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Impact of mode of anesthesia on ischemia modified albumin, operative conditions, and outcome in emergency craniotomies

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ABSTRACT

Background: In neurosurgical procedures, selection of anesthetic techniques can have a substantial role in neurological outcome. Ischemia modified albumin (IMA) is a promising biomarker in strokes either hemorrhagic or ischemic. This work tried to explore the impact of type of the used anesthetics on operative condition, outcome, and if it can affect the level of IMA after emergency craniotomies.

Methodology: Fifty-four patients, 18–69 years of either sex, GCS>8, who underwent emergency craniotomies were enrolled into two groups where anesthesia was maintained by either: isoflurane ≤ 1Mac + fentanyl 1 mcg/kg/h. (Group I (inhalational)) or propofol infusion (100–150 mcg/kg/min) + dexmedetomedine 0.3mcg/kg/h. (Group P (TIVA)). Intraoperative hemodynamics, ICP, brain relaxation score, blood loose, and surgeon satisfaction were assessed. Also, recovery conditions, ICU stay, any complication and mortality, pre- and postoperative IMA and GCS were followed and analyzed.

Results: Group (P) revealed lower but steadier hemodynamics, significantly better brain relaxation score, lower ICP, adequate CPP, fewer patients needed blood transfusion, better surgeon satisfaction, and significantly shorter extubation time with higher sedation. Elevation in postoperative IMA was reported in both groups but the times of increase were significantly lower in group (P) with significant correlation between IMA level and GCS at all times that were detected in both groups. The two groups were comparable regarding postoperative complications, GCS, mortality, and ICU stay.

Conclusion: In emergency craniotomies, the use of TIVA (propofol + dexmetomidine) produced lower ICP, better brain relaxation, and shorter extubation time with lower postoperative IMA level than inhalational anesthetics, which correlate well with GCS.

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1. Introduction

Anesthetic management of patients with traumatic brain injury (TBI) undergoing emergency neurosurgical procedures is crucial for providing neuroprotection with relaxed brain, maintaining adequate cerebral perfusion pressure (CPP), hindering further rise in ICP, and provision of good surgical conditions with rapid, smooth onset and recovery [1].

Providing a balanced anesthesia in neurosurgical varieties become possible with the introduction of safer and rapidly acting intravenous (IV) and inhalational agents [2].

Commonly, inhalational anesthetics induce the reduction of cerebral metabolic rate (CMRO2) and vascular resistance due to their strong cerebral vasodilating property unfortunately, this can cause an increase in cerebral blood flow (CBF) with undesirable raised ICP [3] with a flow-metabolism uncoupling if minimum alveolar concentration (MAC) exceed 1 thus, restricting MAC to 1.0–1.5 is necessary to avoid further deterioration of the brain in patients with elevated ICP [4]. However, easy titration of inhalational agents facilitates preservation of hemodynamic stability [5].

Total Intravenous Anesthesia (TIVA) has increasing popularity in neuroanesthesia as the rapid, short acting used agents like propofol offer rapid emergence, which allows early neurological evaluation; moreover, due to its cerebral vasoconstrictive effect, it helps to circumvent unwanted metabolic and vasodilating actions of inhalational anesthetic [6].

Dexmedetomidine is a pre- and post-synaptic a2-adrenoceptor agonist with distinctive anxiolytic, sedative, analgesic, and anesthetic properties.

Also, there is a raised concern of its ability to maintain the cerebral metabolic to blood flow (CBF) coupling in addition to neuroprotective effect and hemodynamic stability [7,8]. Compared with propofol, it possess shorter arousal time with the suggestion of more beneficial actions of their combined use [9,10].

Ischemia-modified albumin (IMA) is considered as a novel, sensitive biomarker of tissue ischemia. When

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oxygen supply to the tissues decrease, free radicals generate which cause damage of the N-terminus of albumin with the formation of a variant called IMA [11]. Elevated levels after TBI is suggested due to the liberation of reactive oxygen species and is found to have high sensitivity in mortality prediction [12].

Thus, this research hypothesized that as anesthetic agents and technique used in neuroanesthesia can affect the hemodynamics, cerebral blood flow, and metabolic rate thus, it can also affect the level of IMA which is a subtle to any ischemic and oxidative stress conditions; so the current study aimed to search if there is an impact of the type of anesthesia used in emergency craniotomies for mild-to-moderate brain trauma on the level of IMA, which is recently introduced as a specific biomarker of TBI and also on the operative conditions and the outcome with: Primary endpoint was the level of IMA.

Secondary endpoints were intraoperative conditions (e.g., hemodynamics, intracranial pressure (ICP), brain relaxation score (BRS), surgeon satisfaction), postoperative recovery, and clinical outcome (morbidity and mortality) and if there was any correlation between IMA level postoperative Glasgow coma score (GCS).

2. Methodology

After obtaining Institute ethics committee approval (374: 1/2020) and registering with the Clinicaltrials.gov (NCT04490122), we carried out this prospective randomized study in Minia university hospital from MAY 2020 to June 2022 on 54 patients of either sex, age ranging between 18 and 60 years with isolated traumatic brain injuries required emergency craniotomies with Glasgow coma scale (GCS) >8 after gaining informed consent from authorized relative. Those who had polytrauma or isolated extradural hematoma and those who had severe systemic diseases, coagulation disorder, and drug allergy were excluded. Randomization of the recruited patients was performed using computer-generated tables and allocation concealed in sealed envelope (Figure 1) to be opened by the anesthetist in charge just before surgery.

