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Original Article

Comparison of dexmedetomidine versus fentanyl-based total intravenous anesthesia technique on the requirement of propofol, brain relaxation, intracranial pressure, neuronal injury, and hemodynamic parameters in patients with acute traumatic subdural hematoma undergoing emergency craniotomy: A randomized controlled trial

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ABSTRACT

Background: Propofol is one of the most used intravenous anesthetic agents in traumatic brain injury (TBI) patients undergoing emergency neurosurgical procedures. Despite being efficacious, its administration is associated with dose-related adverse effects. The use of adjuvants along with propofol aids in limiting its consumption, thereby mitigating the side effects related to propofol usage. This study aims to compare the safety and efficacy of dexmedetomidine-propofol versus fentanyl-propofol-based total intravenous anesthesia (TIVA) in adult TBI patients.

Methods: A hundred patients posted for emergency evacuation of acute subdural hematoma were enrolled, and they were randomized into two groups of 50 each. Propofol-based TIVA with a Schneider target-controlled infusion model was used for induction and maintenance. Patients in Group F received fentanyl, and those in Group D received dexmedetomidine infusions as adjuvants. Advanced hemodynamic parameters were monitored. Intracranial pressure (ICP) and brain relaxation were measured after dural opening. The mean propofol consumption, number of additional fentanyl boluses, and blood samples for S100b (a biomarker of neuronal injury) were also collected.

Results: The mean propofol consumption in Group D (88.7 ± 31.8 μg/kg/min) was lower when compared to Group F (107.9 ± 34.6 μg/kg/min), ($P = 0.005$). The mean intraoperative fentanyl requirement and postoperative S100b were significantly reduced in Group D. Subdural ICPs and brain relaxation scores were comparable. Hemodynamic parameters were well maintained in both groups.

Conclusion: In TBI, dexmedetomidine as an adjunct to propofol-based TIVA results in a greater reduction in total propofol consumption and intraoperative opioid requirements while maintaining hemodynamic stability when compared to fentanyl.

Keywords: Brain relaxation, Dexmedetomidine, Propofol, fentanyl, Total intravenous anesthesia, Traumatic brain injury

INTRODUCTION

Traumatic brain injury (TBI) is a significant cause of morbidity and mortality worldwide.[7] The pathophysiological changes following TBI are characterized by direct tissue damage, impaired cerebral blood flow (CBF) and autoregulation, tissue edema, oxidative stress, and cerebral metabolic dysfunction. The plausible mechanisms of post-traumatic ischemia include vascular distortion from direct mechanical injury, hypotension in the presence of impaired autoregulation, and vasospasm. Both cerebral ischemia and coexisting edema following TBI are associated with poor neurological outcomes. Hence, anesthesia for emergency neurosurgical procedures in patients with TBI must be tailored to maintain hemodynamic stability, optimize cerebral perfusion, reduce cerebral metabolic rate, lower intracranial pressure (ICP), and ensure adequate brain relaxation.[23]

Both inhalational and intravenous anesthetic regimens have been used in patients with TBI, with no proven supremacy of one modality over the other. Although inhalational anesthetic agents have been shown to offer neuroprotection, they are often associated with an increase in ICP. Compared to inhalational agents, intravenous anesthesia provides better brain relaxation and ICP control, reduces cerebral metabolic demand, maintains flow-metabolism coupling, and minimizes the risk of cerebral ischemia.[28]

Propofol is the most common agent used in intravenous anesthesia regimens in TBI. Its beneficial effects in TBI include a reduction in the cerebral metabolic rate of oxygen, CBF reduction, conservation of cerebral autoregulation and carbon dioxide (CO_2) responsiveness, maintenance of flow–metabolism coupling, decrease in ICP, and neuroprotection. Despite its efficacy, dose-related adverse effects may occur with propofol, including hemodynamic instability, delayed awakening, platelet dysfunction, and lipemia.[3,26,34] In addition, intraoperative doses of propofol have an add-on effect when the same is used for sedation in neuro-critical care postoperatively, thereby increasing the risk of "propofol infusion syndrome."[6] Adding adjuvants along with propofol aids in limiting the total propofol consumption, which, in turn, leads to a reduction in propofol-related adverse effects.[36]

Fentanyl is a commonly used adjuvant in propofol-based total intravenous anesthesia (TIVA) regimens due to its analgesic efficacy, ability to reduce sympathetic response to airway manipulation and surgical stimulation, and cough suppression.[19] However, the use of opioids is associated with respiratory depression, postoperative hyperalgesia, nausea and vomiting, ileus, and urinary retention.

