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ORIGINAL ARTICLE

Effect of Dexmedetomidine Versus Propofol Sedation on the Cerebral Blood Flow Velocity and Cerebral Metabolic Rate of Oxygen in Patients with Traumatic Brain Injury

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ABSTRACT

Background: Every year, Traumatic brain injury (TBI) affects people all over the world in a significant way. In the treatment of TBI, sedatives are employed as neuroprotectors to lower intracranial pressure (ICP) and the cerebral metabolic rate of oxygen (CMRO2).
The aim of the work was to compare the efficacy of dexmedetomidine versus propofol in TBI patients regarding the cerebral blood flow velocity (CBFV), CMRO2 and 28-day mortality.
Methods: This prospective clinical double-blinded randomized study was conducted on 72 patients with TBI. The patients were allocated equally into group D (dexmedetomidine), group P (propofol) and given sedation for 48hrs. Richmond Agitation-Sedation Scale was used for assessment of sedation level. Jugular venous bulb oxygen saturation (SjVO2) and transcranial Doppler measurements of middle cerebral artery (MCA) flow velocity and diameter(d) were recorded at admission, 6 hr, 12hr, 24hr and 48hr.
Results: Both dexmedetomidine and propofol are comparable for managing TBI. There was a significant reduction in cerebral perfusion pressure (CPP) and CMRO2 in each group, but CBF showed an increase with both sedatives. Propofol exhibited a more increase in CBFV. However, neither sedative significantly affected ICP nor 28-mortality rate.
Conclusions: In patients with TBI, dexmedetomidine and propofol sedative agents showed comparable effect on mean arterial pressure (MAP), ICP, CPP, CBF, CMRO2 and mortality rate but HR and mean flow velocity (MFV) were significantly less with dexmedetomidine than propofol. While both sedatives decrease MAP, HR, CPP, CMRO2 and MCA diameter and increase MFV, CBF and SjVO2 when compared to admission values.
Keywords: Dexmedetomidine; Propofol; Traumatic brain injury; Cerebral metabolic rate of oxygen.

INTRODUCTION

TBI primarily affects young, otherwise healthy people and is a leading cause of death and disability among those between the ages of 1 and 44 [1].
Sedative agents play a crucial role in TBI in need of mechanical ventilation, which helps prevent hypoxia and hypercarbia, and reduces the CMRO2, thereby lowering ICP [2].
Over time, various sedative agents have been investigated for use in ICU for TBI patients. Opioids proved effective for pain relief; their sedative doses were associated with high rates of side effects [3].

The most often utilized sedatives in ICU have been benzodiazepines like midazolam and gamma-aminobutyric acid (GABA) receptor agonists, such as propofol.
[4].
Propofol is a widely used sedative-hypnotic anesthetic. Studies have highlighted its beneficial impact on brain hemodynamics, including reducing ICP, CBF, and metabolism while maintaining CPP and MAP. This combination of effects makes propofol neuroprotective during cerebral ischemia [5].
Dexmedetomidine, an α2 adrenergic agonist, is another sedative with several advantages, such as reducing sympathetic activity, providing analgesia, and maintaining patient arousability. It showed a neuroprotective effect in animal studies of TBI by inhibiting cell death, reducing brain tissue damage, axonal injury, and synaptic degeneration [6].
Neuromonitoring is essential in the management of patients in ICU. SjvO2 provides an indirect assessment of cerebral oxygenation and early indications of ischemia from both intracranial and systemic causes [7].
Transcranial Doppler (TCD) is a cost-effective, non-invasive bedside technique which evaluates cerebral hemodynamics by directly visualizing cerebral vessels and assessing flow velocity. This method can be used to calculate ICP, CPP and CMRO2 [8].
Therefore, our study sought to evaluate the impact of using dexmedetomidine versus propofol as neuroprotective sedative agent in TBI.
The primary outcome aimed to assess CBFV to calculate CPP and ICP. While the secondary outcome was assessment of MAP, HR, SjvO2, SaO2, CBF, CMRO2 and mortality rate.

