Original Article

Evaluation of effects of intravenous infusion of dexmedetomidine or lignocaine on stress response and postoperative pain in patients undergoing craniotomy for intracranial tumors: A randomized controlled exploratory study

ABSTRACT

Background: Goals of anesthesia in neurosurgery include stable cerebral hemodynamics and provide relaxed brain to surgeon. Dexmedetomidine and lignocaine as an adjuvant can fulfill these criteria but literature comparing the two are sparse. We compared the effects of intravenous infusion of dexmedetomidine or lignocaine on stress response, postoperative pain, and recovery in patients undergoing craniotomy for intracranial tumors.

Methods: Approval was obtained from IEC, and the study was prospectively registered (CTRI/2022/11/047434). Written and informed consent was obtained from 105 patients fulfilling inclusion criteria, and they were divided into three groups. Group D received intravenous infusion of dexmedetomidine 1 mcg/kg over 15 minutes followed by infusion at rate of 0.5 mcg/kg/h, Group L received intravenous infusion of lignocaine 2 mg/kg over 15 minutes followed by infusion at rate of 1.5 mg/kg/h, and Group N received intravenous infusion of normal saline at the rate of 4–8 ml/h till skin suturing. SPSS v23 (IBM Corp.) was used for data analysis.

Results: There was a significant difference between groups in terms of intraoperative hemodynamic variations, brain relaxation score, extubation criteria, postoperative pain, stress indicator response, and quality of recovery.

Conclusions: Dexmedetomidine as an adjuvant to anesthetic drugs has a better profile than lignocaine in suppressing stress response and preventing hemodynamic variations at intubation, skull pin application, and surgical incision. Dexmedetomidine increases the duration of effective analgesia more than lignocaine, in postoperative period in patients undergoing craniotomy.

Key words: Cortisol, craniotomy, dexmedetomidine, lignocaine, prolactin, stress

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Introduction

A multitude of inflammatory and neuro-endocrine changes occur in body in response to noxious stimuli of surgery. The sympathetic stimulation at the time of laryngoscopy, skull pin insertion, skin incision, tissue dissection, and extubation causes significant change in hemodynamics which may be detrimental to the outcome of craniotomies.[1-3] During craniotomies, a controlled hemodynamics preserve the cerebral homeostasis. Opioids are mainstay drugs, extensively used for the prevention of sympathetic responses but it has undesirable effects of postoperative nausea and vomiting, prolonged sedation, ileus and urinary retention, and respiratory depression.[4,5] Furthermore, in neurosurgeries, rapid recovery from anesthesia to test neurocognitive function and response to surgery is warranted.[6] Opioids are used in higher cumulative doses during neurosurgeries due to the long duration of surgeries, hampering early neurological assessment.

Dexmedetomidine, an α-2 adrenergic agonist, has sedative, analgesic, and sympatholytic properties through its action on locus coeruleus, superficial dorsal horn, and postsynaptic α-2 receptors, respectively. Dexmedetomidine helps in reducing stress response to stimulate events, thus reducing the cerebral catecholamines and providing neuroprotective effect. It produces conscious sedation and helps in early neurological evaluation after surgery.[4,7] Lignocaine, an amide local anesthetic and a class 1b antiarrhythmic agent, exerts its analgesic effects by blocking sodium and potassium channels and presynaptic muscarinic and dopamine receptors, thus reducing the dose and side effects of opioids, which ultimately helps in reducing the length of hospital stay. Lignocaine also has anti-inflammatory effect attributed to direct effect on macrophage and polymorphonuclear granulocyte function and inhibition of release of markers of inflammatory cascade.[8-11] Dexmedetomidine and lignocaine can reduce the requirement of opioids while providing perioperative hemodynamic stability and beneficial effects on postoperative cognition.[12,13] Recently, studies are exploring the usefulness of dexmedetomidine and lignocaine infusion in neurosurgery, but a literature search has not shown enough studies to make a recommendation. There are no studies which head-to-head compares intraoperative and postoperative outcome of "IV" (intravenous) infusion of dexmedetomidine and lignocaine.

In the current study, we hypothesized that the effects of intravenous lignocaine infusion on stress response and postoperative pain in patients undergoing craniotomy will be equal to that of dexmedetomidine. With this background, this study was planned to compare the effects of intravenous dexmedetomidine and lignocaine on intraoperative and postoperative outcomes.

