

Original Article

Effect of Intravenous Infusion of Lidocaine on Pain Reduction after Cesarean Section under General Anesthesia

Anahita Hirmanpour¹, Reihanak Talakoub¹, Hamed Mansouri¹

Abstract

Background: The present study was conducted to evaluate the effect of Lidocaine on pain reduction during and ileus and the need for opioids after caesarean section.

Materials and Methods: This study was randomized double-blind controlled clinical trial. 40 ASA I, II pregnant women were candidates for caesarean section with general anesthesia. They were randomly allocated into two groups of Lidocaine receivers and placebo using randomized block design; the Lidocaine group received 1.5 mg/kg of Lidocaine right before the surgery and then its infusion with a dose of 2 mg/Kg/h until the end of the surgery and the placebo group received normal saline with the same volume and application. Patients' pain intensity was measured using numerical rating scale (NRS), 0 (entering the recovery), 0.5, 1, 4, 12 and 24 hours after the surgery.

Results: Lidocaine decreased the systolic and diastolic pressures of the patients only during the first minute after intubation. There was decrease in mean of arterial blood pressure at the 10th minute after intubation and 40th minute after surgery. In addition, decreased the mean of patients' pain intensity, Diclofenac and Pethidine consumption, side effects (nausea and vomiting), and reduced the time interval before the first time of tolerating oral liquids; but it had effect on infants' Apgar score 1 and 5 minutes after delivery.

Conclusion: Lidocaine was definitely effective on reducing the intensity of pain, opioid and non-steroidal anti-inflammatory drugs consumption and ileus after surgery with the least occurrence of side effects for mothers and infants.

Keywords: Caesarean Section, Postoperative Pain, Lidocaine, General Anesthesia

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1. Anesthesia and Critical Care Research Center, Alzahra Hospital, Department of Anesthesiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding Author: Reihanak Talakoub, MD, Associate Professor, Anesthesiology and Critical Care Research Center, Isfahan University of Medical Science, Isfahan, Iran;
Tel: +98 9131114628
Fax: (+98) 31 37923011
Email: reihanak.talakoub@gmail.com

Introduction

One of the most common complications of caesarean section is postoperative pain (1). Also the most common and important cause of dissatisfaction

among mothers who has been under caesarean section at health centers is postoperative pain (1). Pain, during the first days after delivery, is an important obstacle for taking care of the infant and breastfeeding; therefore specialists' attention for

controlling postoperative pain is necessary (1, 2).

Proper management of postoperative pain has been of great importance during the recent years. The intensity of postoperative pain depends on various factors like patient's perception of pain and threshold, the type and duration of surgery, the type of anesthesia and used anesthetics and patient's mental and psychological condition (example: differences in mental condition in laparotomy for caesarean section against laparotomy for uterus cancer) (1, 3).

The important matter in controlling postoperative pain after caesarean section is reducing morbidity and mother's faster recovery for returning home (4). There are different methods for getting mothers back to the desirable condition for taking care of their infant, breastfeeding, and pain management after caesarean. Like systemic analgesia methods and regional analgesia methods (constant infusion or injecting a dose of analgesic drug to the site of surgery), which would be used after evaluating their complications and advantages and patient's condition (1, 2).

In many Iranian health centers, which is a developing country, the rate of caesarean section is higher than the standard rate (30% of all the deliveries) and this would make it impossible to provide pain control strategies for all the patients (4).

Using non-steroidal anti-inflammatory drugs and opioids is the traditional and most common method for controlling post-operative pain. However there are also some regional analgesic methods which are more powerful than opioid drugs. Also, using narcotic injections compared to regional methods is associated with side effects such as nausea, vomiting, respiratory distress, constipation and dizziness (1, 2). Modern methods such as constant epidural infusion or patient controlled analgesia (PCA), besides needing trained personnel and special facilities, are expensive and associated with some side effects (spinal hematoma). On the other hand, due to low cultural and educational level of the patients who refer to most of the health centers, it is not possible to use advanced pain management devices patient controlled analgesia pumps or PCA (1, 2, 4, 5). Another study has evaluated the effect of using oral painkillers like Dipyron and Morphine right after delivery (1, 2, 5, 6).

