Ain-Shams Journal of Anesthesiology

ORIGINAL ARTICLE Open Access

Comparative study between the effect of dexmedetomidine and lidocaine infusion in lumbar fixation on hemodynamics, fentanyl requirements, and postoperative analgesia

Nayera S. Mohammed*, Mariam K. Habib, Essam A. Abbas, Sahar M. Mahmoud and Ibraheem A. Ramadan

Abstract

Background: Spinal surgery is associated with high incidence of severe postoperative pain difficult to easy control. Appropriate treatment modalities decreased the postoperative morbidity, increased patient satisfaction, allowed early mobility, and decreased hospital costs. Lidocaine was used as intravenous additives to control intraoperative pain and decrease postoperative pain. As lidocaine, dexmedetomidine infusion associated with lower postoperative pain scores decreased the opioid consumption and its related adverse events. The aim of this double blind randomized prospective comparative study was to compare the efficacy of intraoperative dexmedetomidine versus lidocaine infusion on hemodynamics, fentanyl requirements, and postoperative analgesia among 66 patients subjected to lumbar fixation surgery and randomized into group D which received dexmedetomidine 1 μg/kg infusion over 10 min as a loading dose then 0.3–0.5 μg/kg/h after induction of anesthesia as maintenance dose and group X which received lidocaine 0.3–0.5 mg/kg/h after induction of anesthesia.

Results: At 10, 15, 30, and 60 min, the mean arterial blood pressure and heart rate significantly decreased in group D compared to group X, and there was significantly higher total dose of intraoperative analgesic for fentanyl in group X than group D. There was significantly higher numeric rating scale in group X compared to group D at 2, 4, 6, 9, 12, 18, and 24 h postoperative with significant early request of the first analgesia, higher incidence of analgesic needs, and higher dose of postoperative analgesia paracetamol, voltaren, or pethidine in group X compared to group D.

Conclusions: The intraoperative use of dexmedetomidine IV infusion was an alternative mode to decrease the demands of analgesia following spine surgery.

Keywords: Dexmedetomidine, Fixation, Lidocaine, Nausea, Pain, Sedation score, Vomiting

Background

Postoperative pain is one of the most common complications after surgery and associated with higher incidence of nausea and vomiting, increased risk of thromboembolic manifestation, and postoperative cognitive dysfunction. Opioid medications were used commonly to control postoperative pain, but it was associated with higher risk of side effects mainly nausea and constipation (Hurley and Wu 2010).

Dexmedetomidine was a selective alpha 2 agonist as clonidine, but it has a greater affinity to the alpha 2 receptor with hypnotic properties similar to natural sleep and effectively attenuates the stress response to the surgical intervention with minimal or no respiratory depression complication. Also, maintained hemodynamic stability through its function on the central and peripheral alpha 2 receptors leads to reduction of heart rate and the systemic vascular resistance (Bos et al. 2017).

* Correspondence: Lovely_nero2008@yahoo.com
Department of Anesthesiology, Intensive care and Pain Management, Faculty of Medicine, Ain-Shams University, Abbassia, Cairo 11591, Egypt

Perioperative lidocaine infusion is commonly used as analgesic adjunct in enhanced recovery protocols for patients undergoing lumbar fixation surgeries and open and laparoscopic colorectal surgeries to control the intraoperative and postoperative pain scores, decrease opioid consumption, and shorten length of hospital stay and increase patients comfort (Terkawi et al. 2016).

Intravenous lidocaine infusion blockade of the neuronal transmission at the site of injury. Also, it has significant anti-inflammatory properties, reducing the release of cytokines; reduced cytokine-induced cellular damage mediated through mitochondrial adenosine triphosphate (ATP)-gated potassium channels by reducing neutrophil activation decreases intraoperative consumption of inhalational anesthetics and opioids which associated with early return of bowel function (Hollmann and Durieux 2000).

The aim of this study was to compare the efficacy of intraoperative dexmedetomidine versus lidocaine infusion on hemodynamics, fentanyl requirements, and postoperative analgesia.

Methods

This is a double blind randomized prospective comparative study conducted from October 2018 to September 2019 on 66 adult patients from 40 to 60 years, from both sex, American Society of Anesthesiologist (ASA) physical status 1–2, within average body weight, undergoing primary lumbar fixation surgery with 3 h duration of