Dexmedetomidine is a highly selective α-2 agonist which causes cerebral vasoconstriction, decreases the CBF and cerebral metabolic rate (CMR), thereby conserving flow-metabolism coupling, and helps in reducing ICP.[37] Its intraoperative use in various neurosurgical procedures has led to a reduction in the requirements of propofol[1,3,10,16,31,33] and opioids.[9,17,18,20,25,29,30] Hence, the use of dexmedetomidine as an adjunct to propofol in TIVA for patients with moderate to severe TBI may yield multiple benefits such as improved hemodynamic stability, reduction of ICP, and enhanced neuroprotection, to name a few.

TBI is associated with varying degrees of neuronal damage and degeneration, the degree of which determines the severity of TBI.[24] S100b is a low molecular weight calcium-binding protein primarily found in astrocytic glial cells of the central nervous system.[7,8,28] It is a well-established biomarker of brain injury and has been widely used to quantify and prognosticate neuronal damage.[12] Serum levels of S100b are significantly higher in TBI patients when compared to controls.[14] The effect of dexmedetomidine and fentanyl on S100b protein values in TBI patients and if any neuroprotective effect is present is yet to be investigated.

Literature regarding the anesthetic management of head injury using TIVA is sparse, with a lack of consensus on the optimal TIVA regimen for TBI patients. This study aims to compare the safety and efficacy of dexmedetomidine-propofol versus fentanyl-propofol-based TIVA in adult TBI patients undergoing craniotomy and evacuation of hematoma in terms of total propofol consumption, ICP, hemodynamic parameters, and biomarkers of neuronal injury.

MATERIALS AND METHODS

After obtaining approval from the Institute Ethics Committee (JIP/IEC/2021/028), the trial was registered with the Clinical Trials Registry India (CTRI/2021/08/035323). Written informed consent was obtained from a representative family member of subjects satisfying the inclusion and exclusion criteria. One hundred patients belonging to the age group of 18–60 years of either gender, with isolated head injuries, with Glasgow Coma Scale (GCS) <13, scheduled for emergency craniotomy and evacuation of acute traumatic subdural hematoma (SDH) at our hospital were included

in the study. Patients with isolated extradural hematoma, hemodynamically unstable patients (defined as heart rate [HR] <50/min and/or systolic blood pressure (SBP) <90 mm Hg before induction of anesthesia), those who were not consenting to partake in the study, and those planned for conservative management were excluded from the study. Preoperative GCS and computed tomography (CT) brain findings were recorded for all the patients.

Sample size

The number of patients to be included was estimated from the average propofol dosage required for maintenance of anesthesia (4.7 ± 1.6 mg/kg/h) when using propofol target-controlled infusion (TCI).[22] In our study, we expected a difference of 20% with respect to the reduction of the total propofol requirement in patients who received dexmedetomidine and in those who received fentanyl as an adjuvant. Assuming a beta power of 80% and type 1 error of 0.05, the required sample size would be 45 patients in each group. On considering a drop-out rate of 10% and after rounding off, the total sample size was calculated to be 100.

Randomization

Subjects were randomized into two groups, namely, Group F (fentanyl) and Group D (dexmedetomidine), using a computer-generated randomization table. Allocation concealment was achieved using the serially numbered opaque sealed envelope method. A single researcher who was not involved in data collection or patient follow-up opened the envelope. The study drugs (dexmedetomidine or fentanyl) were administered to the patients according to the group allocation. The anesthesiologist conducting the study and the patients were blinded to the study drugs. Dexmedetomidine and fentanyl were diluted with 0.9% normal saline to a concentration of 2 μg/mL in 50 mL.

In the operation theater, standard monitors, including non-invasive blood pressure, electrocardiogram, and pulse oximetry, were attached, and baseline values were noted. A 16 G/18 G intravenous cannula was secured in one of the accessible veins. A preoperative blood sample for the measurement of S100b was collected and stored.

Group F received fentanyl, and Group D received dexmedetomidine as follows: Intravenous loading dose of 1 μg/kg over 10 min (either fentanyl or dexmedetomidine) followed by an intraoperative maintenance infusion of 0.5 μg/kg/h. After the loading dose of the study drug, anesthesia was induced with fentanyl 1 μg/kg and propofol using a TCI pump with a target effect site concentration of 4–5 μg/mL, in accordance with the Schneider model in both groups (21). Intubation was facilitated with rocuronium 1 mg/kg. Post-induction, patients were intubated with an appropriately sized endotracheal tube. The patients were ventilated with 40% fraction of inspired oxygen (FiO_2), and ventilation was adjusted to maintain an end-tidal CO_2 ($EtCO_2$) of 30–35 mm Hg.