The recruited patients were randomized into two groups:

Group I: where anesthesia was maintained with isoflurane ≤ 1Mac + fentanyl 1 mcg/kg hourly (inhalational group)

Group P: anesthesia was maintained with propofol infusion (100–150 mcg/kg/min) + dexmedetomedine 0.3mcg/kg/h.(TIVA group)

In the emergency department, the patient was fully examined, and vital signs and GCS were assessed. Through suitable caliber peripheral veins, two wide bore intravenous cannulae were inserted and secured, then resuscitation of the patients was accomplished with fluids and vasoconstrictor (if needed) to maintain mean arterial pressure (MAP) above 80 mm Hg with sufficient CPP also CT and emergency investigations were performed.

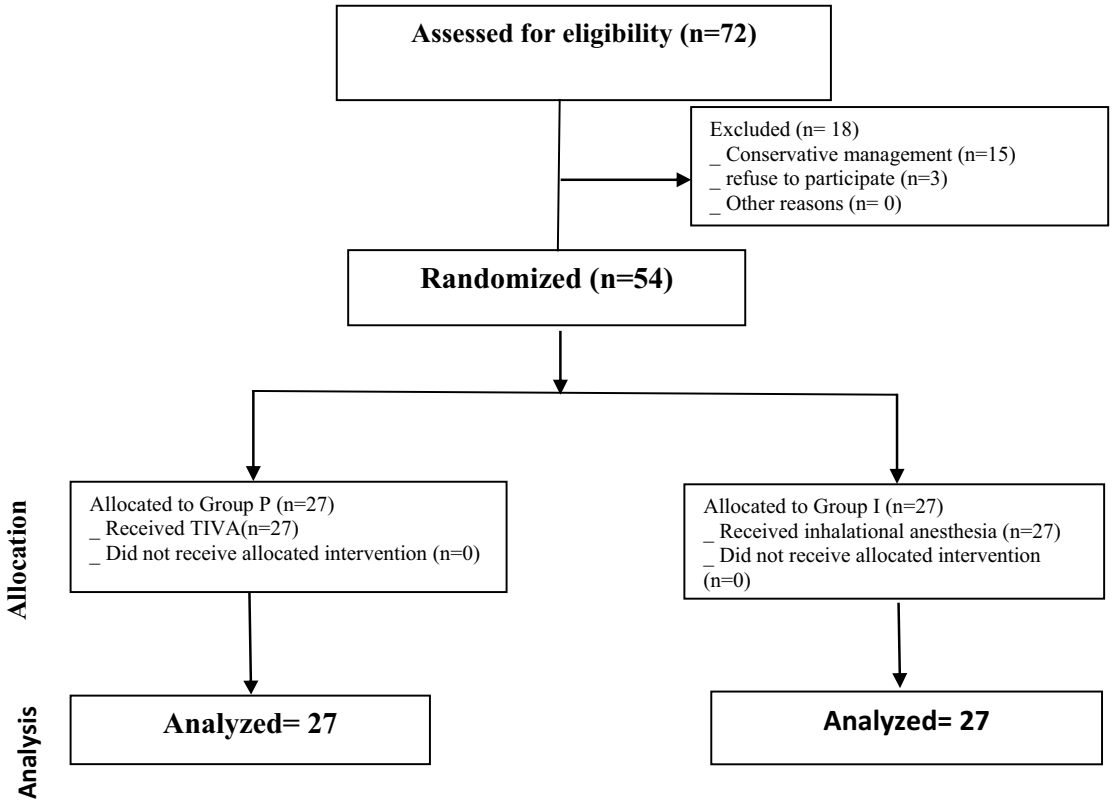

Figure 1. Flow chart.

3. Anesthetic management

On arrival to the operative room, a bedside monitor (NIHON KOHDEN COOPERATION, Tokyo, Japan) with 5 leads-electrocardiogram (ECG), invasive & noninvasive blood pressure (NIBP), Et CO2 and pulse oximetry was applied to the patients, and basal measures were recorded also, first blood sample for IMA was withdrawn at that time simultaneously with re-evaluation of GCS.

Prior to induction of anesthesia, patients of group P received 1 mcg/kg bolus dose of dexmedetomidine (Precedex, Hospira) over 15 minutes through syringe pump. In both groups, after preoxygenation with 100% induction of anesthesia was performed with 2 mcg/kg fentanyl, 1.5–2 mg/kg propofol (Diprivan injectable emulsion, Fresenius Kabi USA), and 0.5 mg/kg atracurium besylate to facilitate intubation, then the patients were gently ventilated for 3 min and intubated with a suitable reinforced cuffed endotracheal tube, connected to mechanical ventilator (Carestation 650- GE-USA) and minute ventilation was modified to preserve an end-tidal CO2 at 28–34 mm Hg with oxygen-air mixture (1:1). Anesthesia was maintained in group I with isoflurane ≤ 1Mac and fentanyl 1 mcg/kg hourly while in group P maintained by propofol 100–150 mcg/kg/min and dexmedetomidine infusion 0.3mcg/kg/h. (infusion was preformed through separate syringe pumps and the rate was precisely titrated according to the vital parameters). Atracurium besylate doses of 0.1 to 0.2 mg/kg were administered for the maintenance of muscle relaxation.

