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Intraoperative Dexmedetomidine in Peripheral or Emergency Neurologic Surgeries of Patients With Mild-to-Moderate Traumatic Brain Injuries: A Retrospective Cohort Study

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Abstract

Background: Although animal models have demonstrated dexmedetomidine (DEX) as neuroprotective in craniocerebral and subarachnoid injuries, but its role in humans remains to be elucidated. The objectives of the study were to compare plasma brain-derived neurotrophic factor (BDNF), cytokine, and superoxide dismutase levels of patients between those who received intraoperative DEX and those who received intraoperative normal saline (NSE) during peripheral or emergency neurologic surgeries.

Methods: Intra- and postoperative data of blood biomarkers and surgical outcomes of patients who underwent peripheral or emergency neurologic surgeries with mild-to-moderate traumatic brain injuries were analyzed retrospectively. Patients received intraoperative DEX group (n = 109) or NSE group (n = 116).

Results: At 15 minutes after intubation and before the operation, in the DEX group, plasma BDNF concentration decreased but remained much higher than the NSE group ($P < .0001$, $q = 15.82$). After 24 hours of surgeries, levels of cytokine were higher in the NSE group than the DEX group ($P < .05$ for all). Dexmedetomidine increased malondialdehyde ($P < .0001$) and superoxide dismutase ($P < .0001$) levels in DEX group.

Conclusions: Intraoperative infusion of DEX may have a neuroprotective, anti-inflammatory, and antioxidant effects during peripheral or emergency neurologic surgeries.

Level of Evidence: III.

Keywords

brain-derived neurotrophic factor, dexmedetomidine, emergency neurologic surgeries, peripheral surgeries, superoxide dismutase, traumatic brain injuries

Introduction

The patients who underwent surgery need good hemodynamic stabilities. Also, the surgeries may create hemodynamic instability, activate the inflammatory cascades, may lead to more destruction of brain, and create complications.[1] For these reasons, the sedation is necessary.[2]

Dexmedetomidine (DEX) is a highly selective α-2 adrenergic receptor agonist.[3] The α-2 receptor agonists have a long track record of use for sedation and analgesia.[4] Animal studies have shown that α-2 agonists are neuroprotective in craniocerebral and subarachnoid injuries,[3,5,6] but this has not been

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definitively shown in humans.[7] The study does not guarantee that DEX may not have adverse effects on the cerebral oxygen supply demand relationship in patients with neurologic injuries.[8] Dexmedetomidine has a significant effect on the central nervous system and decreases the blood flow in the brain and the requirement or needs for cerebral oxygen.[2] It also modifies memory and enhances cognitive ability effects like sedation,[8] analgesic,[3] and anxiolytics.[9] Dexmedetomidine is shown to decrease catecholamine in the brain and improves the perfusion ability in the penumbra.[2] The glutamate level is significantly reduced by DEX, and so injuries at the cellular level is reduced.[6]

Brain-derived neurotrophic factor (BDNF) is protein belonging to the neurotrophic family of growth factors which is present when there is neuronal damage and there is a need for neurogenesis.[7] Therefore, the plasma level of BDNF indicates the extent of neuronal damage.[10] There is a strong positive correlation between the BDNF level in the cortex and that of serum.[11] Therefore, the serum BDNF can be considered as same as the cortical BDNF and is a desirable protein for neuronal health.[10] The commonly used general anesthetics (eg, midazolam) are found to decrease the plasma level of BDNF and also inhibit neuronal activity in the central nervous system.[7]

The objectives of the retrospective analyses of prospectively collected data were to compare the plasma BDNF, cytokine, and superoxide dismutase levels and hemodynamic parameters of patients with mild or moderate traumatic brain injuries between those received intraoperative DEX and those received intraoperative normal saline (NSE) during peripheral or emergency neurologic surgeries.

Materials and Methods

Ethics Approval and Consent to Participate

The designed protocol (GMC/CL/17/2019 dated 21 February 2019) of the established study was approved by the Suzhou Kowloon Hospital review board. The study reporting adheres to the law of China, strengthening the reporting of observational studies in epidemiology (STROBE) statement: cohort studies and the V2008 Helsinki Declaration.

Inclusion Criteria

Patients who underwent peripheral or emergency neurologic surgeries due to fall, motor-bike, car, or cycle accidents, and so on with mild (confusion, disorientation, poor attention, dizziness, and/or loss of memory with/without loss of consciousness for less than 30 minutes and an on admission Glasgow Coma Scale of 13-15) or moderate (loss of consciousness from 20 minutes-6 hours and an on admission Glasgow Coma Scale of 9-12) traumatic brain injuries were included in the study. Patients who had American Society of Anesthesiology status I and II were only included in the analysis.