One of the radial arteries was cannulated with a 20 G cannula. A 7 Fr central line was inserted either in the subclavian vein or the internal jugular vein in all the patients. The cardiac output (CO) monitor (EV1000) was connected to the arterial line and central line, and the values of stroke volume (SV), SV variation (SVV), systemic vascular resistance (SVR), central venous pressure, and CO were obtained. Hemodynamic parameters such as HR, SBP, diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at induction and every minute after induction for 5 min and after that, once in 30 min.

Anesthesia was maintained using propofol with a target plasma concentration between 3 and 4 μg/mL in both groups. In both groups, $EtCO_2$ was maintained at 30–34 mm Hg. HR and invasive blood pressure (IBP) were maintained within 20% of the baseline values.

If the HR and SBP were 20% above the baseline value, a bolus of fentanyl 0.5 μg/kg was given as a rescue measure, followed by an increment in the propofol effect-site concentration by 0.5 μg/mL. The number of additional boluses of fentanyl given was noted. On the contrary, if the HR and SBP were 20% lower, a 200 mL fluid bolus was administered, followed by a reduction in the effect-site concentration of propofol by 0.5 μg/mL. Vasopressors (either phenylephrine or noradrenaline) were given intravenously if the hypotension did not respond to fluids and titration of anesthetics. Normal saline, at the rate of 2 mL/kg/h, was administered in all patients as maintenance fluid.

At the time of scalp incision, mannitol 1 g/kg was administered over 20 min. On the creation of the first burr hole, a 22 G/0.8 mm cannula was placed under the dura and connected to a pressure transducer system through a polyethylene catheter. The zero level of ICP was adjusted with the transducer kept at the level of the mastoid process. The pressure measured was taken to be the ICP at that point in time. CPP was calculated as the difference between MAP and ICP. If the ICP was found to be >25 mm Hg, moderate hyperventilation was done to achieve an $EtCO_2$ of 25–28 mm Hg. Additional boluses of mannitol 0.25–0.5 gm/kg were administered if needed. Once the dura was opened, the brain relaxation score was assessed on a four-point scale ([1] Perfectly relaxed, [2] Satisfactorily relaxed, [3] Firm brain, and [4] Bulging brain), using tactile evaluation by the neurosurgeon who was blinded to the anesthetic technique employed.[27] Brain relaxation was assessed again at the time of dural closure. The infusion of propofol and dexmedetomidine or fentanyl was discontinued when the final skin sutures were applied. At the end of the surgery, the total amount of propofol consumed was calculated, and the

mean propofol consumption was expressed as μg/kg/min, estimated by the total propofol used intraoperatively divided by the duration of the infusion and the patient's body weight. The number of additional boluses of fentanyl given intraoperatively and the total dose of fentanyl in the two groups were compared. A second blood sample for S100b was collected before shifting the patient to the neurotrauma intensive care unit (ICU) for elective ventilation, which was analyzed using the S100b ELISA kit (Elabscience, USA) according to the manufacturer's protocol.

Statistical analysis

All statistical analyses were carried out using Statistical Package for the Social Sciences Version 29.0 (IBM Corp., Armonk, NY). A frequency and percentage scale were used to express the distribution of categorical characteristics, and continuous variables were expressed as mean ± standard deviation. The comparison of the main outcome variable was done using an independent student *t*-test. The categorical variables were compared between the groups using the Chi-square test. All statistical analyses were carried out at a significance level of α error of 5%.

RESULTS

One hundred patients were enrolled in this prospective randomized study. Fifty patients were assigned to each group. One patient in Group D was excluded due to severe persistent bradycardia soon after starting the infusion. Ninety-nine patients (49 in Group D and 50 in Group F) were included in the final analysis [Figure 1]. The two groups were comparable in terms of demographic parameters. The presence or absence of midline shift and that of contusion on CT scan, and the GCS scores at admission were also comparable between the two groups. Twenty-one patients in Group D and 23 patients in Group F were intubated in the emergency medical services department [Table 1]. Subdural ICPs and brain relaxation scores at dural opening, dural closure, and after evacuation of hematoma were also comparable between the two groups [Table 2]. The mean propofol consumption in Group D (88.7 ± 31.8 g/kg/min) was lower when compared to Group F (107.9 ± 34.6 μg/kg/min), with a statistically significant difference (P = 0.005). The number of additional fentanyl boluses and the mean intraoperative fentanyl requirement were significantly decreased in Group D when compared to Group F (group D 22.2 ± 36.4 μg vs. Group F 48.2 ± 43.6 μg) (P = 0.002). There was no statistically significant difference between the two groups with respect to perioperative fluid replacement, vasopressor requirement, blood loss, and blood transfusion [Table 3].