METHODS

Study design
This double-blinded randomized clinical study was done in ICU of Anesthesia, Intensive Care and Pain Management Department, Zagazig University Hospitals from June 2023 to September 2024.
Sample size: Assuming the mean CPP was 54.6 ±1 mmHg vs 53.9±1.1 mmHg, in dexmedetomidine vs propofol group **(Farag et al.,2017)** [9]. At 80% power and 95% CI. The calculated sample was 72 cases divided into 2 equal groups,36 cases in each group, Open Epi Info was used to determine the sample size.
Ethical approval: This study had the approval of the Institution Review Board (IRB) at Zagazig University (Nb:10642) on 29-3-2023. Also, approved from Anesthesia, ICU and Pain Management Department of Zagazig University. Scientific committee obtained patients or first-degree relatives' written consent. The World Medical Association's Code of Ethics (Declaration of Helsinki) was used to conduct this study in human research.
Inclusion criteria:
Gender: both Male and female., Age: 18 - 60 years., Body mass index ≤35 Kg/m2., American Society of Anesthesiologists (ASA) I - I I I and head trauma., Moderate to severe TBI patients diagnosed by CT operated or on conservative treatment.
Exclusion criteria:
We excluded cases with atrioventricular (AV) block with HR under 45, a history of cardiac failure with an ejection fraction below 30%, severe hemodynamic instability prior to admission, known allergies to dexmedetomidine or propofol, pregnancy, severe hepatic disease, elevated creatinine above 2 mg%, or any condition that interferes with the use of a TCD probe like craniotemporal lesions, lacerations, hematomas and thick hair.
Withdrawal criteria:
Patients' first-degree relatives had the ability to withdraw from the research without affecting their medical or surgical treatment plans.
Upon ICU admission, a comprehensive assessment was conducted for each patient. This included taking a detailed medical and surgical history, continuous monitoring of vital signs such as HR, MAP, ECG, oxygen saturation (SpO2) and ensuring adequate resuscitation. Additionally, blood samples were taken to assess serum glucose levels, liver function, serum creatinine, INR, and complete blood count. HR and MAP were monitored continuously but recorded at admission, 6hr, 12hr, 24hr and 48hr.
Seventy-two patients were allocated randomly using a computer-generated table into two equal groups (36 patients for each group):
Group D : Dexmedetomidine was delivered as a loading dosage of 1 mcg/kg over 10 min, then followed by a maintenance dose of 0.5 mcg/kg/hr. for 48 hours.
Group P : Propofol was administered as a loading dosage of 1 mg/kg over 5 min, then a maintenance dose of 0.5 mg/kg/hr. for 48 hours. [10]
Each syringe and its extension tube were wrapped in opaque medical adhesive tape for fully concealing the liquid inside.

A jugular venous bulb catheter was placed and serial SjvO2 samples were obtained. In addition, arterial cannulation was employed to measure arterial oxygen saturation (SaO2), partial pressure of arterial CO2(PaCO2) and partial pressure of arterial oxygen (PaO2).

All parameters (SjvO2, PaO2, PaCO2, SaO2) were recorded at admission, 6hr, 12hr, 24hr and 48hr.

Sedation was adjusted to reach a Richmond Agitation-Sedation Scale (RASS) [11] score of -1 to -2, with evaluations done at admission, 10 minutes, 1 hour, and every 6 hours.

TCD by using (Siemens Acuson X300 Ultrasound Machine, Germany) on MCA through trans temporal window was performed. Various parameters were measured, including peak systolic velocity (PSV) and end diastolic velocity (EDV), while mean flow velocity (MFV) and Pulsatility index (PI) calculated via equation: MFV = [PSV + (EDV × 2)] /3 [12], PI=(PSV–EDV)/MFV [13]. Also, MCA diameter(d=mm) was measured. Non-invasive ICP and non-invasive CPP were calculated using established formulas: nICP(mmHg)=(10.93×PI)-1.28[14], nCPP(mmHg)= MAP×(EDV/MFV) +14[15]. Furthermore, cerebral blood flow volume (CBF) was calculated: CBF (ml blood/min) =MFV×$(d/2)^2$ [16] and the oxygen extraction ratio (OER) as: OER=(SaO2−SjvO2)/SaO2[16]. Then, arterial oxygen content was calculated: CaO2(ml O2/dl) = (SaO2* Hb* 1.39) + (PaO2 x 0.003) [17], where Hb(gm/dl) is the hemoglobin concentration. Lately we calculated cerebral metabolic rate of oxygen: CMRO2(ml O2/dl) =CBF×OER×CaO2[16].

All parameters (PSV, EDV, MFV, PI, ICP, CPP, MCA diameter, OER, CaO2, CBF, CMRO2 were recorded at admission, 6 hr, 12hr, 24hr and 48hr. The patients were followed up for 28 days to record a 28-day mortality rate.

Statistical analysis:

The statistical software SPSS version 27 was used for all analysis. The Shiparo-Wilk and Kolmogorov-Smirnov tests were employed to determine normality. Mean and standard deviation were used to represent normally distributed continuous data, and an independent sample T-test was used to compare continuous data between groups. For continuous data with a non-normal distribution, the median and interquartile range were presented. The Kruskal-Wallis test, followed by Mann-Whitney, was applied to compare non-normally distributed continuous data between groups. Categorical data was displayed as events and percentages, and categorical data were compared between two groups via Chi-square or Fisher Exact tests. Furthermore, a generic linear model was employed to assess repeated observations of data that is normally distributed.

