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# Comparative study between the effect of dexmedetomidine and lidocaine infusion on intraoperative analgesic requirement and hemodynamics during craniotomy

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## ABSTRACT

**Background:** Nowadays, anesthesiologists are evaluating several analgesic adjuncts to minimize opioid use during craniotomy. Some studies have evaluated the analgesic-sparing effect of intravenous infusion of dexmedetomidine and lidocaine on intraoperative hemodynamics and post-operative analgesia. There is a paucity of studies focussing on the intraoperative analgesic requirement. **Aims and Objectives:** The present study compared dexmedetomidine and lidocaine infusion primarily for their effects on intraoperative fentanyl requirements during craniotomy. **Materials and Methods:** This study was done on 70 patients aged 18–80 years, the American Society of Anesthesiologists physical status I–II, having Glasgow Coma Scale 15, undergoing craniotomies. Patients were randomly allocated to receive either dexmedetomidine (group A, n = 35) at a dose of 0.6 mcg/kg bolus over 10 min followed by 0.6 mcg/kg/h infusion or lidocaine (group B, n = 35) at a dose of 1.5 mg/kg bolus over 10 min, followed by 1.5 mg/kg/h infusion till the end of skin suture, respectively. Study drugs were started 10 min before the start of surgery. Intraoperative total fentanyl and propofol consumption, intraoperative hemodynamics, recovery from hypnosis, and time to extubation were recorded. **Results:** The use of dexmedetomidine resulted in considerably less total fentanyl requirement (245.1 vs. 300.7 mcg, P < 0.0001) and total propofol requirement (172.7 vs. 236.7 mg, P < 0.0001) compared with lidocaine. Comparatively better hemodynamics were observed with the use of dexmedetomidine at all the points of observation. **Conclusion:** Dexmedetomidine as an analgesic adjunct can be a better alternative to lidocaine in terms of reduced fentanyl consumption, reduced propofol use and favorable hemodynamics, and early recovery from anesthesia.

**Key words:** Analgesic; Dexmedetomidine; Fentanyl; Hemodynamics; Lidocaine; Propofol

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## INTRODUCTION

During craniotomy, insertion of the skull pin as a part of the head holder to stabilize the head and incision on the dura can lead to considerable periosteal stimulation and immense sympathetic stimulation, resulting in hemodynamic adverse effects.[1] In recent years, practicing anesthesiologists utilized various non-opioid analgesic adjuncts such as dexmedetomidine and lidocaine in the perioperative periods to curtail the use of opioids as a part of enhanced recovery after surgery protocol and to minimize opioid-related adverse events.[2-4]

Perioperative use of intravenous (IV) dexmedetomidine during general anesthesia in adult patients led to extended pain-free periods, reduced pain intensity, and decreased consumption of opioids in the post-operative period.[5] Many studies[6-9] have investigated the analgesic-sparing

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effect of perioperative IV infusion of dexmedetomidine and lidocaine. Some studies[6,7] have reported a considerable reduction of the total dose of analgesic consumption with the use of dexmedetomidine over lidocaine while other studies[8,9] have reported comparable the Visual Analog Scale scores in the post-operative pain assessment. Most of the studies have focused on assessing intraoperative hemodynamics such as heart rate (HR) or mean arterial pressure (MAP) and post-operative pain scores or total analgesics consumption in the post-operative period.

Some studies[10,11] have already focused on the effects of these drugs on intraoperative analgesic consumption. Mohammed et al.[11] observed a considerably higher analgesic (fentanyl) consumption in the intraoperative period with the use of lidocaine infusion compared with dexmedetomidine while Menshawi and Fahim[10] have found no significant difference. Again, the use of dexmedetomidine has led to a considerable reduction of HR and MAP in the intraoperative period in one study[12] while another study[10] reports no significant difference when compared with lidocaine. Thus, a wide variation has been observed in the reported observations of various parameters in different studies. This was the stimulus for further research in this field.