Under complete sterilization, the radial artery of the non-dominant hand was cannulated and zero pressure adjusted for invasive blood pressure monitoring, ABG and all blood samplings. The anesthetic agents were titrated according to the clinical effects and vital parameters. The goals of our intraoperative management protocol were to retain heart rate and blood pressure (BP) within 20% of the baseline value to guarantee adequate CPP, PaO_2 > 100 mmHg, and intracranial pressure (ICP) ≤ 20 mmHg. Thus, if hypotension occurred, it was managed by crystalloids, then anesthetics titration, and lastly by vasopressor, e.g., phenylephrine 100 µg if persistent hypotension was encountered. Symptomatic bradycardia was treated with atropine 0.5 mg i.v. After removal of a bone graft, the surgeon was asked to place a 22 G cannula beneath the dura which was connected through a polyethylene catheter to a pressure transducer and when a stable uninterrupted wave was recorded, intracranial pressure was measured; thereafter, the cannula was withdrawn and opening of the dura was done [13]. On opening the dura, evaluation of the brain relaxation state (BRS) was accomplished using a four-point scale (1 = slack brain, 2 = mild, 3 = moderate, and 4 = severe brain herniation). Another assessment of BRS was performed before closure of the dura [14].

In case the ICP was found high (>22 mmHg), hyperventilation was performed to lower the $EtCO_2$ around 25–28 mm Hg, also mannitol boluses of 0.25–0.5 g/kg could be used if necessary. Intraoperatively, any blood loose was calculated and replaced. About 15 min before the end of the surgery, dexmetomidine was stopped, and near the completion, all anesthetic agents were off, muscle relaxants were reversed with 0.05 mg/kg neostigmine + 0.02 mg/kg atropine, and the patients were extubated. Recovery profile (extubation time (time from reverse administration till tube removal), modified Aldrete score and Ramsay sedation score [15,16]) was recorded then the patients were transported with full monitoring to the surgical intensive care for follow up.

Postoperatively the following parameters were assessed and analyzed:

- GCS at 1 h, 6 h, 24 h, and 48 h postoperatively.

-The other samples for IMA analysis were obtained at 1 h, 6 h, and 24 h and any correlation with GCS level was statistically analyzed.

-Any postoperative complications, length of ICU stay, and mortality.

4. Ischemia modified albumin (IMA) analysis

Blood samples of IMA were centrifuged at 2500 rpm for 20 min and the serum stored at –80°C. IMA was measured using Elisa kit (Human Ischemia modified albumin Elisa kit, Bioassay, China). The kits and samples were warmed to room temperature before use. Samples were added to the reagents and the plate was covered with a scalar then incubated for 1 h at 37°C. The plate was washed 5 times with the wash buffer. The substrate solutions A and B were added to the plate then incubated for 10 min at 37°C in the dark. The stop solution was added where the blue color was changed immediately into yellow. Finally, the optical density (OD value) was determined by a microplate reader within 10 min after adding the stop solution.

5. Statistics

5.1. A-Sample Size

With aid of power calculation of a prior study data [17] where the mean IMA in group S was 0.76±0.09 & in group P was 0.83±0.9, **27** patients was required in each group to offer 80% power for Independent samples T test at 0.05 significance by using G Power 3.1 9.2 software.

5.2. B-Statistical method

IBM SPSS version 25 statistical package software (IBM; Armonk, New York, USA) was used for analysis. Parametric quantitative data were summarized as

mean ± SD and minimum and maximum of range. For non-parametric quantitative data by median (IQR), Number and % were applied for qualitative data.

Independent samples T-test was used to compare parametric quantitative data between the two groups and Mann–Whitney test for non-parametric. Analyses between the two times within each group were performed for parametric quantitative data by paired samples T-test, while the chi-square test was used to compare categorical variables. Pearson's correlation coefficient was used to assess correlations between variables. P-value less than 0.05 was considered statistically significant.

6. Results

Statistical analysis of our data showed that the two studied groups were comparable regarding the demographic parameters and the preoperative CT findings (Table 1).

Mean arterial blood pressure (MAP) and heart rate (HR) showed more stability in (P) group with significantly lower values recorded from 15 min (MAP) and after intubation (HR) and continued inwards. Intragroup comparison, group (P) revealed significant lower MAP and HR values compared to the preoperative (baseline) almost timepoints while swinging recorded in group (I) with significantly lower MAP at 5 and 15 min but significantly higher immediately after intubation, at 30 min and before extubation. Also, HR showed lowering at 15 min and rising after intubation and before extubation (Tables 2 and 3).

Significantly better intracranial pressure (ICP) and brain relaxation scores (BRS) were observed in group (P) than group (I). Also, brain relaxation score [2] at dura closure was significantly better when compared to that at the dura opening [1] (Table 4). The two groups showed normal cerebral perfusion pressure (82 ± 10.5 and 74.1 ± 7.8) that statistically was significantly lower in group (P) actually, it was more ideal (normal CPP range 60–80 mmHg).

Analysis of the other operative data showed significantly higher number of patients required blood transfusion in group (I) (26 Vs 21 *p-value 0.043)* while the amount of bl. transfused, fluid and the need for vasoactive drugs were comparable. The surgeon satisfaction score was significantly better in group (P).

Table 1. Demographic data and preoperative CT findings.