RESULTS

From June 2023 to February 2024, eighty-three individuals who had TBI were evaluated for enrollment into this research in the ICU of the Anesthesia, Intensive Care, and Pain Management Department at Zagazig University Hospital. Eleven individuals were eliminated from the trial (5 refused consent and 6 did not match the inclusion standards), whereas 72 case with TBI agreed to participate and were randomly assigned to propofol group (n=36) and dexmedetomidine group (n=36) **(figure 1).**

The average age of included patients was 38.5±3.24 years old. Most of them were men. Additionally, the mean Glasgow Coma Scale (GCS) was 6.28±1.16 in group P and 6.53±1.23 in group D. Most of the patients had an ASA grade I. There were non-significant differences between the two groups in terms of patient features at admission. (**Table 1**).

The MAP was not significantly different between the two groups. While the MAP showed a significant decrease at all time points in each group when compared to at admission values **(figure 2)**.

Dexmedetomidine significantly decreases HR more than propofol at intervals from 6hr to 48hr. In addition, both drugs significantly reduce HR with a more reduction in group D than at admission values **(figure 3)**.

This study demonstrated significant increases in PSV, EDV, and MFV in both groups with a more increase in propofol group. **(Table 2).**

In terms of PI, no significant difference was observed between the two sedatives. Furthermore, there was no noticeable change in ICP when comparing the two sedatives. **(table 2).**

Additionally, CPP showed no significant difference between the two sedatives. Conversely, both groups showed a significant reduction in CPP at 6, 12, 24, and 48 hours when compared to their values at admission. **(table 3).**

Regarding MCA diameter, both groups showed a significant decrease. Conversely, CBF increased significantly with both sedatives **(table 3).**

Arterial O2 saturation remained unaffected by either sedative, indicating no significant impact on oxygen delivery. However, a notable difference between the

two groups was observed in Sjvo2 at 6, 12 and 48hrs. Sjvo2 was significantly lower in group D than in group P. The two sedatives' effects on CMRO2 were not statistically different. However, CMRO2 levels in each group at 6 hours were significantly lower than those upon admission. **(table 4).**

The 28-day mortality rate was higher in group P (11.1%) than in group D (8.3%) but without significant difference **(table 1).**

Table (1): Patients characteristics data at admission, Glasgow Coma Scale and 28-day mortality rate.

		Group P (N=36) mean±SD		Group D (N=36) mean±SD		P value
Age(years)		38.25±3.24		39.40±2.90		0.117
BMI(kg/m2)		26.27±2.49		27.26±6.62		0.4
Random blood sugar (RBS)(mg/dL)		103.37±23.52		105.91±23.25		0.64
Gender		N	%		N	%
Male		30	83.3%	29	80.6%	0.759
Female		6	16.67%	7	19.4%	
Glasgow Coma Scale (GCS)		6.28	1.16	6.53	1.23	0.37
ASA status+ T(trauma)		**N**	**%**	**N**	**%**	
I		20	55.6%	21	58.3%	0.83
II		14	38.9%	12	33.3%	
III		2	5.6%	3	8.3%	
28-day mortality	No	32	88.9%	33	91.7%	
	Yes	4	11.1%	3	8.3%	0.99

(Data expressed as mean±SD or %. P value <0.05 is considered significant).

Table (2): Effect of Propofol or Dexmedetomidine Sedation on peak systolic velocity, end diastolic velocity, mean flow velocity and Pulsatility index.