The HR, SBP, DBP, and MAP were recorded at induction, 5 min post-induction, and at 30-min intervals after that. The HR before induction and at various predetermined time points were comparable between the two groups [Figure 2a]. The MAP was comparable between both groups at baseline. The difference in MAP between the two groups at 60 min and 90 min was statistically significant (P = 0.01 at both time points), with MAP being significantly lower in Group D [Supplementary Table 1 and Figure 2b]. The CO was significantly lower in Group D when compared to Group F at various predetermined time points [Supplementary Table 2 and Figure 3a]. However, the SV did not differ significantly between the two groups [Supplementary Table 3 and Figure 3b]. The SVV and SVR were also comparable in both groups at all-time points [Supplementary Tables 2 and 3, Figure 4a and b]. The number of tracheostomized patients, length of ICU stay, duration of hospitalization, and in-hospital mortality were found to be comparable between the two groups [Table 4]. Baseline values of S100b were significantly higher in Group D as compared to Group F (P = 0.005). We also observed a subsequent increase in the S100b values from baseline in Group F (P = 0.01) and a subsequent reduction from baseline in Group D (P = 0.21). However, all values of the biomarker were within clinically acceptable limits [Table 5].

DISCUSSION

This randomized controlled trial was formulated to compare dexmedetomidine-based TIVA versus fentanyl-based TIVA in patients with acute traumatic SDH undergoing emergency craniotomy. To the best of our knowledge, there are no studies available comparing the two adjuvants, namely, fentanyl and dexmedetomidine, with propofol in the intraoperative period. The primary outcome of the study was to compare the intraoperative mean propofol consumption between the two groups. Our results demonstrate that the total amount of propofol consumed was lower in the dexmedetomidine-based anesthetic regimen in comparison to the fentanyl-based protocol.

Mean propofol consumption

The mean propofol consumption was lower in the dexmedetomidine group (88.7 ± 31.8 μg/kg/min) in comparison to the fentanyl group (107.9 ± 34.6 μg/kg/min) by approximately 18%, and this difference was statistically significant (P < 0.005). In a study by Joy *et al*., a 30% reduction in the mean propofol consumption was observed with the dexmedetomidine-based anesthetic regimen in patients undergoing elective neurosurgical procedures.[16] Chakrabarti *et al*. studied the effect of dexmedetomidine as an adjunct to propofol on the recovery characteristics

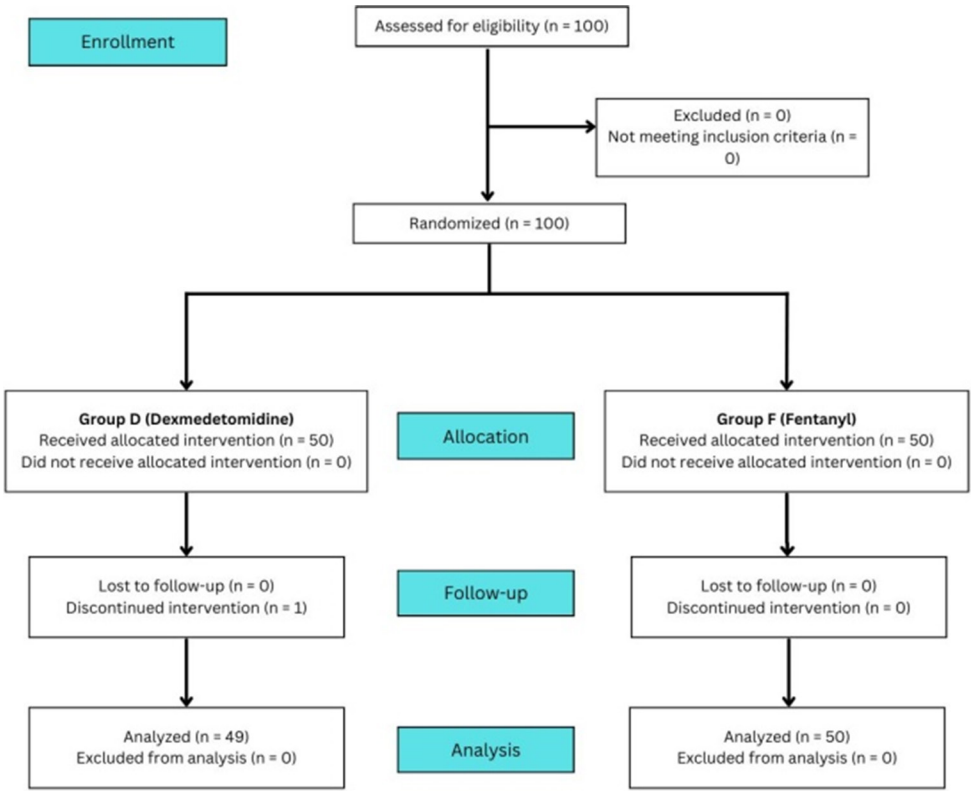

Figure 1: CONSORT Flow diagram.

