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Research Article

BISPECTRAL INDEX GUIDED EVALUATION OF PROPOFOL AS ANAESTHETIC ADJUVANT WITH ISOFLURANE IN PATIENTS UNDERGOING CRANIOTOMY AND EXCISION OF SPACE OCCUPYING LESION: A RANDOMIZED CONTROLLED DOUBLE BLIND STUDY

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A B S T R A C T

Background: Neuroprotection is the cornerstone of anaesthetic management in neurosurgery and is provided by both intravenous and inhaled anaesthetics. A combined technique with both agents may be easy to titrate, may allow to combine the neuroprotective effect of both, and reduce the anaesthetic dose used.

Aims and objectives: To evaluate propofol as anaesthetic adjuvant to Isoflurane in patients undergoing craniotomy and excision of space occupying lesion. The primary objective was to find out BIS guided optimum dose of propofol for infusion during intra operative course. The secondary objectives were to assess haemodynamic stability, reduction in requirement of opioids and isoflurane intra operatively, level of post operative sedation and any possible side effects.

Materials and Methods: Total 75 adult patients scheduled for craniotomy and excision of space occupying lesion under general anesthesia were recruited and divided randomly into three groups containing 25 patients each. Group A- maintenance dose of propofol @100 µg/kg/min iv.Group B- maintenance dose of propofol @150 µg/kg/min iv.Group C- maintenance infusion of TPN (20% intralipid) as placebo. Isoflurane was titrated to keep BIS between 40 to 60 and fentanyl(1µg/kg) was given if BIS value >60 despite isoflurane@1vol%. Haemodynamic parameters, reduction in requirement of opioids and isoflurane, level of post operative sedation (Ramsay Sedation Score) and any possible side effects were assessed.

Results: The requirement of Isoflurane (ISO Vol%) was significantly lesser in Groups-A&B as compared to Group-C at all the times during surgery. There was a decrease in mean MAP value followed by a gradual increase in all three groups, the decrease being much more in group-B as compared to groups-A&C. Patients given propofol infusions were calm and cooperative during extubation with stable haemodynamics and had earlier response to verbal commands.

Conclusions: Intraoperative infusion of propofol decreases requirement of inhalational agent and opioid analgesia significantly and patients are calm and cooperative during extubation with stable haemodynamics and early awakening. Propofol @100 µg/kg/min iv provides better haemodynamic stability.BIS is an indispensable tool in assessing intraoperative awareness and decreasing the requirement of inhalational agent.

INTRODUCTION

Anaesthetic management during neurosurgical procedures is a critical issue and ensuring haemodynamic stability is fundamental in order to preserve cerebral autoregulation [1]. A topic that has created quite a lot of debate is which is the best anaesthetic method for patients with cerebral and spinal pathologies as well as head injury. Two modalities are in use at the present time: total intravenous anaesthesia (TIVA) and inhaled anaesthetics. They both have advantages and drawbacks. Neuroprotection is the cornerstone of anaesthetic management in neurosurgery [2].Review of literature shows that both anaesthetic modalities have neuroprotective properties. It is critical to assess the effect of inhaled or intravenous anaesthetics during the procedure, as well as the time and quality of the recovery. It seems common sense to think that a combined technique with intravenous and inhaled agents may be easy to titrate, may allow to combine the neuroprotective effect of both agents, and reduce the anaesthetic dose used.

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Aims and Objectives

This study was done to evaluatepropofol as anaesthetic adjuvant to Isoflurane in patients undergoing craniotomy and excision for space occupying lesion (SOL). The primary objective was to find out BIS guided optimum dose of propofol for infusion intraoperatively. The secondary objectives were to assess haemodynamic stability, reduction in requirement of opioids and isoflurane, level of post operative sedation and any possible side effects intraoperatively.

MATERIALS AND METHODS

After getting approval from our Institutional Ethics Committee (No. 799/Ethics/R.Cell-18), this randomized, double-blind, placebo controlled clinical trial was done over a period of one year.This study is registered with Clinical Trials Registry of India (CTRI/2018/06/014411).