Variable	Group I (N = 27)	Group P (N = 27)	*P-value*
Age (y)	29.8 ± 11.3	31.9 ± 12.8	*0.524*
Mean ± SD			
Sex	23(85.2%)	23(85.2%)	*1*
Male	4(14.8%)	4(14.8%)	
Female			
Weight (kg)	76.3 ± 10.2	78.1 ± 9.5	*0.501*
Mean ± SD			
Height (m)	1.7 ± 0	1.7 ± 0	*0.791*
Mean ± SD			
BMI	26.1 ± 2.7	26.9 ± 2.8	*0.304*
Mean ± SD			
ASA I	25(92.6%)	24(88.9%)	*0.639*
ASA II	2(7.4%)	3(11.1%)	
Preoperative CT findings:			
Fissures:	9(33.3%)	14(51.9%)	*0.169*
Brain edema	22(81.5%)	21(77.8%)	*0.735*
Subdural hematoma (SDH)	7(25.9%)	7(25.9%)	*1*
Subarachnoid hemorrhage (SAH)	5(18.5%)	5(18.5%)	*1*
Midline shift >5 mm	18(66.6%)	17(63%)	*0.239*
Contusion	8(29.6%)	10(37%)	*0.564*
Pneumocephalus	5(18.5%)	4(14.8%)	*0.715*

No significant difference among studied groups (P value >0.05). Data presented as mean ± SD or %.

Table 2. Mean arterial blood pressure (MAP) (mmHg).

Time interval	Group I N = 27	Group D N = 27	*p-value*
Preoperative *Mean ± SD*	92.9 ± 9.7	94.7 ± 10.1	*0.486*
Immediately After intubation	96.8 ± 10.3 #	94.4 ± 8.7	*0.358*
Mean ± SD			
5 min	86.5 ± 11#	85.5 ± 8.4#	*0.708*
15 min	84.6 ± 11.4#	78.9 ± 8.4 #	*0.043**
30 min	98 ± 11.6 #	84.5 ± 8.1 #	*<0.001**
60 min	96.5 ± 11.8	83.7 ± 8.2 #	*<0.001**
90 min	95.6 ± 13	81.3 ± 10.3 #	*<0.001**
Immediately before extubation	103.7 ± 11.5#	94.1 ± 8.8	*0.001**
Mean ± SD			
After extubation *Mean ± SD*	94.5 ± 9.7	85.6 ± 8#	*0.001**

Data presented as mean ± SD *: Significance at P value < 0.05 between the two group. #: Significant between each time with the baseline within the group.

Table 3. Heart rate (beat/min).

Time interval	Group I N = 27	Group D N = 27	*P-value*
Preoperative	99.8 ± 12.3	93.1 ± 16.9	*0.099*
Mean ± SD			
After intubation	109.4 ± 10	93.1 ± 12	***<0.001****
Mean ± SD			
5 min	95.6 ± 8.6	#	***<0.001****
Mean ± SD		81.1 ± 9.3	
15 min	88.5 ± 10.1	#	***<0.001****
Mean ± SD		72.4 ± 7.6	
30 min	106 ± 13.5	#	***<0.001****
Mean ± SD		74.8 ± 7	
60 min	103.4 ± 13.6	#	***<0.001****
Mean ± SD		69.6 ± 6.8	
90 min	103.5 ± 12.5	69.2 ± 6	***<0.001****
Mean ± SD			
Immediate before extubation	113.4 ± 14.7	#	***<0.001****
		80.2 ± 6.5	
After extubation	102.8 ± 10.5	72.4 ± 7.6	***<0.001****
Mean ± SD			

Data presented as mean ± SD *: Significance at P value < 0.05 between the two group. #: Significant between each time with the baseline within the group.

Table 4. Intracranial pressure (ICP), cerebral perfusion pressure (CPP) and brain relaxation score.

Variable	Group I (N = 27)	Group P (N = 27)	P-value
ICP (mm Hg) *Mean ± SD*	19.7 ± 2.5	15.6 ± 3	***<0.001****
CPP (mmHg) at dura opening	82 ± 10.5	74.1 ± 7.8	***0.003****
Brain relaxation score (BRS) at dura opening [1] *Median +IQR*	3	2	
	(2-3)	(1-3)	***0.049****
Brain relaxation score (BRS) at dura closure [2] *Median +IQR*	2	2	***<0.001****
	(2-2)	(1-2)	
P- value (BRS 1 vs 2)	***0.007****	***0.024****	

Data presented as mean ± SD or median + IQR *: Significance at P value < 0.05 between the two group.

Recovery parameters detected significantly shorter extubation time with higher sedation in group(P) but the modified Aldrete score was statistically insignificant. The two groups were comparable regarding the anesthetic and the operative time (Table 5).

Regarding IMA, the two groups showed significant increase in IMA level at all timepoints compared to the preoperative levels; however, the values in group (P) were lower. Comparison between the two groups detected a significantly lower IMA level in group (P) at time of 6 h postoperatively compared to group (I). Analysis of the degree or of increase in each group relative to the baseline showed higher times of elevation in group I with high significance difference when compared to that in group P (Table 6 and Figure 2).

As shown in Table 7, the two studied groups were comparable in terms of GCS, length of ICU stay, postoperative complications, and mortality.

Table 5. Operative and recovery data.

Variable	Group I (N = 27)	Group P (N = 27)	*P-value*
Blood loss (ml)	1337 ± 385.5	1229.6 ± 464.8	**0.478**
Blood Transfusion (%) *No*	1(3.7%)	6(22.2%)	***0.043****
Yes	26(96.3%)	21(77.8%)	
Fluid (ml)	1203.7 ± 346.9	1333.3 ± 392.2	*0.176*
Need for Vasoactive (%) *No*	27(100%)	25(92.6%)	*0.150*
Yes	0(0%)	2(7.4%)	
Surgeon satisfaction Very poor	0(0%)	0(0%)	***<0.001****
Poor	2(7.4%)	0(0%)	
Satisfied	16(59.3%)	1(3.7%)	
Good	8(29.6%)	13(48.1%)	
Excellent	1(3.7%)	13(48.1%)	
Extubation time (min)	12.6 ± 1.7	10.5 ± 2.1	***<0.001****
Modified Aldrete score	12	12	*0.809*
Median ± IQR	(11-12)	(11-12)	
Ramsay sedation score	2	3	***<0.025****
Median ± IQR	(2-3)	(2-3)	
Anesthesia time (min)	176.7 ± 22.7	174.8 ± 34.9	*0.818*
Mean ± SD			
Operative time (min)	143.3 ± 21.3	138 ± 40.5	*0.544*
Mean ± SD			

Data presented as mean ± SD, median ± IQR or % *: Significance at P value < 0.05 between the two groups.