Table 1: Comparison of demographic parameters between the two groups.

Variables	Group D (Mean±SD) (*n*=49)	Group F (Mean±SD) (*n*=50)	*P*-value
Age (years)	40.2±13.6	40.8±13	0.79
Weight (kg)	64.8±11.2	63.3±9.8	0.48
Gender (%)			
Male	39 (78)	38 (76)	0.81
Female	11 (22)	12 (24)	
GCS at admission	8.2±3.7	8.8±3.9	0.45
Midline shift (>5 mm) (%)	33 (66)	34 (68)	0.83
Contusion present (%)	28 (56)	33 (66)	0.30
Received intubated (%)	21 (42)	23 (46)	0.69
Duration of surgery (min)	224.7±40.6	232.1±49.3	0.42

Group D: Dexmedetomidine group, Group F: Fentanyl group, SD: Standard deviation, GCS: Glasgow Coma Scale, *n*: Number of patients. *P*<0.05 is considered significant.

Table 2: Comparison of brain relaxation score and ICP between the two groups.

Variables	Group D (Mean±SD) (*n*=49)	Group F (Mean±SD) (*n*=50)	*P*-value
ICP (mm Hg)	20.9±2.6	20.6±3.2	0.68
CPP (at the time of dura opening)	60.4±13.9	59.5±14.9	0.74
Brain relaxation score (dural opening) (%)			
1	3 (6.1)	1 (2)	0.48
2	12 (24.5)	12 (24)	
3	11 (22.4)	17 (34)	
4	23 (46.9)	20 (40)	
Brain relaxation score (dural closure) (%)			
1	8 (16.3)	10 (20)	0.90
2	20 (40.8)	17 (34)	
3	16 (32.7)	17 (34)	
4	5 (10.2)	6 (12)	
Bone flap	24 (49)	21 (42)	0.49
Replaced *in situ* Kept in the abdomen	25 (51)	29 (58)	

ICP: Intracranial pressure, CPP: Cerebral perfusion pressure, SD: Standard deviation, Group D: Dexmedetomidine group, Group F: Fentanyl group, *n*: Number of patients. *P*<0.05 is considered significant.

and analgesic requirements in patients undergoing cerebellopontine angle surgery under bispectral index (BIS) guidance.[5] The authors of the study reported a significant reduction in the requirements of propofol (1.74 g vs. 2.18 g) in patients receiving dexmedetomidine. Similar reductions in the induction and maintenance doses of propofol have been observed in other procedures, such as elective abdominal surgeries, sedation for non-operating room procedures, and spine surgery.[1,3,10,15,16,30,31,33] This effect could be attributed to

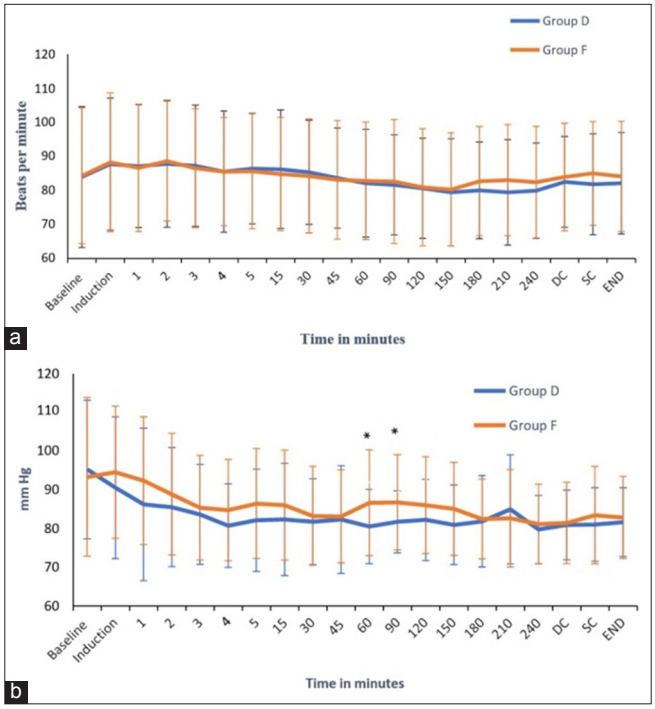

Figure 2: (a) Comparison of HR between the two groups. (b) Comparison of MAP between the two groups. DC: Dural closure, SC: Skin closure, END: End of the surgery, HR: Heart rate, MAP: Mean arterial pressure, *: $P < 0.05$.