Total 75 patients in the age group of 18-60 years with ASA physical status I or II and having GCS of 12 or above scheduled for craniotomy and excision of SOL under general anesthesia with an expected duration of surgery around 4 – 5 hours were recruited. Exclusion criteria included hypertension, allergic reactions to propofol, pregnancy, breastfeeding, deranged liver and kidney function and refusal to give written/informed consent. Patients were divided randomly into three groups containing 25 patients each.

Group A patients were given maintenance dose of propofol by infusion at 100 µg/kg/min iv.

Group B patients were given maintenance dose of propofol by infusion at 150 µg/kg/min iv.

Group C(Placebo) patients were given maintenance dose of TPN (20% intralipid- imitating propofol in morphological characteristics) by infusion intravenously.

At the time of preanaesthetic check-up, patients posted for elective craniotomy for SOL and satisfying inclusion criteria were approached and explained about the study and the possibility of being randomly allocated into any of the study groups. After agreeing for participation, they were asked to sign the consent form. On the day of surgery, the patient was randomly allocated into any of the three groups with the help of computer generated random number by anaesthetist A, who was not involved in conduct of anaesthesia. Infusions were prepared by anaesthetist A containing propofol 10mg/ml to a volume of 50 ml.

After the patient was taken to the operating room, all monitors (pulse oximetry, ECG, NIBP, BIS) were attached and baseline readings were recorded. Premedication was done with fentanyl 2µg/kg and induction with propofol 2mg/kg. Vecuronium was given at a dose of 0.1 mg/kg and trachea intubated with appropriate size tube. Maintenance was carried out with oxygen and nitrous (50:50 ratio); intermittent doses of vecuronium 0.02 mg/kg (to keep Train of Four count less than 3) and isoflurane as inhalational agent (guided by BIS). Following this, infusion of propofol was started by anaesthetist A.After setting the infusion rate as per the group allocation, screen of infusion pump displaying infusion rate was covered so that it was not visible to the anesthetist B (involved in intraoperative monitoring). The anaesthetist A thereafter left the operating room. Further monitoring and titration of inhalational agent (isoflurane) was done by anaesthetist B.

In case of higher BIS scores despite isoflurane being used as 1 vol%, fentanyl (1µg/kg) was to be given as repeat analgesic dose to maintain BIS value <60. Intraoperatively, if any hypotensive episode occurred, fluid bolus was to be given (10-20ml/kg) and isoflurane to be titrated. Further, if severe hypotension was found then infusion was to be stopped and the respective case was excluded from our study. The infusions were stopped after dural closure. After extubation, patient's level of sedation was assessed with the help of Ramsay Sedation Score [3] (Table 1).

The patient Outcomes were Assessed on the Basis of

- Haemodynamic parameters – HR, BP (MAP) and SPO_2
- Requirement of additional doses of fentanyl as 1µg/kg
- Requirement of isoflurane (as vol%) to maintain a BIS between 40 to 60
- Ramsay sedation score (Table 1) at 5 minutes , 1 hour and 2 hours after extubation

Statistical Analysis

The results were analyzed using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) Version 23**.** Discrete (categorical) data were summarized as proportions and percentages (%) and quantitative data were summarized as mean ± SD.The statistical tests used were Chi Square Test, One-way ANOVA and Kruskal Wallis H Test. A p value <0.05 was considered statistically significant.

Sample size

The sample size has been calculated using the formula{n=[16σ2/d2] +1}and with reference to study done by Ortiz J *et al*, (2014)[4]comparing the effects of anaesthesia with propofol, isoflurane, desflurane and sevoflurane. Total 75 patients were included, 25 in each group**.**

RESULTS

The three groups were comparable with respect to mean age, weight and gender distribution (Table 2).