Table 6. Ischemia modified albumin (IMA) level (U/ml).

Time	Group I N = 27	Group p N = 27	*p-value*
Preoperative	86.6 ± 11	87 ± 12.7	*0.902*
Mean ± SD			
1 hrPostoperative	96.5 ± 12.1	#	*0.262*
Mean ± SD		92.6 ± 13.1	
6 hrs.	102.9 ± 11	#	***0.023****
Mean ± SD		95 ± 13.8	
24 hrs.	96.8 ± 12	#	*0.115*
Mean ± SD		91.5 ± 12.3	
Degree of increase in IMA in each group relative to the preoperative level			
1hrPostoperative	(7.9–13.9)	(4.7–8.5)	***<0.001****
Median ± IQR	9.9	6.5	
6 hrs.	(14–25.9)	(6–21.1)	***<0.001****
Median ± IQR	16.7	8.2	
24 hrs.	(4.9–19)	(4.3–6.9)	***0.002****
Median ± IQR	12.2	5.5	

*: Significance at P value < 0.05 between the two group. #: Significant between each time with the baseline within the group.

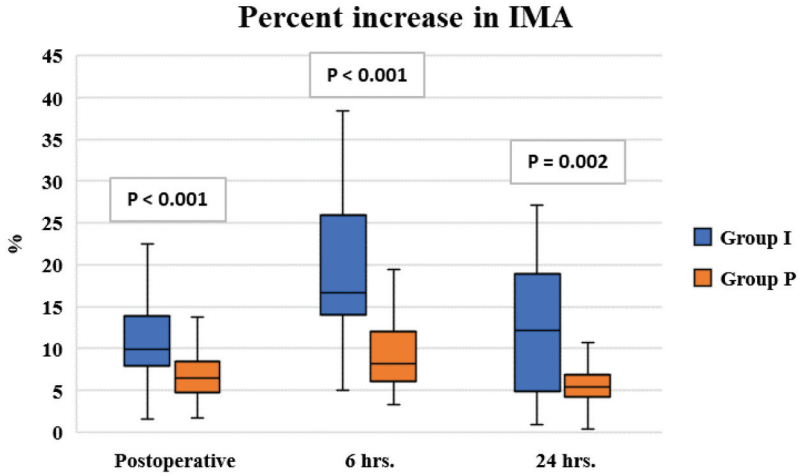

Figure 2. **%** of increase in IMA.

Significantly better GCS was found at 6, 24, and 48 h in comparison with preoperative with intermediate-to-strong correlation between IMA level and GCS (r = *−0.568 in group* ***I***, and *−0.734in group* ***P***, *p-value <0.001**) were detected in both groups (Figure 3).

7. Discussion

Traumatic brain injury (TBI) is frequently and commonly faced in emergency department and is considered the prominent cause of disability and death. Despite wide and successful utilization of inhalational

Table 7. Glasgow coma score (GCS), ICU stay, postoperative complications and mortality.

Variable	Group I (N = 27)	Group P (N = 27)	*P-value*
GCS *(Mean ± SD)*	12 ± 1.6	11.9 ± 1.7	*0.933*
Preoperative			
1h Postoperative	12.1 ± 1.5	12 ± 1.7	*0.730*
6 hrs.	12.5 ± 1.2#	12.4 ± 1.2#	*0.908*
24 hrs.	12.8 ± 0.7#	12.8 ± 0.8	*0.860*
48 hrs.	12.9 ± 0.6#	12.9 ± 0.5#	*0.999*
ICU stay *(Mean ± SD)*	2.1 ± 1.2	2.6 ± 1.6	*0.291*
postoperative Complications (%)	18(66.7%)	19(70.4%)	*0.770*
No	9(33.3%)	8(29.6%)	
Yes			
Ischemia	3(11.1%)	2(7.4%)	*0.639*
Convulsion	3(11.1%)	3(11.1%)	*1*
Pneumocephalus	4(14.8%)	2(7.4%)	*0.386*
Wound infection	1(3.7%)	0(0%)	*0.313*
Bradycardia	0(0%)	2(7.4%)	*0.150*
Recollection	0(0%)	1(3.7%)	*0.313*
Mortality (%)	0(0%)	1(3.7%)	*0.313*

Data presented as mean ± SD or % *: Significance at P value < 0.05 between the two group. #: Significant between each time with the baseline within the group.