Methods

This prospective randomized controlled exploratory study was conducted in the Department of Anesthesiology between February 2022 and September 2023. Institutional Ethic Clearance was obtained. The study adhered to the Declaration of Helsinki's ethical guidelines (2013) for human experimentation. Written informed consent was taken from all patients, and study was registered at the Central Trials Registry India (CTRI/2022/11/047434).

Primary objectives were the evaluation of effects on (i) intraoperative hemodynamic variations, (ii) response to noxious stimulus of surgery, and (iii) postoperative pain as evaluated by "CPOT" (critical care pain observation tool).[14] Secondary objectives were to assess brain relaxation score, incidence of "POCD" (postoperative cognitive dysfunction), quality of recovery, and effects on extubation criteria. One hundred and five patients of "ASA" (American society of anesthesiologist) grade I–II, aged 18–60 years having "GCS" (Glasgow coma scale) score 13–15, scheduled for elective craniotomy for intracranial tumor excision were included. Exclusion criteria were, uncontrolled hypertension/diabetes/heart disease, 2nd- and 3rd-degree heart block, active beta-blocker users, psychiatric disorders, or history of substance abuse.

Patient meeting inclusion criteria were randomly allocated into three groups by computer-generated table of non-repetitive random numbers and blinding was done by sealed envelope technique by an anesthesiologist not involved in the study. Group D patients received bolus IV infusion of dexmedetomidine 1 mcg/kg over 15 minutes followed by 0.5 mcg/kg/h till skin suturing. Group L patients received bolus IV infusion of lignocaine 2 mg/kg over 15 minutes followed by 1.5 mg/kg/h till skin suturing. Group N patients received bolus IV infusion of 20 ml normal saline over 15 minutes followed by 4–8 ml/h till skin suturing. Total amount of drug for bolus infusion was diluted with normal saline upto 20 ml in all three groups to ensure proper blinding. For continuous IV infusion, study drugs were diluted in such concentration that the rate of infusion was between 4 and 8 ml/hr. Study drug preparation and infusion were done by an anesthesiologist not involved in the study. Data collection was done by primary investigator. The participants, anesthesiologist in charge of the case, and primary investigator were all blinded to intervention (triple blinded).

Patients were kept nil-per-oral for solids for six hours. No sedative premedication was prescribed. After shifting patients to the operating room, electrocardiography, non-invasive blood pressure, and pulse oximeter were attached and BIS. Bolus IV infusion of the study drug was given over 15 minutes followed by pre-oxygenation and anesthesia induction with IV fentanyl 2 mcg/kg; propofol (1–2.5 mg/kg); and vecuronium (0.1 mg/kg). Airway was secured by cuffed endotracheal tube. Anesthesia was maintained with sevoflurane, air-oxygen mixture (60:40), and intermittent bolus of IV vecuronium and fentanyl. Controlled ventilation was initiated to maintain end-tidal CO_2 of 32–35. According to institutional protocol, IV mannitol (0.5 gm/kg) was used in all supratentorial tumors. Invasive blood pressure monitoring was achieved with radial artery cannulation while triple lumen 7 FG central line was inserted in subclavian/Internal jugular vein. No scalp block or local anesthetic infiltration at pin site was administered.

"HR" (heart rate), "SBP" (systolic blood pressure), "MAP" (mean arterial pressure), and BIS were recorded at the following time points: baseline; after study drug bolus infusion; before intubation, at intubation; 2, 5, and 15 min after intubation; before skull pin application, at skull pinning with Mayfield clamp; 5, 10, and 15 min after skull pinning and then every 15 minutes till end of surgery. During surgery, a note of the above parameters was also made just before incision and at incision. HR, SBP, and MAP were also noted at extubation and 2, 5, and 10 min after extubation. If SBP or HR values exceeded baseline values by >20% at laryngoscopy or skull pin insertion, an additional dose of propofol (3 ml bolus) was administered. If any such change was observed intraoperatively, fentanyl 50 mcg was administered. Persistent hypertension or tachycardia was controlled by esmolol (0.5 mg/kg). Hypotension (MAP below 20% of baseline) and bradycardia (HR below 20% of baseline) were managed by mephentermine 3 mg IV bolus or atropine 0.4 mg IV, respectively.