### Aims and objectives

Hence, the present study aimed to compare the intraoperative fentanyl requirement (primary outcome measure) between the patients receiving IV infusions of dexmedetomidine or lidocaine infusions. Other outcome measures were intraoperative propofol requirement, intraoperative vital parameters (HR and mean arterial blood pressure), and the time to recovery.

## MATERIALS AND METHODS

This prospective double-blinded randomized study was started after receiving clearance from the Institutional Ethics Committee (IPGME&R/IEC/2020/614-B, dated December 09, 2021) and obtaining written informed consent from each patient.

Seventy patients of either sex, aged 18–80 years, weighing between 50 and 80 kg with the American Society of Anesthesiologists (ASA) physical status I and II with the Glasgow Coma Scale score 15, scheduled for elective craniotomy surgery for 2–3 h duration were included in this study. Patients with known hypersensitivity to study drugs, those with renal, hepatic, or cardiac insufficiency, those suffering from psychiatric illness or on long-term sedatives, and unwilling patients were excluded.

### Sample size calculation

The sample size calculation using the methods described by Charan et al.[13] In a previous study,[10] the intraoperative fentanyl consumption was noted as 104.68±18.54 and 92.87±11.67 with the use of lidocaine and dexmedetomidine, respectively. Hence, the standard deviation of the control group was rounded off to 18. It was assumed that a difference of a minimum of 25 mcg of intraoperative fentanyl consumption with the use of dexmedetomidine would be clinically important to detect. Thus, the effect size was 25. Considering 1:1 group allocation, with the power of the study at 80% and allowing an alpha error of 5%, the sample size was calculated to be 8.6 (approximated to 9) for each group. The sample size was increased to 35 per group to achieve an increased confidence interval of the population data, to have a greater chance of normal distribution, and to address the attrition issue.[14]

A detailed pre-anesthetic check-up and necessary investigations were done before surgery. On the day of surgery, after the arrival of the patient to the patient preparation room, 18-gauze IV cannula was inserted and normal saline was started. The patient was connected to a multichannel monitor (non-invasive blood pressure, electrocardiogram, and pulse oximeter), and baseline parameters were recorded. Bispectral index (BIS) monitor electrodes were placed on the skin of the forehead after cleaning it with alcohol and the level of anesthesia was assessed with the BIS monitor (model VISTA, Aspect Medical System, USA).

Study participants were randomly allocated into two groups to receive infusion dexmedetomidine (Group A, n=35) or preservative-free 2% lidocaine (Group B, n=35). Randomization was done with computer-generated tokens, and concealment of allocation was done by serially numbered opaque sealed envelope technique. The trial participants and investigators were kept blind.

An independent nurse who was not involved with the study loaded the syringes with study solutions. She prepared the syringes containing either dexmedetomidine at 4 mcg/mL or lidocaine at 10 mg/mL. She handed over the respective syringe according to the group allocation, keeping the conducting anesthesiologist blind about the contents.

Ten minutes before the induction of anesthesia IV infusion of the study drug solutions was started in both the groups at a rate of 0.9 mL/kg/h. This infusion rate corresponds to 0.6 mcg/kg of dexmedetomidine or 1.5 mg/kg of lidocaine. After the loading dose, the infusion rate was reduced to 0.15 mL/kg/h, which translates into 0.6 mcg/kg/h of dexmedetomidine and 1.5 mg/kg/h of lidocaine.

The volumes, appearance, and infusion rates were similar in both groups, and thus, the particular intervention was kept blinded to the investigators. The patients remained blinded owing to anesthetized conditions. Data about intraoperative outcomes were observed and recorded by a researcher who remained blinded throughout the study.