Exclusion Criteria

Alcoholic patients (a long-term addiction to alcohol), patients on treatment with antipsychotic medications and psychiatric illness, and patients with American Society of Anesthesiology status III and IV were excluded from the analyses.

Cohort

Patients who received intraoperative DEX (Precedex, Pfiezer Inc, New York, NY) were included in the DEX group and those who received intraoperative NSE (Baxter Pvt Ltd., Deerfield, IL) were included in the NSE group. All the patients irrespective of which group they belong were given oral 5 mg diazepam (Valium Roche Laboratories Inc., Little Falls, NJ) and lidocaine (Xylocaine Spray, AstraZeneca, Cambridge, Massachusetts) applied on the skin of patients' arms so that they would not feel any pain during puncture). Each patient had intravenous catheters (Rusch Inc., Gerlingen, Germany) inserted in each arm. One catheter was for measurement of the plasma concentration of BDNF and another was for anesthesia and volume measurement. When each patient was brought into the operating room, each one was administered 500 mL of Ringer's lactate (Baxter Pvt. Ltd) for the purpose of rapid volume expansion inside the vessel.

Anesthesia Method

Patients of the DEX group were received intraoperative DEX 1 μg/mL and patients of the NSE group were received NSE. The anesthetists who prepared these solutions were not a member of the operation team. In the DEX group, patients were administered DEX 1 μg/kg/h by intravenous infusion which was done for 15 minutes (average). Along with this, 1% wt/vol propofol (Propoven; APP Pharmaceuticals Inc, Los Angeles, CA) was infused until the eyelid reflex of the patient was lost. After this, 1.5 μg/kg fentanyl (Sublimaze; SPL Pharmaceuticals, Illinois) and 0.1 mg/kg cis-atracurium (Nimbex; Abbvie Inc, Lake Bluff, IL) were administered by the intravenous route until neuromuscular relaxation was observed. The anesthetics were the same during all these intubations. The induction of preoperative anesthesia and management of anesthesia was in the same manner in the NSE group except NSE was administered in place of DEX. Maintenance of anesthesia in both groups was done by continuous infusion of propofol. Sometimes, fentanyl and cisatracurium were both administered to maintain the patients' analgesic effect and muscular relaxation, respectively. Continuous waveform capnography was maintained between 4.7 and 6.0 kPa. The bispectral index was monitored and maintained between 35 and 65.

When surgery had finished, before the closure of the skin, 35 to 50 μg fentanyl injected to each patient to decrease the pain from the operation. Anesthesiologists (minimum 3 years of experience) of the institutes were performed all anesthetic procedures.

Data Collections

Data (electronic) regarding pathological findings, heart rate, the Bispectral index, and surgical outcomes of patients were collected from the medical records of the institutes after getting permission from the competent authorities.

Blood Biomarkers

All pathological analyses performed by pathologists (minimum 3 years of experience) of the institutes.

Brain-Derived Neurotrophic Factor Levels

Throughout the operation, blood samples of 5 mL were withdrawn from each patient. The blood samples were withdrawn at the patient in a normal state or baseline (immediately preoperative), at 15 minutes after intubation, although the operation was yet to commence, after skin closure, at 10 minutes after extubation in the postanesthesia care unit, and at 24 hours after the surgery. All the blood samples were placed in sterile ethylene diamine tetraacetic acid tubes (Vacumed; FL Medical, Miami, Florida), and it underwent centrifugation at 2500 rpm (GCC-S; Thomas Scientific, Swedesboro, New Jersey). These samples were stored at -70°C temperature. Brain-derived neurotrophic factor concentration was measured by enzyme-linked immunosorbent assay (Human BDNF ELISA Kit; Proteintech Group Inc, Chicago, Illinois).[7]

Cytokine Measurements

One day after surgeries, 10-mL venous blood was collected in a sterile tube. Interleukin (IL)-6, tumor necrosis factor-α (TNF-α), and IL-1β levels were evaluated by a solid-phase, 2-site chemiluminescent enzyme immunometric assay procedure (Euro DPC Ltd, Gwynedd, Wales).[12]

Malondialdehyde Level

In 0.5 mL of blood plasma, 2.5 mL of 100 g/L trichloroacetic acid (Mark Specialties, Berlin, Germany) was added. This mixture was put in a centrifuge tube and allow to rest in boiling water for 15 minutes. Allow to cool the mixture and absorbance was measured at 532 nm using Visible Spectrophotometer (4800; Double-beam, Shimadzu, Tokyo, Japan).[5] Malondialdehyde level was measured 24 hours after the surgery.