One of the commonly used analgesic drug in this field is Lidocaine which is used as an antiarrhythmic IB class drug for treating ventricular tachycardia and sometimes myocardial ischemia. This drug has analgesic and anti-hyperalgesia effects (7). Lidocaine is not teratogenic and it is a safe drug in its therapeutic doses and, except for neonatal inter-scalp injections that could cause neonatal toxicity, it has few side effects. Lidocaine has a low excretion into breast milk and its half-life is 90 to 120 minutes. Using Lidocaine during early pregnancy would not increase the risk for embryonic defects but it would decrease the blood supply for the placenta and increase the uterine myometrium tone. In high dose injections, it would temporarily and transiently decrease the Apgar score of infants (1, 5, 6). Furthermore, Lidocaine is an inexpensive, easily injectable and relatively safe drug (7).

The mechanisms of anesthetic drugs are numerous. The anesthetic effect of drugs, when prescribed before trauma to the tissue, is based on the preventive theory of central pain sensitization. Prescribing anesthetics before trauma would linger the pharmacokinetic effects of the anesthetic method (1).

Therefore the anesthetic drug would be administered through different methods of intramuscular, intravenous, epidural, regional peripheral nerve block, slowly intraperitoneal injection or subcutaneous injection (8, 9). The effect of Lidocaine on pain reduction in surgeries has previously been studied. In a study, local injection of Lidocaine before making the incision in caesarean section led to pain reduction during the early hours after the surgery in mothers without any side effects; it also reduced the need for opioids. Also injecting IM injection, SC injection or both of Lidocaine after making the incision in caesarean section into rectus abdominus muscle would reduce post-operative pain and the duration of hospitalization (6).

Therefore, considering the importance of pain control after caesarean section, preventive use of analgesic agents during surgery could be reasonable for reducing post-operative pain (7). Considering the advantages of local injection methods and the appropriateness of lidocaine for this matter, this study evaluated the effect of intravenous injection of

Lidocaine during caesarean section with general anesthesia on pain, ileus and the need for opioids after surgery.

Methods

This study was a randomized controlled double-blind clinical trial which was conducted from winter 2015 to autumn 2015 at Al-Zahra and Beheshti hospitals after taking permission from ethics committee of Isfahan University of Medical Sciences. ASA I and II term pregnant women (more than 37 weeks), who were candidates for caesarean section with general anesthesia were enrolled in the study.

The exclusion criteria were: receiving antiarrhythmic drugs, having any previous diagnosed allergy to Lidocaine, having diabetes, having neurologic problems, being an addict, chronic use of opioids or analgesics, having any type of heart blocks, having any type of arrhythmia, having a history of myopathy, having renal or hepatic problem or a GFR < 40% and having a heart problem or EF < 45%. Surgeries that lasted more than 2 hours, were associated with complications such as bladder injury which required urology intervention, hysterectomy, blood transfusion (due to major bleeding) which led to acid-base disorders and diagnosed or pregnancy-related treatment-resistant hypotension, were also led to patient's exclusion. Participants were allocated into two groups of Lidocaine receivers and placebo (normal saline) through block random allocation

The drug and the placebo were prepared and coded in similar syringes by an anesthesia technician. The person who injected the syringes was different from the one who prepared them. The Lidocaine group received 1.5 mg/kg of Lidocaine right before the surgery and its infusion with a dose of 2 mg/kg.h lasted from clamping the umbilical cord and taking out the neonate until the end of the surgery and putting the bandages.

Patients of the placebo group received similar doses of normal saline. Then necessary measures for general anesthesia and then transfer to the recovery room were performed. Patients were monitored for ECG, SPO₂ and NIBP from the beginning and all of the vital signs of the patients were measured and recorded before the induction, before intubation, 1, 5 and 10 minutes after intubation and then every half an

hour until the end of the surgery. Also, after the surgery and the infusion ended, patients' vital signs were recorded every 15 minutes at the recovery room.

Patients' pain intensity at 0, 0.5, 1, 4, 12 and 24 hours after the surgery were measured and recorded.

Pain's scoring was based on numerical rating scale (NRS) and the scales were no pain (0), mild (1-4), moderate (5-7) and severe (8-10); an NRS of 4 or more required intervention and treatment. Treatment was first started by prescribing Diclofenac 100 mg suppository and in case the pain did not stop, 50 mg of Pethidine was injected intravenously.