Before induction, the arterial cannula was inserted in the radial artery after performing Allen's test for continuous invasive hemodynamic monitoring in an attempt to monitor stroke volume variation (SVV) and cardiac output. Initially, patients received pre-oxygenation with 100% oxygen for 3 min. Both the groups received pre-emptive injection paracetamol (15 mg/kg). Before induction, patients of both groups received bolus fentanyl (2 mcg/kg). Induction of anesthesia was done using propofol 2 mg/kg IV in the running fluid. After checking mask ventilation, an injection of rocuronium bromide (0.9 mg/kg) was administered through the IV route and the airway was secured with an endotracheal tube of appropriate size after mask ventilation for 90 s. Adequacy of muscle relaxation was judged clinically with adequate jaw relaxation. The correct position of the endotracheal tube position was confirmed by capnography. The patients were mechanically ventilated with an anesthesia machine (GE Care station 620) using volume-controlled mode. A circle system was used for ventilation of the lungs to maintain $EtCO_2$ between 35 and 40 mm Hg and peak airway pressure <30 mm Hg. After intubation, central venous catheterization was done.

In the intraoperative period, anesthesia was maintained with IV infusion of propofol (1%) using a target-controlled infusion pump (Schnider model) with a target concentration being 3–4 mcg/mL depending on demographic characteristics. An additional dose of propofol at 0.5 mg/Kg was used to maintain BIS value within 40–60. To maintain the target MAP between 70 and 80 mmHg, the rate of propofol infusion was adjusted accordingly. IV fluid requirement was addressed as per goal-directed fluid therapy (SVV <13%). Muscle relaxation was maintained with rocuronium top-up doses (0.1 mg/kg) titrated with clinical monitoring, $EtCO_2$ tracings, and ventilation curves.

Both groups received injection fentanyl 25 mcg IV in aliquots when HR or MAP was increased >30% of the baseline, after excluding the other probable causes of tachycardia such as bleeding, awareness, and dehydration. On commencement of skin closure, propofol infusion was discontinued. The amount of propofol and fentanyl consumption was calculated and recorded. The study drug solution was stopped at the end of skin closure. The "recovery from hypnosis" was defined as the time duration from the stoppage of the study solution up to achieving a BIS score of 80.

After achieving spontaneous eye opening and regular respiration, the reversal of the neuromuscular block was attempted using injection neostigmine (50 mcg/kg) and injection glycopyrrolate (10 mcg/kg). Then patients were extubated and the time was noted. Extubation time was measured from the stoppage of study drug infusion to the point of tracheal extubation, and after extubation, patients were transferred to the post-anesthesia care unit and then shifted to the ward when the Aldrete score was achieved more than 9. HR and MAP were recorded before intubation, after intubation, pinning, skin incision, dura incision, and at 30, 60, 90, 120, and 150 min of the intraoperative period as well as immediately after post-extubation.

We defined intraoperative bradycardia as HR <50 beats/min (bpm) and considered treatment with 0.5 mg of atropine. Hypotension (defined as a 20% decrease in the MAP from the baseline) was treated with an aliquot of 250 mL of normal saline and increments of ephedrine 3 mg IV.

The data were tabulated in Microsoft Excel and analyzed with SPSS V.24 software. The continuous variables have been expressed with mean and standard deviation. The categorical variables have been expressed with frequency and percentage. Independent t-test and Chi-square test are used for the comparisons. The $P \leq 0.05$ was considered statistically significant.

## RESULTS

The data from all 70 patients were available for analysis (Figure 1). The study spanned from January 2022 to December 2022, for 1 year. The two groups of patients were comparable in respect of demographic data and duration of surgery (Table 1).

The patients receiving intraoperative dexmedetomidine infusion required about 50–70 mg less propofol in the intraoperative period to maintain vital parameters within permissible limits. Similarly, patients receiving intraoperative dexmedetomidine infusion consumed about 55 mcg less fentanyl in the intraoperative period. Both the differences were statistically significant. A quicker recovery from hypnosis and faster extubation were noted in patients receiving dexmedetomidine infusion compared with those receiving lidocaine infusion (Table 2).

