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ORIGINAL ARTICLE

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The impact of intraoperative intravenous lidocaine infusion on early postoperative pain after complex spine surgeries

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Abstract

Background This study aimed to assess the effect of intravenous lidocaine infusion affected on early postoperative pain control after complex spin surgeries.

Ninety patients who were scheduled for complex spine surgery were included in this prospective double-blinded controlled trial. They were randomly assigned to one of two groups: L and P. Patients in group L received a loading dose of lidocaine 1 mg/kg then followed by 1.5 mg/kg/h infusion till the end of the surgery, while in group P, lidocaine was replaced with normal saline.

Results The pain score assessed by VAS at rest showed statistically significant lower values in group L at 30 min, 8, 12, and 24 h postoperatively. VAS during movement was significantly higher in group P only after 24 h postoperatively. The entire dose of intraoperative fentanyl consumed was significantly lower in group L. The time elapsed to ask for the first dose of rescue analgesia was significantly longer in group L. The first rescue dose of nalbuphine was significantly lower in group L. In group P, the overall dose of narcotics consumed in the first postsurgical day was significantly higher.

Conclusions When compared to placebo, lidocaine infusion significantly reduced the postoperative pain scores, as well as the entire dose of intraoperative and postoperative narcotics used.

Keywords Intravenous lidocaine, Complex spine surgery, Visual analog scale

Background

Complexity in spine surgery refers to the revision of previous back or neck spine surgery, scoliosis correction, and surgery of more than three spinal segments (Batko et al. 2020). Complex spine surgeries are followed by severe pain which is a challenging task for the anesthesia team to control by well-planned pain control strategies which have a positive effect on postoperative outcomes. Feld et al. (2003) the postoperative pain can be explained by massive tissue damage and sensory nerve stimulation, and the large doses of intraoperative opioids initiate postoperative hyperalgesia (Koppert and Schmelz 2007).

Recent research has looked into the usage of multimodal opioid-free pain control strategy in the perioperative period. Non-opioid medications used during surgery have been shown to diminish opioid usage after surgery. Lidocaine may be an effective perioperative pain reliever (Lockwood and Misra 2020). Lidocaine is characterized by a favorable safety profile offering central and peripheral analgesia (Bailey et al. 2018; Tully et al. 2020) and

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when given by intravenous infusion tissues become more saturated, and the first peak half-life will be less dominant., it's duration of action is sustained, and lidocaine concentration levels keep rising (Berk and Silberstein 2018). The goal of our study was to evaluate how intraoperative IV lidocaine infusion altered early pain control after complex spinal surgeries.

Methods

We performed a prospective, randomized controlled double-blinded trial with an allocation ratio 1:1 in parallel groups from August 2021 to December 2022. After receiving ethical approval (FMASU M D 153/2021), all patients provided informed consent. The study was carried out on 90 patients who underwent complex spine surgery under general anesthesia. This trial was registered prospectively (PACTR202206745131592).

Patients were subdivided into two groups, 45 patients each. We included adult patients less than 60 years old with the American Society of Anesthesiologists (ASA) Physical Status Class I to III scheduled for complex spinal surgeries. Exclusion criteria covered patient refusal, uncooperative patient, neuro-psychiatric illness, unilateral or bilateral lower limb weakness (Bromage score 2 or more) (Craig and Carli 2018) (participants with neurological disorders were excluded from ASA III status), allergy to any used medications, severe renal impairment, severe hepatic disease, morbid obesity with body mass index (BMI) more than 40 kg/m^2, history of drug abuse, and administration of analgesics 24 h preoperatively.

The drug was prepared in un-labeled syringes by one of the researchers and was put in closed different colored envelopes and was handled by another anesthesiologist who was blinded to the content of the syringe and not involved or interested in the study. Using a 50-ml syringe containing lidocaine 1% (10 mg/ml), patients in group L received 1 mg/kg (0.1 ml/kg) with induction, then 1.5 mg/kg/h (0.15 ml /kg/h) infusion until the procedure was completed, while in the patients in group P, the lidocaine was replaced with normal saline.