Parameter (Cm/second)	Time	Group P (Mean ± SD)	Group D (Mean ± SD)	P value	P1	P2
PSV(peak systolic velocity)	Admission	55.85 ± 4.20	52.99 ± 4.09	0.26		
	1 hour	75.82 ± 4.50	67.54 ± 3.70	**0.000**		
	6 hours	76.64 ± 4.30	66.54 ± 4.50	**0.000**	**0.000**	**0.000**
	12 hours	77.65 ± 4.40	65.64 ± 3.30	**0.000**	**0.000**	**0.000**
	24 hours	77.60 ± 4.50	67.46 ± 4.40	**0.000**	**0.000**	**0.000**
	48 hours	72.64 ± 4.31	68.50 ± 2.86	**0.000**	**0.000**	**0.000**
EDV(end diastolic velocity)	Admission	25.31 ± 2.20	22.80 ± 2.90	0.70		
	1 hour	35.19 ± 4.20	29.50 ± 4.10	**0.01**		
	6 hours	35.19 ± 4.20	29.60 ± 4.30	**0.01**	**0.000**	**0.000**
	12 hours	34.99 ± 3.60	29.64 ± 4.25	**0.01**	**0.000**	**0.000**
	24 hours	36.12 ± 3.90	28.73 ± 4.50	**0.000**	**0.000**	**0.000**
	48 hours	36.25 ± 4.40	30.88 ± 3.60	**0.04**	**0.000**	**0.000**
MFV(mean flow velocity)	Admission	34.50 ± 2.30	32.10 ± 2.10	**0.03**		
	1 hour	48.70 ± 3.00	42.80 ± 3.20	**0.000**		
	6 hours	48.60 ± 3.10	42.60 ± 3.35	**0.000**	**0.000**	**0.000**
	12 hours	48.90 ± 2.95	42.40 ± 3.00	**0.000**	**0.000**	**0.000**
	24 hours	49.50 ± 3.35	43.00 ± 3.10	**0.000**	**0.000**	**0.000**
	48 hours	49.30 ± 3.30	43.50 ± 3.90	**0.001**	**0.000**	**0.000**

Parameter (Cm/second)	Time	Group P (Mean ± SD)	Group D (Mean ± SD)	P value	P1	P2
Pulsatility index (PI)	at admission	1.05 ±0.16	1.03±0.16	0.55		
	6hr	1.08 ±0.14	1.09±0.17	0.66	0.427	0.151
	12hr	0.99 ±0.23	1.06±0.18	0.13	0.230	0.483
	24hr	0.97 ±0.22	1.04±0.16	0.38	0.101	0.803
	48hr	1.11 ±0.26	1.05±0.18	0.17	0.270	0.640

Data expressed as mean±SD or %. P value <0.05 is considered significant. P value indicate the statistical difference between both groups. P1: indicate the statistical difference between values 6,12,24 and 48 hours to that at admission in group P. P2: indicate the statistical difference between values 6,12,24 and 48 hours to that at admission in group D.

Table (3): Effect of propofol or dexmedetomidine sedation on noninvasive intracerebral pressure (nICP), noninvasive cerebral perfusion pressure (nCPP), middle cerebral artery (MCA) diameter and cerebral blood flow (CBF) in patients with TBI.

Parameter	Time	Group P (Mean ± SD)	Group D (Mean ± SD)	P value	P1	P2
nICP(mmHg)	at admission	10.08±1.65	9.84±1.67	0.56		
	6hr	10.36±1.39	10.44±1.86	0.65	1.000	0.45
	12hr	9.40±2.44	10.21±1.96	0.13	0.178	1.000
	24hr	9.36±2.42	9.82±1.97	0.38	0.223	1.000
	48hr	10.76±2.78	9.98±1.91	0.17	0.248	1.000
nCPP(mmHg)	at admission	83.65±11.98	81.22±10.39	0.612		
	6hr	65.89±9.15	68.47±11.47	0.560	**0.000**	**0.002**
	12hr	58.26±11.37	61.13±12.78	0.578	**0.000**	**0.000**
	24hr	56.29±13.27	57.31±12.53	0.853	**0.000**	**0.000**
	48hr	58.23±15.63	58.71±12.93	0.937	**0.000**	**0.000**
MCA diameter (mm)	at admission	4.38±0.55	4.31±0.55	0.769		
	6hr	4.16±0.56	4.11±0.55	0.828	**0.000**	**0.000**
	12hr	4.01±0.52	3.98±0.47	0.903	**0.000**	**0.000**
	24hr	4.00±0.49	3.89±0.45	0.578	**0.000**	**0.000**
	48hr	3.94±0.52	3.81±0.50	0.532	**0.000**	**0.000**
CBF (ml/min)	at admission	279.43±63.37	274.04±65.66	0.840		
	6hr	482.34±155.34	439.70±142.51	0.491	**0.000**	**0.001**
	12hr	523.14±190.56	481.37±198.09	0.604	**0.001**	**0.005**
	24hr	548.79±214.56	491.13±187.19	0.490	**0.000**	**0.005**
	48hr	536.23±197.99	476.45±180.62	0.448	**0.000**	**0.005**

Data expressed as mean±SD or %. P value <0.05 is considered significant. P value indicate the statistical difference between both groups. P1: indicate the statistical difference between values 6,12,24 and 48 hours to that at admission in group P. P2: indicate the statistical difference between values 6,12,24 and 48 hours to that at admission in group D.

Table (4): Effect of propofol or dexmedetomidine sedation on Sjvo2, SaO2, OER and CMRO2 in patients with TBI.