Considerably lower MAPs (Table 3) and HRs (Table 4) were noted at most of the time points in the intraoperative period in patients receiving dexmedetomidine in comparison with those receiving lidocaine infusions in

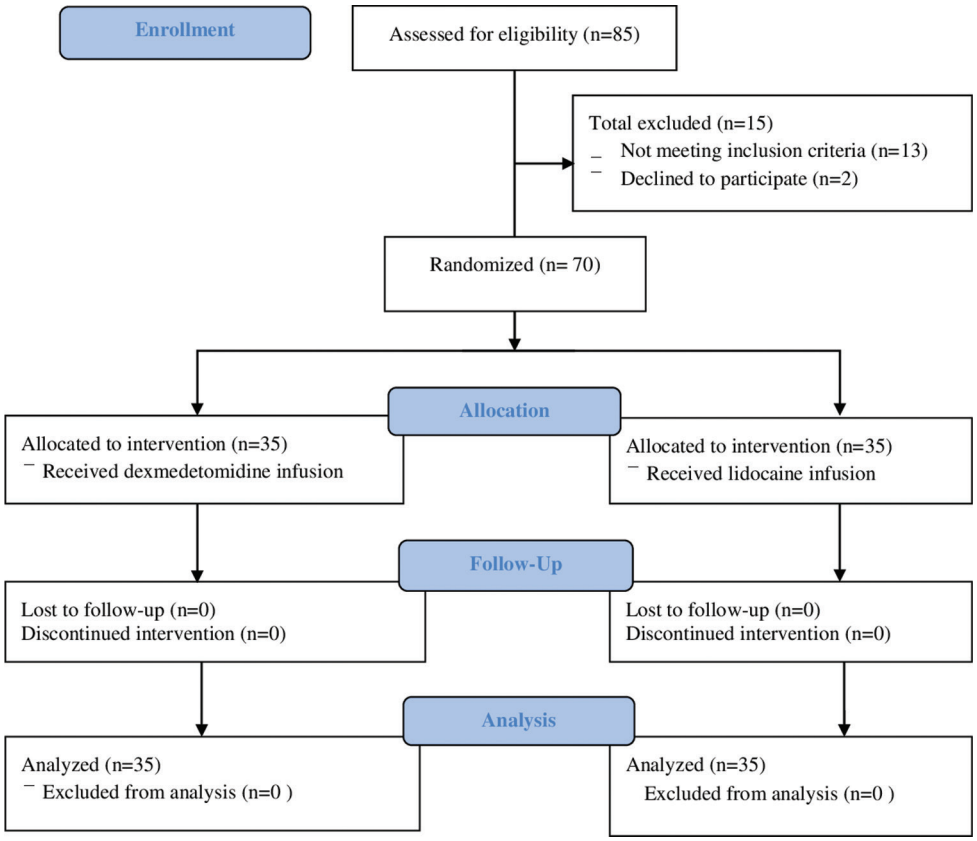


**Figure 1:** Consort flow diagram showing patient recruitment and follow-up

**Table 1: Demographic parameters**

| Parameters | Dexmedetomidine (n=35) | Lidocaine (n=35) | P-value |
|---|---|---|---|
| Age (years) | 47.5±9.8 | 47±6.7 | 0.81 |
| Weight (kg) | 64.7±2.5 | 65.2±3.8 | 0.535 |
| Gender (M/F) * | 19/16 | 20/15 | 0.81 |
| ASA-PS (I/II) * | 18/17 | 15/20 | 0.473 |
| Duration of surgery (min) | 155.7±18.7 | 148.8±14.8 | 0.094 |

Data presented as mean±deviation and analyzed with student's unpaired t-test. The categorical data marked with * are analyzed using the Chi-square test. The *P*<0.05 is considered statistically significant. ASA-PS: American Society of Anesthesiologists-physical status