Superoxide Dismutase Level

In 0.5 mL of blood plasma, 1.0-mL ethanol/chloroform mixture (6:4 ratio; Mark Specialties, Berlin, Germany) was added and centrifuged. The inhibition of nitro blue tetrazolium reduction was measured in the Xanthine/Xanthine Oxidase system. The half of inhibition of the nitro blue tetrazolium reduction was considered as one unit of superoxide dismutase activity.[5] Superoxide dismutase level was measured 24 hours after the surgery.

Statistical Analysis

InStat version 3.01 (GraphPad, San Diego, California) was used for statistical analysis. Mann-Whitney U test[5] was performed for continuous data and Fisher exact test[10] was performed for categorical data. Tukey test (considering critical value [q] > 3.332 as significant) was performed for post hoc analysis of continuous data which were found significant in the Mann-Whitney U test. The results were considered significant at a 95% level of confidence.

Results

Enrollment

From September 1, 2018 to February 1, 2019, there were 357 patients underwent dental, maxillofacial, ophthalmic, orthopedic, emergency neurologic, or plastic/reconstructive surgeries and had mild or moderate traumatic brain injuries at the department of surgeries in the Affiliated Huai'an Hospital of Xuzhou Medical University, Huai'an, Jiangsu, China; the Shandong energy Zaozhuang Mining Group Central Hospital, Zaozhuang, Shandong, China; and the Suzhou Kowloon Hospital, Shanghai Jiao Tong University School of Medicine, Suzhou, Jiangsu, China. Among them, 57 patients were alcoholic, 32 patients on treatment of antipsychotic drugs, 24 patients with psychiatric illness, 12 patients with American Society of Anesthesiology status III (substantive functional limitations), and 7 patients with American Society of Anesthesiology status IV (constant threat to life). Therefore, they were excluded from the analysis. Data regarding pathological findings, heart rate, the Bispectral index, and surgical outcomes of 225 patients who received intraoperative DEX group (n = 109) or NSE group (n = 116) were included in the analyses. The flow chart of the analyses is presented in Figure 1.

Demographical Characters

There was no significant difference between the demographical and clinical characteristics of the enrolled patients at the time of the admission ($P > .05$ for all, Table 1). All the enrolled patients had a higher blood pressure than the normal range (80/120 mm Hg) at the time of admission to hospitals.

Brain-Derived Neurotrophic Factor Levels

At 15 minutes after intubation and before the operation, in the DEX group, plasma BDNF concentration came down but remained much higher than the NSE group (166.27 ± 33.24 pg/mL vs 122.25 ± 16.29 pg/mL, $P < .0001$, $q = 15.82$). Administering propofol along with DEX kept the BDNF level steady in the DEX group. After skin closure (164.25 ± 31.12 pg/mL vs 158.55 ± 18.45 pg/mL, $P = .094$) and 10 minutes after extubation (161.29 ± 28.26 pg/mL vs 153.29 ± 27.15 pg/mL, $P = .078$), the plasma BDNF concentrations of the DEX group were almost steady in both groups. In the NSE group after skin closure, the plasma