The mean heart rate (HR) at baseline (before premedication) in the three groups were 87.36±7.09/min(Group-A), 86.24±7.29/min(Group-B) and 84.68±8.01/min(Group-C) which decreased initially to minimum values of 63.76±2.85/min, 62.84±2.76/min and 72.29±4.19/min respectively in the three groups and later on increased gradually in all the three groups(Fig. 1). The differences in mean heart rates among the groups were not significant at baseline($p=0.448$) and after premedication($p=0.191$) and intubation($p=0.071$) however, the differences became highly significant at the time of head pinning($p<0.001$) and skin incision($p<0.001$) which persisted upto 1 hr post-extubation ($P<0.001$ at all times).

On comparing the mean HR between Group-A and Group-B, no significant difference was found except between the time of skin incision and dural flap and at the time of extubation (Table 3).The mean HR in Group-A was lower than Group-C at all the time intervals except at baseline however the difference became significant at the time of head pinning ($p<0.001$) which persisted upto 1hr post-extubation ($P\leq0.05$ at all time intervals) (Table-3). The mean HR in Group-B was lower than Group-C at all the time intervals except at baseline however the difference became significant at the time of head

pinning ($p<0.001$) and persisted upto 1 hr post-extubation ($P\leq0.05$ at all time intervals) (Table 3).

The mean MAP in Group-A at baseline (before premedication) was 88.32±3.72 mmHg which decreased progressively to a minimum value 72.60±1.89 mmHg and after that it increased gradually to the maximum value80.92±2.78 mmHg and at 2 hrs post-extubation, the mean MAP was 77.60±3.33 mmHg (Fig. 2).The mean MAP in Group-B at baseline (before premedication) was 89.28±3.58 mmHg which decreased to the minimum value 61.24±1.88 mmHg and later-on, it increased gradually to a maximum value of 81.48±4.22at extubation. The value at2 hrs post-extubationwas 78.36±3.24 mmHg (Fig. 2).The mean MAP in Group-C at baseline (before premedication) was 89.80±5.89 mmHg which decreased to the minimum value 73.06±2.14 mmHg and again increased to 77.88±2.74 mmHg at 2 hrs post-extubation (Fig. 2).

Though there was no significant difference in mean MAP at baseline, the difference became significant after premedication ($p=0.010$), and highly significant at the time of intubation ($p<0.001$) which persisted upto 1 hr post-extubation ($P\leq0.05$ at all times) (Fig. 2).

On comparing the MAP differences of Group-A & Group-B, significant differences were observed at the time of head pinning, between time of dural flap to skin and soft tissue closure and at 1 hr post-extubation, the maximum difference being 12.92 mmHg (Table 4). The maximum difference in mean MAP between Groups-A & C was 11.40±1.29 mmHg seen at the time of Scalp dissection. Significant differences were observed in mean MAP between the groups-A & C at the time of intubation, which persisted upto 60 min of Tumour dissection. After that, difference again became highly significant at extubation and persisted upto 1hr post-extubation (Table 4). The mean MAP in Group-B was lesser than Group-C at all the time intervals except at 2 hr post-extubation and the differences were significant at all these times (except at baseline and at 1 hr post-extubation, maximum difference being 14.70 mmHg (Table 4).

The mean BIS in Groups-A,B and C at baseline (before premedication) were 98.60±1.12, 98.64±1.11 and 98.36±1.29 respectively, which decreased slightly after premedication. The BIS values were well maintained between 40 and 60 during anaesthesia (between intubation and extubation) and thereafter it again increased to 87.36±2.00, 87.04±2.92 and 88.32±1.82 respectively in the three groups(Fig. 3). The differences in BIS among the groups were not found to be significant ($P>0.05$) at any time except for a short time after premedication and intubation.

The requirement of Isoflurane (ISO Vol%) was significantly higher in Group-C as compared to Groups-A&B at all the times during surgery (Fig 4 and Table 5). The requirement of Isoflurane was higher in Group-A as compared to Group-B, however the differences were not significant at the time of head pinning, skin incision, scalp dissection and dura flap ($p>0.05$). The differences became significant at the time of craniotomy and during tumour dissection and it persisted till the skin and soft tissue closure (Fig. 4 and Table 5).