**Table 2: Intraoperative propofol and fentanyl requirement**

| Parameters | Dexmedetomidine (n=35) | Lidocaine (n=35) | P-value |
|---|---|---|---|
| Total fentanyl required | 245.1±25.9 | 300.7±22.1 | <0.001 |
| Total propofol required (mg) | 172.7±7.6 | 236.7±17.5 | <0.001 |
| Recovery from hypnosis (min) | 6.8±1.4 | 7.6±1.3 | 0.009 |
| Time to extubation (min) | 18.3±4.4 | 23.2±3.8 | <0.001 |

Data presented as mean±deviation and analyzed with student's unpaired t-test

the intraoperative period. There was no bradycardia and hypotension as per our set definition (data not presented). Seven patients in the dexmedetomidine group and five patients in the lidocaine group developed low MAP (65–70 mm Hg). Eleven patients in the dexmedetomidine group and 10 patients in the lidocaine group sustained low HR (53–60 bpm) but did not require any treatment as per set protocol.

## DISCUSSION

The present study finds that patients receiving intraoperative dexmedetomidine infusion consumed about 55 mcg less fentanyl consumption in the intraoperative period in comparison with lidocaine infusion. The observation of the present study is in line with that observed by Mohammed et al.,[11] who found considerably lower consumption

**Table 3: Trend of mean arterial pressure between the groups**

| Parameters | Dexmedetomidine (n=35) | Lidocaine (n=35) | P-value |
|---|---|---|---|
| MAP baseline | 73.8±3.3 | 75.3±4.5 | 0.118 |
| MAP post-intubation | 84.3±3.9 | 87.1±4.2 | 0.006 |
| MAP before pinning | 82.4±4.4 | 85.9±5.0 | 0.003 |
| MAP after pinning | 83.9±3.1 | 87.7±3.9 | <0.001 |
| MAP pre-incision | 75.9±2.9 | 82.1±5.4 | <0.001 |
| MAP post-incision | 83.5±2.4 | 84.9±4.1 | 0.079 |
| MAP before incising dura | 80.6±3.4 | 85.8±3.8 | <0.001 |
| MAP after incising dura | 81.5±4.2 | 88.2±5.6 | <0.001 |
| MAP 30 min | 78.8±5.5 | 83.9±7.1 | 0.001 |
| MAP 60 min | 78.9±5.4 | 84.2±7.2 | <0.001 |
| MAP 90 min | 78.9±4.8 | 85.8±5.5 | <0.001 |
| MAP 120 min | 80.2±3.1 | 85.6±5.2 | <0.001 |
| MAP 150 min | 81.1±3.0 | 86.0±4.5 | <0.001 |
| MAP post-extubation | 83.9±3.2 | 87.6±2.7 | <0.001 |

Data presented as mean±deviation and analyzed with student's unpaired t-test, MAP: Mean arterial pressure

**Table 4: Trend of heart rate between the groups**

| Parameters | Dexmedetomidine (n=35) | Lidocaine (n=35) | P-value |
|---|---|---|---|
| HR baseline | 91.5±7.4 | 90.1±7.3 | 0.411 |
| HR post-intubation | 81.6±3.6 | 82.2±5.7 | 0.599 |
| HR before pinning | 69.9±8.7 | 73.5±8.2 | 0.081 |
| HR after pinning | 76.8±4.0 | 80.0±5.1 | 0.005 |
| HR pre-incision | 70.0±8.2 | 74.4±6.4 | 0.015 |
| HR post-incision | 79.0±3.4 | 81.4±5.0 | 0.022 |
| HR before incising dura | 69.6±8.1 | 73.1±7.5 | 0.059 |
| HR after incising dura | 77.8±3.8 | 80.8±4.5 | 0.004 |
| HR at 30 min | 69.7±7.8 | 71.8±8.1 | 0.275 |
| HR at 60 min | 69.6±7.8 | 73.3±5.6 | 0.027 |
| HR at 90 min | 66.9±7.6 | 64.3±7.7 | 0.155 |
| HR at 120 min | 67.0±8.5 | 70.1±5.1 | 0.067 |
| HR at 150 min | 69.8±7.3 | 73.5±4.8 | 0.016 |
| HR post-extubation | 78.3±3.4 | 78.9±6.7 | 0.622 |

