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Research Article

Safety and Efficacy of Perioperative Lidocaine Infusion- A Prospective, Controlled Study

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ABSTRACT

Background: After introduction of synthetic opioids, in 1960s, safe and stress-free opioid balanced anesthesia has been developed. Opioids have well known side effects such as respiratory depression, immunosuppression, muscle rigidity, negative inotropism, nausea, vomiting, hyperalgesia, urinary retention, postoperative ileus and drowsiness which are clinically important. Perioperative opioids are important factor of opioid epidemic in USA and other countries. Therefore, there is increased interest in perioperative use of non-opioid analgesics especially lidocaine.

Patients and Methods: 185 adult patients, undergoing various elective surgical procedures, were divided into; control group I (105 patients) [Fentanyl Group], and group II (80 patients) [Opioid Free Anesthesia Group]. Patients of both groups received at anesthetic induction; lidocaine 1.5 mg/kg bolus followed by 1.5 mg/kg/h infusion intraoperatively, and 2 mg/Kg/h infusion for 2-8 hours postoperatively. Both groups received other analgesic adjuvants such as diclofenac 75 mg, paracetamol 1 gm, and $MgSO_4$ 30-50 mg/kg intraoperatively. A supplemental fentanyl 1 mcg/kg was used if there is increase of mean arterial pressure (MAP) and/ or heart rate (HR) more than 20% above base line. 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: Supplemental intraoperative fentanyl was needed in 8.6% of cases in group I, and in 30% of cases in group II. Group II also needed a higher minimum alveolar concentration (MAC) of sevoflurane during first 30 minutes. Both groups needed analgesia immediately post extubation if surgeries were less than 3 hours. After 8 hours of lidocaine infusion, there was no need for additional opioids for 24 hours and only paracetamol 1 gm and/or diclofenac 75 mg were enough in both groups. No significant differences in bowel function were observed between the 2 groups. There are no clinically detected or observed toxicity or side effects due to lidocaine infusion.

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

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pain score after recovery was 0-3, versus 3-7 if the duration of lidocaine infusion was 40-150 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

INTRODUCTION

Balanced anesthesia is the cornerstone of current anesthetic practice for many decades. According to this concept, which had been proposed by J. Lundy, using of lower doses of more than one anesthetic agent improves outcomes [1]. After introduction of synthetic opioids, in 1960s, safe and stress free opioid balanced anesthesia has been developed. Opioids have many side effects such as respiratory depression, immunosuppression, muscle rigidity, negative inotropism, nausea, vomiting, hyperalgesia, urinary retention, postoperative ileus, and drowsiness which are clinically important [2]. Perioperative opioids are important factor of opioid epidemic in USA and other countries [2-5]. Therefore, there is increased interest in perioperative use of non-opioid analgesics especially lidocaine [6].

Many clinical trials and reviews demonstrated benefits of lidocaine perioperative infusion in different types of surgery [6,7-13]. In the current study, our concern was about safety and efficacy of perioperative infusion of lidocaine with and without of opioids. We will assess intraoperative fentanyl consumption, VAS pain score at immediate recovery time and after 24 hours postoperatively, and analgesic requirements were recorded. Postoperative bowel function was also monitored.

PATIENTS AND METHODS

This is a prospective non-randomized, controlled clinical trial conducted in the Research Institute of Clinical Medicine, Tbilisi, Georgia between 4th February 2019 and 30th December 2019. After approval of the ethics committee; 185 adult patients were enrolled. American Society of Anesthesiologists (ASA) physical status I-III, patients aged 18-80 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. Patient demographics and characteristics of performed surgeries are presented in Tables 1 and 2 respectively.

Table 1: Patient demographics.

Variables	Group I Fentanyl (n=105)	Group II Opioid FreeAnesthesia (n=80)
Age(years)	48 (18-77)	52 (20-79)
Gender (M), n (%)	35(33)	29 (36)
Body mass index (kg m^{-2})	28 (23-38)	27 (22-35)
ASA I	5	4
ASA II	95	73
ASA III	5	3
Smoking history (%)	25 (24)	21(26)
Hypertension (%)	77 (73)	59 (74)
Diabetes mellitus (%)	11 (10)	5 (6)

Table 2: Types of surgery.