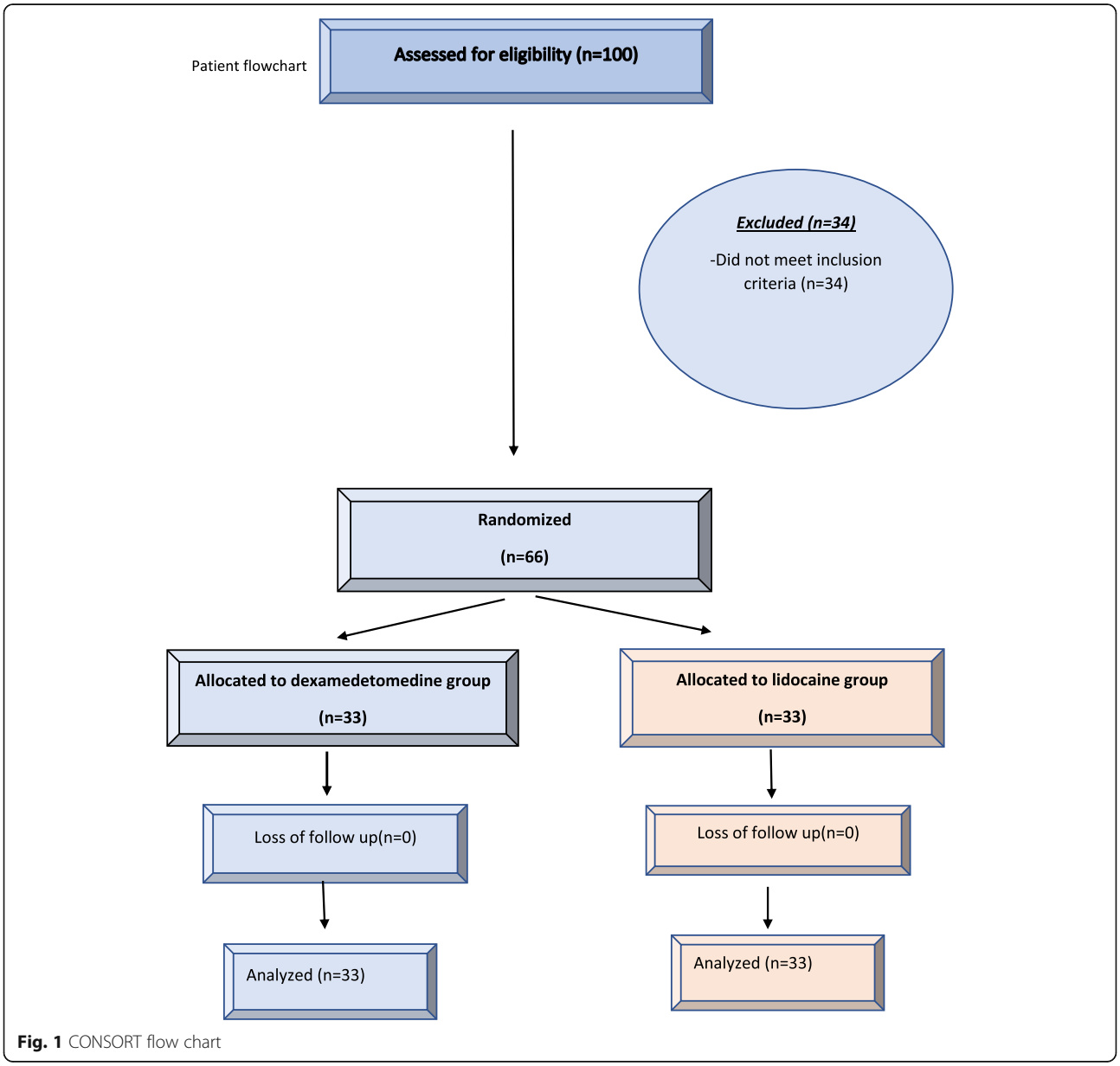

Fig. 1 CONSORT flow chart

surgery, randomized into 2 equal groups, each consisting of 33 patients, namely, group D in which patients received dexmedetomidine 1 μg/kg infusion over 10 min as a loading dose then 0.3–0.5 μg/kg/h after induction of anesthesia as maintenance dose and group X which included patients who received lidocaine 0.3–0.5 mg/kg/h after induction of anesthesia till the end of the operation after approval of the Ethical Committee and written informed consent from all participants were obtained.

Exclusion criteria included patients with history of allergy to dexmedetomidine and lidocaine, presence of significant dysfunction (cardiovascular, neurological, respiratory, hepatic and/or renal problems) (ASA 3–4), patients with any abnormal vital signs especially hypotension and/or bradycardia, polytrauma patients, patients who refused to participate, addict patient, and pregnant female.

All patients were subjected to history taking, clinical examination, and routine investigations according to their medical history performed.

Four syringes were prepared and coded by a clinical pharmacist and statistician; 2 of them for loading dose one contains 100 μg of dexmedetomidine diluted in 50 cc normal saline infusion, and the other contains 50 cc normal saline. The last 2 syringes were for maintenance; one of them contains 200 μg of dexmedetomidine diluted in 50 cc normal saline (the concentration were 4 μg /ml), and the other contains 200 mg of lidocaine diluted in 50 cc normal saline (the concentration was 4 mg/ml) infusion. Participating patients were randomly allocated to the different groups using computer-generated software, results concealed in opaque, sealed envelopes.