Parameter	Time	Group P (Mean ± SD)	Group D (Mean ± SD)	P value	P1	P2
SjvO2(%)	at admission	51.06 ± 10.51	51.28 ± 9.34	0.95		
	6hr	75.59 ± 3.93	69.96 ± 5.21	0.01	**0.000**	**0.000**
	12hr	76.81 ± 2.71	73.16 ± 3.76	0.01	**0.000**	**0.000**
	24hr	75.24 ± 2.92	73.01 ± 4.18	0.27	**0.000**	**0.000**
	48hr	75.64 ± 4.49	71.50 ± 3.53	0.04	**0.000**	**0.000**
SaO2(%)	at admission	97.2 ± 1.60	97.1 ± 1.70	0.80		
	6hr	97.2 ± 1.72	97 ± 1.75	0.85	1.000	0.817
	12hr	97.1 ± 1.64	97 ± 1.70	0.95	0.080	0.814
	24hr	97 ± 1.61	96.9 ± 1.78	0.90	0.061	0.647
	48hr	97.1 ± 1.42	96.9 ± 1.65	0.85	0.792	0.634
OER	at admission	0.47 ± 0.11	0.46 ± 0.11	0.717		
	6hr	0.22 ± 0.05	0.25 ± 0.05	0.219	**0.000**	**0.000**
	12hr	0.21 ± 0.03	0.23 ± 0.04	0.560	**0.000**	**0.000**
	24hr	0.23 ± 0.04	0.23 ± 0.04	0.836	**0.000**	**0.000**
	48hr	0.22 ± 0.05	0.23 ± 0.05	0.643	**0.000**	**0.000**
CMRO2(ml/min)	at admission	22.52±7.36	21.77±7.10	0.662		
	6hr	17.88±6.06	18.45±6.36	0.701	**0.001**	**0.032**
	12hr	18.59±6.97	18.44±8.12	0.932	0.119	0.318
	24hr	20.66±7.51	20.30±9.71	0.861	1.000	1.000
	48hr	20.33±8.37	18.88±7.37	0.438	1.000	0.532

Data expressed as mean±SD or %. P value <0.05 is considered significant. P value indicates the statistical difference between both groups. P1: indicate the statistical difference between values 6,12,24 and 48 hours to that at admission in group P. P2: indicate the statistical difference between values 6,12,24 and 48 hours to that at admission in group D.

*Sjvo2: jugular venous bulb oxygen saturation SaO2: arterial oxygen saturation,
OER: oxygen extraction ratio, CMRO2: cerebral metabolic rate of oxygen

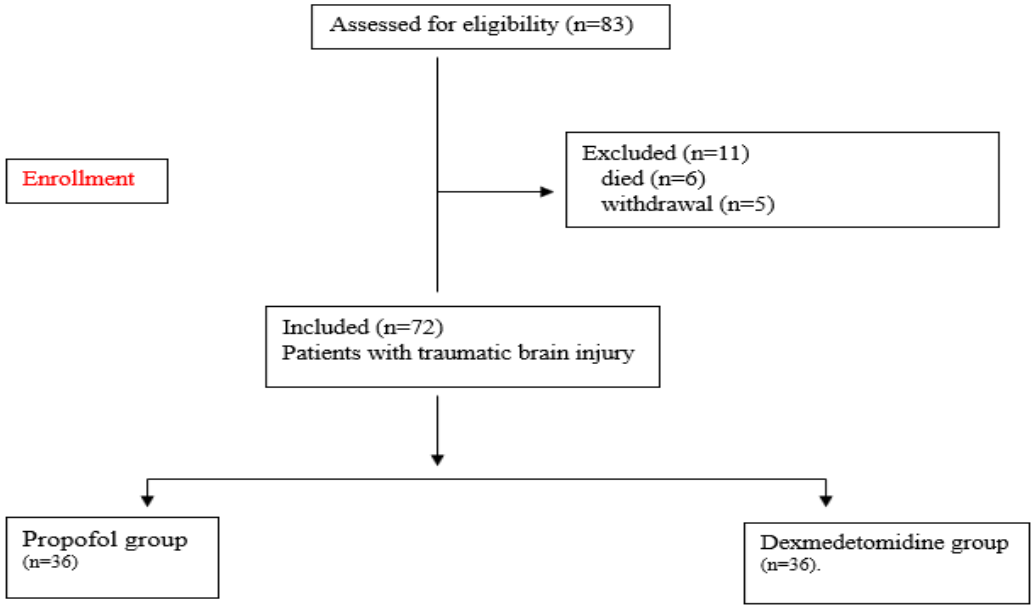

Figure (1): Flow chart of patients with traumatic brain injury.