Data presented as mean±deviation and analyzed with student's unpaired t-test, HR: Heart rate

(286 vs. 876 mcg) of a total dose of intraoperative analgesics (fentanyl) in patients receiving dexmedetomidine compared with lidocaine. Another study by Menshawi and Fahim[10] also reports lower consumption of intraoperative analgesics with the use of intraoperative infusion of dexmedetomidine over lidocaine (about 93 mcg vs. 105 mcg, respectively). Contrast reporting does exist in two recent studies[16,17] that observed that the mean intraoperative fentanyl consumption was comparable with the use of intraoperative dexmedetomidine and lidocaine.

The amount of intraoperative fentanyl consumption varied widely in different studies. For example, the reported amount of intraoperative fentanyl requirement was found to be 20.5 mcg[16], 104.7 mcg[10], 229.5 mcg,[17] and 876 mcg[11] in groups using lidocaine while it was 26.5 mcg, 92.9 mcg, 229.7 mcg, and 286 mcg, respectively, in groups using dexmedetomidine in those studies. Several factors contributed to heterogeneity among different studies. For example, the duration of surgery varied in different studies from <1 h[8], 2–2.5 h[10,11,18,19], and >3 h[17,20]. Variations in the intraoperative analgesics, volatile anesthetics, and the presence or absence of initial bolus dose of dexmedetomidine and lidocaine – all have contributed to the heterogeneity among different studies[8,16]. This heterogeneity can explain the variation in the absolute values of intraoperative analgesic consumption.

IV lidocaine infusion was found to be as effective as dexmedetomidine in reducing the requirement of rescue tramadol.[21] In another study, Cho et al.,[8] observed a comparable analgesic-sparing effect between dexmedetomidine and lidocaine infusions. Both infusions led to a reduction of fentanyl requirements in the early post-operative period after laparoscopic cholecystectomy. Opioid-sparing effect of dexmedetomidine has already been reported.[5,22] In children undergoing intracranial surgeries, IV infusion of dexmedetomidine in the intraoperative period was found to be superior to lidocaine for their opioid-sparing analgesia.[20]

The present study also found a lower consumption of anesthetic agent propofol with the use of dexmedetomidine compared with lidocaine. Menshawi and Fahim[10] also

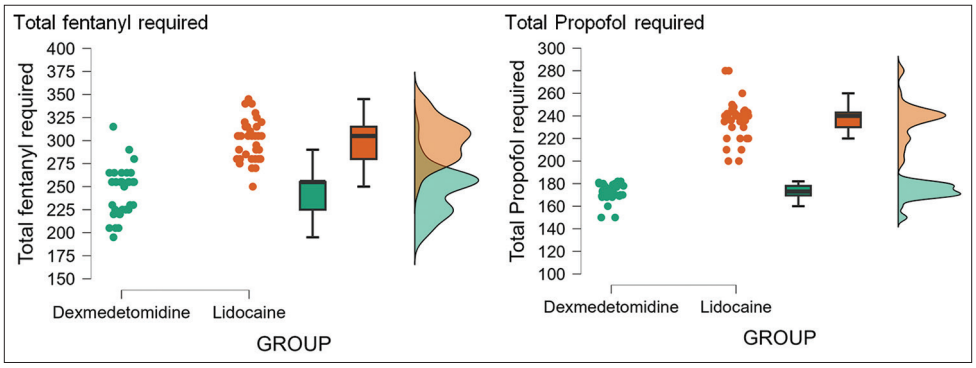


**Figure 2:** Rain cloud plots of intraoperative fentanyl and propofol requirement. The rain-cloud plot is a combined illustration of data distribution (the 'cloud'), along with jittered raw data (the 'rain'). The reader can easily have a clear visible impact about the data distribution and there is nothing to be 'hidden away'. It offers much utility and flexibility and appears better than a boxplot plus raw data in revealing bimodal or other crucial facets of the data.[15]

observed a similar trend of lower propofol consumption with the use of dexmedetomidine over lidocaine (1.53 mg/kg vs. 1.82 mg/kg, respectively). Additional treatment with dexmedetomidine or lidocaine has led to a reduction in intraoperative propofol consumption with the use of either of the drugs in comparison with the control group.[7]