Stress response to surgery was evaluated by blood sugar, serum cortisol, and serum prolactin (ADVIA Centaur, Siemens Healthcare Pvt. Ltd. NY, USA) at baseline, 12 hours and 24 hours after the end of surgery. "BRS" (brain relaxation score) was assessed by surgeon on a 4-point Likert scale (1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm brain, 4 = bulging brain). At skin suturing, all patients were given IV paracetamol 15 mg/kg and ondansetron 0.1 mg/kg. Maintenance drugs were stopped after skin suturing. Decision regarding extubation or continued elective ventilation was taken after consulting the surgical team. According to standard anesthesia protocol, trachea was extubated. Time of response to verbal commands, eye opening, and extubation after stopping study drug infusion was noted. Extubated patients were transferred to post-anesthesia care unit, and patients requiring elective ventilation were shifted to ICU.

Quality of recovery was assessed in extubated patients by "RASS" (Richmond Agitation–Sedation Scale) score at extubation, 1 hour, 6 hours, 12 hours, and 24 hours. CPOT score was used for postoperative pain evaluation at 1 hour, 6 hours, 12 hours, and 24 hours. Postoperatively if CPOT score was >2, time from end of surgery was noted, and inj. paracetamol 1 gm IV was administered. Preoperative cognition was assessed using "HMSE" (Hindi mini mental state examination) score and was compared to values at 24-hour postoperatively.[15]

As there is no study comparing infusion dexmedetomidine and infusion lignocaine in neurosurgery for change of serum cortisol level 12 hours after surgery, this study was planned as exploratory study and a total sample size of 105 subjects (35 in each group) was taken fulfilling the criteria of central limit theorem. Data were coded and recorded in MS Excel spreadsheet program. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive statistics were elaborated as means/standard deviations, medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Group comparisons for continuously distributed data were made using an independent sample *t*-test. For non-normally distributed data, Wilcoxon test was used. Chi-squared test was used for group comparisons of categorical data. In case, the expected frequency in the contingency tables was found to be <5 for >25% of the cells, Fisher's exact test was used instead. Non-parametric tests were used to make statistical inferences as data were not normally distributed. Kruskal–Wallis test and Friedman test were used to compare the three groups wherever applicable. Statistical significance was kept at $P < 0.05$.

Results

One hundred and five patients were assessed and included in the study and randomly allocated into three groups (Groups D, L, and N) with thirty-five (n = 35) patients in each group. Three patients in group D and one patient in group L had massive blood loss causing hemodynamic instability requiring inotropes. Hence, these four patients were excluded from the statistical analysis [Figure 1: Consort diagram of the study].

Patients in three groups were similar in demographic profiles, ASA grade, tumor location, duration of anesthesia and surgery, extubation status, and total blood loss [Table 1].