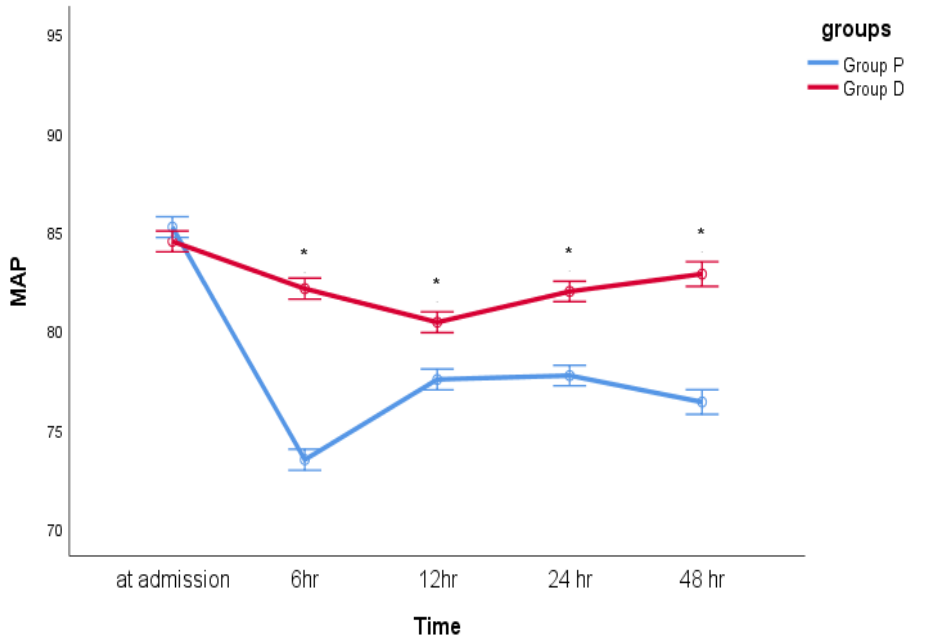

Figure (2): line chart for effect of propofol or dexmedetomidine sedation on mean arterial pressure (MAP) in patients with TBI.

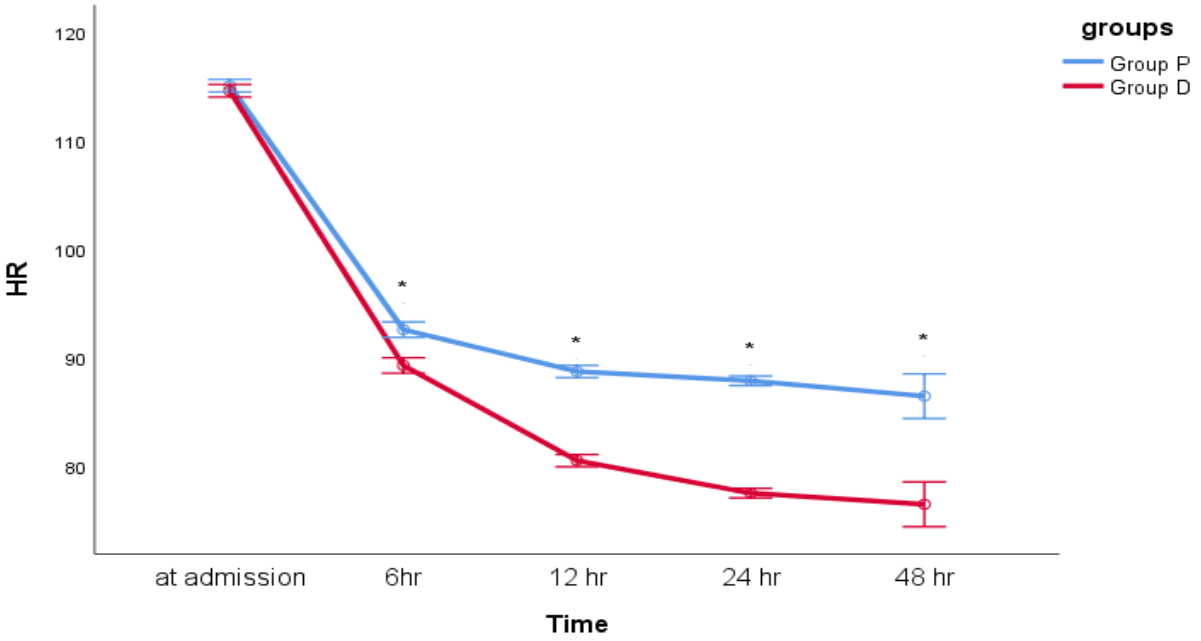

Figure (3): line chart for effect of propofol or dexmedetomidine sedation on heart rate (HR) in patients with TBI.