The repeated dose of fentanyl was required only in group C in 13 (52.0%) cases at the time of skin incision, in 10 (40.0%) cases at the time of scalp dissection and flap and in 11 (44.0%) cases at the time of craniotomy (Table 6). The difference in percentage of patients who required repeated dose of fentanyl among the groups at each of the above said times was found to be significant ($p<0.01$).

At 5 min post-extubation, the maximum mean Ramsay sedation score in Group-C (2.44±0.51) was found to be significantly higher ($p<0.05$) than the other two groups (2.00±0.00). At 1 hr and 2 hr post-extubation, the mean Ramsay sedation score of the three groups were exactly the same (2.00±0.00) (Table 7).

Table 1 Ramsay Sedation Scale

Grade	Degree of sedation/arousability of the patient
1	Patient is anxious and agitated or restless, or both
2	Patient is cooperative, oriented and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

Table 2 Demographic profile

Variable	Group-A	Group-B	Group-C	F-value	p-value
	Mean+SD	Mean+SD	Mean+SD		
Age(yrs)	42.20+10.90	40.16+9.24	42.60+9.17	0.45	0.642
Weight(Kg)	62.64+11.08	64.24+9.07	64.56+8.63	0.28	0.754
Gender	Group-A No. (%)	Group-B No. (%)	Group-C No. (%)	Chi sq	p-value
Female	11(44.0%)	10(40.0%)	13(52.0%)	0.753	0.686
Male	14(56.0%)	15(60.0%)	12(48.0%)		

Table 3 Bi-group Comparison of difference in Heart Rate between the groups

Heart Rate	Gr A vs Gr B		Gr A vs Gr C		Gr B vs Gr C	
	Mean Diff.	p-value	Mean Diff.	p-value	Mean Diff.	p-value
Before premedication	1.12	0.857	2.68	0.418	1.56	0.742
After premedication	2.44	0.349	-0.59	0.937	-3.03	0.198
INTUBATION	1.00	0.761	-2.23	0.261	-3.23	0.064
Head pinning	-2.24	0.166	-13.50	<0.001	-11.30	<0.001
Skin incision	-5.48	<0.001	-17.20	<0.001	-11.80	<0.001
Scalp dissection and flap	-5.64	<0.001	-20.10	<0.001	-14.40	<0.001
Craniotomy	-5.48	<0.001	-21.40	<0.001	-16.00	<0.001
Dura flap	-2.72	0.043	-15.60	<0.001	-12.90	<0.001
Tumor dissection 0 min	-2.04	0.093	-13.80	<0.001	-11.80	<0.001
Tumor dissection 20 min	0.12	0.992	-13.70	<0.001	-13.80	<0.001
Tumor dissection 40 min	1.56	0.201	-12.10	<0.001	-13.60	<0.001
Tumor dissection 60 min	0.88	0.565	-11.80	<0.001	-12.60	<0.001
Tumor dissection 100 min	0.12	0.990	-12.00	<0.001	-12.10	<0.001
Tumor dissection 120 min	0.72	0.682	-10.90	<0.001	-11.60	<0.001
Tumor dissection 160 min	0.63	0.843	-7.88	<0.001	-8.51	<0.001
Dural closure	-0.20	0.961	-10.70	<0.001	-10.50	<0.001
Skin and soft tissue closure	0.00	1.000	-9.96	<0.001	-9.96	<0.001
Post extubation 0 min	5.36	<0.001	-23.20	<0.001	-28.60	<0.001
Post extubation 5 min	0.80	0.794	-15.40	<0.001	-16.20	<0.001

Post extubation 1 hr	1.12	0.688	-4.28	0.007	-5.40	<0.001
Post extubation 2 hr	-2.39	0.144	-3.48	0.020	-1.08	0.668

