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Original article

Impact of Lignocaine infusion on anaesthetic drug requirement and post-operative recovery outcome in major elective non cardiac surgery under general anaesthesia: A descriptive observational study from Maharashtra

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ABSTRACT

Background: Multimodal analgesia demands use of drugs in perioperative period producing adequate pain relief without affecting the quality of recovery by attenuating drug-related adverse effects.Systemic lignocaine has effective analgesic, anti-inflammatory, and anti-hyperalgesia properties and improves the quality of recovery after surgery. Its systemic effects on hemodynamic and anaesthetic requirements were not well explored.Therefore, aprimary objective of this study aims at 1) Impact on anaesthetic drug requirement: muscle relaxant and volatile anaesthetic agent (ETSevoflurane),intraoperative opioidand hemodynamic stability. 2) The secondary objective waspost-operative outcomeand post op analgesia in major elective non cardiac surgery under GA.**Methodology:** Currentstudy investigated the impact of lignocaine infusion by comparing two groups: one Group[L], receiving lignocaine infusion 1.5mg/kg bolus followed by infusion of 2mg/kg/hr. in addition to standard anaesthesiaand control Group [C] receiving only standard anaesthesia.ET-Sevoflurane,total opioid,muscle relaxant, postoperative outcome like Extubation time, Eye opening time,and verbal response, requirement of rescue analgesic Inj. Tramadolfor 1 to4hourspostop were evaluated.**Results:** ET Sevoflurane concentration was lower in group[L] [1.22% (SD 0.342) Vs. 2.35% (SD 0.226)]Amountof muscle relaxant was lower in group[L][34.11± 0.69Vs. 46.78± 7.646mg, 30% reduction] Time to extubation [T1][5.8±2.4Vs. 9.635 ±0.85 min], response to verbal command [(L)8.28 ±2.86Vs.(C)14.33 ±1.31min)]. Postoperativeanalgesic[2/48 (L)Vs. 16/48(C) patients]. Hemodynamics like MAP, SBP, DBP and HR were lower in [L] group and remained optimum. No sedation noted,no adverse effects.**Conclusion:**Lignocaine infusion reducesperioperative opioids and anaesthetics. It achieves hemodynamic stability and reduces requirement of analgesics for

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post-operative pain. Lignocaine infusiongiven as an adjunct in the perioperative period benefits as analgesic plus anaesthetic sparing in anaesthesia practice.

Key words: Lignocaine, Muscle relaxant, Sevoflurane, Extubation, Infusion.

Introduction:

This is a descriptive study was approved by Institutional Ethical committee of MIMER Medical College, Talegaon (D), Pune No. (IEC/MIMER/2021/775) and all participants provided with written informed consent. This study was conducted between November 2021 to July 2023 in tertiary care hospital of western Maharashtra.Ninety-six adult patients participated.

Post-operative nausea vomiting (PONV) and pain are the common hazards of General Anaesthesia. These are most disturbing and discomforting to an anesthetising patient. These untoward effects are increased by volatile agents and increased doses of opioid [1]. Thinking about opioids risks in the postoperative period [1]; found an increased interest in the use of non-opioids analgesic adjuncts. [2]Non-opioid analgesics have been increasingly used due to concerns about opioid safety in the postoperative period.One such promising drug of potential interest is IV lignocaine, which can be administered intra- and/or postoperatively in order to decrease postoperative pain and improve recovery outcomes. Injection Lignocaine (also known as lidocaine) is an amino-amide local anesthetic (LA) that has gained attention for its potential benefits when administered intravenously during surgical procedures.The half-life of lignocaine is 1.5 to 2 hours after a bolus dose; however, the half-life of lignocaine can be prolonged with infusion durations.It has been used widely in chronic and neuropathic pain management and postoperative analgesia via IV infusion. [2]

In the majority of trials, the clinical effect of lignocaine exceeded the duration of the infusion by more than 8.5hrs, which is 5.5 times the half-life of the compound.The reported benefits of perioperative lignocaine infusion include reductions in pain, nausea, ileus duration, opioid requirement, and length of hospital stay.

With this background study aims to observe the impact of lignocaine infusion on anaesthetic drug requirements postop analgesia, hemodynamic stability and postoperative recovery outcomes. It also demonstrated its usefulness as an adjunct in perioperative period.