Preoperatively, all participants were thoroughly evaluated by medical history, physical examination, and investigations (complete blood count, kidney and liver function testing, coagulation profile, and electrocardiography (ECG)). All patients were taught about the whole anesthetic procedure, as well as about the visual analog scale (VAS) (Aldrete 1995), with 0 denoting no pain and 10 denoting the most excruciating imaginable pain.

All participants had a peripheral IV cannula inserted and were monitored by 5 lead electrocardiography (ECG), pulse oximetry, non-invasive blood pressure, capnography, and urine output (UOP). Preoperative 0.020 mg/kg midazolam was given 20 min before induction of general anesthesia. General anesthesia was induced by 2 µg/kg IV fentanyl, propofol 2 mg/kg, and atracurium 0.5 mg/kg. Endotracheal intubation was done to secure the patient's airway, after which mechanical ventilation was used for keeping the patient's end-tidal CO_2 ($ETCO_2$) within 35 to 40 mm Hg. Anesthesia maintenance was done with 1–2 MAC isoflurane delivered in an oxygen/air (50%: 50%) mixture to keep systolic blood pressure within the 20% baseline limit. Before skin incision, an IV infusion of 60 mg ketorolac started over 30 min. Before extubation, all patients received 1gm of acetaminophen (paracetamol) via IV infusion.

If patients developed tachycardia (HR ≥ 20% of the basal readings) and/or hypertension (BP ≥ 20% of the basal readings) a dose of fentanyl 0.5 µg/kg would be delivered and repeated within 10 min if no response occurred.

In patients who developed hypotension (BP ≤ 90/60), a bolus of 500 ml crystalloid was given, and, if still no response, ephedrine 5 mg IV was given to be repeated within 10 min if there was no response happened.

At the end of the surgery, reversal of muscle relaxant was done by neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. then extubation was done after the full return of the conscious level and motor power. All participants were transferred to the PACU. The discharge from PACU after the Modified Alderete score values of 9 and above was accomplished (White and Song 1999).

All patients were given paracetamol 1 g injection every 8 h. Nalbuphine 5 mg slowly IV was delivered as rescue analgesia when VAS was ≥ 4 and was repeated every 20 min till the pain subsided or if the patient demanded additional analgesia.

Patient-reported outcomes

As a primary outcome, we recorded VAS at rest and movement (lower limbs raising actively or passively) at the predetermined intervals of 30 min, 4, 8, 12, and 24 h postoperatively. Then we compared the following as a secondary outcome, the total dose of narcotic (fentanyl) used intraoperatively, the time elapsed till the need of the first dose of rescue analgesia (nalbuphine), the first dose of rescue analgesia, the overall dose of nalbuphine used in the first postoperative day, complications after surgery including postoperative nausea and vomiting (PONV), hypotension, arrhythmia, delirium, convulsions, and monoplegia or paraplegia.

Statistical analysis

The Statistical Package for Social Science (SPSS) version 22.0 was used to analyze the data. Quantitative data were expressed as mean ± standard deviation (SD) or median (IQR) when demonstrated. The frequency and percentage

of qualitative data were used. A *P*-value of 0.05 or higher was considered significant.

Sample size

Using the G power program for sample size calculation, setting power at 80% and alpha error at 5% reviewing results from a previous study (Koppert et al. 2004) showed that patients who received lidocaine reported less pain during movement and the control group exhibited significantly more pain during movement especially during second and third postoperative 24 h, assuming a medium effect size difference regarding the pain score between the two groups ($d=0.3$), and after 10% adjustment for dropout rate, sample size of at least 90 patients (45/group) will be needed.