DISCUSSION

In this study, the MAP showed a decrease with both propofol and dexmedetomidine but without significant difference between both sedatives. This finding aligns with previous research done by Khallaf et al. [2] who investigated the effects of propofol and dexmedetomidine sedation on Sixty TBI patients and observed non-significant difference in MAP.

However, Tarabrin et al. [18] compared dexmedetomidine and propofol in 84 mechanically ventilated TBI patients found that patients on dexmedetomidine had a significant lower MAP at various time points (e.g., 90 and 180 minutes) compared to the propofol group which contradicts with our study. This difference may be attributed to Tarabrin et al. used a higher dose of dexmedetomidine (1.4- 5mcg/kg/hr) but in our study 0.5mcg/kg/hr. In addition, that study monitored the effect of sedatives on a shorter period than ours that was 48hrs. Also, Hao et al. [19] who studied the efficacy of dexmedetomidine and propofol on 90 patients with moderate and severe TBI revealed that the dexmedetomidine's MAP was noticeably lower than the propofol group. This contrast may be attributed to that some patients in their study who achieved poor sedation efficacy received a bolus injection of either morphine or pethidine which may be attributed to make these results not match with our results.

The HR showed a significant decrease in each group upon time of sedation meaning that both sedatives lower HR, but dexmedetomidine had a more significant reduction than propofol from 6hrs to 48hrs. Agreeing with this, Tarabrin et al. [18] found that both propofol and dexmedetomidine reduce HR in TBI patients under mechanical ventilation, with dexmedetomidine resulting in a more pronounced HR reduction over time. After 180 minutes, the dexmedetomidine group's heart rate (75 beats per minute) was far lower than the propofol group's (86 beats per minute). However, Hunt et al. [20] examined 83 TBI patients who were given either propofol or dexmedetomidine lasting over 6 hours and found no statistically significant variation in heart rate between the two sedatives. This contrast may be attributed to the inclusion of a larger number of patients than ours that was 72 patients. Also, longer duration of follow up may be considered as propofol group and dexmedetomidine group recorded a range of (24-153) and (33-267) hours comparatively to 48hrs in our study. Also, some patients received additive sedatives for the management of their sedation.

Our study revealed that Propofol exhibited considerably greater PSV, EDV, and MFV than dexmedetomidine from 6 to 48 hours, with both groups showing a significant increase throughout the sedation period compared to admission values.

In addition, there was a significant decrease in MCA diameter with both propofol and dexmedetomidine upon all time of infusion which indicated the cerebral vasoconstrictive effect of both sedatives which may explain the increase in flow velocities which aligns with Bauerschmidt et al. [21] who reviewed cerebral vasoconstrictive effect of both propofol and dexmedetomidine.

In contrast, Steiner et al. [22] investigated how increasing propofol plasma concentrations affects pressure autoregulation in ten patients with head injuries using target-controlled infusions. It concluded that flow velocity in MCA at high propofol plasma levels (6-8 mg/kg/hr) was significantly less than moderate concentration (3-4 mg/kg/hr). That contrast may be attributed to the use of larger doses than in our study (0.5mg/kg/hr).

Also, Arulvelan et al. [23], studied 30 normal individuals. The cerebral hemodynamic indicators were evaluated using the MCA flow velocity via TCD. Bilateral MFV and PI measurements were made at baseline and 10 minutes after receiving a shot of dexmedetomidine at a dosage of 1 mcg/kg. Following dexmedetomidine infusion, MFV dramatically reduced in both hemispheres ($P < 0.05$), but PI values significantly increased. That contrast may be attributed to different types of population who were free of intracranial pathology. Also, the shorter duration of follow up (10 min) than our study (48 hr).

Furthermore, Ludbrook et al. [24] studied Seven patients admitted for orthopedic operation and MCA flow velocity were measured at induction with propofol. The use of propofol caused a significant reduction in MCA velocity. That contrast may be due to different methods as that study investigated propofol in non-traumatized patients and as anesthesia for short time during induction.

In our study, there was not a significant variation between dexmedetomidine and propofol regarding the pulsatility index (PI). Additionally, there was not a significant variation between the two groups' ICPs. Agreeing with, Khallaf et al.[2]

who compared the efficacy of propofol and dexmedetomidine in 60 head injured patients and observed non-significant difference over 48hrs of study regarding ICP. Also, Grille et al. [25] studied dexmedetomidine impact on twelve severe TBI patients and found non-significant differences between the values of ICP after drug infusion in relation to the baseline values.
In contrast, **Aryan et al.** [26] obtained data of 39 patients who underwent neurosurgeries and later on received dexmedetomidine in ICU and found that the mean ICP decreased. This contrast may be attributed to different population as percentage of patients with head trauma included in was only (31%).