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Study design: This is a descriptive study comparing two groups. Study group, Group [L] receiving Lignocaine infusion along with standard GA and control group, Group [C] receiving only standard GA protocol for non-cardiac surgery lasting for 2-3 hours.

Considering reduction of 30% in the anaesthetic doses as shown in pilot study at Type I error α=0.1 and allowable error 20%, the minimum estimated sample size was 96 participants. They were divided in two groups. The formula used was:

$$n = \frac{(Z\alpha)^2\, pq}{(l)^2} = \frac{(1.28)^2 \times 30 \times 70}{(6)^2} = 96$$

Where Zα= 1.28 at α=0.1 p=30 q= (100-p) =70 and l= 20% of p= 6

Study criteria:

Inclusion criteria:

- Adult patients posted for elective non cardiac surgery lasting for 2-3 hours under general anaesthesia
- Age 18 to 65 yrs.
- ASA Physical Status grading I-II
- Hemodynamically stable patients
- Patients without co-morbid medical illness.

Exclusion Criteria:

- Patients having H/O allergic reaction to Lignocaine.
- Patients with Hepatic and Renal disorder.
- BMI>35kg/m^2
- Chronic abuse of NSAID or opioid.
- Patients on Beta blockers
- H/O Obstructed sleeps apnoea (OSA)
- Co-morbid diseases like Diabetes/ Hypertension/Ischemic heart disease / Heart block and on anticoagulant
- Mallampatti class III-IV
- Pregnant women and Lactating mothers

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- H/O Respiratory; CNS and Psychiatric disorders.

Exclusion criteria are equally important to define a homogenous study population and minimize confounding variables.

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Methodology

Preoperative phase:

Participants were connected to multipara monitor device for ECG, pulse oximeter and NIBP monitoring in the recovery room. Group [L] received 1.5mg/kg preservative free intravenous bolus Lignocaine injection over 15 minutes before GA along with IV Ringer lactate solution. Group [C] participants received only IV Ringer lactate infusion.Patients were shifted to OT after 15 minutes.Serious side effects, such as neurologic changes and cardiac toxicity, were not observed.

Intraoperative Material and Monitoring:

In the operation theatre (OT), the standard routine protocol used for GA was as follows:

Following premedication with inj. Glycopyrrolate, Midazolam and Ondansetron IV, induction of anaesthesia was achieved by injection Fentanyl 2mg/kg and injection Propofol 1-1.5mg/kg till the loss of consciousness.Neuromuscular blockade was achieved with injection Atracurium 0.5 mg/kg. Patients were intubated with Portex cuffed endotracheal tube of appropriate size. Injection Paracetamol 1gm IV was started before incision. Anaesthesia was maintained with 66% N_2O and 33% O_2.and Sevoflurane with intermittent incremental doses of injection Atracurium in the dose of 0.1mg/kg; to achieve surgical plane of anaesthesia. Incremented doses of injection Atracurium were given only after seeing a notch in the EtCO2. Inj. Fentanyl was given additionally if tachycardia observed. Patients were ventilated mechanically to achieve end-tidal CO_2 concentration between 33 to 40 mmHg. Any change in these hemodynamic parameters (e.g., HR, SBP, and MAP) was acted upon by altering the concentration of Sevoflurane and addition of injection Fentanyl 0.5mg/kg. Nearing to closure, infusion was stopped. Neuromuscular blockade was reversed by inj. Neostigmine (0.05mg/kg) and inj. Glycopyrrolate (0.01 mg/kg).

Post-operative assessment:

Recovery outcome was evaluated using pain scores, time for extubation, eye opening time, obeying verbal response after adequate reversal condition. Rescue Tramadol was given when VAS>5. Total consumption of Muscle relaxant, End Tidal inhalational anaesthetic agent and consumption of opioid injection were noted. Post op dose of Rescue analgesic was

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calculated. Patients were also observed for Nausea, vomiting and any other side effects like Sedation, hypotension and Bradycardia.

STATISTICAL ANALYSIS: Data was analysed using SPSS version (24.0).For the continuous data, Student's t test and Mann–Whitney U tests were performed. To compare means, standard two-sample t tests were used. For categorical data, Chi square test was used.