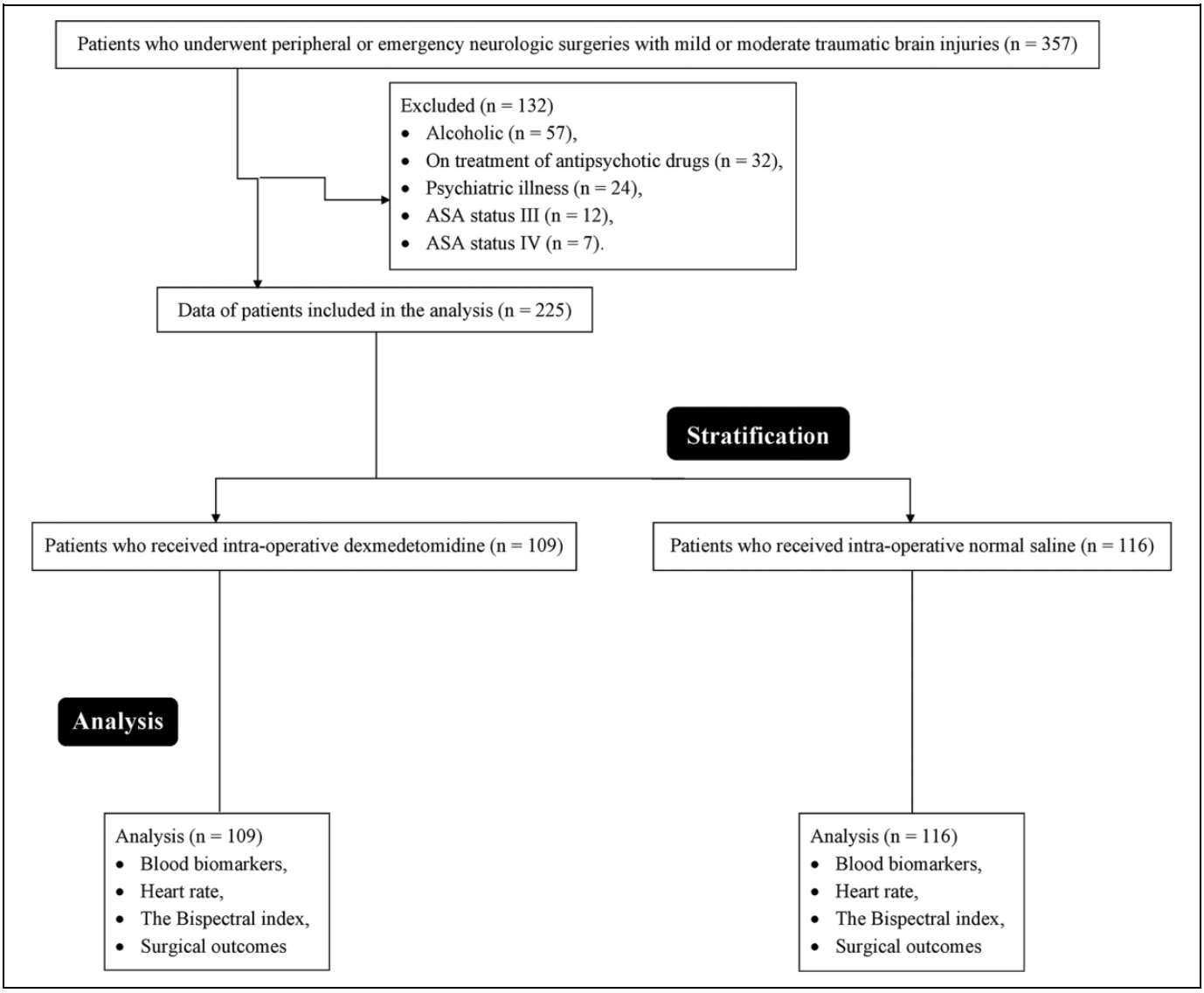

Figure 1. Flow chart of the study.

BDNF concentration increased due to the natural physiological response to the wound caused by the surgery. But 10 minutes after the extubation, in the NSE group, due to the absence of any trigger, the serum BDNF level again decreases while in the DEX group because of DEX, the serum level of BDNF almost remained the same. Twenty-four hours after the surgeries, in the DEX group (173.21 $\pm$ 31.12 pg/mL), the serum BDNF level remained higher than those of the NSE group (123.29 $\pm$ 26.25 pg/mL). While in the NSE group, it came down ($P < .0001$, $q = 17.04$). Dexmedetomidine application in the DEX group ultimately led to high the BDNF plasma concentration as compared to NSE group (Figure 2).

Cytokine Measurements

After surgeries, IL-6, TNF-α, and IL-1β levels were increased in all patients. However, after 24 hours of surgeries, there were significantly higher levels of cytokine measurements in the NSE group than the DEX group ($P < .05$ for all, Table 2).

Heart Rate

Changes in the heart rate during the operation were also noted. The records are shown in Table 3. The heart rate of patients belonging to the DEX group was lower as compared to the NSE group during the time of DEX injection, applying anesthesia, and during intubation. The lowest recorded heart rate in the DEX group patient was 50 bpm which was recorded just after anesthesia which returned to normal of 71 bpm after intratracheal intubation was done. No other serious consequences like hypotension were found. In general, heart rates were fewer in the DEX group than in the NSE group throughout the operation.