Patients were kept fasted, as per the American Society of Anesthesiologists physical status guidelines. All patients were premedicated with midazolam 1–2 mg i.v. at the preparation room before admitted to operation room. Upon arrival to the operating room, standard monitoring equipment was attached [an electrocardiogram leads II and V5, a pulse oximeter and entropy electrodes, and a noninvasive blood pressure monitor]. Baseline vital parameters, such as heart rate (HR) and mean arterial blood pressure (MAP), were noted prior to induction of anesthesia.

Begin giving loading dose dexmedetomidine 1 μg/kg infusion over 10 min in group D. Then, anesthesia was induced by administration of 2 mg/kg intravenous propofol and 2 μg/kg fentanyl. Endotracheal intubation was facilitated by intravenously injecting 0.5 mg/kg atracurium. Anesthesia was maintained using oxygen [O_2], with isoflurane (1.2–1.5%), and capnogram was attached. Then, top up doses atracurium guided by nerve stimulator (train of four (TOF) 0.15–0.25 indicates adequate surgical relaxation) to maintain neuromuscular relaxation. Lungs were mechanically ventilated to keep the end tidal carbon dioxide ($ETCO_2$) within 35–40 mmHg.

After intubation, patients who were in group D received dexmedetomidine 0.3–0.5 μg/kg/h as maintenance dose. And group X received lidocaine 0.3–0.5 mg/kg/h after induction of anesthesia until the end of the operation. Give fentanyl 0.5–1 μg/kg if HR increased or mean blood pressure increase > 20% of baseline after exclusion of other causes of tachycardia (bleeding, dehydration, awareness).

At the end of surgery, inhalational anesthesia was discontinued at beginning of skin closure, and infusion was stopped at the end of operation. Patients were turned to the supine position, and the neuromuscular block was reversed using neostigmine [0.05 mg/kg] and atropine [0.001 mg/kg]. The endotracheal tube was removed when the patients met the criteria of extubation (return of gag reflex, facial grimace, and purposeful motor movements) and were transferred to the post-anesthesia care unit. Patients were then discharged from the post-anesthesia care unit (PACU) when an Aldrete score > 9 was achieved.

The outcomes included assessment of the vital signs, blood pressure and heart rate, 5 min and 10 min, after beginning infusion then every 30 min intraoperative. Assessment of pain was by the Numeric Rating Scale (NRS-11) that is an 11-point scale for patient self-reporting of pain (Frattali 1999) immediately postoperative, then at 1st 24 h, every 2 h in the 1st 6 h, every 3 h in the 2nd 6 h, and every 6 h in the remaining 12 h; number of patients required postoperative rescue analgesia, first time of rescue analgesia, and total consumption of rescue analgesia either intraoperative or postoperative were documented. Patient with mild pain received paracetamol (15 mg/kg), patient with moderate pain received NSAID, and patient with severe pain received pethidine (50 mg IV). And assessment of the sedation level post-operative was carried out by modified Ramsay Sedation Scores (RSS).

Incidence of bradycardia, hypotension, and vomiting was recorded and treated probably. Infusion was stopped if HR < 50 and give atropine (0.01 mg/kg) repeated if needed or hypotension by decreasing mean blood pressure > 30% of baseline and give ephedrine (5 mg IV bolus) and repeated if needed. Patient with nausea and vomiting received 1–2 mg granisetron.

Statistical analysis

Sample size was calculated using PASS® version 11 program, setting the type-1 error (α) at 0.05 and power at 80%. Results from a previous study of Talke et al. (Talke et al. 2000) reported that heart rate was slower with dexmedetomidine (73 ± 11 bpm) than control (83 ± 20 bpm). Calculation according to these values produced a minimal sample size of 33 cases per group, estimated

Table 1 Comparison between group D and group X according to demographic data

Demographic data	Group D (n = 33)	Group X (n = 33)	t/χ^{2a}	p value
Age (years)				
Range	30–60	30–60	1.618	0.104
Mean ± SD	45.90 ± 8.72	44.98 ± 8.55		
Sex				
Male	24 (72.7%)	22 (66.7%)	1.213[a]	0.23
Female	9 (27.3%)	11 (33.3%)		
ASA				
I	26 (78.8%)	24 (72.7%)	0.213[a]	0.556
II	7 (21.2%)	9 (27.3%)		
Weight (kg)				
Range	60–100	60–100	1.213	0.131
Mean ± SD	81.60 ± 15.50	97.83 ± 15.19		
Duration of surgery (min)				
Mean ± SD	105.38 ± 17.92	109.52 ± 12.86	1.476	0.113

t independent sample *t* test, *ASA* American Society of Anesthesiologist, *SD* standard deviation
[a]χ^2 Chi-square test

effect size according to Cohen's d = (83 − 73)/16.140012 = 0.619578.