In this study, the CPP showed a significant decrease with propofol and dexmedetomidine in each group separately at 6, 12, 24 and 48 hrs when compared to at admission values. While there was non-significant difference between either propofol or dexmedetomidine groups. This agrees with Khallaf et al. [2] who compared the efficacy of propofol and dexmedetomidine in 60 head injured patients and observed non-significant difference in CPP over 48hrs of study. Additionally, after administering a loading dose of dexmedetomidine to 30 patients who did not exhibit any cerebral pathology, Arulvelan et al. [23] discovered that CPP values were considerably lower in both hemispheres ($P < 0.05$) following dexmedetomidine infusion.
However, Aryan et al. [26] obtained data of 39 patients who underwent neurosurgeries and later on received dexmedetomidine in ICU and found that when dexmedetomidine was given, the mean ICP decreased and the CPP slightly increased. This contrast may be attributed to different population as percentage of patients with head trauma included in was only (31%).

In our study, both sedatives increased CBF at 6, 12, 24, and 48 hours compared to admission. While there was no significant variation between either groups. Aryan et al.[26] obtained data of 39 patients who underwent neurosurgeries and later on received dexmedetomidine in ICU and concluded that there was improvement in CPP and CBF after dexmedetomidine infusion.
In contrast, Oshima et al. [27], investigated propofol efficacy on CBF and CMRO2 on 10 healthy humans. The results showed that propofol reduced CBF and CMRO2 with no effect on the extraction of oxygen. This contrast may be attributed to a different population in healthy rather than TBI patients. Also, the average dose of propofol was higher (6-8 mg/kg/hr.) compared to our study (0.5mg/kg/hr.).

In our result, both propofol and dexmedetomidine had non-significant effect on arterial oxygen saturation (SaO2) in either group. However, Sjvo2 showed a more significant reduction in group D than group P at interval time from 6, 12 and 48 hours. In addition, both sedatives significantly decreased O2 extraction ratio (OER) when compared to admission values but without significant difference between both groups. The CMRO2 showed non-significant difference between propofol and dexmedetomidine but a significant reduction regarding CMRO2 was observed in each group at 6 hours after initiating sedation.
Agreeing with that, Flower et al. [28] in a systematic review discussed various studies on sedation methods in TBI patients, including propofol and dexmedetomidine. It highlighted that both agents could reduce CMRO2 effectively. Also, Wang et al. [16] examined the impact of dexmedetomidine on non-TBI patients (n=15), TBI patients (n=20) and found that there was a reduction in CMRO2, but it was not significant between the two groups.
In addition, Guo et al. [29] studied 90 patients who had interventional embolization of cerebral aneurysms and were classified equally into A and B groups. Group A received intravenous dexmedetomidine over 10 minutes pre induction of anesthesia. Group B got equal amount of normal saline via the same procedure. They concluded that dexmedetomidine reduced oxygen extraction and enhanced cerebral oxygen metabolism.

Our study found non-significant difference in the 28-day mortality rate with either propofol or dexmedetomidine, with mortality rates of 11.1% and 8.3%, respectively (P value = 0.99). Kawazoe et al. [30] explored the impact of dexmedetomidine on 201 adults in critical conditions and found non-significant improvement in 28-day mortality rates compared to non-dexmedetomidine sedation strategies with propofol or other. In contrast, Xu and Xiao [31] utilized database of Medical Information Mart for Intensive Care (MIMIC) to evaluate the outcome of dexmedetomidine in 2673 TBI patients. They observed a lower significance in-hospital mortality with dexmedetomidine in contrast to those

who did not receive it. This may be related to the large population involved in their study and recording of 6 months mortality. Also, Wan Hassan et al. [32], examined 110 patients with severe TBI who had emergency brain surgery and contrasted the results of target-controlled propofol infusion with sevoflurane anesthesia. Patients were divided into two equal groups, monitored during surgery and in ICU, then monitored for outcome measures until they were discharged. Their study concluded the mortality rate with propofol was about 27.3 % with a mean of ICU duration 8.4 days and a mean ward duration 14.2 days. The contrast here may be related to the shorter time of follow up than in our study and surgical intervention performed.

CONCLUSIONS:

In patients with TBI, dexmedetomidine and propofol sedative agents showed comparable effect on MAP, ICP, CPP, CBF, CMRO2 and mortality rate but HR and mean flow velocity (MFV) were significantly less with dexmedetomidine than propofol. While both sedatives decrease MAP, HR, CPP, CMRO2 and MCA diameter and increase MFV, CBF and SjVO2 when compared to admission values.

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