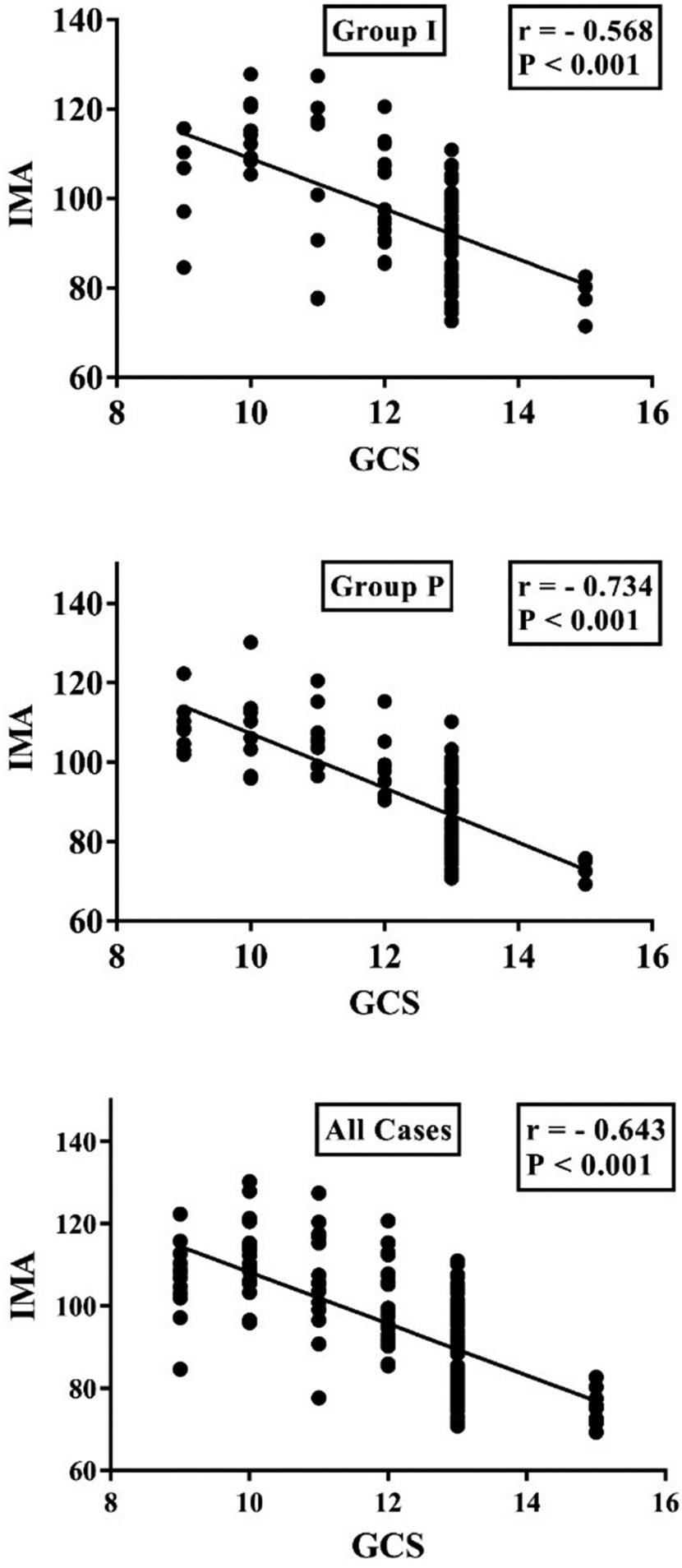

Figure 3. Correlation between IMA level and GCS in both groups.

anesthetics and TIVA in neurosurgeries, there is no clear consensus of the superiority of one over the other or standard proposal for the priority of either technique in these risky circumstances [18].

This research dealt this issue from another aspect which is the impact of using TIVA or inhalational technique on operative conditions and outcome in traumatically injured brain patients also, investigating the suggestion of impact of the type of anesthesia on IMA a biomarker which recently proved to have a prognostic value in TBI. As traumatic brain injuries are usually accompanied with release of oxygen-free radicals due to the associated ischemia, hypoxia, ischemic reperfusion injury thus, these are favorable conditions for IMA generation. To the best of our knowledge, studies concerning the impact of mode of anesthesia on IMA are not available.

Our results showed comparability of the enrolled patients regarding their demographics and preoperative CT findings. Those who received TIVA (group P) had lower but steadier hemodynamics, significantly better brain relaxation score, and lower ICP. Also, significantly lower number of patients needed blood transfusion, better surgeon satisfaction, and shorter extubation time with higher sedation were encountered in those patients who received TIVA. Elevation in postoperative IMA was reported in both groups but the degree of increase was significantly lower in group (P) with significant correlation between IMA level and GCS at all timepoints was detected in both groups. Postoperative complications, GCS, mortality, and ICU stay were comparable.

Maintenance of hemodynamic stability is a major anesthetic goal in these critical neurosurgical procedures which facilitate attainment of optimal (CPP) (60–70 mm of Hg) and reduction of ICP. In this research, hemodynamics were maintained in both groups, but stability was more obvious in TIVA group in most timepoints which was accompanied by a parallel significant lowering of ICP in dura opening with adequate CPP which statistically seems to be significantly lower (74.1 ± 7.8 in TIVA group (P) Vs 82 + 10.5 in group I) but it is in favor of group P as this CPP actually is considered optimal. Also, brain relaxation was significantly better in TIVA group both at dural opening and before dural closure. All these factors provided better operative conditions with lower blood loss although it was statistically insignificant, the number of patients who needed blood transfusion was significantly lower in TIVA group (P), consequently surgeon satisfaction was significantly higher.

In this study, subdural ICP was chosen which is considered by other investigators a good tool of estimating ICP and found it more pertinent than lumbar CSF pressure and explained their opinion that the increasing effect of oedema or space occupying lesion on ICP should be more prominent in subdural assessment due to their close localization moreover, the presence of brain herniation can hinder CSF pathway, thus lumbar CSF pressure would be unreliable [13].