After being transferred to the ward, patients who received standard treatment with Diclofenac and Pethidine, based on their own request and NSR of 4 or more, received another suppository of Diclofenac and if needed, 50 mg of IM Pethidine. The time of entering the recovery room and the time for the first request for pain killers at the recovery room and the ward were recorded. The extra doses of Diclofenac and Pethidine were also measured and recorded. Regarding sedation, patients were categorized into 4 groups of 0 = alert, I = sleepy but arousable, II = stupor and III = coma.

Side effects after surgery including lightheadedness, numbness and tingling in the extremities, nausea, vomiting and severe drowsiness were recorded. The duration of anesthesia, from the time of induction of anesthesia until transferring to the recovery room was calculated and recorded.

The duration of extubation, from the time of cutting the anesthetic until removing the tracheal tube was calculated and recorded. If the patient had hypotension of SBP < 90 mmHg or less than 20% of the baseline pressure drop, 5 mg of Ephedrine was injected intravenously. In case of Bradycardia (HR < 50), 0.5 mg Atropine was prescribed.

The duration of staying in the recovery room was measured and recorded from the time of entering until the time of being discharged from the recovery room based on modified aldreet score. Infant's Apgar score was measured and recorded 1 and 5 minutes after birth. The sample size was estimated to be 20 for each group with a confidence interval of 95%, test power of 0.84 and accuracy of 0.5. Data were analyzed using SPSS 21 (Chicago, Illinois, USA). A p value of less 0.05 was considered significant. For

analyzing qualitative data, t test and chi-square were used. Mann-Whitney test was used for analyzing categorical variables. Variance analysis with repeated measures, Newman-Kelus test and post hoc student tests were used for analyzing hemodynamic variables at different times in both groups.

Results

Forty pregnant women were enrolled as the participants for this study. Demographic characteristics and the duration of surgery and recovery are respectively presented in tables 1 and 2.

The mean changes of systolic and diastolic blood pressure had a significant difference between both groups only one minute after intubation ($p < 0.05$) (Figure 1, 2).

The mean of changes in the arterial blood pressure of patients, at the same time intervals, had a significant difference between both groups 10 and 40 minutes after the surgery ($p < 0.05$) (Figure 3).

The mean of changes in the patients' heart rate, at the same time intervals, had a significant difference between both groups 1 minute after intubation ($p < 0.05$) (Figure 4).

The mean of changes in patients' oxygen saturation, at the same time intervals, had a significant difference between both groups 40 minutes after the surgery ($p < 0.05$) (Figure 5).

The mean of changes in patients' blood pressure, heart rate and oxygen saturation are shown in diagrams 1 to 5.

Measurement times on the horizontal axis of diagrams 1 to 5

Measurement time on the basis of intubation	1	2	3	4	5	6	7	8	9	10	11	12
	Right before	1 minutes after	5 minutes after	10 minutes after	40 minutes after	70 minutes after	100 minutes after	130 minutes after	160 minutes after	190 minutes after	220 minutes after	250 minutes after

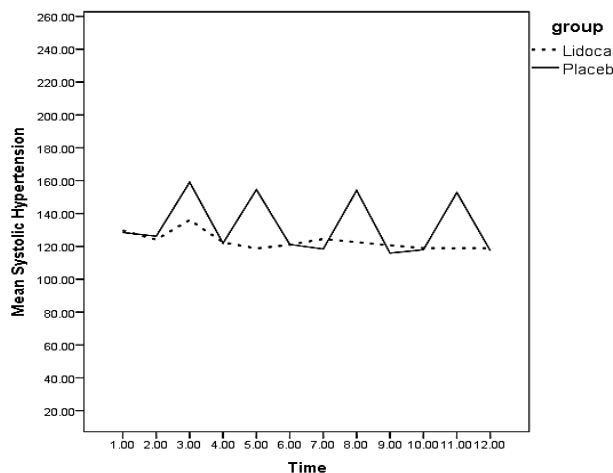


Figure 1. The linear diagram of the mean of systolic blood pressure for each studied group separately (mmHg).