Our data were analyzed using the Statistical Package for Social Sciences, version 20.0 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent sample t test of significance was used when comparing between two means, and Mann-Whitney U test for non-parametric data between two-groups. Chi-square (χ^2) test of significance was used to compare proportions between qualitative parameters. The confidence interval was set to 95%, and the margin of error accepted was set to 5%. So, the p value ≤ 0.05 was considered significant, p value ≤ 0.001 was considered as highly significant, and p value > 0.05 was considered insignificant.

Results

One hundred patients were assessed for eligibility, 34 patients were not excluded nor met inclusion criteria, and remaining 66 patients were randomly divided to one of each group (Fig. 1). In the current study, the majority of

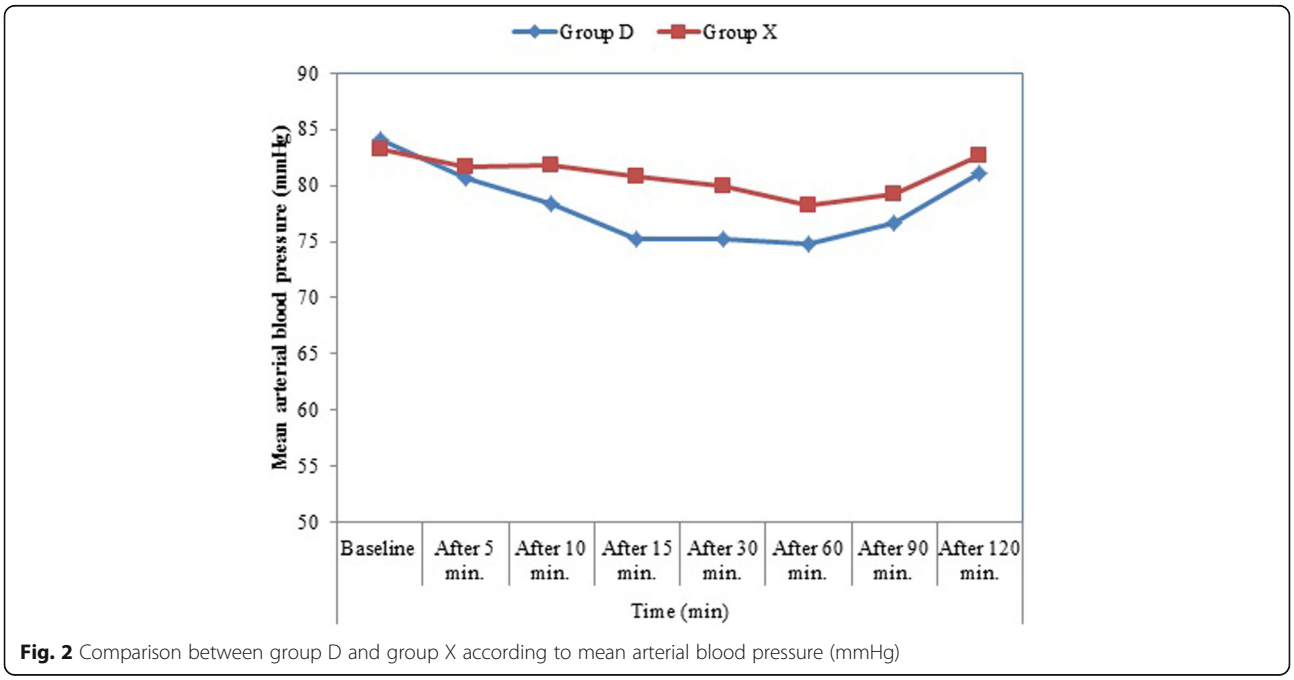

Fig. 2 Comparison between group D and group X according to mean arterial blood pressure (mmHg)

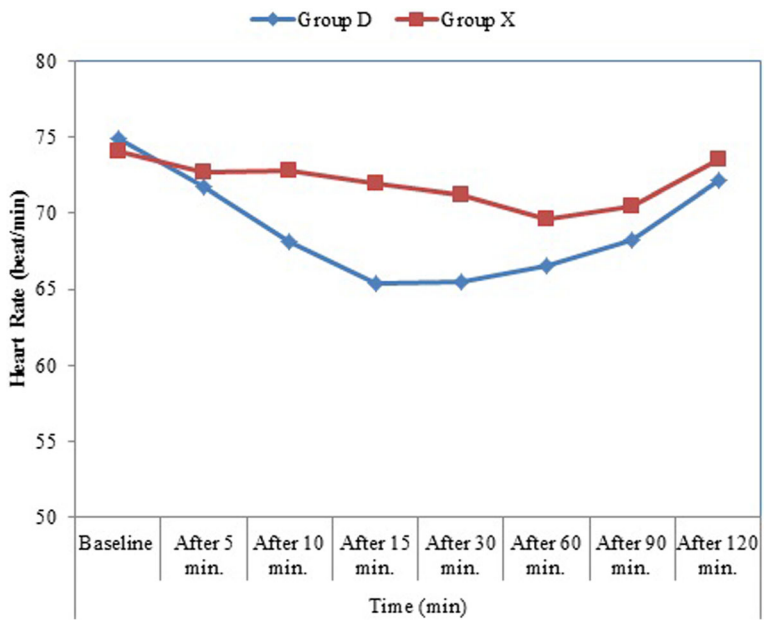

Fig. 3 Comparison between group D and group X according to heart rate (beat/min)

studied cases was male (72.7% and 66.7%) with no statistically significant difference between groups according to demographic data as age, gender, ASA, weight, and duration of surgery (p = 0.104, 0.23, 0.556, 0.131, and 0.113 respectively) (Table 1).