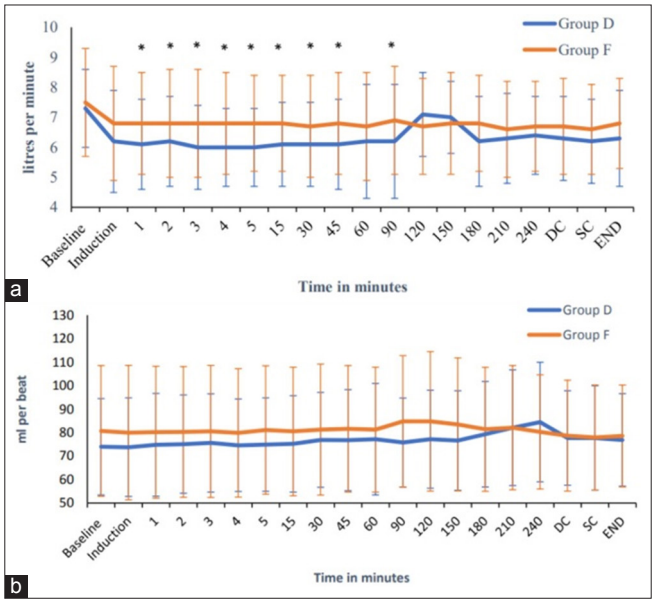

Figure 3: (a) Comparison of CO between the two groups. (b) Comparison of SV between the two groups. DC: Dural closure, SC: Skin closure, END: End of the surgery, CO: Cardiac output, SV: Stroke volume, *: $P < 0.05$.

its α-2 agonist activity on the locus coeruleus, giving rise to an anesthetic-sparing effect.[35]

Table 3: Comparison of intraoperative parameters between the two groups.

Variables	Group D (Mean±SD) (*n*=49)	Group F (Mean±SD) (*n*=50)	*P*-value
Total propofol consumption (mg)	1281.07±505.09	1573.4±640.4	0.007
Mean propofol consumption (μg/kg/min)	88.7±31.8	107.9±34.6	0.005
Mean fentanyl bolus dose (μg)	22.2±36.4	48.2±43.6	0.002
Fentanyl bolus (*n*) (%)			
0	29 (59.1)	12 (24)	0.001
1	8 (16.3)	22 (44)	
2	10 (20.4)	6 (12)	
3	2 (4)	6 (12)	
4	0 (0)	4 (8)	
Quantity of intraoperative intravenous fluids (mL)	3158.5±832.4	3291±874.7	0.44
Urine output (mL)	1007.1±583.3	955.8±504	0.64
Blood loss (mL)	649.2±238	687.2±373.3	0.55
PRBC given (*n*) (%)	16 (33.3)	17 (34)	0.95
Requirement of vasopressor (*n*) (%)	8 (16.3)	6 (12)	0.54

SD: Standard deviation, Group D: Dexmedetomidine group, Group F: Fentanyl group, PRBC: Packed red blood cells, $P<0.05$ is considered significant, *n*: Number of patients

Table 4: Comparison of pre- and post-operative S100b values between the two groups.

S100b values (pg/mL)	Group D (Mean±SD) (*n*=49)	Group F (Mean±SD) (*n*=50)	*P*-value (comparison between the groups)
Preoperative	28.0±14.6	22.3±10.5	0.005
Postoperative	24.5±14.7	26.8±13.9	0.31
P-value (comparison within the group)	0.21	0.012	

SD: Standard deviation, Group D: Dexmedetomidine group, Group F: Fentanyl group, *n*: Number of patients. $P<0.05$ is considered significant.

Brain relaxation and other intraoperative parameters

We did not find any difference in brain relaxation and ICP after dural opening between the two groups. Günes *et al.* compared the hemodynamic profiles, cerebral mechanics, and recovery characteristics of patients undergoing elective neurosurgical procedures receiving dexmedetomidine-

