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Dr. Sunil Jain
Senior Consultant, Department
of Anaesthesiology, Metro
Hospital and Cancer
Research Center, Jabalpur,
Madhya Pradesh, India

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Perioperative lidocaine infusion: A controlled clinical trial to evaluate the safety and efficacy of its use

Dr. Sunil Jain

Abstract

Aim: To evaluate the Safety and Efficacy of Perioperative Lidocaine Infusion.

Material and Methods: This was prospective non-randomized, controlled clinical trial done in the Department of Anesthesia, Metro Hospital and Cancer Research Center, Jabalpur, Madhya Pradesh, India. Total 100 patients were included in this study. All surgeries were performed under general anesthesia and patients were divided into two groups. Group I (Controlled Fentanyl Group) and Group II (Opioid Free Anesthesia Group). Intraoperative fentanyl consumption and visual analog scale (VAS) pain score assessment at immediate recovery time as well as after 24 hours postoperatively were assessed and analgesic requirements were recorded.

Results: In the current study there were no significant differences between the 2 groups as regarding age, sex, body weight, BMI, and ASA physical status. Therefore, mentioned variables would have minimal influence on the assessed parameters when comparing the safety and efficacy of perioperative lidocaine infusion with or without fentanyl adjustment at the induction of anesthesia. Comparison between the groups showed a significant difference in amount of Propofol during induction and difference in intraoperative fentanyl requirements. Patients in group I; supplemental fentanyl was needed in 4 cases (8%) while in group II fentanyl was needed in 16 cases (32%). In group II, 72% of cases i.e. in 36 patients' anesthesia were opioid-free. In group I propofol dose for induction of anesthesia was significantly lower than in group II. These differences were statistically significant. In group II patients; there was more hyperdynamic reactions to skin incision (rise of heart rate and mean arterial blood pressure more than 30% above baseline) and there was a need of higher MAC (1.41) of sevoflurane during the first 30 minutes of surgery. After 8 hours of continuous lidocaine infusion, there was a low VAS of pain score and minimal or no need of additional opioid or non-opioid analgesia during 24 hours. After laparoscopic colorectal and cholecystectomy surgery postoperative bowel sound recovery time in both groups of patients was clinically equal. There were neither perioperative complications nor clinical signs of lidocaine toxicity detected perioperatively.

Conclusion: Safety and efficacy of perioperative lidocaine infusion have been demonstrated. Opioid free anesthesia (OFA) is possible in 70% of cases. Post-operative lidocaine infusion for 5-8 hours was sufficient for pain relieve with minimal non opioid analgesia for 24 hours.

Keywords: Lidocaine, perioperative infusion, opioid, balanced anesthesia, multimodal analgesia

Introduction

Inadequate pain relief after surgery causes undesirable effects. On the other hand, excessive use of opioids produces several adverse effects and might delay recovery^[1, 2]. Therefore, a multimodal analgesia regimen is recommended in the perioperative setting as it provides superior analgesia and reduces opioid requirement^[3]. Intravenous (IV) lidocaine is a widely studied drug for multimodal analgesia. IV lidocaine at the doses between 1.5–3 mg. kg⁻¹. h⁻¹ produces analgesic, antihyperalgesic, and anti-inflammatory effects^[4]. Besides, a low dose of lidocaine is relatively safe and more feasible for perioperative use^[4-7]. Additional benefits of lidocaine infusion include a reduction in the incidence of postoperative nausea and vomiting, early return of bowel motility and improved quality of recovery^[8].

Corresponding Author:
Dr. Sunil Jain
Senior Consultant, Department
of Anaesthesiology, Metro
Hospital and Cancer
Research Center, Jabalpur,
Madhya Pradesh, India

Several studies have shown that perioperative lidocaine infusion reduces postoperative pain intensity and opioid consumption, while others have found lidocaine to be ineffective [8]. These inconsistent findings may be due to variation in surgical procedure, dose and duration of lidocaine infused. Interestingly, a current update from Cochrane based meta-analysis found a weak evidence for IV lidocaine compared to placebo on early postoperative pain scores and overall opioid requirements [9]. On the contrary, other recently published meta-analyses have shown improvement in postoperative pain-related outcomes with lidocaine infusion during laparoscopic cholecystectomy [10, 11]. Although lidocaine infusion was effective for postoperative analgesia in open inguinal hernia surgery [12], its use has not been reported in totally extraperitoneal (TEP) laparoscopic inguinal hernioplasty. Therefore, the aim of the present study was to evaluate the Safety and Efficacy of Perioperative Lidocaine Infusion.

Material and Methods

This was prospective non-randomized, controlled clinical trial done in the Department of Anesthesia, Metro Hospital and Cancer Research Center, Jabalpur, Madhya Pradesh, India, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient.

Methodology

Total 100 patients were included in this study. American Society of Anesthesiologists (ASA) physical status I-III, patients aged 18-70 years old, of both sexes, who were undergoing different types of non-cardiac surgery. Contraindications were patients with lidocaine allergy, complete atrioventricular block, bradycardia and hepatic insufficiency.