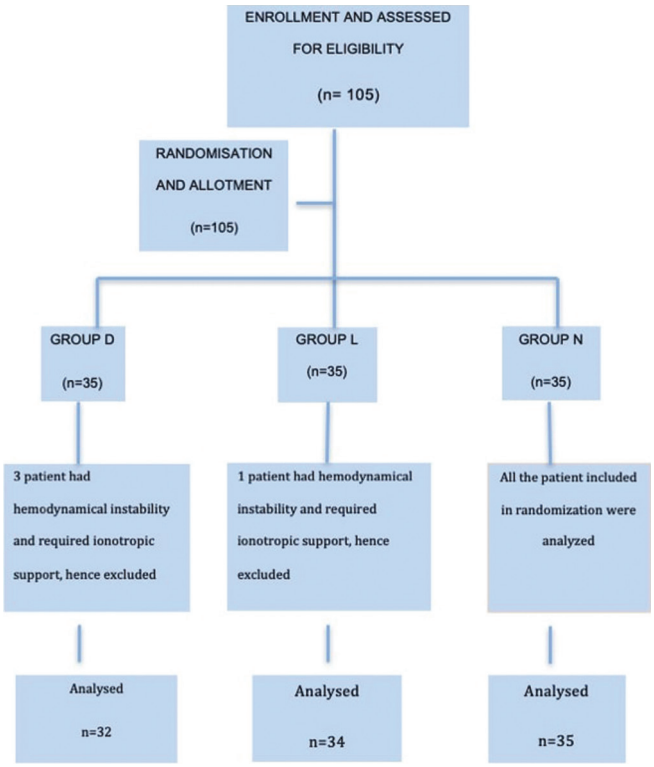

Figure 1: CONSORT flow diagram of the study

Patients in group N showed maximum change (delta increase) in HR, SBP, and MAP at intubation, skull pinning, incision, and extubation [Table 2]. Total fentanyl requirement was significantly less in group D in comparison with other groups while patients in group L required significantly less fentanyl in comparison with group N [Table 3]. Although the time to eye opening, verbal response, and extubation was significantly less statistically in group N, the difference clinically was very less [Table 3]. Postoperatively, time to first complaint of pain (as perceived by CPOT >2) was significantly more in group D in comparison with other groups while it was significantly more in group L in comparison with group N. Postoperatively, HMSE score in all the extubated patients was more than 23, indicating the absence of POCD in any patients [Table 3]. Although BRS as assessed by the surgeon was comparable in three groups at dural opening, it was significantly better in groups D and L at the time of dural closure [Table 3]. Change in serum cortisol from baseline to 12-hr and 24-hr postoperative period was not significant in any group. There was significant decrease in serum prolactin value at 12-hr and 24-hr postoperative period in groups D and N. While the increase in blood sugar level from baseline to 12-hr and 24-hr postoperative period was not significant in group D, it was significant in group N at both time points. Blood sugar level significantly increased at 12 hours in groups L and N while the increase was not significant in group D. At 24 hours, the change in blood sugar was significant only in group N [Table 4].

Although the majority of the patients in all three groups had a RASS score of zero (alert and calm) at extubation and at 1 hour postoperatively, recovery profile was significantly better in group D in comparison with other groups. All the extubated patients in all three groups were alert and calm (RASS 0) at 6, 12, and 24 hours postoperatively [Table 5]. In dexmedetomidine group, four (12.5%) patients reported hypotension and bradycardia while one patient reported nausea. In lignocaine group, two (5.9%) patients reported bradycardia, seven (20.6%) reported nausea and one patient had vomiting. In control group, nine (25.7%) patients reported nausea while two of them vomited. The difference in incidence of hypotension and nausea was statistically significant.

Discussion

In our study, dexmedetomidine showed significantly more stable hemodynamics at stimulating events in comparison with other two groups while lignocaine showed significantly better control of hemodynamics in comparison with control. Results of our study were in line with many other studies where authors used dexmedetomidine in craniotomies.[1,4,6,16,17] Mahajan *et al*.[10] compared lignocaine with normal saline in craniotomies and observed that heart rate and MAP remained stable at skull pinning and extubation in lignocaine group but the difference was not significant which could have been due to an ongoing baseline remifentanil infusion in all patients. Stating a similar result to the above study, Peng *et al*.[8] did not find significant difference between normal saline and lignocaine for MAP and HR in craniotomies. Our results were in concordance with the results of study by Chandra *et al*.[18] where authors used lignocaine in craniotomy and found that in comparison with placebo, values of HR and MAP were lower in lignocaine group at intubation, headpin fixation, skin incision, and extubation.

In our study, although change in serum cortisol level at postoperative time points was not significant in any group, the serum level decreased at both postoperative time points in dexmedetomidine and control group, while it increased in lignocaine group at both the time points. There was significant decrease in serum prolactin level at both postoperative time points in dexmedetomidine and control group, while in lignocaine group the serum level non-significantly increased at 12 hr and decreased at 24 hr postoperatively. At 12 hours, blood sugar significantly increased in lignocaine and control group while the increase was not significant in dexmedetomidine group. Increase in blood sugar at 24 hours was significant only in control group. Pharmacodynamic properties of dexmedetomidine could

Table 1: Demographic profile and clinical characteristics of patients

Parameters	Group			*P*
	D (*n*=32)	L (*n*=34)	N (*n*=35)	
Age (Years) (mean±SD)	40.75±11.29	39.29±12.42	43.49±15.66	0.417[1]
Gender				0.919[2]
Male	16 (50.0%)	17 (50.0%)	19 (54.3%)	
Female	16 (50.0%)	17 (50.0%)	16 (45.7%)	
Weight (Kg) (mean±SD)	57.06±7.24	56.88±8.20	60.94±9.07	0.096[3]
ASA Grade				0.879[2]
I	26 (81.2%)	26 (76.5%)	27 (77.1%)	
II	6 (18.8%)	8 (23.5%)	8 (22.9%)	
Location of tumor				0.879[2]
Supratentorial	23 (71.9%)	25 (73.5%)	27 (77.1%)	
Infratentorial	9 (28.1%)	9 (26.5%)	8 (22.9%)	
Duration of Anesthesia (min) (mean±SD)	404.22±51.29	376.62±56.85	392.29±61.83	0.147[1]
Duration of surgery (min) (mean±SD)	300.47±46.81	279.41±54.55	289.29±53.54	0.357[3]
Extubation Status				0.311[2]
Extubated	28 (87.5%)	29 (85.3%)	26 (74.3%)	
Not Extubated	4 (12.5%)	5 (14.7%)	9 (25.7%)	
Total Blood loss (ml) (mean±SD)	864.06±467.36	700.59±385.35	902.86±649.20	0.277[3]