Our results are in accordance with other researchers who reported significantly lower ICP with better brain relaxation in severe TBI patients who were anesthetized by propofol based anesthesia (TIVA) than those received isoflurane; however, they recorded comparability of hemodynamics in both groups and attributed that to their excessive monitoring of hemodynamics and precised fluid replacement to preserve optimal CPP [19].

On contrary, a meta-analysis reported that the beneficial lowering effect on ICP and higher CPP exerted by propofol-maintained anesthesia unfortunately, it was not accompanied by a parallel improvement in operative conditions or brain relaxation, the authors justify this as all the participants of the included studies were undergoing elective supratentorial tumors resection, and had GCS of 15 with normal or slightly raised ICP, thus the effect of propofol on brain relaxation was not expected to be large [20].

In this research, the addition of dexmedetomidine in TIVA group certainly has a pivotal role in exerting the recorded valuable effects specially on hemodynamics as higher grade of stability was recorded; the most important was blunting the increase in HR and Bl.P after intubation which was absent in group I and the ʳise of MAP and HR was obvious at these two critical times. The blunting effect was attributable to the loading dose administered 15 min prior to the induction of anesthesia, also dexometomidine effect was demonstrable at recovery with significant shorter extubating time in calm sedated patients with easy arousability, more hemodynamic stability without respiratory depression .

In addition to anesthetic and analgesic properties, its capability of providing hemodynamic stability, and preserving cerebral homeostasis [8], many recent studies proved protective effect of dexometomidine on vital organs, e.g., brain and heart. Also, it can improve outcome in neuronal injury of various causes as ischemia, hypoxia, anesthetic-induced, oxidative stress, neuroinflammation, and cerebral injury reperfusion injury (CIRI). It exerts these actions through different mechanisms as facilitating transmitters, immune preservation, anti-inflammatory, and anti-apoptotic actions [21,22].

Ischemia-modified albumin (IMA) is a variant of human serum albumin with decreased capability to bind metal ions such as copper. It was originally introduced as an early marker of cardiac ischemia. However, it is found to increase in a number of ischemic conditions which is noncardiac in its origin as D.M., peripheral vascular disease, hemorrhagic strokes, and glaucoma [23,24].

In the current research, we hypothesized that as the anesthetic agents have different effects on cerebral blood flow and metabolic rate (CMRO2), CPP, ICP, and hemodynamics; thus, it can affect the IMA level which is very sensitive to any ischemic or hypoxic conditions. Our results showed that postoperative IMA increased in comparison with the preoperative (baseline);

however, the recorded values were lower in group P compared to group I even the difference was statistically insignificant except at the time of 6 h; however, analysis of the degree of increase in each individual group clarifies the difference as where IMA increased by 6.5, 8.2, and 5.5 times the baseline in group P (TIVA). It increased by 9.9, 16.7, and 12.2 times in group I at the same time intervals. As the demographics and operative circumstances were comparable between the two studied groups, we can suggest that the type of anesthesia had a pivotal role in altering the IMA levels. Although serial sampling for IMA were not available due to financial factors, the selected timepoints were suitable and coincide with the kinetics of IMA that rise within minutes of ischemic insult (which make it valuable in early prediction of ischemia before the occurrence of irreversible necrosis) and remain raised for 6 to 12 h and its normal levels are retained after 24h.

Importantly, the recorded elevation in IMA showed moderate-to-strong correlation with postoperative GCS ($r = 0.568$ *in group* ***I***, and -0.734*in group* ***P*** $p < 0.001$) in both groups which makes IMA a promising biomarker in emergency craniotomies.

Our results are in agreement with earlier study that investigated IMA level after TBI and reported elevated levels of IMA, which correlate with GCS and considered it as a highly sensitive and specific predictor of mortality [12]). Also, significantly elevated IMA levels were detected in cases with cerebral hemorrhage and TBI with an interesting justification of the presence of ischemic or a traumatic "penumbra" [25,26].

In other terms, traumatic injuries can induce regional ischemic areas which enhance the formation of IMA [27].

Finally, the two groups were comparable regarding postoperative complications, ICU stay, and mortality. As noticed in the current research results, the only reported death case was in group P, actually, this patient came to the hospital aspirated with bad general condition and unfortunately suffering postoperative recollection, and aspiration pneumonia which was the leading cause of death after about 25 days of hospitalization.

8. Limitations

This study has several limitations; first, it included mild-to-moderate TBI only (GCS>8) which make the extrapolation of the study results to severe traumatized patients is improper.

Second, the frequency of sampling of IMA was limited to the timepoints reported in the study due to financial causes. Certainly, to investigate the predictive utility of a certain biomarker, larger serial samples are mandatory.

Third, follow up of the patients and neurological outcome was limited to the hospital period; so follow up of 28 days and long-term outcome is recommended for future studies.

9. Conclusion

Mode of anesthesia has an impact on operative conditions, outcome, and IMA levels as the use of TIVA (propofol + dexometomidine) produced lower ICP, better brain relaxation, shorter extubation time than inhalational anesthetic with lower postoperative IMA levels, which correlates well with GCS that can be considered as an important biomarker in TBI.

Disclosure statement

No conflict of interest.

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References

[1] Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury. Neurosurgery. 2017;80(1):6–15. Fourth Edition. Neurosurgery

[2] Kannabiran N, Bidkar PU. Total intravenous anesthesia in neurosurgery. J Neuroanaesthesiol Crit Care. 2018;5 (3):141–149

[3] Prabhakar H, Singh GP, Mahajan C, et al. Intravenous versus inhalational techniques for rapid emergence from anesthesia in patients undergoing brain tumor surgery. Cochrane Database Syst Rev. 2016 9;9(9):1–73.