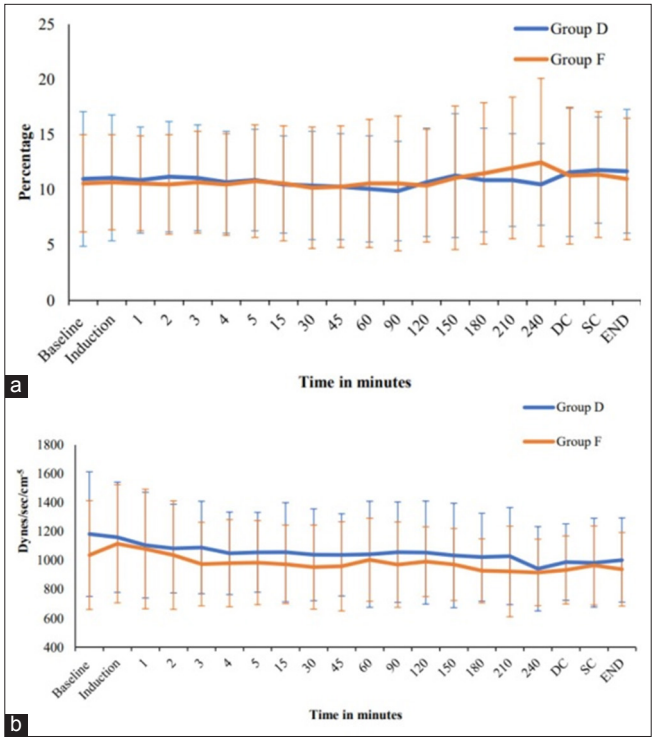

Figure 4: (a) Comparison of SVV between the two groups. (b) Comparison of SVR between the two groups. DC: Dural closure, SC: Skin closure, END: End of the surgery, SVV: Stroke volume variation, SVR: Systemic vascular resistance.

remifentanil versus propofol-remifentanil anesthesia.[11] The authors did not report a statistically significant difference in the brain relaxation scores between the two study groups. Preethi *et al*. observed better brain relaxation under propofol-based TIVA as compared to inhalational anesthesia in patients with TBI undergoing emergency craniotomy for evacuation of the hematoma.[28] Since TIVA was used in both groups in our study, there was no significant difference in brain relaxation after dural opening and after hematoma evacuation between the two groups.

Intraoperative blood loss, the total amount of crystalloids, colloids, and blood products administered, and the requirement of vasopressors and blood transfusion were comparable in both groups.

Hemodynamic parameters

Hemodynamic parameters were well maintained in both groups. This finding is reflected in the studies conducted by Song *et al*. and Tanskanen *et al*., who did not notice any episodes of bradycardia and/or hypotension while using dexmedetomidine in patients undergoing craniotomy.[32,33] To obtain a more accurate assessment of the hemodynamic status, our study incorporated monitoring of advanced hemodynamic parameters, such as CO, SV, SVV, and SVR [Supplementary Tables 2 and 3]. CO was significantly reduced in the dexmedetomidine group as compared to the fentanyl group at various time points. However, it was within the clinically acceptable range at all-time points in both groups [Supplementary Table 2]. The extensive hemodynamic monitoring instituted in our study may have been responsible for the prompt recognition and mitigation of any hemodynamic instability that might have occurred.

Additional fentanyl boluses

There was a significant reduction in the additional intraoperative fentanyl requirement in the dexmedetomidine group in comparison to the fentanyl group in our study. Joy *et al*. and Chakrabarti *et al*. demonstrated similar results in their study, where the total opioid consumption was significantly lower in the dexmedetomidine group.[16,5] Similarly, Andleeb *et al*. reported a lower fentanyl consumption in dexmedetomidine and ketamine groups in comparison to the control group.[2] This finding buttresses the analgesic efficacy of dexmedetomidine and its potential to be used as an adjuvant to propofol in TIVA, thereby mitigating the adverse effects associated with opioids.

That being said, few other studies have demonstrated no significant reduction in intraoperative opioid usage with the addition of dexmedetomidine.[25,39] However, in the studies mentioned above, the analgesic under scrutiny was remifentanil, whose unique pharmacological profile may have contributed to the said findings. Further studies comparing fentanyl and dexmedetomidine as adjuvants to TIVA with respect to their effect on perioperative opioid requirements are warranted.

Brain biomarkers

The baseline levels of S100b were elevated in the dexmedetomidine group, as compared to the fentanyl group. However, there was a reduction in the postoperative biomarker values in the dexmedetomidine group, a finding that can be attributed to the neuroprotective and anti-apoptotic effects of the drug.[4,21] The S100b value in the fentanyl group was seen to rise in the postoperative period, possibly due to the lack of similar neuroprotective effects of fentanyl.[38] Bindra *et al*. studied the neuroprotective effects of intraoperative dexmedetomidine among patients with temporal lobe epilepsy undergoing temporal lobectomy.[4] Their study reported lower perioperative values of S100b in patients receiving dexmedetomidine. In a meta-analysis of 879 randomized controlled trials, dexmedetomidine was shown to reduce the surges in S100b values and to mitigate the stress-related increases in HR, MAP, and ICP in patients with ischemic brain injury. Literature regarding similar effects of dexmedetomidine in patients with TBI is

Table 5: Comparison of postoperative outcome parameters between the two groups.