RESULTS:

Table 1: Baseline demographic data of the study population

Variable name	**Group L (n-48)**	**Group C (n-48)**	**P value**
Age(years)	35.62 ±15.54	37.31±14.44	0.582
ASA PS			
I	12(25%)	14(29.16%)	0.648
II	36(75%)	34(70.84%)	
III	0	0	
Weight (Kg)	54.22 ±10.41	57.95±10.53	0.0812
Duration of surgery (hours)	2.35 ±0.79	2.65 ±0.80	0.0648
Alderete score	9.020 ± 0.144	8.87 ± 0.33	0.0046

Interpretation:

- Most demographic and clinical characteristics (age, ASA status, weight, and duration of surgery) show no statistically significant differences between groups ($p > 0.05$), indicating well-matched groups.
- The Alderete score shows a statistically significant difference ($p < 0.05$), suggesting better post-anesthesia recovery in Group L

Figure 1: Bar diagram showing types of surgery the patients underwent

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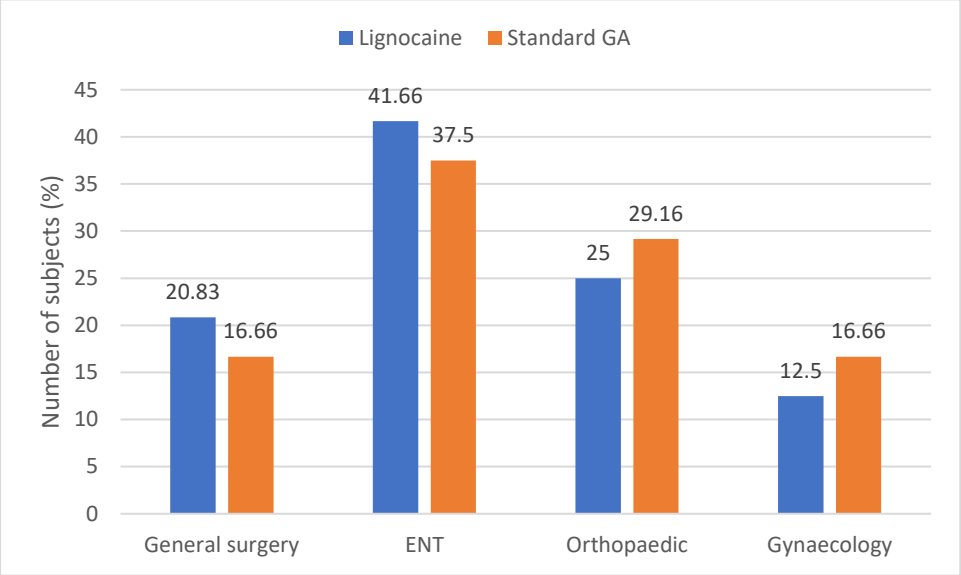

Table2: Distribution according to opioid consumption

	Standard GA	GA with Lignocaine	P value
Fentanyl opioid used (mg)	120±3.247	75±2.66	0.042
Post op analgesic No. of patients	16/48 (33.33%)	2/48(4.12%)	0.013

Consumption of perioperative opioid and post op analgesics were much less with Lignocaine infusion ($p<0.05$)this represents a 37.5% reduction in fentanyl requirement with lignocaine and 87.6% reduction in the number of patients requiring post-operative analgesics. These findings strongly support the clinical benefits of adding lignocaine to the GA protocol for both intraoperative and post-operative pain management

Table 3: Anaesthetic drugs required

	Conventional GA	**GA with Lignocaine**	**P value**
ET-Sevoflurane %	2.359±0.226	1.227±0.342	0.001

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Dose of Muscle relaxant in (mg)	46.66±7.700	34.11±0.69	0.001

1. ET-Sevoflurane Concentration:

- Conventional GA: 2.359% (±0.226)
- GA with Lignocaine: 1.227% (±0.342)
- The difference is statistically significant (p = 0.001)
- This shows that adding Lignocaine resulted in approximately 48% lower Sevoflurane requirements

2. Muscle Relaxant Dosage:

- Conventional GA: 46.66 mg (±7.700)
- GA with Lignocaine: 34.11 mg (±0.69)
- The difference is statistically significant (p = 0.001)
- This indicates about 27% lower muscle relaxant requirements when Lignocaine was used

The data suggests that adding Lignocaine to the GA protocol significantly reduced the requirements for both Sevoflurane and muscle relaxants. This could potentially lead to faster recovery times and fewer side effects