1=One-way ANOVA, 2=Chi-squared test, 3=Kruskal–Wallis test, Significant at $P<0.05$

Table 2: Hemodynamic changes in various groups

Parameter		Group			Kruskal–Wallis Test		Adjusted *P* value for pairwise comparison		
		D	L	N	χ^2	*P*	D-L	D-N	L-N
Delta HR	Intubation	11.03 (6.95)	11.32 (5.46)	15.63 (5.48)	12.152	0.002	0.954	0.004	0.017
	Skull pinning	13.41 (9.55)	22.26 (8.68)	29.83 (9.07)	39.280	<0.001	0.002	<0.001	0.011
	Incision	7.03 (7.86)	17.18 (9.00)	21.69 (8.54)	36.424	<0.001	<0.001	<0.001	0.229
	Extubation	12.56 (7.96)	9.62 (8.09)	15.94 (12.59)	5.356	0.069	0.421	0.768	0.063
Delta SBP	Intubation	13.69 (6.64)	13.71 (5.01)	21.23 (7.93)	26.783	<0.001	0.989	<0.001	<0.001
	Skull pinning	21.25 (13.88)	38.12 (13.95)	44.00 (9.80)	31.624	<0.001	<0.001	<0.001	0.435
	Incision	10.50 (12.02)	29.18 (14.42)	35.66 (9.76)	40.063	<0.001	<0.001	<0.001	0.234
	Extubation	12.97 (10.61)	11.76 (10.84)	26.71 (20.74)	11.306	0.004	0.990	0.019	0.007
Delta MAP	Intubation	9.09 (6.80)	10.59 (6.82)	14.71 (6.10)	6.651	0.002	0.627	0.002	0.028
	Skull pinning	15.34 (11.91)	26.79 (11.84)	30.06 (8.81)	24.637	<0.001	0.001	<0.001	0.461
	Incision	7.47 (8.50)	20.94 (9.71)	26.11 (9.17)	42.076	<0.001	<0.001	<0.001	0.145
	Extubation	10.16 (10.58)	7.88 (7.22)	17.49 (13.72)	8.310	0.016	0.924	0.097	0.019

Delta (change) indicates increase in values; Results in mean (SD); Significant at $P<0.05$

have played a role in inhibiting the rise of stress hormones. The similar result seen in control group can be due to the use of higher dose of fentanyl in them. Sustained rise in blood glucose even in postoperative period can be explained by the fact that in major surgeries the increase in blood glucose can remain elevated for more than 24 hours due to relative lack of insulin along with peripheral insulin resistance.[3] Uyar *et al*.[2] found that after skull pin insertion dexmedetomidine group showed increased values of plasma cortisol, prolactin, and glucose but the rise was not significant. In contrast to this, our study did not show increased values of hormones as upon noxious stimuli cortisol values start to increase and peak at around 4 hours while we analyzed hormones at 12 hours and 24 hours.[19] Wang *et al*.[20] in their meta-analysis found that cortisol level was significantly lower in dexmedetomidine group in comparison with placebo at 24 hours and 48 hours postoperatively. Wang *et al*.[21] in their meta-analysis concluded that perioperative use of dexmedetomidine significantly decreases cortisol levels in comparison with saline-based control but not significantly in comparison with active comparators.

In concordance with other studies, we found that dexmedetomidine and lignocaine significantly reduced the opioid requirement.[1,5,10,16,18,22] Kundra *et al*.[7] did not find significant difference in opioid requirement in dexmedetomidine group, the reason could be the use of lower dose of dexmedetomidine that too without loading dose. A relaxed brain in neurosurgery is an essential requirement as it improves surgical condition, helps surgeons reach the area of interest, and very importantly reduces the risk of ischemia in areas of brain under the retractor.[23] We found

Table 3: Comparison of change in BIS at stimulating time points, total fentanyl and propofol used, extubation criteria, time at first complaint of pain (CPOT >2), HMSE score for postoperative cognition and brain relaxation score