*p-values are calculated using Tukey Post hoc test

Table 4 Bi-group Comparison of difference in MAP between groups

MAP	Gr A vs Gr B		Gr A vs Gr C		Gr B vs Gr C	
	Mean Diff.	p-value	Mean Diff.	p-value	Mean Diff.	p-value
Before premedication	-0.96	0.734	-1.480	0.483	-0.51	0.913
After premedication	1.84	0.408	-2.600	0.171	-4.44	0.008
INTUBATION	-0.83	0.790	-6.240	<0.001	-5.40	<0.001
Head pinning	-3.44	0.024	-10.600	<0.001	-7.20	<0.001
Skin incision	-2.11	0.198	-9.840	<0.001	-7.72	<0.001
Scalp dissection and flap	-1.32	0.565	-11.400	<0.001	-10.10	<0.001
Craniotomy	0.92	0.728	-11.300	<0.001	-12.20	<0.001
Dura flap	3.72	<0.001	-6.160	<0.001	-9.88	<0.001
Tumor dissection 0 min	8.32	<0.001	-4.080	<0.001	-12.40	<0.001
Tumor dissection 20 min	11.56	<0.001	-2.360	0.017	-13.90	<0.001
Tumor dissection 40 min	12.88	<0.001	-1.840	0.025	-14.70	<0.001
Tumor dissection 60 min	12.92	<0.001	-1.560	0.032	-14.40	<0.001
Tumor dissection 100 min	11.88	<0.001	-1.230	0.134	-13.10	<0.001
Tumor dissection 120 min	11.28	<0.001	-1.000	0.206	-12.20	<0.001
Tumor dissection 160 min	10.91	<0.001	0.352	0.856	-10.50	<0.001
Dural closure	10.20	<0.001	-0.120	0.977	-10.30	<0.001
Skin and soft tissue closure	4.76	<0.001	0.880	0.191	-3.88	<0.001
Post extubation 0 min	-0.56	0.850	-7.480	<0.001	-6.92	<0.001
Post extubation 5 min	-2.08	0.075	-6.920	<0.001	-4.84	<0.001
Post extubation 1 hr	-2.88	0.005	-4.960	<0.001	-2.08	0.054
Post extubation 2 hr	-0.76	0.665	-0.280	0.946	0.48	0.849

Table 5 Bi-group Comparison of difference in ISoVol% between groups

ISO Vol%	Gr A vs Gr B		Gr A vs Gr C		Gr B vs Gr C	
	Mean Diff.	p-value	Mean Diff.	p-value	Mean Diff.	p-value
Head pinning	0.05	0.142	-0.332	<0.001	-0.38	<0.001
Skin incision	0.05	0.105	-0.432	<0.001	-0.48	<0.001
Scalp dissection and flap	0.03	0.497	-0.420	<0.001	-0.45	<0.001
Craniotomy	0.08	0.008	-0.448	<0.001	-0.53	<0.001
Dura flap	0.05	0.062	-0.236	<0.001	-0.29	<0.001
Tumor dissection 0 min	0.09	0.006	-0.212	<0.001	-0.30	<0.001
Tumor dissection 20 min	0.13	<0.001	-0.248	<0.001	-0.38	<0.001
Tumor dissection 40 min	0.14	<0.001	-0.232	<0.001	-0.37	<0.001
Tumor dissection 60 min	0.12	<0.001	-0.252	<0.001	-0.37	<0.001
Tumor dissection 100 min	0.12	<0.001	-0.236	<0.001	-0.35	<0.001
Tumor dissection 120 min	0.11	<0.001	-0.260	<0.001	-0.37	<0.001
Tumor dissection 160 min	0.23	0.036	-0.235	0.037	-0.47	<0.001
Dural closure	0.17	<0.001	-0.228	<0.001	-0.40	<0.001
Skin and soft tissue closure	0.16	<0.001	-0.132	<0.001	-0.30	<0.001

Table 6 Number of patients Requiring repeated Dose of Fentanyl

Repeat dose of fentanyl	Group-A		Group-B		Group-C		chi sq	p-value
	No.	%	No.	%	No.	%		
Skin incision	0	0.0%	0	0.0%	13	52.0%	31.452	<0.001
Scalp dissection and flap	0	0.0%	0	0.0%	10	40.0%	23.077	<0.001
Craniotomy	0	0.0%	0	0.0%	11	44.0%	25.781	<0.001