The mean of patients' intensity of pain based on NRS at the time of entering the recovery room, 15 minutes into the recovery room and then 4, 12, and 24 hours after the surgery had a significant difference

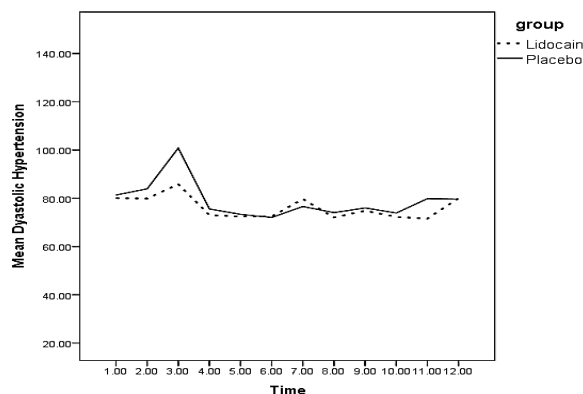


Figure 2. The linear diagram of the mean of diastolic blood pressure for each studied group separately (mmHg).

between both groups ($p < 0.05$). No significant difference was observed between both groups at any other measurement time ($p > 0.05$) (Figure 6).

The mean of consuming extra doses of Diclofenac suppository, at the moment of entering the recovery room, 15 and 60 minutes into the recovery

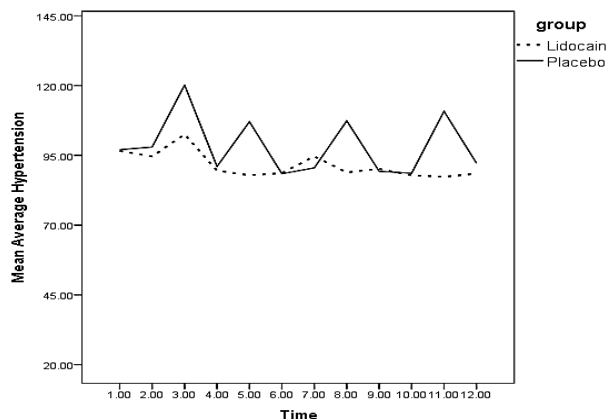


Figure 3. The linear diagram of the mean of arterial blood pressure for each studied group separately (mmHg).

and 4 and 12 hours after the surgery was significantly lower in the Lidocaine receiving group compared to the placebo group; their difference was significant ($p < 0.05$). Considering the injection of extra doses of Pethidine, at the moment of entering the recovery room and 15 minutes into the recovery room and also 4 hours after the surgery, it was lower in the Lidocaine receiving group compared to the placebo group and their difference was significant ($p < 0.05$) (Figures 7 and 8).

The level of drowsiness at all the measurement times had no significant difference between both groups ($p > 0.05$) (Figures 9, 10, 11).

The frequency of the incidence of nausea and vomiting had a significant difference between both groups ($p < 0.05$) (Figure 12).

The frequency of the incidence of side effects had no significant difference between both groups ($p > 0.05$) (Figure 13).

The mean of Apgar score of infants one and five minutes after birth showed no significant difference between both studied groups ($p > 0.05$).

Discussion

The present study revealed that intravenous bolus injection of Lidocaine during surgery would decrease systolic and diastolic blood pressure and heart rate during the first minute after laryngoscopy and endotracheal intubation. However, according to previous studies, which had not used (10-12) this drug, could be effective on hemodynamic stability of pregnant women during laryngoscopy and

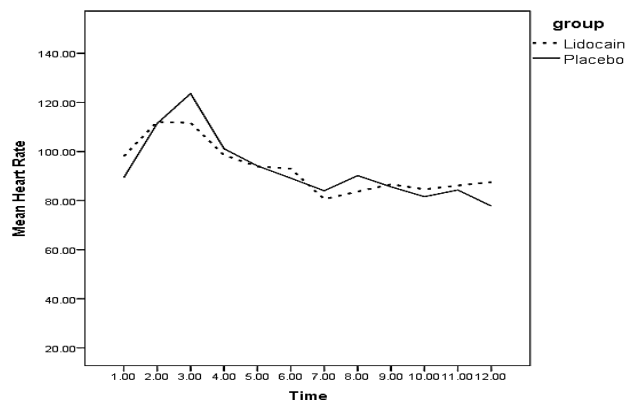


Figure 4. The linear diagram of patients' heart rate for each studied group separately.