In the current study, at 10, 15, 30, and 60 min, the mean arterial blood pressure and heart rate significantly decreased in group D compared to group X as p = 0.037, 0.029, 0.009, and 0.018, respectively for MAP and 0.041, 0.014, 0.013, and 0.026 respectively for HR (Figs. 2 and 3).

Table 2 shows a highly statistically significant higher mean value of group X compared to group D according to total dose of intraoperative analgesic for fentanyl.

There was statistically significant higher mean value of numeric rating scale in group X compared to group D at 2, 4, 6, 9, 12, 18, and 24 h postoperative, as p = 0.035, 0.032, 0.020, 0.026, 0.009, 0.025, 0.024 respectively (Fig. 4).

Table 3 shows statistically significant short time of mean value of group X compared to group D according to time of first analgesia (min).

Also, there was statistically significant difference between groups according to needs for analgesia as in group D; 57.6% of cases required one dose, versus (100%) in group X, with statistically significant difference between groups according to needs for analgesia (Table 4).

The required dose of postoperative analgesia paracetamol, voltaren, or pethidine in group X (751.39 ± 90.71, 100.84 ± 12.17, and 133.91 ± 16.17) was significantly higher than in group D (430.34 ± 73.16, 57.75 ± 9.82, and 76.70 ± 13.04) as p = 0.013, 0.017, 0.017 respectively. The incidence of nausea and vomiting was significantly higher in group X (39.4% and 36.4%) than group D (18.2% and 9.1%) as p = 0.015 and 0.008 respectively (Fig. 5).

Table 5 shows statistically significant difference between groups according to Ramsay Sedation Scores from after surgery, after 2 h and after 4 h as p = 0.019, 0.023, and 0.034 respectively, as group D is more sedated.

Discussion

In the current study, we described the use of intraoperative dexmedetomidine versus lidocaine infusion in lumbar fixation surgery at 10, 15, 30, and 60 min; the mean arterial blood pressure and heart rate significantly decreased in group D compared to group X. This may be

Table 2 Comparison between group D and group X according to intraoperative analgesic for fentanyl

Intraoperative analgesic for fentanyl (1 μg/kg)	Group D (n = 6)	Group X (n = 20)	t test	p value
Total fentanyl dose	286	876	13.347	< 0.001**

t independent sample t test, SD standard deviation
**Highly significant as p < 0.001

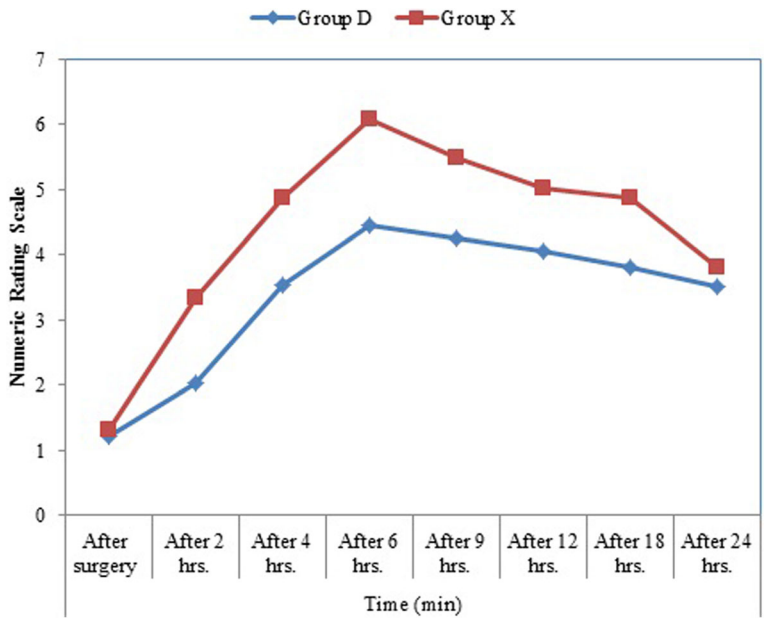

Fig. 4 Comparison between group D and group X according to numeric rating scale

explained by binding of dexmedetomidine to α2-adrenoreceptors within the peripheral and central nervous systems in either pre-, post-, and extra-synaptic sites which in turn decreased the norepinephrine release also hypotension resulting from vasodilatation associated with dexamedetomedine is mediated through three α2-adrenoreceptors (α2a, α2b, and α2c) within the vascular endothelial cells respond by causing a. Also, the centrally located α2a and α2c adrenoreceptors had an important role in development of hypotension associated with dexmedetomidine. As regard to lidocaine, it has a stabilizing effect on the heart and blood pressure, possibly by direct myocardial depressant effect, a peripheral vasodilating effect, and through its anti-inflammatory activity, but this effect is less potent than dexmedetomidine (Weerink et al. 2017).

