interval, (p<0.001). (Figure & II).

Discussion

Elevated LDH levels can serve as a reliable indicator of hepatic injury, as supported by prior research[11], and are also indicative of organ dysfunction, potentially contributing to significant postoperative complications. Studies have demonstrated that patients experiencing postoperative complications have notably higher mortality and recurrence rates, with increases of 43% and 38%[12], respectively, compared to those without such complications.

There are few researches investigating the prognostic significance of lactate monitoring specifically in patients

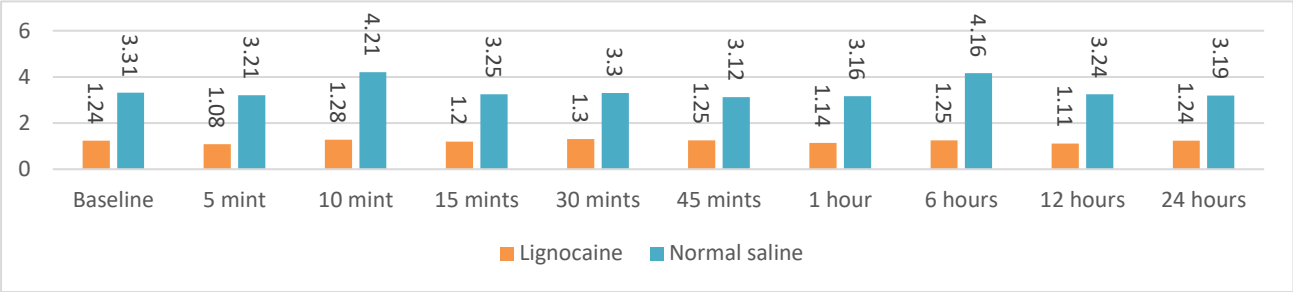

Figure I. Distribution of VAS score at rest among both the groups.

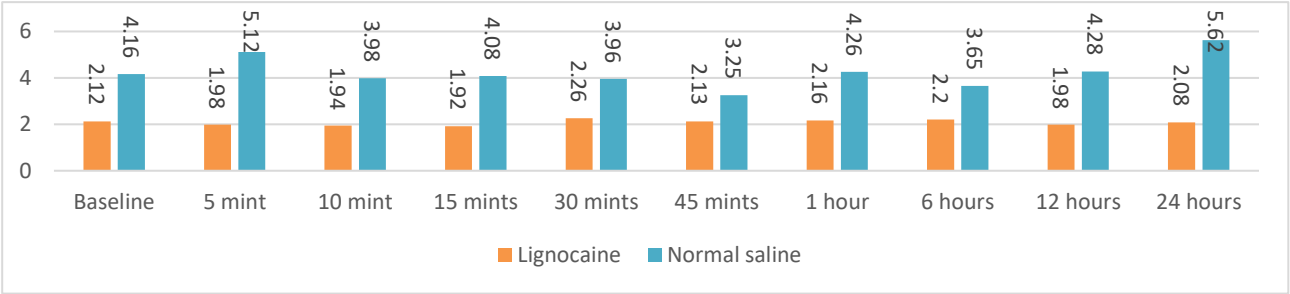

Figure-II. Distribution of VAS score at movement over time among both the groups.

undergoing elective major abdominal surgery, with most studies focusing on heterogeneous groups of critically ill patients in ICU and emergency department settings, predominantly those with sepsis, trauma, shock, or severe respiratory failure.[13]

In this study majority of patients were male in both lignocaine 55% and placebo 60% group. Ho et al[14] conducted a study that involved fifty-eight patients, with 42 of them being male, who were randomized, with 29 in each arm (lidocaine and control). The median age of the patients was 64 years (ranging from 51 to 70 years), and their body weight ranged from 64 kg to 89 kg, with a median of 75 kg.

In this study postoperative VAS score at rest and at movement over time of lignocaine group was lower than the normal saline group at each time interval. In their study, González-Callejas et al[15] discovered a robust correlation between lactate dehydrogenase (LDH) concentrations and postoperative pain levels. This finding suggests that can serve as a valuable biochemical predictor to identify patients who are likely to require more potent analgesics for effective and aggressive pain management following surgical procedures. Ahuja et al[16] study concluded that low level of postoperative serum LDH and lactate levels in patients who were given intravenous lignocaine as compared to those who received normal saline during bowel surgery.

The impact of lidocaine on postoperative outcomes was less significant than what was observed in the recent meta-analysis conducted by Sun et al[17] analysis who revealed a noteworthy decrease in the time to 1st flatus and bowel movement by 11.11 hours and 15.11 hours, respectively. Additionally, there was a reduction in hospital length of stay by 0.71 days, as well as lower rest pain scores. In this study mean time to flatus of lignocaine and normal saline group was 66.80±8.87 hours and 87.41±7.55 hours.

Birklein et al[18] and Julius et al[19] found that venous lactate levels remained unchanged, while skin lactate levels were significantly elevated in patients with complex regional pain syndrome (CRPS) compared to control subjects (2.95 mmol/L vs. 1.74 mmol/L; $p < 0.005$), indicating a likely increase in anaerobic glycolysis, possibly due to chronic tissue hypoxia.

Forkasiewicz et al[20] study revealed that elderly hepatocellular carcinoma (HCC) patients undergoing hepatic arterial chemoembolization experienced improved long-term prognosis and enhanced clinical efficacy, with prolonged survival time, when they had low levels of serum LDH compared to those with high levels. In a study involving 40 patients, Harvey et al[21] found that while the lidocaine group showed faster recovery of bowel movement and earlier discharge compared to the control group, there were no significant differences observed in opioid consumption, flatus recovery, or Visual Analog Scale (VAS) pain scores at 6-, 18-, or 24-hours' post-surgery.

Conclusion

Patients undergoing bowel surgery who received intraoperative IV lignocaine exhibited lower postoperative serum LDH and lactate levels compared to those who received normal saline. It was also concluded that indirectly intravenous lignocaine also improves postoperative outcomes by reducing pain and hospital stay.

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