Table 1. Demographical, Anthropological, and Clinical Parameters of the Enrolled Patients.[a]

Characteristics	DEX Group	NSE Group	Comparisons Between Groups
Patients Included in the Analysis	109	116	*P* Value
Gender			
Male	85 (78)	84 (72)	.358
Female	24 (22)	32 (28)	
Age (years)			
Minimum	18	18	.228
Maximum	60	60	
Mean ± SD	38.45 ± 5.43	39.54 ± 7.81	
Ethnicity			
Han Chinese	98 (90)	104 (89)	.999
Mongolian	8 (7)	9 (8)	
Mongolian	2 (2)	2 (2)	
North Korean refugee	1 (1)	1 (1)	
A Glasgow Coma Scale			
9	15 (14)	14 (12)	.996
10	35 (32)	35 (30)	
11	41 (37)	44 (38)	
12	7 (6)	9 (8)	
13	5 (5)	7 (6)	
14	3 (3)	3 (3)	
15	3 (3)	4 (3)	
Body mass index (kg/m2)	24.51 ± 1.52	24.89 ± 1.88	.098
American Society of Anesthesiology physical status			
I	72 (66)	83 (72)	.391
II	37 (34)	33 (28)	
Blood pressure (mmHg)			
Systolic	135 ± 9	133 ± 7	.063
Diastolic	85 ± 6	83 ± 9	.053
The interval between the injury occurring and surgery being performed (h)	18 ± 6	17 ± 7	.253
Type of surgeries			
Dental	39 (36)	35 (30)	.111
Maxillofacial	45 (41)	48 (41)	
Ophthalmological	12 (11)	5 (4)	
Orthopedic	9 (8)	18 (16)	
Neurologic (emergency type)	2 (2)	7 (6)	
Plastic/reconstructive	2 (2)	3 (3)	
Interleukin-6 level (pg/mL)	458.12 ± 55.45	443.55 ± 58.45	.057
Tumor necrosis factor-α level (pg/mL)	13.92 ± 2.21	13.01 ± 4.89	.077
Interleukin-1β level (pg/mL)	5.81 ± 1.12	6.12 ± 2.23	.193

Abbreviations: DEX, dexmedetomidine; NSE, normal saline; SD, standard deviation.

[a]Continuous data are shown as mean ± SD and categorical data are shown as frequency (percentage). For statistical analysis, Mann-Whitney *U* test was performed for continuous data and Fisher exact test was performed for categorical data. A $P < .05$ was considered significant. American Society of Anesthesiology physical status: I: Normal patient, II: patient with mild disease.

The Bispectral Index

Since the induction of anesthesia to skin closure, the Bispectral index values found higher in the DEX group than the NSE group (Table 4).

Surgical Parameters

The general properties like duration of the surgery ($P = .109$), the postanesthesia care unit stay ($P = .0624$), volume therapy ($P = .07$), amount of bleeding during surgery ($P = .06$), and postoperative nausea ($P = .353$) in the both groups were not significantly different. Propofol ($P < .0001$) and fentanyl ($P < .0001$) doses for induction were fewer in the DEX group than in the NSE group. Intraoperative DEX infusion increased malondialdehyde ($P < .0001$) and superoxide dismutase ($P < .0001$) levels in the DEX group. The hospital stay of patients of the DEX group was comparatively fewer than those of the NSE group ($P < .0001$, Table 5). Mortality was not recorded between the incidence of traumatic brain injury and surgery in any of patient.

Discussion

The study demonstrated that DEX returned the BDNF level to baseline 24 hours after the surgery. Even in between 15 minutes