In harmony with our finding, Anis et al. found that dexmedetomidine attenuation of the HR was statistically highly significant compared with that of lidocaine (L), as the maximum increase in the mean values of the HR in group L was less than 20% from the baseline value and was not associated with a significant increase in the mean values of the MAP, and this may be explained by different surgical procedures in their study (Anis et al. 2016).

Similarly, Prasad et al., found that there was fall in HR and MAP when compared to the baseline value. Compared to group L, fall in HR and MAP was highly significant in group D (dexmedetomidine) (p = 0.000) (Prasad et al. 2015).

In contrast, among 90 female patients who underwent elective abdominal gynecological surgeries and were enrolled in the Menshawi and Fahim, the MAP and HR had no significant difference between groups D and L (Menshawi and Fahim 2019).

In the current study, the total dose of intraoperative analgesic for fentanyl was significantly higher in group X than group D. This was explained by the anesthetic and opioid-sparing effects of dexmedetomidine (Dunn et al. 2016).

Moharram and Mostafa enrolled 60 patients scheduled for elective lumbar spine instrumentation divided into (group C) who received placebo and dexmedetomidine group (group D) and found a significant reduction in intraoperative fentanyl consumption by dexmedetomidine

Table 3 Comparison between group D and group X according to time of first analgesia (min)

Time of first analgesia (min)	Group D (n = 33)	Group X (n = 33)	t test	p value
Mean ± SD	159.64 ± 30.27	124.78 ± 24.66	4.277	0.009*

t independent sample t test, SD standard deviation
*Significance as p value < 0.05

Table 4 Comparison between group D and group X according to needs for analgesia

Needs for analgesia	Group D (n = 33)	Group X (n = 33)	χ^2	p value
1st dose	19 (57.6%)	33 (100%)	3.164	0.009*
2nd dose	13 (39.4%)	24 (72.7%)	3.146	0.010*
3rd dose	2 (6.1%)	13 (39.4%)	3.119	0.011*

χ^2 Chi-square test
*Significant as $p < 0.05$

infusion when compared with the control group (Moharram and Mostafa 2019).

Also, Menshawi and Fahim found no significant difference between groups L and D in the total intraoperative fentanyl consumption (Menshawi and Fahim 2019).

In the present study, at 2, 4, 6, 9, 12, 18, and 24 h postoperative, the numeric rating scale was significantly higher in group X compared to group D mediated by dexmedetomidine binding to the central and spinal cord α2-receptors which resulted in decreased substance P and glutamate release (Weerink et al. 2017).

Similarly, Andjelković et al. found that the distribution of the average VAS differed significantly between dexmedetomidine group (DG) and lidocaine group (LG) (p = 0.028) and between control group (CG) and LG (p = 0.023) (Andjelković et al. 2018). In contrast, according to Cho et al., no significant difference was observed in VAS score among group L and group D during the first 24 h after LC (Cho et al. 2014).

In the present study, the time to first analgesic was statistically significantly delayed in group D than group X. Also, there was significantly higher incidence of requesting analgesia in group X. Similarly, Manne et al. observed an increase in the time to receive first rescue analgesia, with a decrease in total analgesic requirements in the first 24 postoperative hours among patients who received dexmedetomidine infusion (Manne et al. 2014).

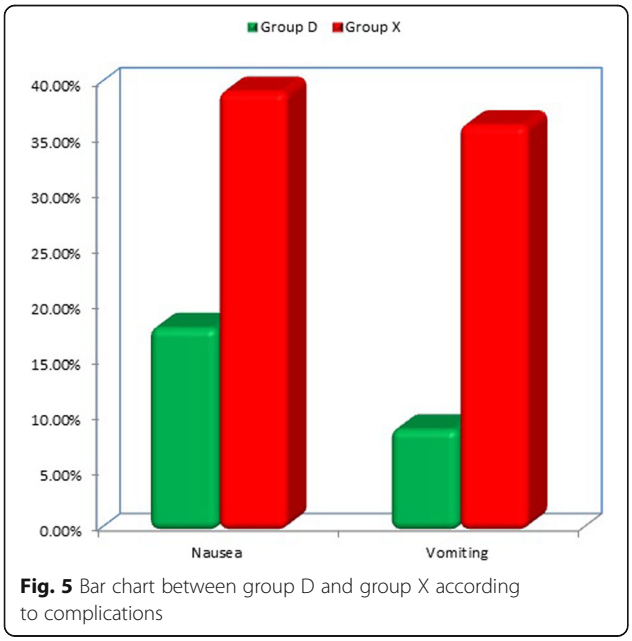

Fig. 5 Bar chart between group D and group X according to complications

In agreement with our results, according to Menshawi and Fahim, the time to the first postoperative analgesic requirement was significantly longer in group D when compared with groups L and C (Menshawi and Fahim 2019).