Table 7 Comparison of Ramsay sedation score among the Three Groups

Ramsay sedation score	Group-A		Group-B		Group-C		Kruskal Wallis H test	
	Mean	SD	Mean	SD	Mean	SD	chi sq	p-value*
Post extubation 5 min	2.00	0.00	2.00	0.00	2.44	0.51	25.44	<.001
Post extubation 1 hr	2.00	0.00	2.00	0.00	2.00	0.00	0.00	1.000
Post extubation 2 hr	2.00	0.00	2.00	0.00	2.00	0.00	0.00	1.000

*p-value is calculated using Kruskal Wallis test

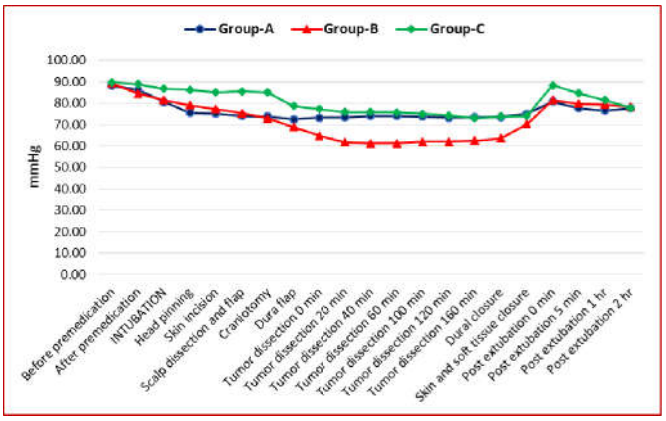

Figure 1 Comparison of Heart Rate among the Three Groups

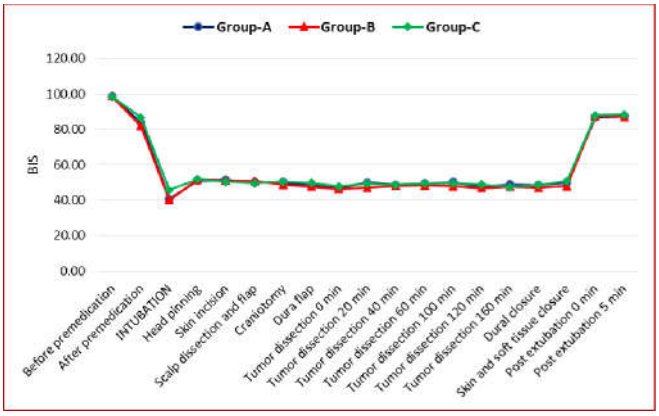

Figure 2 Comparison of MAP among the Three Groups

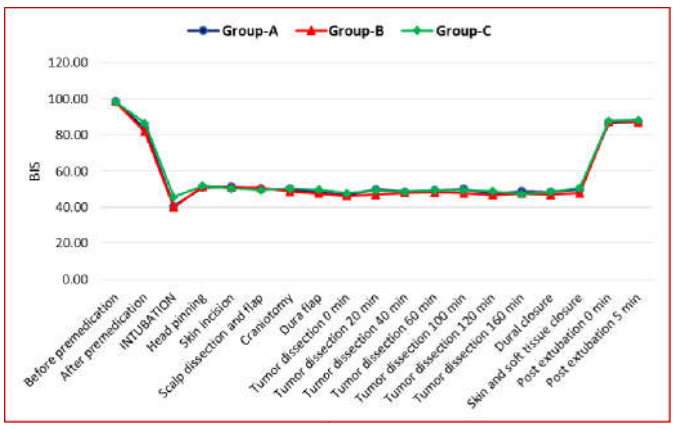

Figure 3 Comparison of BIS among the Three Groups

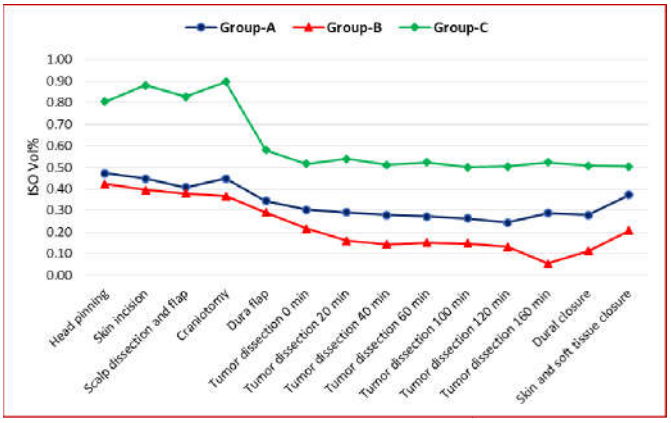

Figure 4 Comparison of ISO Vol% among the Three Groups

DISCUSSION

Propofol and isoflurane have well proven roles as intravenous and inhalational anaesthetics respectively in neurosurgery [5]. The patients having intracranial pathology especially space occupying lesions in brain are usually in a state of delicate intracranial homeostasis. Maintenance of an optimal cerebral perfusion pressure (CPP) is a key factor in managing these patients during perioperative period. Induction of anaesthesia, laryngoscopy and endotracheal intubation may produce deleterious effects on mean arterial pressure (MAP), intracranial pressure (ICP) & therefore on CPP. The control and manipulation of cerebral blood flow (CBF) are central to the management of ICP during anaesthesia because CBF varies according to vasoconstrictor-vasodilator response of anaesthetic agent.

Most studies have shown that propofol either decreases or does not change ICP [6]. At the same time MAP is decreased almost in same magnitude or more. Thus CPP is decreased in most circumstances.

On the other hand, early neurological assessment is essential following most neurosurgical operations. Thus we need to use drugs and techniques that should not cause any hindrance to this objective. The standard use of isoflurane doesn't allow quick neurological assessment of these patients following their use. The kinetics of propofol allows both induction and continuous intravenous maintenance of anesthesia with rapid recovery of consciousness [7].It has also been shown to be superior to inhalational anaesthesia in terms of rapid awakening.