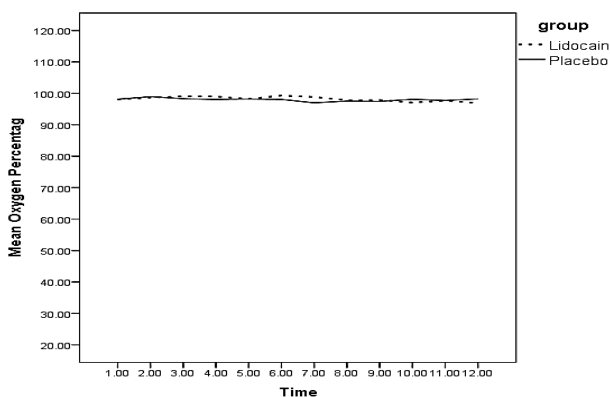


Figure 5. The linear diagram of patients' oxygen saturation for each studied group separately.

endotracheal intubation. Furthermore, pain intensity and consumption of extra doses of analgesic drugs were lower in the Lidocaine receiving group compared to the placebo group.

The effect of local application of Lidocaine for pain reduction during surgeries has been previous studied. In one study, local injection of Lidocaine before making the incision in caesarean section, with no side effects for the mother, decreased the pain during the first hours after surgery and also decreased the need for opioids. Also subcutaneous injection of Lidocaine or intramuscular injection into rectus abdominis or both after making the incision in caesarean section would decrease post-operative pain intensity and duration of hospitalization (1, 6, 13). Intravenous injection during and after abdominal surgeries in different studies (14), would decrease the duration of hospitalization and would also decrease ileus, as the most important factor in lingered hospitalizations. Also patients would experience less

Table 1: Frequency distribution and dispersion of demographic characteristics for each group.

Variable	Lidocaine receiving group	Placebo group	P value
Age (years)	29.3 ± 3.3	29.3 ± 4.6	0.938
Gestational age (weeks)	39.9 ± 0.5	38.4 ± 1.1	0.066
Height (cm)	160 ± 4.8	161.5 ± 6.4	0.408
Weight (kg)	80.9 ± 12	79.75 ± 10.4	0.749
Body Mass Index (BMI)	31.59 ± 4.4	30.49 ± 2.8	0.345

- Variables are presented as mean ± SD
- P values less than 0.05 indicate statistically significant difference

Table 2: Comparing the mean duration of surgery and recovery between both groups.

Variable	Lidocaine receiving group	Placebo group	P value
Duration of surgery (minutes)	59.75 ± 18.3	51.5 ± 10.2	P ≥ 0.05
Duration of recovery	60 ± 0.0	60 ± 0.0	P > 0.05

- P values less than 0.05 indicate statistically significant difference

Measurement times on the horizontal axis of diagram 6

Measurement time on the basis of intubation	1	2	3	4	5	6	7	8
	At the time of entering the recovery room	15 minutes into the recovery room	30 minutes into the recovery room	45 minutes into the recovery room	60 minutes into the recovery room	4 hours after the surgery	12 hours after the surgery	24 hours after the surgery