The MAP and HR were found to be considerably decreased with the use of dexmedetomidine compared with lidocaine.[11] In a recent study, Ibrahim et al.[17] also found a considerable reduction in MAP with the use of dexmedetomidine in comparison with lidocaine. They observed considerable bradycardia with the use of dexmedetomidine over lidocaine. However, another study[23] reported that dexmedetomidine did not produce significant bradycardia probably due to avoidance of the loading dose. IV infusion of 0.6 μg/kg dexmedetomidine initiated before induction can maintain hemodynamic stability in the intraoperative period and can decrease cough during emergence from anesthesia in patients undergoing laparoscopic cholecystectomy.[22]

The present study observes that the use of dexmedetomidine led to considerably earlier recovery from hypnosis and a shorter time to extubation. In the absence of objective monitoring, the level of analgesia and anesthesia was titrated to maintain a close range at the cost of variable recovery time. Although the time to extubation was statistically significant, no inference can be drawn regarding its clinical significance. Further study with attention to the above issues can generate evidence in this aspect. The present study is in contrast with the study of Menshawi and Fahim[10] which reports about comparable recovery time from anesthesia between the use of dexmedetomidine and lidocaine.

Lidocaine infusion can be effective for acute post-operative pain control in major surgery owing to its opioid-sparing effect and acceptable safety profile. It is considered a simple intervention that carries minimal risk when administered correctly and can be useful, especially when the regional local anesthetic techniques are not feasible.[24] It can be beneficial for patients in terms of reducing the length of hospital stay and minimizing the incidence of chronic pain related to surgical procedures.[25] Weibel et al.,[26] expressed uncertainty about the effect of perioperative lidocaine infusion on opioid consumption and early post-operative pain scores compared with placebo. They found the quality of evidence to be limited owing to inconsistency of study quality. They opined that lidocaine probably has no clinically relevant effect on pain scores beyond 24 h.

In patients undergoing pelvi-abdominal cancer surgeries, intraoperative infusion of dexmedetomidine or lidocaine, both have led to attenuation of proinflammatory cytokines and stress response in the post-operative period.[27] The analgesic, antihyperalgesic, and anti-inflammatory effects of IV lidocaine can occur due to sodium channel blockade and inhibition of N-methyl-D-aspartate receptors.[28] Dexmedetomidine has anti-nociceptive and sedative properties owing to specific α 2-adrenergic receptor agonistic activity. IV dexmedetomidine has a role as post-operative analgesia, which yields reduced consumption of opioids.[29] In a dose-response study, Durrani et al.,[30] reported that the mechanism of analgesia with IV lidocaine may not follow a concentration-effect connection. The authors hypothesized that the analgesic response to IV lidocaine can be a quick "break in pain" over a narrow dosage and concentration range, independent of lidocaine dose.[31]

## Limitations of the study

It was not possible to measure the concentration of lidocaine and dexmedetomidine. The use of modern equipment (such as a processed EEG monitor) to assess analgesia and hypnosis in an objective manner[31] was not possible owing to logistic issues. In the present study, only clinical parameters were used to assess analgesic and anesthetic requirements in the intraoperative period.

Clinical monitoring was used to assess the effects of neuromuscular blockade and reversal. The sample size was a small and single-center study. Further, study addressing these issues can yield precise results and can be a future scope.

## CONCLUSION

Intraoperative infusion of dexmedetomidine can be a better alternative to lidocaine infusion as an analgesic adjunct in view of lower consumption of fentanyl and propofol during craniotomy surgery. Maintaining comparatively lower MAP and HR throughout the intraoperative period without clinically significant adverse events appears to be an additional advantage.

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