But in the study by Bakan et al., they found that intraoperative administration of the intravenous dexmedetomidine and lidocaine was associated with decreased postoperative opioid use in laparoscopic cholecystectomy and delayed the first rescue analgesia up to 6 h postoperatively compared with conventional opioid-based anesthesia (Bakan et al. 2015).

In this study, the required dose of postoperative analgesia paracetamol, voltaren, or pethidine in group X was significantly higher than in group D. Dexmedetomidine contains analgesic properties therefore reducing opioid requirements intraoperatively as well as postoperatively. The present study is supported by previous studies; the intravenous dexmedetomidine infusion reduced the requirement for fentanyl in the PACU (Park et al. 2012; Kaur and Singh 2011; Feld et al. 2006).

Similarly, Garg and colleagues found a 54% decrease in opioid requirement post-operatively when dexmedetomidine was used (Garg et al. 2016).

But discordances with study by Anis et al. found that the total dose of pethidine given to patients in both lidocaine and dexmedetomidine groups was less than 50 mg, and this was statistically non-significant (Anis et al. 2016).

Limitation of this study included small sample size; we did not measure the serum level of lidocaine as the loading and maintenance dose was similar to previous studies that reported no detectable side effects. Also, the effect of both drugs was not seen in hypertensive and cardiac patients as those patients were excluded from the study although they have apriority of pain control, and pain assessment was done only at rest only in this study and not during active movement.

Further studies on a larger sample size were recommended, and using different doses of both drugs may be helpful to detect an optimal dose of lidocaine and dexmedetomidine. It will be more useful to study in high-risk hypertensive and cardiac patients and to correlate

Table 5 Comparison between group D and group X according to Ramsay Sedation Scores

Ramsay Sedation Scores	Group D (n = 33)	Group X (n = 33)	z test	p value
After surgery	4.15 ± 0.25	2.06 ± 0.25	4.320	0.019*
After 2 h	3.11 ± 1.71	2.17 ± 1.38	3.450	0.023*
After 4 h	3.04 ± 1.23	2.08 ± 1.51	2.332	0.034*
After 6 h	2.16 ± 1.53	2.00 ± 1.64	0.303	0.157
After 9 h	2.10 ± 1.38	2.14 ± 0.90	0.787	0.377
After 12 h	2.11 ± 1.27	2.15 ± 1.64	0.707	0.403
After 18 h	2.14 ± 1.23	2.11 ± 1.57	0.281	0.286
After 24 h	2.08 ± 1.11	2.06 ± 1.56	0.115	0.735

z Mann-Whitney test
*Significant as $p < 0.05$

between uses of either drugs and plasma catecholamine levels, which reflected the stress response, and it was necessary to evaluate postoperative pain on movement in farther studies.

Conclusion

Our results suggest the unique role of dexmedetomidine infusion added to routine general anesthesia in significantly decreased postoperative pain intensity and decreased the need for rescue analgesics than lidocaine infusion, among patients that underwent lumbar fixation surgery.

Abbreviations

ASA: American Society of Anesthesiologist; ATP: Adenosine triphosphate; CBC: Complete blood count; CG: Control group; DG: Dexmedetomidine group; ECG: Electrocardiogram; $ETCO_2$: End tidal carbon dioxide; GABA: γ-Aminobutyric acid; GIT: Gastrointestinal tract; HR: Heart rate; KFT: Kidney function test; LFT: Liver function test; LG: Lidocaine group; MAP: Mean arterial blood pressure; NRS-11: Numeric Rating Scale; PACU: Post-anesthesia care unit; PT: Prothrombin time; PTT: Partial thromboplastin time; RBS: Random blood sugar; TOF: Train of four

Acknowledgements

Not applicable

Authors' contributions

IA designed the study, revised literature, followed the patients, and critically reviewed the manuscript. MK designed the study, analyzed the data, and wrote and critically revised the manuscript. EA and SM revised literature and followed the patients. NS collected the data, performed the analysis, and wrote the manuscript. All authors approved the final version of the manuscript.