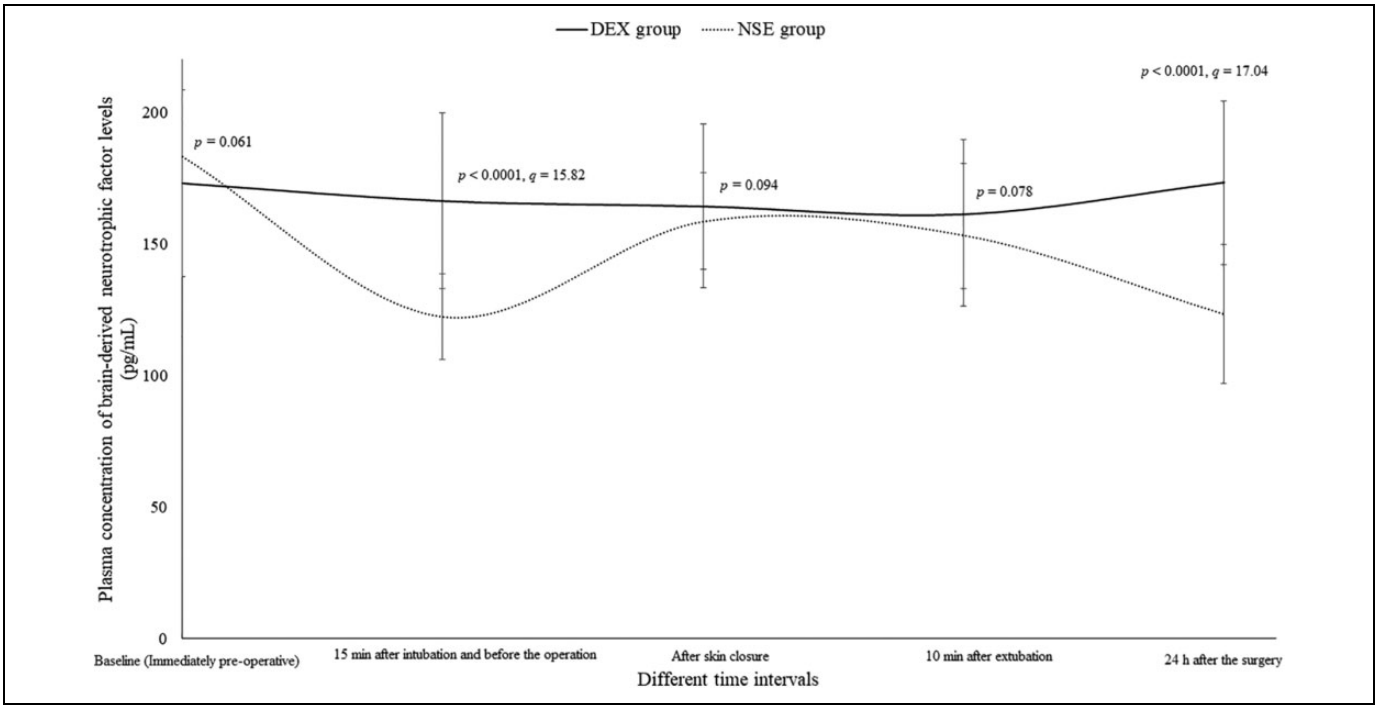

Figure 2. Plasma concentration of brain-derived neurotrophic factor levels at different time intervals. Data are shown as mean ± SD. The Mann-Whitney *U* test was performed for statistical analysis. Tukey test was performed for post hoc analysis. A $P < .05$ and $q > 3.332$ were considered as significant.

Table 2. Cytokine Measurements.[a]

Parameters	DEX Group				NSE Group					
Level	BL	EL	Comparison Between BL and EL		BL	EL	Comparison Between BL and EL		Comparisons Between Groups at EL	
Patients Included in the Analysis	109	109	*P* Value	*q* Value	116	116	*P* Value	*q* Value	*P* Value	*q* Value
Interleukin-6 level (pg/mL)	458.12 ± 55.45	481.12 ± 60.12[b]	.004	4.14	443.55 ± 58.45	511.14 ± 61.63	<.0001	12.12	.0003	5.25
Tumor necrosis factor-α level (pg/mL)	13.92 ± 2.21	16.85 ± 3.41[b]	<.0001	8.27	13.01 ± 4.89	20.25 ± 4.45	<.0001	19.24	<.0001	10.29
Interleukin-1β level (pg/mL)	5.81 ± 1.12	6.45 ± 1.13[b]	<.0001	4.18	6.12 ± 2.23	8.45 ± 3.01	<.0001	11.03	<.0001	10.64

Abbreviations: BL, baseline (immediately preoperative); DEX, dexmedetomidine; EL, after 24 hours of surgery; NSE, normal saline.
[a]Data are shown as mean ± SD. Mann-Whitney *U* test was performed for statistical analysis. Tukey test was performed for post hoc analysis. A $P < .05$ and $q > 3.332$ were considered as significant.
[b]Significant fewer than NSE group at EL.

after the intubation and before the starting of operation and 10 minutes after extubation, the plasma BDNF concentrations were not reduced significantly in the DEX group. Comparatively, in the NSE group, fluctuation of the plasma BDNF level during surgeries was observed and saw significant reduction at 24 hours after the surgery. The study also demonstrated that 15 minutes after the intubation of DEX and anesthesia may be the appropriate time to understand the effects of on the changes in the plasma concentration of BDNF. The current study, along with many other studies,[6,7] shows that the application of anesthetics may affect the plasma BDNF concentration. There is significant evidence that the plasma BDNF has a neuroprotective role.[7,13] The BDNF plays an important role in neuroprotection by activating the phosphatidylinositol 3-kinase (PI3K)/