Parameter		Group			Kruskal–Wallis/*Chi-Squared Test		Adjusted *P* value for pairwise comparison		
		D	L	N	χ^2	*P*	D-L	D-N	L-N
Total fentanyl (mcg)		180.31 (41.54)	242.35 (48.62)	289.29 (49.43)	48.824	<0.001	<0.001	<0.001	0.011
Total propofol (mg)		99.38 (24.49)	109.71 (23.93)	122 (25.87)	11.774	0.003	0.275	0.002	0.198
Extubation criteria	Time to verbal response (min)	15.96 (2.65)	15.62 (2.72)	12.77 (2.05)	21.588	<0.001	0.952	<0.001	<0.001
	Time to eye opening (min)	16.54 (2.87)	16.21 (2.72)	13.35 (1.85)	21.398	<0.001	0.982	<0.001	<0.001
	Time to extubation (min)	17.57 (2.83)	17.34 (2.81)	14.42 (1.92)	20.636	<0.001	0.988	<0.001	<0.001
Time (hrs) At CPOT >2		3.94 (1.48)	2.38 (0.95)	1.56 (0.63)	48.104	<0.001	<0.001	<0.001	0.005
HMSE	Preop	29.69 (0.82)	30.00 (0.70)	29.57 (1.01)	4.640	0.098	0.316	0.955	0.113
	24-hour Postop	28.75 (0.95)	28.97 (1.11)	28.34 (1.26)	4.850	0.088	0.625	0.628	0.081
*BRS at dural opening	Score 1	7 (21.9%)	8 (23.5%)	4 (11.4%)	1.941	0.379	1.000	0.493	0.493
	Score 2	25 (78.1%)	26 (76.5%)	31 (88.6%)					
*BRS at dural closure	Score 1	25 (78.1%)	24 (70.6%)	8 (22.9%)	24.944	<0.001	0.578	<0.001	<0.001
	Score 2	7 (21.9%)	10 (29.4%)	27 (77.1%)					

Results in mean (SD); BIS—bispectral index; mcg—microgram; min—minutes; hrs—hours; CPOT—critical care pain observation tool; HMSE—Hindi mini mental state examination; significant at $P<0.05$, BRS—Brain relaxation score

Table 4: Stress indicator response in various groups

Marker	Group	Baseline	12-hour postoperative	24-hour postoperative	*P* (intragroup)	
					Baseline-12 hours*	Baseline-24 hours*
Serum cortisol	D (*n*=32)	7.45 (0.78-14.31)	3.7 (1.28-14.41)	5.5 (2.01-10.4)	0.911	0.340
	L (*n*=34)	1.38 (0.6-13.19)	4.23 (1.63-9.91)	3 (1.07-11.45)	0.437	0.993
	N (*n*=35)	4.16 (0.88-9.93)	3.26 (1.34-15.69)	3.88 (1.46-13.71)	0.293	0.608
	P# (Intergroup)	0.515	0.985	0.662		
Serum prolactin	D (*n*=32)	9.37 (6.11-19.88)	6.97 (4.96-9.89)	6.65 (3.88-10.98)	0.025	0.005
	L (*n*=34)	8.66 (5.27-19.67)	8.92 (4.1-12.6)	6.08 (4.38-13.27)	0.144	0.065
	N (*n*=35)	13.51 (5.91-26.29)	7.99 (5.25-13.44)	8.21 (5.02-12.42)	0.001	0.002
	P# (Intergroup)	0.506	0.585	0.578		
Blood sugar	D (*n*=32)	105.5 (98-121.5)	113 (104-122)	110.5 (101-119)	0.064	0.354
	L (*n*=34)	106 (96-115)	118 (104-128)	106 (98.5-130)	0.001	0.371
	N (*n*=35)	103 (95-108)	108 (98-133)	104 (98-118)	0.001	0.037
	P# (Intergroup)	0.106	0.588	0.663		

Result in median (IQR), IQR—interquartile range, significant at $P<0.05$. # - one-way ANOVA test used for intergroup comparison. * - paired *t*-test used for comparison of change in parameter from baseline to 12 and 24 hours

that brain was significantly more relaxed in dexmedetomidine and lignocaine group in comparison with control while the difference between them was not significant. Results of our studies are in concordance with many other studies.[4,18,24-26]