Results

Ninety patients completed the study (Fig. 1, Table 1). The postoperative VAS assessed at rest showed significantly lower values in group L than in group P at the measured points of time (30 min, 8, 12, and 24 h postoperatively) with *p*-values (0.002, 0.008, 0.048, and 0.001, respectively), but there was no statistically significant difference between both groups at 4 h postoperatively with *P* value 0.052. On the other hand, the postoperative VAS assessed at movement showed non-significant differences between both groups at

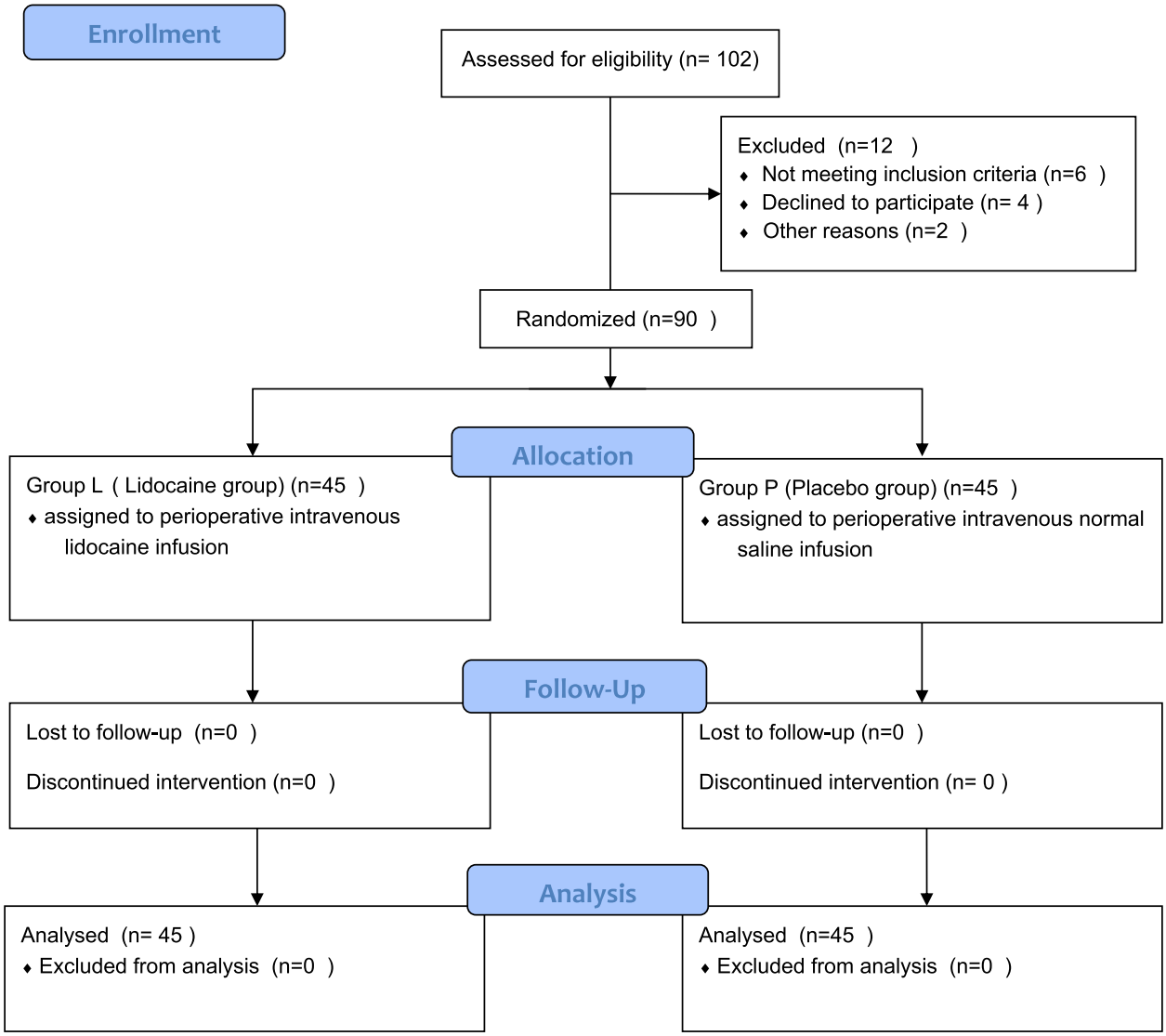

Fig. 1 Consort trial flow diagram

Table 1 Comparison between groups as regards demographic data, intraoperative data and complications