Table 4:Distribution according to hemodynamic changes

Time in hours	SBP(Mean ±SD)	DBP(Mean +SD)	MAP (Mean +SD)	HR
Pre op	124.67 ±16.14	79.26 ±11.09	89.57 ±13.95	90.39 ±13.87
0.5	115.31 ±16.3	74.78 ±13.0	83.37 ±14.18	88.44 ±13.40
1	111.55 ±16.65	71.28 ±13.05	81.64 ±12.84	86.09 ±12.03
1.5	110.33 ±15.55	70.92 ±12.99	79.63 ±14.67	83.44 ±12.42
2	111.05 ±15.14	71.09 ±11.14	80.60 ±13.91	83.23 ±12.29
2.5	111.67 ±14.72	71.30 ±11.36	80.97 ±13.70	84.12 ±12.32
3	108.90(12.98)	67.74(11.60)	78.51(11.98)	79.38(10.85)

The average **Mean Arterial Pressure** [83.37mm Hg (SD: 14.18)], **Systolic blood pressure** was also lower [115.31 mmHg (SD:16.30)], **Diastolic Blood Pressure**was [74.78mm Hg(SD :13.0)] as was the mean heart rate [88.44 beats/min (SD: 13.40), 95% CI with power of 80%

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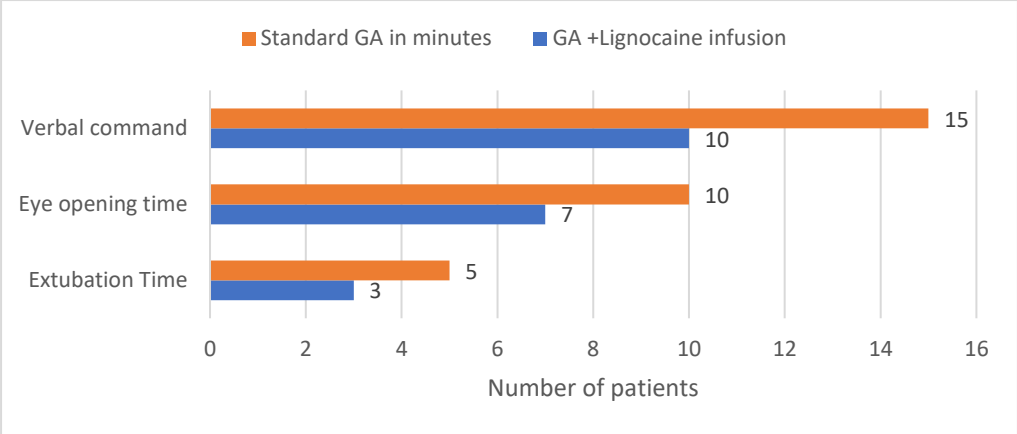
(Mentioned at 30 min. 1 hr,1.5hr 2hr,2.5hr,3hr)Pre -op is mentioned table 4. All the values of Hemodynamic status like MAP, SBP, DBP and HR were lower and remained more or less with normal limits throughout the surgical duration after IV Lignocaine Bolus+ Infusion. Intravenous lignocaine reduces volatile anaesthetic requirements(40-50%) and lowers blood pressure and heartRate. No difference in sedation score. No adverse effects.

Figure 2:Bar diagram showing post op recovery outcome



<u>This bar graph compares two groups - Standard GA (General Anesthesia) and GA with Lignocaine infusion - across three metrics:</u>

Shows faster response to verbal command, Quicker eye opening, Demonstrates faster extubation in Lignocaine group. The data suggest that patients receiving GA with Lignocaine infusion consistently showed faster recovery times across all three parameters compared to standard GA alone. The Largest difference appears to be verbal command response time(5 min. diff.) followed by eye opening time(3 min. diff.), and extubation time (2 min. diff.)

<u>DISCUSSION</u>:

Since lignocaine infusion's first clinical use in 1961, various meta-analyses have established the efficacy of IV lignocaine use. The results of these reviews showed remarkable reduction of pain and/or opioid requirements during the first 24 hours postoperatively. It also reduces anaesthetic requirements by approximately one third.[3]Less expensive and safety profile made it useful in perioperative period. Several animal studies were carried out to reveal its efficacy. *Bailey et al*. concluded that perioperative lignocaine infusions reduced the presence of procedure-related pain longer after surgery. [3]