Accordingly, we planned this study to evaluate the intraoperative conditions and patient outcomes in neurosurgical patients using propofol as anaesthetic adjunct with isoflurane. We compared two different doses of propofol i.e., 100 µg/kg/min iv and 150 µg/kg/min iv as maintenance infusion during craniotomy and excision of SOL to find out BIS guided optimum dose of propofol for infusion during intraoperative course. We also assessed haemodynamic stability, reduction in requirement of opioids and isoflurane intraoperatively, level of postoperative sedation and any possible side effects intraoperatively.

In our study, the mean HR in Group-A had decreased progressively to the minimum value 63.76±2.85/min and after that it gradually increased to a mean value 75.40±3.96/min after 2 hrs post-extubation. Similarly, in Group B, the HR decreased to a minimum value 62.84±2.76/min and increased gradually thereafter. However, in group C less variation in HR was noted, minimum HR being 72.29±4.19/min.

This was similar to the study conducted by Mi *et al.*[8], where a combination of propofol with fentanyl lead to decrease in HR in all groups due to the prevention of stress response by fentanyl and its myocardial depressing effect. They observed greater hemodynamic and electroencephalograph responses to intubation in patients who received propofol than in those who received both propofol and fentanyl.

In studies done by Galletly DC *et al.*[9] and Ebert TJ *et al.*[10], transient increase in HR were observed during induction of anaesthesia with propofol, which occured during or soon after injection. Tachycardia persisted for approximately 1 min and then HR remained steady at a value little different from control values.

Apart from the initial tachycardia, a general increase in HR during propofol anaesthesia was observed by Howell S *et al.* [11], Ebert TJ *et al.* [10], Ebert TJ *et al.* [12] in their studies while Grounds TM *et al.* [13] observed no increase, or even a decrease after a bolus injection of propofol. Similarly, no increase in HR was noted after propofol infusion in studies done by Samain E *et al.* [14], Cullen P *et al.* [15], Lepage JM *et al.* [16], Claeys M *et al.* [17] and Mulier JP *et al.* [18] which is similar to the results of our study.