Demographic data		Lidocaine group ($n=45$)	Placebo group ($n=45$)
Age (years)		46.78 (10.99)	44.56 (10.88)
Sex	**Male**	44.4%	46.7%
	Female	55.6%	53.3%
BMI		31.04 (3.75)	30.76 (3.34)
ASA	**I**	62.2%	62.2%
	II	28.9%	31.1%
	III	8.9%	6.7%
Type of spine surgery	**Multi level**	62.2%	55.6%
	- Redo	28.9%	31.1%
	- Scoliosis	8.9%	13.3%
Operation time (h)		6.25 (1.89)	6.74 (1.64)
Anesthesia time (h)		6.92 (2.01)	7.62 (1.74)
PONV		4.4%	2.2%
Shivering		11.1%	15.6%
Hypotension		2.2%	4.4%
Monoplegia or paraplegia		0%	2.2%
Arrythmia		No cases detected	
Convulsions		No cases detected	
Delirium		No cases detected	

Data expressed as mean ± SD, proportion, t = Student t test, χ^2 = chi square test

the measured points of time (30 min, 4, 8, and 12 h postoperatively) except after 24 h when VAS was lower in group L in a comparison with group P with p-value < 0.001 (Figs. 2 and 3).

The total fentanyl dose delivered intraoperatively showed a statistically significant difference between group L and group P with p-value < 0.001. The time elapsed till the need for the first rescue analgesic