In our study, time to eye opening, time to response to verbal opening, and time to extubation, all were statistically significantly less in control group, although clinically the difference appeared non-significant. The longer time to extubation in comparison with ours could be due to the use of higher dose of fentanyl.[1,6] Ilhan *et al*.[4] in their study stopped dexmedetomidine infusion earlier than that of our study which could have resulted in lesser time to extubation. Results of our study matched the results of Peng *et al*.[8] and Mahajan *et al*.[10] where time to extubation was longer in lignocaine group in comparison with control. Extubation of trachea can be associated with airway response leading to agitation, coughing, bronchospasm, increased bleeding from the surgical site, and raised intracranial pressure.[27] We found that none of the patients in dexmedetomidine group was agitated or anxious postoperatively, and a maximum number of patients in dexmedetomidine group were calm and cooperative at extubation. Prathapadas *et al*.[6] found that there was no statistically significant difference in RASS score at extubation and in postoperative period between dexmedetomidine and control group. Song *et al*.[22] found that in comparison with control, significantly more number of patients were cooperative and oriented in postoperative period in dexmedetomidine group. Our results are similar to Kothari *et al*.[28] where authors found significantly less agitation and restlessness at extubation in dexmedetomidine group in comparison with lignocaine. The trauma of surgery, by stimulating immune cascade and release of inflammatory mediators, may provoke POCD.[29]

Table 5: Comparison of quality of recovery at extubation and one hour into postoperative period in patients who were extubated in the operating theatre at the end of surgery

RASS	Group			Fisher's Exact Test		Adjusted *P* value for pairwise comparison		
	D (*n*=28)	L (*n*=29)	N (*n*=26)	χ^2	*P*	D-L	D-N	L-N
Extubation				21.752	0.002	0.038	<0.001	0.288
Score -2	2 (7.1%)	0 (0.0%)	0 (0.0%)					
Score -1	8 (28.6%)	5 (17.2%)	2 (7.7%)					
Score 0	18 (64.3%)	17 (58.6%)	12 (46.2%)					
Score 1	0 (0.0%)	6 (20.7%)	8 (30.8%)					
Score 2	0 (0.0%)	1 (3.4%)	4 (15.4%)					
1 Hour postoperative								
Score -2	0 (0.0%)	0 (0.0%)	0 (0.0%)	12.8	0.008	0.148	0.010	0.121
Score -1	0 (0.0%)	0 (0.0%)	0 (0.0%)					
Score 0	25 (89.3%)	22 (75.9%)	13 (50.0%)					
Score 1	3 (10.7%)	3 (10.3%)	9 (34.6%)					
Score 2	0 (0.0%)	4 (13.8%)	4 (15.4%)					

RASS: Richmond Agitation–Sedation Scale (4: combative, 3: very agitated, 2: agitated, 1: restless, 0: alert and calm, −1: drowsy, −2: light sedation, −3: moderate sedation, −4: deep sedation, and − 5: unarousable); Significant at $P<0.05$

Studies suggest the beneficial role of dexmedetomidine and lignocaine in postoperative cognition.[13,29] None of the patients in the present study showed signs of postoperative cognitive dysfunction. Bradycardia and hypotension which are well-known side effects of dexmedetomidine responded well to rescue drug and intravenous fluids. Higher reporting of nausea in lignocaine and control group could be due to the use of higher dose of opioid.

There were few noteworthy limitations. Firstly, it was a single-center study. Second, as the study drugs were used as continuous infusion for long duration, using the targeted plasma concentration for study drugs could have avoided some side effects. Lastly, we couldn't measure serum level of inflammatory markers IL-6 and TNF-α.

Conclusion

Dexmedetomidine as an adjuvant to anesthetic drugs has a better profile than lignocaine in preventing stress response and hemodynamic variations at intubation, skull pin application, and surgical incision. Dexmedetomidine increases duration of effective analgesia in postoperative period in patients undergoing craniotomy and thus can attenuate hemodynamic changes associated with pain. The opioid requirement decreases significantly when dexmedetomidine is used as an adjuvant, and thus, it can help in reducing the opioid-related side effects postoperatively. Dexmedetomidine provides better quality of recovery in comparison with lignocaine. Lignocaine has a better side effect profile than dexmedetomidine when latter is used in the dose as used in this study. As the literature for comparison of dexmedetomidine and lignocaine in neurosurgery are scarce, more number of studies with flexible-dose regimens are needed to strike balance between benefit and side effects of drugs.

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Conflicts of interest

There are no conflicts of interest.

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