Table 3. Changes in Heart Rate of Patients During Surgery.[a]

Time of Measurement	Heart Rate (Beats per Minute)		Comparisons Between Groups	
	DEX Group	NSE Group		
Patients included in the analysis	109	116	*P* Value	*q* Value
Baseline (immediately preoperative)	77 ± 6.5	79 ± 7.6	.051	NA
Study drug injection	64 ± 5.3	77 ± 7.8[b]	<.0001	20.76
Anesthesia induction	52 ± 3.1	66 ± 5.6[b]	<.0001	28.14
Intubation	85 ± 8.9	92 ± 6.7[b]	<.0001	9.99

Abbreviations: DEX, dexmedetomidine; NA, not applicable; NSE, normal saline; SD, standard deviation.
[a]Data are shown as mean ± SD. Mann-Whitney *U* test was used for statistical analysis. Tukey test was performed for post hoc analysis. A $P < .05$ and $q > 3.332$ were considered as significant.
[b]Significantly higher than the DEX group.

Table 4. The changes in Bispectral Index Value During Surgery.[a]

Time of Measurement	DEX Group	NSE Group	Comparisons Between Groups	
Patients included in the analysis	109	116	*P* Value	*q* Value
Baseline (immediately preoperative)	97.9 ± 0.4	98.1 ± 1.1	.075	NA
Anesthesia induction	41.8 ± 0.5	40.2 ± 0.6[b]	<.0001	33.4
Intubation	63.5 ± 2.6	55.8 ± 3.9[b]	<.0001	29.72
Skin cut	55.5 ± 3.2	50.9 ± 2.9[b]	<.0001	58.69
Skin closure	61.5 ± 3.15	60.12 ± 2.15[b]	.0002	6.54

Abbreviations: DEX, dexmedetomidine; NA, not applicable; NSE, normal saline; SD, standard deviation.
[a]Data are shown as mean ± SD. Mann-Whitney *U* test was used for statistical analysis. Tukey test was performed for post hoc analysis. A $P < .05$ and $q > 3.332$ were considered as significant.
[b]Significantly lower than the DEX group.

Table 5. The Surgery-Related Results.[a]

Parameters	DEX Group	NSE Group	Comparisons Between Groups
Patients included in the analysis	109	116	*P* Value
Duration of surgery, minute	112.25 ± 11.81	109.82 ± 10.85	.109
Propofol for induction, mg	40.65 ± 5.85[b]	89.88 ± 11.91	<.0001
Fentanyl for induction, mg	25.12 ± 5.45[b]	38.45 ± 8.15	<.0001
Postanesthesia care unit stay, minutes	245.12 ± 18.19	240.45 ± 19.15	.0624
Volume therapy, mL	1545 ± 180	1595 ± 230	.072
Blood loss during surgery (mL)	95.89 ± 11.32	98.99 ± 13.12	.06
[c]Malondialdehyde level (nM/g)	20.45 ± 5.45[d]	15.34 ± 6.45	<.0001
[c]Superoxide dismutase (U/mg)	0.06 ± 0.009[d]	0.02 ± 0.001	<.0001
Postoperative nausea during the hospital stay	15 (14)	7 (6)	.071
Hospital stay (days)	4 ± 0.5[b]	5 ± 0.4	<.0001

Abbreviations: DEX, dexmedetomidine; NSE, normal saline; SD, standard deviation.
[a]Continuous data are shown as mean ± SD, and categorical data are shown as frequency (percentage). For statistical analysis, Mann-Whitney *U* test was performed for continuous data and Fisher exact test was performed for categorical data. A $P < .05$ was considered significant.
[b]Significantly fewer than NSE group.
[c]Measured 24-hour after surgeries.
[d]Significantly higher than the NSE group.

Akt signaling pathway.[14] Dexmedetomidine, in addition to increasing the plasma BDNF concentration, also increases vascular endothelial growth factor which ultimately serves a positive role in neuroprotection. Dexmedetomidine enhances the BDNF (BDNF4 and BDNF5) transcription and the BDNF protein cortical expression in vivo.[6] Dexmedetomidine can keep stabilizing the BDNF levels during peripheral or emergency neurologic surgeries.