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The detailed mechanism of action includes its binding with sodium channel potassium Channels, calcium channels, G-coupled protein receptors, N -methyl-D-aspartate (NMDA) receptors, the glycinergic system and its interaction with general anaesthetic agents which has synergism. [3] Lignocaine has anti-inflammatory properties and prevents central nervous system hyperalgesia. Lignocaine infusion in humans is evaluated for its pain relief, cytokine response, PONV, acceleration of hospital discharge.[4-8] The analgesic effect is through suppression of generating impulse from damaged nerve fibres and proximal dorsal root ganglion. NMDA receptors cause inflammatory response. [9,10] There is an abruption of neural transmission at the site of tissue injury which results in reduction of neurogenic inflammation. Such mechanisms are thought to contribute to the anti neuro inflammatory effects of lignocaine and may explain its clinical benefits in the management of acute and chronic pain. [11-13]

We have studied our patients of ENT, General Surgery, Gynaecological, Orthopaedic patients posted for major surgeries lasting for 2-3 hrs. under General Anaesthesia. We have studied 96 patients for post-operative pain relief for 1-4hrs. in recovery period and found less requirement of Intravenous Injection Paracetamol or Injection Tramadol. In our patients we have used 1.5mg/kg bolus dose of injection Lignocaine 15 minutes prior to OT and 2mg/kg dose after induction as an infusion and continued throughout. We stopped infusion 30 minutes prior finishing and the ET concentration of Volatile agent Sevoflurane was adjusted to MAC value

Ahn et al[12] in2015 did IV lignocaine Vs. Placebo study in 50 inpatient Laparoscopic colectomy patients with similar dose as in our study of 1.5mg/kg as bolus followed by infusion 2mg/kg/hr. and found that decreased use of Fentanyl PCA pump and fentanyl use for 24 hrs. Postoperatively, less painscore, higherpatients' satisfaction for pain control.

Saadavy *et al*[13]in 2010did double blind randomised placebo-controlled study with 2mg/kg as bolus followed by 2g/kg/hr. infusion till end of surgery for 120 in-patients operated for Laparoscopic cholecystectomy and found decreased VAS score for abdominal and shoulder pain and postoperative morphine consumption.

In 1975 Suzuki *et al*[14]studied neuromuscular effect of Lignocaine infusion by ulnar nerve stimulation in patients undergoing general anaesthesia by comparing test stimulus and conditioning stimulus and found that there was prolonged neuromuscular relaxation in

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lignocaine group. This shows that there is muscle relaxant sparing nearly by 30% during GA. Our study is in comparison with this (Average 34mg Vs. 45 mg of NMBA Atracurium)

Although lignocaine was initially studied and proven to have clear analgesic effects following laparoscopic and open abdominal surgeries, it has now been shown to be applicable in different clinical settings peri-operatively including following spinal, breast, ENT and other surgeries.[17] We have used Lignocaine infusion to all major ASA grade I and II surgeries, and patients without co-morbidity.Lignocaine reduced postoperative pain at 1–4 hours and 24 hours after surgery but not after 48 hours

Pain Management: Lignocaine infusion has been associated with lower pain scores post-surgery. Patients reported reduced pain intensity both at rest and during movement for up to 48 hours following surgery, suggesting that lignocaine can provide sustained analgesia.

Specifically, one study found a mean pain-free period of over 5 hours in patients receiving lignocaine compared to significantly shorter durations in control groups. [18]

Reduction in Opioid Requirements: **Decreased Opioid Consumption**: The use of lignocaine infusion is linked to a marked reduction in opioid requirements post-operatively. Studies have shown that patients receiving lignocaine used significantly less morphine in the first 24 hours after surgery compared to controls (4.5 mg vs. 19.85 mg) and had a longer time before requesting additional analgesia (approximately 9.56 hours vs. 1.82 hours)

This opioid-sparing effect not only enhances patient comfort but also reduces the risk of opioid-related side effects.Standard anesthesia was used across all four studies. Kang, et al. did not include any additional IV opioids intra-operatively. [16]

Reduction in Anaesthetic Requirements:

Lignocaine infusion has been shown to provide significant anaesthetic-sparing effects during major non-cardiac surgeries lasting 2-3 hours under general anaesthesia. This effect is primarily attributed to its analgesic, anti-nociceptive, and anti-arrhythmic properties, which contribute to reduced requirements for other anaesthetic agents.Studies indicate that intravenous (IV) lignocaine infusion can significantly decrease the dosage of anaesthetic agents required during surgery. For instance, one study by *Lauwick S et al*reported a reduction in Sevoflurane requirements by approximately 30.5% when combined with lignocaine compared to control groups receiving saline. This reduction helps maintain