Type of surgery	Group I Fentanyl (n=105)	Group II OpioidFree Anesthesia (n=80)
Major open abdominal and colorectal surgery	6	9
Laparoscopic and colorectal surgery	19	10
Head and neck surgery	5	7
Laparoscopic esophageal surgery	5	5

Laparoscopic cholecystectomy	49	28
Breast surgery	2	5
Abdominal hernia surgery	14	9
Appendectomy	5	7

Methodology

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 (105 patients); induction was done with fentanyl 2 μkg/kg, propofol 1.4-2.0 mg/kg, atracurium 0.5 mg/kg. While in group II (80 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 $MgSO_4$ 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.

Statistical analysis

Statistical differences were evaluated and means of quantitative data were compared using Student's t-test. Analysis was performed in Stata version 15.0. P<0.05 means that differences were statistically significant.

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 9 cases (8.6%) while in group II fentanyl was needed in 29 cases (30%). In group II, 70% of cases i.e. in 56 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.

Table 3: Results.

Parameter	Group I Fentanyl (n=105)	Group II Opioid Free Anesthesia(n=80)	Significance
Propofol for induction (mg/kg)	1.42 (± 0.3)	1.83 (± 0.5)	P<0.05
Heart rate after incision	75.1 (± 10.2)	98.0 (± 11.3)	P<0.05
Sevoflurane MAC	1.12 (± 0.6)	1.40 (± 0.5)	P<0.05
MAP after skin incision	89.2 (± 9.1)	110.1 (± 11.2)	P<0.05
Intraoperative fentanyl (number of patients, %)	9 (8.6%)	29 (30%)	P<0.05
Time of anesthesia (min)	114.2 (50-240)	109.3 (45-220)	P>0.05
Pain score after recovery	5.1 (± 1.7)	5.3 (± 1.8)	P>0.05
Pain score after 24 h	1-3	1-3	-
bowel sound recovery time (min)	150.6 ± 27.1	152.4 ± 28.1	P>0.05

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 (1.4) 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 (7 cases).After 8hours 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 24hours. 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.

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 [14]. 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 [15] can be obtained from lidocaine. In 1961 Bartlett et al. had shown that systemic lidocaine is effective for relief of postoperative pain [16]. 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 [6,7-13]. 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 [6,12,17,18]. 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 [19-21].

Our cohort of patients was predominantly with different types of abdominal surgery and 12 cases of head and neck surgery (thyroidectomy, cystectomy) 7 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 Guinotet al. (2019) who concluded that OFA for cardiac surgery is related to higher incidence of increased blood pressure [12]. 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 30% 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 then 2.5-3 hours (laparoscopic colorectal surgery) pain score after recovery was 0-3. In other cases (duration of surgery/ anesthesia 40-150 min) pain score after recovery was 3-7 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 postoperative infusion for 8 hours may be sufficient for pain control up to 72 hours [12]. Other authors are recommending 24 hours postoperative 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 [11]. 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 [22].

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 [6,9].

CONCLUSION

We have demonstrated safety and effectiveness of perioperative lidocaine infusion for different types of surgery. Analgesic effect of lidocaine lasts longer than its half-life. According to our results; optimal combination of opioid and non-opioid analgesia techniques is essential. Postoperative opioid consumption is minimal during first day after surgery. Opioids should continue to be a part of multimodal pain management in the perioperative period. Limitation of this study is its non-randomized and non-blind character in addition to the use of lidocaine as well as other analgesic adjuncts in both groups. Perioperative analgesia (type, quality, quantity, and monitor) is still one of the actual problems of anesthesiology and this field is great area for more prospective randomized clinical trials.

AUTHOR'S CONTRIBUTION

V. Shoshiashvili proposed the clinical trial, made and executed the study, wrote, supervised and reviewed the manuscript. A. EL-Molla proposed, wrote, reviewed, and supervised the manuscript. F. Aboul Fetouh shared, reviewed and supervised the proposal. R. AL-Otaiby shared and reviewed the manuscript. A. Kandil critically reviewed the manuscript. O. Shaalan reviewed the manuscript. Y. Ali reviewed and shared the manuscript. All Authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

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