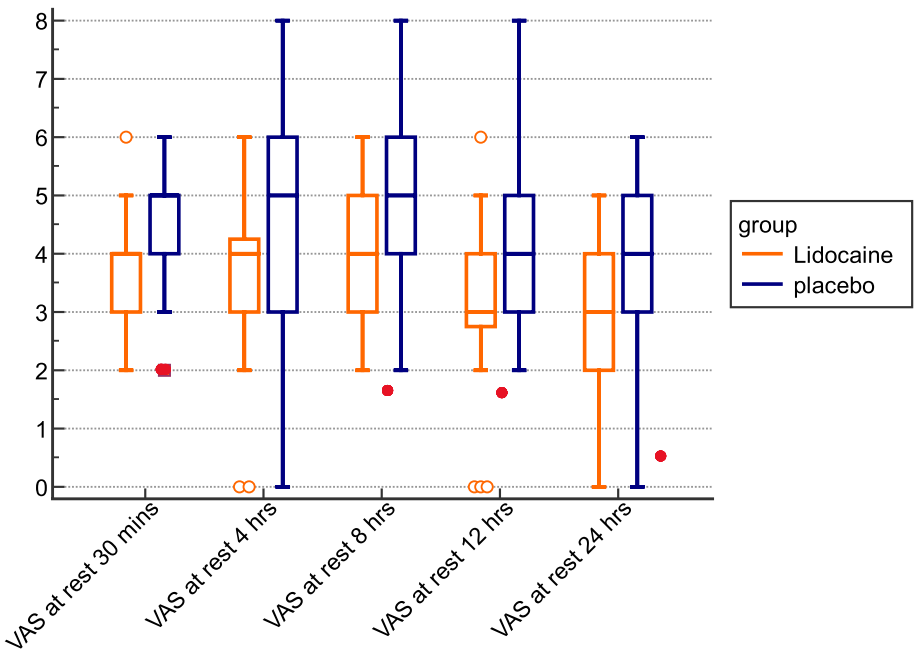

Fig. 2 Comparison between groups as regards VAS at rest

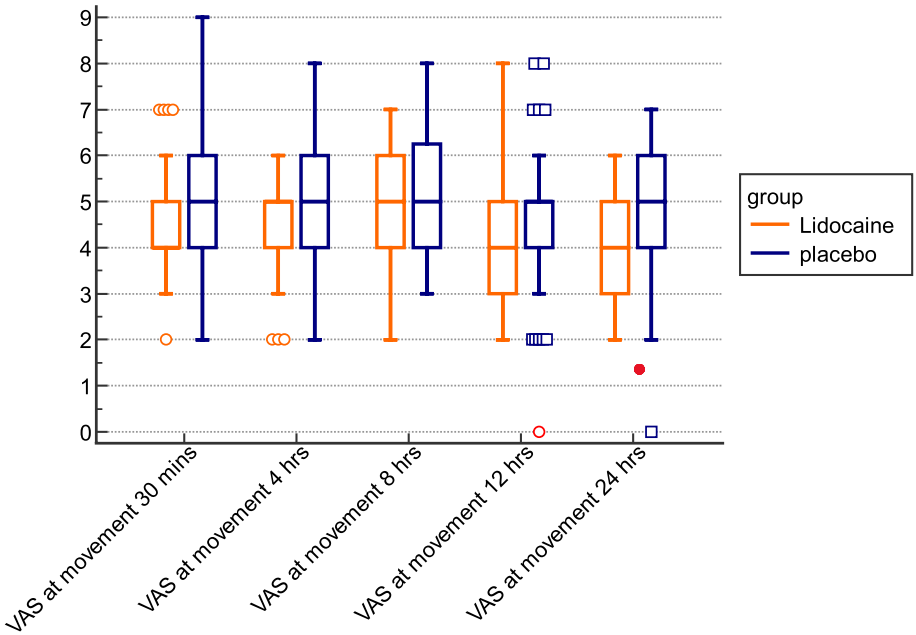

Fig. 3 Comparison between groups as regards VAS at movement. Red circle indicates a significant difference

postoperatively was significantly prolonged in group L than in group P with *p*-value < 0.001. Furthermore, the first dose of rescue analgesia was significantly lower in group L than group P (5.981.51 and 9.042.83 mg, respectively, with *p* value < 0.001), while the total dose of postoperative rescue analgesia given to patients during the first 24 postoperative hours showed statistically significant higher values in group P than group L with *P*-value < 0.001 (Table 2).

Discussion

In our study, the data revealed that VAS values at rest were statistically higher at 30 min, 8, 12, and 24 h postoperatively in the placebo group. Despite VAS at movement being clinically better at the same time points in the lidocaine group, it showed statistically non-significant values except after 24 h post-operation. We can explain these results by fear of patients to move so as not to exaggerate the pain and for fear of postoperative surgical complications.

The time elapsed till the need for the first dose of rescue analgesic was significantly prolonged in the lidocaine group. Also, the overall dose of intraoperative narcotics consumed as well as the first rescue analgesia was significantly higher in the placebo group, and that the entire dose of rescue analgesia was significantly higher in the same group.

Our findings regarding increased postoperative analgesic efficacy of intraoperative lidocaine infusion were consistent with other studies in which IV lidocaine was found to diminish postsurgical pain in various types of surgery, including complex spine surgeries. Major abdominal surgery, like major spine surgery, appears to cause substantial tissue damage, and lidocaine is used to provide analgesia for both types of surgery (Farag et al. 2013). This can be explained as lidocaine has a modulatory effect on the emergence of the surgically induced inflammatory process as it triggers the release of the anti-inflammatory mediators. Therefore, IV lidocaine has been proven to diminish pain, PONV, and other

Table 2 Total dose of intraoperative fentanyl used, time till request, the first and total dose of rescue analgesia used postoperatively

	Lidocaine group (*n* = 45)	Placebo group (*n* = 45)	*t*	*p*-value
Total intraop.fent dose (mcg)	187.11 (43.93)	300.44 (57.92)	10.5	**< 0.001**
Time till 1st rescue (h)	6.89 (2.15)	3.06 (1.93)	8.89	**< 0.001**
Dose of 1st rescue (mg)	5.98 (1.51)	9.04 (2.83)	6.41	**< 0.001**
Total dose of rescue (mg)	14.62 (3.30)	20.02 (3.55)	7.48	**< 0.001**

complications after surgery (Lahav et al. 2002; Herroeder et al. 2007).