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adequate sedation levels while minimizing potential side effects associated with higher doses of anaesthetics. [20]

Multimodal Analgesia Strategy: The integration of lignocaine into a multimodal analgesia regimen enhances overall pain management strategies by addressing multiple pathways of pain perception, thereby improving patient outcomes without relying heavily on opioids[9]

To achieve desired clinical effects, levels of plasma between 0.5 and 5 mcg/ml are required. All studies administered a bolus dose of lignocaine at induction; we gave bolus of same dose 15 minutes prior to OT to know any adverse effects plus due to its pharmacological action, our patients came calm and quiet and do not raise their heart rate inside OT.All studies also continued intravenous infusions of lignocaine during surgery; dosing for the infusions ranged from 1.3 mg/kg/h to 3 mg/kg/h. We kept same dose range of 2mg/kg/h of infusion thought procedure and stopped 30 minutes prior.

Opioids were used during induction in two study groups: one[21] using Sufentanil (0.15 mcg/kg) and one[15] using fentanyl (2 mcg/kg). In five studies, intra- and postoperative nonopioid analgesia was administered; agents included acetaminophen (15 mg/kg or 1 gm), ketorolac (0.5 mg/kg or 30 mg), and/or metamizole (1 g). All ten studies administered postoperative opioids for pain control and measured the number of opioids required as a study outcome. We used only injection Tramadol 100mg. as rescue analgesics.

The results of perioperative lignocaine administration on pain control in laparoscopic abdominal surgery were mixed when considering the group of studies. Four studies[22-25] did not find any statistical improvement in patient self-reported pain on numeric rating scales (NRS) or visual analogue scores (VAS) in the lignocaine group, while the remaining six studies[26-28] described lower pain scores with lignocaine administration. As with patient-reported pain scores, this reduction in opioid use was primarily seen in the first 24 hours after surgery.

In our study, there were no signs of adverse events or toxicity as perioral numbness or metallic taste or shivering or convulsion. Patients were wide awake and there was no mental confusion postop.

Our study was comparable with above mentioned studies. There was nearly 27% reduction in dose of muscle relaxant and nearly 48% reduction in the use of inhalational agent Sevoflurane. The hemodynamic stability was achieved throughout surgery with

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optimal heart rate (HR), SBP, DBP and MAP.This helped to achieve optimal oligemic field during surgery which results in minimal tissue handling and thereby reducing postoperative pain. Lignocaine being anti-inflammatory provide adequate analgesia in the perioperative period.

Since there was reduction in the use of Sevoflurane, post op agitation was not observed as an adverse outcome, when one uses Sevoflurane for the long time.

Extubation time was less and Smooth without cough on tube. Patients were slightly drowsy but arousable and responded to verbal command within 5-10 minutes. There was no hangover of sedation and the hemodynamic remained stable throughout. There was no Lignocaine Toxicity observed to any patient. All patients were reversed adequately. Extubation time was not prolonged compared to conventional GA protocol patients. Verbal command and Eye-opening time was slightly delayed due to mild sedation.Post-operative analgesia was excellent and patients were ambulated early.

Safety and Adverse effects

Lignocaine infusion is generally considered safe, with studies reporting no significant adverse effects or toxicity associated with its use. The administration protocol typically involves an initial bolus followed by a continuous infusion, which has been shown to effectively manage both pain and hemodynamic stability during surgery as well as sparing of anesthetics.

Conclusion:

- The administration of intravenous lignocaine during major elective non-cardiac surgeries is expected to lower anesthetic drug requirements and improve postoperative recovery outcomes. By evaluating these parameters, this study aims to contribute valuable insights into the efficacy of lignocaine as an adjunctive therapy in surgical anesthesia management. Further research may solidify its role in enhancing patient outcomes across various surgical disciplines and to establish optimal dosing strategies and explore its efficacy across different surgical studied procedures beyond those already.
- The integration of lignocaine infusion into perioperative care protocols can enhance recovery outcomes for patients undergoing major elective non-cardiac surgeries. By reducing reliance on opioids, it not only mitigates potential opioid-related side effects but

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also accelerates recovery processes such as bowel function and overall hospital discharge readiness.

- In conclusion, the application of IV lignocaine infusion during major elective surgeries appears promising for improving anesthetic management and postoperative recovery outcomes.

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