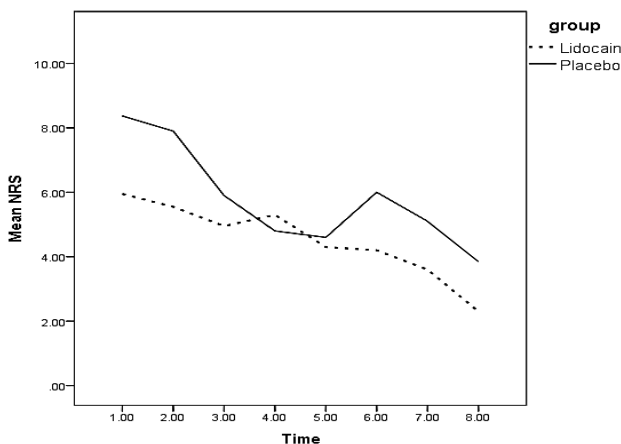
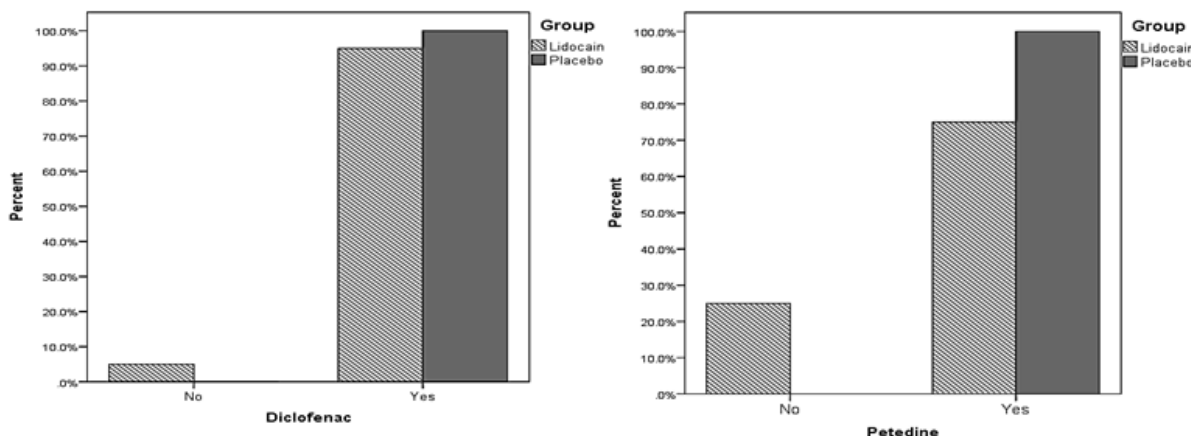


Figure 6. The linear diagram of patients’ intensity of pain based on intensity.

nausea and vomiting during the first 24 hours after surgery and would need less Morphine (15, 16). The present study also approved the reduction of nausea

and vomiting and less consumption of opioids. Intravenous injection of Lidocaine in radical prostatectomy, along with similar effects, was also effective in return of bowel functions (17). Intravenous injection of Lidocaine would decrease the intensity of permanent pain in women after breast surgeries (18).

Lidocaine had similar analgesic effects after cholecystectomy surgeries and laparoscopic cholecystectomy; it led to a decrease in the need for opioids, faster resolve of ileus and sooner discharges of the patient from the hospital (7, 19, 20). The present study also approved the safe and uncomplicated analgesic and hyper analgesic effect of Lidocaine (21) in pregnant women who were candidates for caesarean section. One of the limitations of this study was not measuring the serum level of Lidocaine, but considering all the conducted monitoring and patients’ vital signs, no toxicity was



Figures 7 & 8. The frequency histogram for consuming Diclofenac suppository & Pethidine in each group separately.

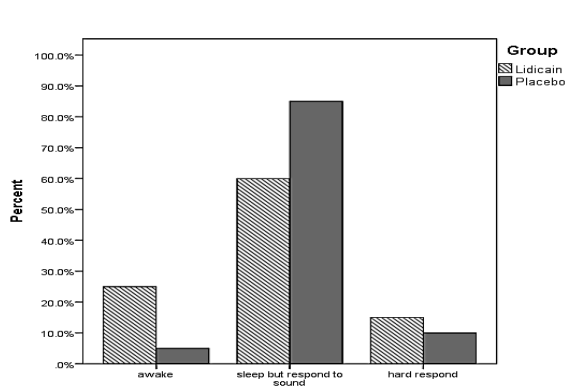


Figure 9. The frequency histogram for the level of drowsiness in both groups at the time of entering the recovery room.

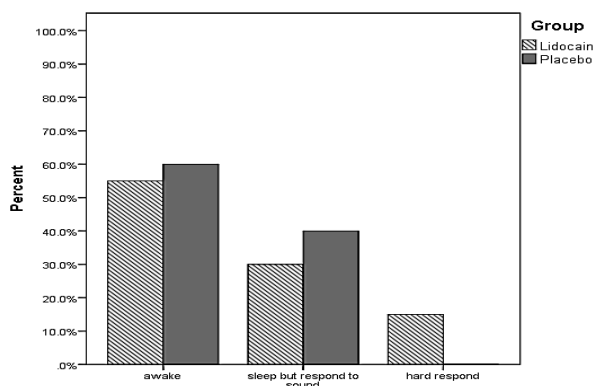


Figure 10. The frequency histogram for the level of drowsiness in both groups 30 minutes into the recovery room.