Our results went in accordance with the findings of Baral et al. (2010), who revealed that perioperative intravenous lidocaine infusion at a dosage of 1.5 mg/kg IV bolus followed by 1.5 mg/kg/h infusion on pain severity at rest and movement in patients underwent upper abdominal surgeries, and also a total postoperative analgesic requirement, were considerably lower in the group of lidocaine.

To a further extent, Ibrahim et al. (2018) demonstrated that IV lidocaine, administered during surgery as a bolus followed by an infusion, effectively diminished the severity of long-term postoperative back pain up to three months after spinal fusion surgery. This can be explained as when lidocaine was given by infusion intravenously it lasts far beyond the time of infusion and may be justified by constant lidocaine concentrations in the cerebrospinal fluid (Tsai et al. 1998).

This was also confirmed by Farag et al. (2013), who discovered that lidocaine was significantly superior to placebo on pain scores and significantly better on the cumulative postoperative morphine dosage during the first 48 h post complex spine surgeries. Patients who received lidocaine reported well-promoted quality of life at one and three months after surgery.

In contrast, Dewinter et al. (2017) proved that there was no significant difference in cumulative morphine requirements between the lidocaine and placebo groups in the first postoperative day in patients who underwent posterior spinal arthrodesis. Besides, groups did not differ in terms of pain score at rest at any time, as well as PONV incidence. Remifentanil was used in this study as a rescue analgesia that might play a role in these results.

As regard the total intraoperative opioid consumption, we met a notable lower dose in the lidocaine group compared to placebo, which is in line with the results of Chandra et al. (2022) and Zhang et al. (2022).

Our results concerning the postoperative complications revealed non-considerable variation between both groups. Unfortunately, one of the patients in the placebo group developed early postoperative monoplegia, and this was attributed to surgical reasons, not pharmaceutical.

This went with Groudline et al. (1998) who tested IV lidocaine infusion on forty patients who underwent radical retropubic prostatectomy at lidocaine bolus (1.5 mg/kg) and infusion (3 mg/min, unless if body weight was 70 kg, then 2 mg/min) and recorded that there were no adverse events associated with the lidocaine infusion in any patient. Lidocaine blood levels did not exceed toxic levels (>5 g/mL). All patients who received IV lidocaine infusion showed minimal side effects, then toxicity from perioperative lidocaine infusion was extraordinarily uncommon.

As regards postoperative nausea and vomiting (PONV), our results have been promoted by Farag et al. (Koppert et al. 2004) who cleared up the non-significant difference between both groups among PONV. On the other side, Xu et al. (2021) confirmed that PONV had a lower incidence in the cases of the lidocaine group who underwent hepatectomy.

We would like to point out that our study has some constraints, including a limited sample size, likewise, we did not analyze serum concentration levels of lidocaine in our cases.

Conclusion

We draw the conclusion that lidocaine was highly effective in maintaining postoperative analgesia after complex spine surgeries in terms of pain scores following surgery, time to that first analgesic necessity, and total intraoperative and postoperative analgesic intake with no difference regarding post-operative complications.

Abbreviations

ECG	Electrocardiography
ASA	American Society of Anesthesiologists
VAS	Visual analog scale
IV	Intravenously
$ETCO_2$	End-tidal CO_2
MAC	Minimal alveolar concentration
PONV	Postoperative nausea and vomiting

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Authors' contributions

AF contributed to the idea and revision of the study; TA and EH contributed to the conception and design of the study, organized the data collection, and interpreted the results, SH checked the statistical analysis and revised the manuscript critically. All authors read and accept the final manuscript.

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Availability of data and materials

It is not applicable.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee at the Faculty of Medicine, Ain Shams University Hospital, Cairo, Egypt (FMASU M D 153/2021) It is included as a scanned gif. It is registered on Pan African trial registry.org with ID (PACTR202206745131592). All patients provided informed consent at Ain Shams University hospitals.

Consent for publication
It is not applicable.

Competing interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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