[4] Sakabe T, Matsumoto M. Effects of anaesthetic agents and other drugs on cerebral blood flow, metabolism and intracranial pressure. In: Cottrell JE, Young WL, editors. Cottrell and young's neuroanaesthesia. 5th ed. Philadelphia: Elsevier; 2010. p. 78–94.

[5] McCulloch TJ, Thompson CL, Turner MJ. A randomized crossover comparison of the effects of propofol and sevoflurane on cerebral hemodynamics during carotid endarterectomy. Anesthesiology. 2007 Jan;106(1):56–64.

[6] Deiner S. Highlights of anesthetic considerations for intraoperative neuromonitoring. Semin Cardiothorac Vasc Anesth. 2010;14(1):51–53.

[7] Kim SY, Kim JM, Lee JH, et al. Efficacy of intraoperative dexmedetomidine infusion on emergence agitation and quality of recovery after nasal surgery. Br J Anaesth. 2013;111(2):222–228.

[8] McAuliffe N, Nicholson S, Rigamonti A, et al. Awake craniotomy using dexmedetomidine and scalp blocks: a retrospective cohort study. Can J Anaesth. 2018;65 (10):1129–1137.

[9] Shen SL, Zheng JY, Zhang J, et al. Comparison of dexmedetomidine and propofol for conscious sedation in awake craniotomy: a prospective, double-blind, randomized, and controlled clinical trial. Ann Pharmacother. 2013;47(11):1391–1399.

[10] Tachibana S, Tanaka S, Yamakage M. Successful anesthetic management using dexmedetomidine sequentially with propofol in the asleep-awake-asleep

technique for elderly patients undergoing awake craniotomy. Case Rep Anesthesiol. 2020 Mar;2020:6795363.
[11] Gunduz A, Turedi S, Mentese A, et al. Ischemia-modified albumin levels in cerebrovascular accidents. Am J Emerg Med. 2008;26(8):874–878.
[12] Radwan TAM, Fahmy RS, El Emady MFM, et al. Ischemia-modified albumin as a biomarker for prediction of poor outcome in patients with traumatic brain injury: an observational cohort study. J Neurosurg Anesthesiol. 2021;33(3):254–257.
[13] Petersen KD, Landsfeldt U, Cold GE, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. Anesthesiology. 2003;98(2):329–336.
[14] Raghava A, Bidkar PU, Prakash MS, et al. Comparison of equiosmolar concentrations of hypertonic saline and mannitol for intraoperative lax brain in patients undergoing craniotomy. Surg Neurol Int. 2015;6(1):73.
[15] Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth. 1995;7(1):89–91.
[16] Riessen R, Pech R, Tränkle P, et al. Comparison of the RAMSAY score and the richmond agitation sedation score for the measurement of sedation depth. Crit Care. 2012;16(1):326.
[17] Erturk E, Topaloglu S, Dohman D, et al. The comparison of the effects of sevoflurane inhalation anesthesia and intravenous propofol anesthesia on oxidative stress in one lung ventilation. Biomed Res Int. 2014;360936:1–4.
[18] Hassan WMNW, Nasir YM, Zaini RHM. Shukeri WFWM. target controlled infusion propofol versus sevoflurane anaesthesia for emergency traumatic brain surgery: comparison of the outcomes.malays. J Med Sci. 2017;24:73–82.
[19] Preethi J, Bidkar PU, Cherian A, et al. Comparison of total intravenous anesthesia vs. inhalational anesthesia on brain relaxation, intracranial pressure, and hemodynamics in patients with acute subdural hematoma undergoing emergency craniotomy: a randomized control trial. Eur J Trauma Emerg Surg. 2021;47(3):831–837.
[20] Chui J, Mariappan R, Mehta J, et al. Comparaison entre propofol et agents volatils pour le maintien de l'anesthésie pendant les interventions de craniotomie non urgentes : revue méthodique et méta-analyse. Can J Anaesth. 2014;61(4):347–356.
[21] Li F, Wang X, Deng Z, et al. Dexmedetomidine reduces oxidative stress and provides neuroprotection in a model of traumatic brain injury via the PGC-1α signaling pathway. Neuropeptides. 2018;72:58–64.
[22] Li J, Xiong M, Nadavaluru PR, et al. Dexmedetomidine attenuates neurotoxicity induced by prenatal propofol exposure. J Neurosurg Anesthesiol. 2016;28(1):51–64.
[23] Unchiti K, Leurcharusmee P, Samerchua A, et al. The potential role of dexmedetomidine on neuroprotection and its possible mechanisms: evidence from in vitro and in vivo studies. Eur J Neurosci. 2021;54(9):7006–7047.
[24] Kara I, Pampal HK, Yildirim F, et al. Role of ischemic modified albumin in the early diagnosis of increased intracranial pressure and brain death. Bratisl Lek Listy. 2017;118(2):112–117.
[25] Abboud H, Labreuche J, Meseguer E, et al. Ischemia-modified albumin in acute stroke. Cerebrovasc Dis. 2007;23(2–3):216–220.
[26] H-M W, Huang S-C, Vespa P, et al. Redefining the pericontusional penumbra following traumatic brain injury: evidence of deteriorating metabolic derangements based on positron emission tomography. J Neurotrauma. 2013;30(5):352–360.
[27] Colak T, Duman C, Bamaç B, et al. Ischemia modified albumin levels following mild closed head trauma in the rat. Turkiye Klinikleri J Med Sci. 2010;30(4):1171–1176