observed with this drug and the applied dosage. But conducting further studies with larger sample size and measurement of the serum level of Lidocaine is recommended. Another limitation of this study was not measuring the chronic pain of the patients after caesarean section. Since, the helpful effect of Lidocaine in controlling chronic pain after surgeries (18, 22, 23) has been approved, future studies could assess this matter; because in the present study patients could only be observed for 24 hours after the surgery. Therefore prescribing Lidocaine during the induction and also during the caesarean section, with no adverse effect on mothers' hemodynamics during the surgery or infants' Apgar score, could decrease the intensity of pain and also nausea and vomiting after surgery. It could also lead to a significant reduction in the use of opioids and pain killers after surgery and ileus (in case of any). Since this drug has a suitable price and could be applied easily, it could

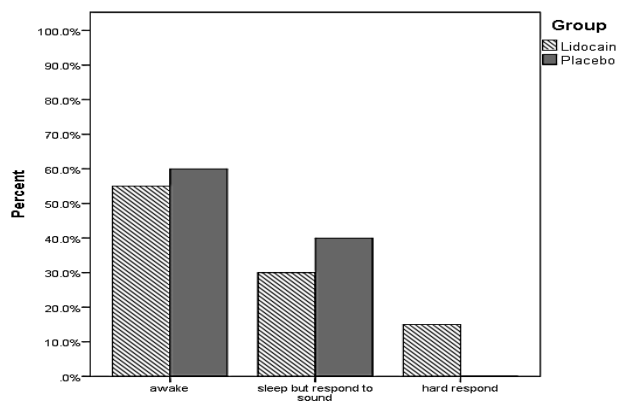


Figure 11. The frequency histogram for the level of drowsiness in both groups 60 minutes into the recovery room.

be afforded for being used during caesarean sections.

Table 3: Determining and comparing the mean of Apgar score of infants in both the studied groups.

Variable	Lidocaine group	receiving Placebo group	P value
The mean of Apgar score 1 minute after birth	8.55	8.70	0.701
The mean of Apgar score 5 minutes after birth	9.95	10.95	0.395

• P values less than 0.05 indicate statistically significant difference

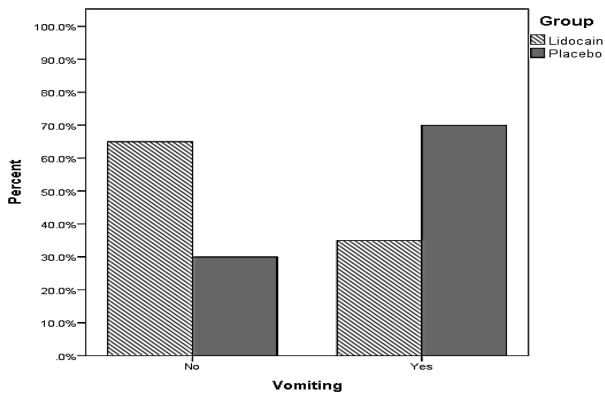


Figure 12. The frequency histogram for nausea and vomiting in both groups.

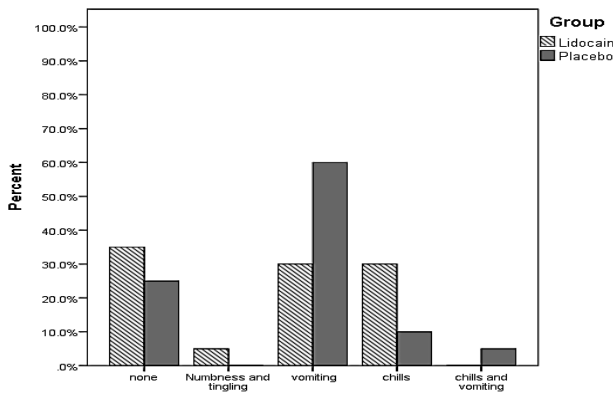


Figure 13. The frequency histogram for the incidence of side effects after surgery for both groups.

Conclusion

Using systemic Lidocaine during surgery with a bolus dose of 1.5 mg/kg and infusion dose of 2 mg/kg/h during caesarean section with general anesthesia, along with the hemodynamic stability of the mother after laryngoscopy and endotracheal intubation, could significantly decrease the intensity of post-operative pain, consumption of opioids and

non-steroidal anti-inflammatory drugs and also ileus after the surgery.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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