All surgeries were performed under general anesthesia and patients were divided into two groups. Group I (Controlled Fentanyl Group) and Group II (Opioid Free Anesthesia Group). After application of standard ASA, non-invasive monitors, in group I (50 patients); induction was done with fentanyl 2 µg/kg, propofol 1.4-2.0 mg/kg, atracurium 0.5 mg/kg. While in group II (50 patients); induction was done same as Group I but without fentanyl i.e. propofol and atracurium were given also. Patients of both groups received 1.5 mg/kg lidocaine intravenous bolus over 30 seconds at induction time, then intraoperative lidocaine infusion: 1.5 mg/kg/h followed by 2 mg/kg/h postoperatively for 2-8 hours. Anesthesia was maintained by sevoflurane 1-1.5 Minimum Alveolar Concentration (MAC). Other analgesic adjuvants were used in form of MgSO₄ 30-50 mg/kg, paracetamol 1000 mg, and diclofenac 75 mg intraoperatively. A supplemental fentanyl 1 mcg/kg was used if there was increase of mean arterial pressure (MAP) and/or heart rate (HR) more than 20% above base line. Muscle relaxation was maintained by infusion of atracurium 0.5 mg/kg/h, which was discontinued 20-30 minutes before termination of anesthesia. Intraoperative fentanyl consumption and visual analog scale (VAS) pain score assessment at immediate recovery time as well as after 24

hours postoperatively were assessed and analgesic requirements were recorded. Postoperative bowel function was also monitored by auscultation until recovery.

Results

In the current study there were no significant differences between the 2 groups as regarding age, sex, body weight, BMI, and ASA physical status. Therefore, mentioned variables would have minimal influence on the assessed parameters when comparing the safety and efficacy of perioperative lidocaine infusion with or without fentanyl adjustment at the induction of anesthesia. Comparison between the groups showed a significant difference in amount of Propofol during induction and difference in intraoperative fentanyl requirements. There was tendency to tachycardia and increase in mean arterial pressure (MAP) after skin incision and during the first 30 minutes of surgery in non-opioid group as shown in Table 3. For patients in group I; supplemental fentanyl was needed in 4 cases (8%) while in group II fentanyl was needed in 16 cases (32%). In group II, 72% of cases i.e. in 36 patients' anesthesia were opioid-free. In group I propofol dose for induction of anesthesia was significantly lower than in group II. These differences were statistically significant.

In group II patients; there was more hyperdynamic reactions to skin incision (rise of heart rate and mean arterial blood pressure more than 30% above baseline) and there was a need of higher MAC (1.41) of sevoflurane during the first 30 minutes of surgery. In all cases immediately after awaking and extubation, there was a need of additional analgesia (single injection was given in form of 50 mcg fentanyl, or morphine hydrochloride 4 mg intravenously). Additional analgesia after extubation was depended on time of surgery and duration of intraoperative lidocaine infusion. In cases, when surgery and consequently lidocaine infusion were longer than 3 hours, there was no or minimal need of additional analgesia after recovery (5 cases). After 8 hours of continuous lidocaine infusion, there was a low VAS of pain score and minimal or no need of additional opioid or non-opioid analgesia during 24 hours. After laparoscopic colorectal and cholecystectomy surgery postoperative bowel sound recovery time in both groups of patients was clinically equal. There were neither perioperative complications nor clinical signs of lidocaine toxicity detected perioperatively.

Table 1: Demographic profile of the patients

Parameter	Group I Fentanyl (n = 50)	Group II Opioid free anesthesia (n = 50)
Age (years)	49 (18-69)	51 (20-70)
Gender (M), n (%)	18 (36)	20 (40)
Body mass index (kg m ⁻²)	18 (23-38)	17 (22-35)
ASA I	3	5
ASA II	44	41
ASA III	3	4
Smoking history (%)	10 (20)	12 (24)
Hypertension (%)	35 (70)	36 (72)
Diabetes mellitus (%)	6 (12)	2 (4)

Table 2: Types of surgery

Type of surgery	Group I Fentanyl (n = 50)	Group II Opioid free anesthesia (n = 50)
Major open abdominal and colorectal surgery	5	5
Laparoscopic and colorectal surgery	8	6
Head and neck surgery	3	4
Laparoscopic esophageal surgery	3	3
Laparoscopic cholecystectomy	22	14
Breast surgery	1	3
Abdominal hernia surgery	5	6
Appendectomy	3	5

Table 3: Outcome of the patients

Parameter	Group I Fentanyl (n = 50)	Group II Opioid free anesthesia (n = 50)	Significance
Propofol for induction (mg/kg)	1.38 (± 0.4)	1.79 (± 0.6)	P<0.05
Heart rate after incision	74.8 (± 10.4)	97.4 (± 11.7)	P<0.05
Sevoflurane MAC	1.13 (± 0.5)	1.41 (± 0.6)	P<0.05
MAP after skin incision	89.6 (± 9.5)	110.8 (± 11.9)	P<0.05
Intraoperative fentanyl (number of patients, %)	4 (8%)	16 (32%)	P<0.05
Time of anesthesia (min)	113.9 (52-245)	110.1 (44-222)	P>0.05
Pain score after recovery	5.2 (± 1.8)	5.4 (± 1.9)	P>0.05
Pain score after 24 h	1-3	1-3	-
bowel sound recovery time (min)	151.1 ± 26.8	151.6 ± 27.8	P>0.05