Funding

We did not receive any financial support

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due [Publishing the clinical data about any study conducted in our hospitals and approved by the institutional ethical committee is against the policy of the Faculty of Medicine, Ain-Shams University unless there is a reasonable request] but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the ethical committee of Ain Shams University with approval number (FMASU M D 248/2018); the participants provided written consent.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Received: 26 August 2020 Accepted: 9 November 2020
Published online: 25 November 2020

References

Andjelković L, Novak-Jankovič V, Požar-Lukanovič N, Bosnić Z, Spindler-Vesel A (2018) Influence of dexmedetomidine and lidocaine on perioperative opioid consumption in laparoscopic intestine resection: a randomized controlled clinical trial. J Inter Med Res 46(12):5143–5154. https://doi.org/10.1177/0300060518792456

Anis S, Samir G, ElSerwi H (2016) Lidocaine versus dexmedetomidine infusion in diagnostic laparoscopic gynecologic surgery: a comparative study. Ain-Shams J of Anaesthesiol 9(4):508–516. https://doi.org/10.4103/1687-7934.198265

Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, Kadioglu H et al (2015) Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Braz J Anesthesiol 65(3):191–199. https://doi.org/10.1016/j.bjane.2014.05.001

Bos M, Janssen M, Smeets A, Temel Y, Zundert A, Ackermans L (2017) Use of dexmedetomidine during deep brain stimulation for Tourette syndrome: a case report and review of the literature. Anaesth Cases 5(1):13–17. https://doi.org/10.21466/ac.UODDDBS.2017

Cho K-R, Lee J-H, Kim M-H, Lee W-J, Lim S-H, Lee K-M et al (2014) Effect of perioperative infusion of lidocaine vs. dexmedetomidine on reduced consumption of postoperative analgesics after laparoscopic cholecystectomy. Anesth Pain Med 9(3):185–192

Dunn LK, Durieux ME, Nemergut EC (2016) Non-opioid analgesics: novel approaches to perioperative analgesia for major spine surgery. Best Pract Res Clin Anaesthesiol 30(1):79–89. https://doi.org/10.1016/j.bpa.2015.11.002

Feld JM, Hoffman WE, Stechert MM, Hoffman IW, Ananda RC (2006) Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. J Clin Anesth 18(1):24–28. https://doi.org/10.1016/j.jclinane.2005.05.009

Frattali C (1999) National Institutes of Health, Warren Grant Magnuson Clinical Center. ASHA 41(4):46

Garg N, Panda NB, Gandhi KA, Bhagat H, Batra YK, Grover VK et al (2016) Comparison of small dose ketamine and dexmedetomidine infusion for postoperative analgesia in spine surgery—a prospective randomized double-blind placebo controlled study. J Neurosurg Anesthesiol 28(1):27–31. https://doi.org/10.1097/ANA.0000000000000193

Hollmann MW, Durieux ME (2000) Local anesthetics and the inflammatory response: a new therapeutic indication? Anesthesiology 93(3):858–875. https://doi.org/10.1097/00000542-200009000-00038

Hurley RW, Wu CL (2010) Acute postoperative pain. Millers Anesth 7:2757–2787

Kaur M, Singh P (2011) Current role of dexmedetomidine in clinical anesthesia and intensive care. Anesth Essays Res 5(2):128–133 0.4103/0259-1162.94750

Manne GR, Upadhyay MR, Swadia V (2014) Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative

analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian J Anaesth 58(6):726–731. https://doi.org/10.4103/0019-5049.147164
Menshawi MA, Fahim HM (2019) Dexmedetomidine versus lidocaine as an adjuvant to general anesthesia for elective abdominal gynecological surgeries. Ain-Shams J Anesthesiol 11(1):12–21. https://doi.org/10.1186/s42077-019-0027-9
Moharram AA, Mostafa RH (2019) Efficacy of dexmedetomidine infusion without loading dose as a potent hypotensive agent in lumbar fixation surgery. Open Anesth J 13(1):68–74 0.2174/2589645801913010068
Park J-K, Cheong SH, Lee KM, Lim SH, Lee JH, Cho K et al (2012) Does dexmedetomidine reduce postoperative pain after laparoscopic cholecystectomy with multimodal analgesia? Korean J Anesthesiol 63(5):436–440. https://doi.org/10.4097/kjae.2012.63.5.436
Prasad S, Matam U, Ojili G (2015) Comparison of intravenous lignocaine and intravenous dexmedetomidine for attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation. J Dr NTR Univ Health Sci 4(2):86–90. https://doi.org/10.4103/2277-8632.158579
Talke P, Chen R, Thomas B, Aggarwall A, Gottlieb A, Thorborg P et al (2000) The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. Anesth Analg 90(4):834–839. https://doi.org/10.1213/00000539-200004000-00011
Terkawi AS, Tsang S, Kazemi A, Morton S, Luo R, Sanders DT et al (2016) A clinical comparison of intravenous and epidural local anesthetic for major abdominal surgery. Region Anesth Pain M 41(1):28–36. https://doi.org/10.1097/AAP.0000000000000332
Weerink MA, Struys MM, Hannivoort LN, Barends CR, Absalom AR, Colin P (2017) Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmacokinet 56(8):893–913. https://doi.org/10.1007/s40262-017-0507-7

Publisher's Note