After 24 hours of surgeries, there were significantly fewer levels of cytokine measurements in the DEX group than the

NSE group. Any trauma or injury from surgery may activate the hypothalamic–pituitary–adrenal axis and activates hormone secretion and pro-inflammatory cytokines. Tumor necrosis factor-α and IL-6 are also considered as a mediator of neuroinflammation in the central nervous system.[4] Once the above secretion of inflammation mediators occurs, it may result in nerve cells swelling and necrosis, damaging neurological function. Tumor necrosis factor-α also has some absolute neurotoxic effect.[10,12] A pilot study has shown that DEX was successful in reducing the release of IL-6.[12] The studies have also shown that DEX has reduced the release of TNF-α.[12,15] The results regarding cytokine measurements of the current study were contradicted with the results of a randomized double-blinded trial.[15] Dexmedetomidine not only enhance the BDNF concentration but also cause a reduction in inflammation during peripheral or emergency neurologic surgeries.

The study found that the DEX group patients were more stable as compared to the NSE group patients in terms of their heart rates and the Bispectral index values. The results regarding hemodynamic parameters of the current study were parallel with the results of a double-blind, randomized trial.[7] It is certain that due to the antisympathetic effect of DEX, patients of the DEX group had seen their heart rates and the Bispectral index values to be steady. It had been seen that DEX could revert the reduced the plasma concentration of BDNF which is caused by anesthetics and it lasts for 24 hours after the surgery. This fact needs to be clarified more than whether it can be correlated with the rise in the level of the BDNF.

In addition to these, DEX is found to increase the malondialdehyde level and thus enhance superoxide dismutase activities. During peripheral or emergency neurologic surgeries, there are different noxious and harmful stimuli in the body. From incision itself to exposure of the viscera, all the stimuli affect postoperative healing.[7] Moreover, during surgeries, neural damage is also quite high which is generally impossible to avoid.[5] Superoxide dismutase has strong antioxidation property, and it plays a role in preventing radical injury in the human body.[5,9] Dexmedetomidine may decrease the oxidative stress of the human body due to surgeries.

The dose of intraoperative DEX was kept 1 μg/kg. Dexmedetomidine has little evidence of respiratory depression, especially in the elderly population in nonintubated conditions.[16] So, the dose of DEX kept 1 μg/kg.

In limitations of the study, for example, retrospective analysis, lack of positive control group, and have chances of bias. A large randomized trial is required to state the hypothesis clearly. The clinical outcomes were not analyzed due to the short postoperative period used for analysis. There is a different immune response to surgeries in men and women. Age and the other demographical parameters may have also affected immune responses. Dexmedetomidine also has an effect on postoperative pain and behavioral responses.[15] The effects of sex, age, and the demographical parameters on immune response did not evaluate. Also, clinical and functional recoveries, for example, postoperative pain and behavioral responses, did not evaluate. The study did not compare cognitive scores or neurological status at the discharge of the hospitals.

Conclusions

The study showed the comparison of BDNF, cytokine, and superoxide dismutase levels and hemodynamic parameters between patients receiving intraoperative DEX and those receiving intraoperative NSE as a tool to express neuroprotection in the patients undergoing peripheral or emergency neurologic surgeries with mild-to-moderate brain injury. Patients receiving intraoperative DEX had BDNF returned to baseline (immediately preoperative) at 24 hours after surgery and those receiving NSE had decreased BDNF at 24 hours compared to baseline (immediately preoperative). Intraoperative infusion of DEX can have a neuroprotective role as DEX would be actively involved in anti-inflammatory action and increasing antioxidants like superoxide dismutase. Dexmedetomidine did clinically decrease heart rate values in that group, but it did not result in any hypotensive events. This results in neurogenesis and healing in the central nervous system at the appropriate time. Therefore, DEX may be considered one of the key drugs in patients undergoing peripheral or emergency neurologic surgeries with mild-to-moderate traumatic brain injuries due to trauma.

Authors' Note

All authors read and approved the manuscript for publication. QD was the project administrator, contributed to software, formal analysis, validation, and literature review of the study. XZ contributed to conceptualization, resources, data curation, investigation, and literature review of the study. PC contributed to software and literature review of the study and draft, review, and edited the manuscript for intellectual content. The authors agree to be accountable for all aspects of work ensuring integrity and accuracy. The data sets used and analyzed during the current study available from the corresponding author on reasonable request.

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Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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