Discussion

Medications of different classes can be used for analgesia in perioperative period, such as dexmedetomidine, clonidine, ketamine, gabapentin, paracetamol, NSAIDs, ketamine, lidocaine, and magnesium sulphate. Therefore, opioid based analgesia may be replaced by the multimodal analgesia [13]. There are different methods of multimodal analgesia, including OFA, but no rational strategy has been provided for choosing the drug combinations. Lidocaine infusion is a cornerstone of them as many advantages associated with opioids-such as analgesia and autonomic nervous system control [14] can be obtained from lidocaine. In 1961 Bartlett *et al.* had shown that systemic lidocaine is effective for relief of postoperative pain [15]. Since lidocaine effectiveness had been shown for management of different pain conditions including peripheral and central pain as well as chronic, acute, and perioperative pain in different types of surgery [16-23]. It had been shown that by using lidocaine in addition to other analgesics-such as paracetamol, NSAIDs, and magnesium sulphate-it is possible to provide opioid-free anesthesia in many fields of surgery and it may be important for outcome of cancer surgery [16, 22, 24, 25]. However it does not mean that we do not need opioids. It is still debatable and rational approach is needed to avoid "friendly fire" in our practice [26, 28]. Our cohort of patients was predominantly with different types of abdominal surgery and 7 cases of head and neck surgery (thyroidectomy, cystectomy) 4 cases of breast surgery (mastectomy, sector resection). We have shown that in most of cases OFA is possible, but opioids supplements give a better hemodynamic stability. Our results are in agreements with Pierre-Grégoire Guinot *et al.* (2019) who concluded that OFA for cardiac surgery is related to higher incidence of increased blood pressure [22]. We have not found any adverse effects of opioid adjustment (prolonged recovery, nausea, vomiting, ileus or hyperalgesia). Therefore, multimodal analgesia must be balanced. Antinociceptive action of lidocaine infusion was time dependent. In OFA group II, at induction of anesthesia, there was hypertension during the first 0.5-1 hour of surgery. Magnesium sulphate, paracetamol, and diclofenac were not helpful as high MAC of sevoflurane (>1) was

needed and in 32% of cases fentanyl was added. After 0.5-1 hour sevoflurane MAC gradually decreased (<1). This time dependency has been seen after patient recovery too. If duration of lidocaine infusion was more than 2.5-3 hours (laparoscopic colorectal surgery) pain score after recovery was 0-3. In other cases (duration of surgery/anesthesia 40-160 min) pain score after recovery was 3-8 hours. Postoperative lidocaine infusion for 5-8 hour was sufficient for pain relief and minimizing of opioid use up to 24 hours. For this reason, it is interesting that according to some authors' intraoperative lidocaine infusion and post-operative infusion for 8 hours may be sufficient for pain control up to 72 hours [22]. Other authors are recommending 24 hours post-operative infusion, which is safe, effective (pain score decrease was more prominent 36 hours after lidocaine infusion had been terminated) and can be provided without ECG monitoring [21]. Proposed mechanisms of the lidocaine prolonged activity are the anti-inflammatory properties that are more potent compared to traditional anti-inflammatory drugs. Also, lidocaine attenuates peripheral nociceptors sensitization and central hyperexcitability through its sodium channel blocking action. Other proposed mechanisms are: muscarinic antagonism, glycine inhibition, reduction in the production of excitatory amino acids, reduction in the production of thromboxane A2, release of endogenous opioids, and reduction in neurokinins [29]. We have shown the effectiveness of lidocaine infusion and its combination with other analgesics, including opioids, for abdominal, breast and head and neck surgeries. For laparoscopic abdominal surgery we are using lidocaine infusion and there is no need of epidural anesthesia for these types of surgery. According to the literature review perioperative lidocaine infusion correlated with decreased visual analogue scale pain scores at 1 to 4 hours and 24 hours postoperatively. Other benefits include decreased opioid requirements, reduced nausea, and vomiting. These benefits were seen in patients undergoing laparoscopic and open abdominal surgery, genitourinary, breast surgery, cardiothoracic surgery and spine surgery [16, 19].

Conclusion

Safety and efficacy of perioperative lidocaine infusion have been demonstrated. Opioid free anesthesia (OFA) is possible in 70% of cases. Antinociceptive action of lidocaine is time dependent and no immediate analgesia was needed after extubation if the duration of intraoperative lidocaine infusion was more than 3 hours as the VAS pain score after recovery was 0-3, versus 3-7 if the duration of lidocaine infusion was 40-160 minutes. Post-operative lidocaine infusion for 5-8 hours was sufficient for pain relieve with minimal non opioid analgesia for 24 hours. Keywords: Lidocaine; Perioperative infusion; Opioid; Balanced anesthesia; Multimodal analgesia

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