Outcome parameters	Group D (Mean±SD) (*n*=49)	Group F (Mean±SD) (*n*=50)	*P*-value
Tracheostomy (*n*) (%)	19 (38)	14 (28)	0.25
Expired (*n*) (%)	8 (16)	4 (8)	0.20
Days on ventilator	3.8±2.6	3.1±3.7	0.30
ICU stay (days)	5.2±3.1	4.4±4	0.27
Hospital stay (days)	9.0±5.7	7.1±4.7	0.07
GCS at discharge	11.3±4	11.8±3.8	0.69

SD: Standard deviation, Group D: Dexmedetomidine group, Group F: Fentanyl group, ICU: Intensive care unit, GCS: Glasgow Coma Scale, *n*: Number of patients. *P*<0.05 is considered significant.

lacking. To the best of our knowledge, this is the first study reporting a plausible neuroprotective role of intraoperative dexmedetomidine in TBI patients.

Course of hospital stay

The length of ICU stays, number of ventilator days, length of hospitalization, number of patients requiring tracheostomy, and the in-hospital mortality were comparable between the two groups in our study [Table 4]. The findings indicate that there was no significant impact on long-term outcomes created by the use of the study drugs intraoperatively. A meta-analysis concerning outcomes of dexmedetomidine versus propofol sedation in critically ill patients requiring mechanical ventilation in the ICU revealed no significant difference in the length of ICU stay.[13] Due to the lack of robust data on similar outcome measures in patients undergoing neurosurgery for TBI, further research is warranted to study the same in perioperative settings.

Limitations of the study

Our study is unique in exploring the neuroprotective role and propofol-sparing effects of dexmedetomidine, among other outcome measures, in the setting of TBI. Nevertheless, our study has certain limitations. We did not measure the plasma concentrations of propofol, dexmedetomidine, or fentanyl. Furthermore, the comparison of the cost-effectiveness of the study drugs was not part of our study. Considering the relatively short duration of action of the study drugs and the lack of significant long-term effects on the outcome measures, the follow-up was not extended beyond patient discharge from the hospital.

CONCLUSION

Based on the findings of our study, we conclude that dexmedetomidine, when used as an adjunct to propofol-based TIVA, results in a greater reduction in the total propofol consumption and intraoperative opioid requirement while maintaining hemodynamic stability when compared to fentanyl. Subdural ICPs, brain relaxation scores at dural opening, dural closure, and after evacuation of hematoma were comparable between the two groups. There was no statistically significant difference between the two groups with respect to perioperative fluid replacement, requirement of vasopressors, blood loss, and blood transfusion. Although the MAP and CO were lower in the dexmedetomidine group, they were well within the normal limits. The two groups were comparable in terms of other hemodynamic parameters, such as SV, SVV, and SVR. Serum levels of S100b showed a reduction from their baseline value in the dexmedetomidine group, supporting the neuroprotective role of dexmedetomidine in TBI. Further studies are needed to confirm the neuroprotective role of dexmedetomidine in TBI patients.

Transparency, rigor, and reproducibility summary

The study design and analysis plan were preregistered on August 2, 2021, at the Clinical Trials Registry India (CTRI/2021/08/035323). The prespecified sample size was 50 per group, yielding a statistical power of 80% for the detection of a 20% reduction in the total propofol requirement in patients who received dexmedetomidine and in those who received fentanyl as an adjuvant. All subjects were assigned to Group F (fentanyl) and Group D (dexmedetomidine) using a computer-generated randomization table, yielding groups that did not differ in baseline characteristics. One hundred subjects were enrolled, and primary outcomes were assessed in 99 subjects (50 in Group F, 49 in Group D) after excluding 1 patient in Group D due to severe persistent bradycardia soon after the commencement of drug infusion. All primary outcomes were assessed by investigators blinded to group assessment. The data and analytic code have not been deposited at any external site due to hospital policy but are partially available on request. The findings have not yet been replicated or externally validated. The manuscript is open-access.

Author contributions

VC: Methodology, Investigation, Writing-original draft; PB: Conceptualization, Methodology, Supervision; SS: Conceptualization, Visualization, Supervision; MK: Visualization, Supervision; BV: Data curation, Supervision; PC: Methodology, Writing-review, and editing; JJ: Data curation, Formal analysis; RR: Methodology, Writing-review, and editing.

Ethical approval

The research/study approved by the Institutional Review Board at Jawaharlal Institute of Postgraduate Medical Education and Research, number JIP/IEC/2021/028, dated July 06, 2021.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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