Maintenance of stable haemodynamics is an important part of neuroanesthesia practice. Severe hypotension can jeopardise the CPP. Similarly, perioperative hypertension is associated with intracranial hypertension, which may result in intracranial haemorrhage and aggravation of brain oedema [19]. Propofol produces dose-dependent decrease of systemic vascular resistance [20] and reduction of cardiac output [21].

In our study, we observed highly significant differences in MAP among the groups at most of the time intervals. There was a decrease in mean MAP value followed by a gradual increase in all three groups. However, the decrease in MAP was much more in group B (minimum MAP 61.24±1.88 mmHg) as compared to group A (minimum MAP 72.60±1.89 mmHg) and group C (minimum MAP 73.06±2.14 mmHg). Thus, it was concluded that propofol given in a dose of 100 µg/kg/min, shows better haemodynamic stability as compared to a higher infusion dose of 150 µg/kg/min.

Kanaya N *et al.* [22], in their study, had also shown that induction of anaesthesia with propofol was associated with significant decreases in mean blood pressure in a BIS-dependent manner. Hernandez *et al. [23],* carried out a study with propofol–ketamine, midazolam–ketamine and propofol–fentanyl combinations and observed stable haemodynamics in patients who received propofol and ketamine, whereas patients who had received midazolam–ketamine had significantly higher number of hypertensive peaks.

With the help of BIS monitoring, we were able to decrease the isoflurane requirement to the extent that for maximum time during tumour dissection, isoflurane was used at low values of 0.2 to 0.3 vol% in group A and almost stopped in group B but requirement of isoflurane was higher in group C (~0.5 vol%). Also, similar BIS values were found in the control group, but at a cost of higher requirement of isoflurane. Similarly, in a

study conducted by Cordella *et al* [24], twenty-four patients underwent elective surgery under general anesthesia that was administered through Target Controlled Infusion (TCI) for effect-site concentration (Ce) of Propofol and Remifentanil, targeting the BIS in the 40-60 intervals. They demonstrated decreased incidence of intraoperative awareness using BIS.

Regarding the analgesic effect of propofol, our study showed significant results as the repeated dose of fentanyl was required only in group C patients at the time of skin incision, scalp dissection and flap and during Craniotomy. This was consistent with a study conducted by Anker-Moller *et al [25]*. They assessed the analgesic properties of thiopental and propofol in 12 healthy patients exposed to laser stimulation and reported that sub-hypnotic doses of propofol increased the pain threshold to laser stimulation and decreased the amplitude of pain-evoked potentials.

The emphasis in present clinical practice is to facilitate early awakening along with improved quality of emergence. Early awakening allows for a timely detection of a neurological complication and reintervention if necessary. Emergence time in our study was the time from switching off of N_2O to extubation following which the patient can be subjected to neurological examination.

In our study, at 5 minutes post extubation, Ramsay sedation score was 2 in all the patients in both groups A and B whereas it was significantly higher in control group. This was due to higher volume of isoflurane used. There was no statistically significant difference in sedation score at 1 hour or 2 hr post-extubation. The time taken to response to verbal commands was significantly higher in the control group when compared to the other two groups as isoflurane requirement was higher in control group. This finding was consistent with results of study conducted by Bastola *et al* [26] in which they observed following neuromuscular reversal, the time to respond to verbal commands among the patients were significantly prolonged with use of sevoflurane when compared to propofol. Also, in a study done by Miura *et al* [27], Propofol was associated with a better recovery profile and neurological condition than isoflurane, as indicated by shorter extubation and OR discharge times and better postoperative consciousness.

CONCLUSIONS

We conclude that propofol if used as an intraoperative infusion, blunts the sympathetic response to laryngoscopy and intubation, head pinning, skin incision, scalp dissection, craniotomy, tumour dissection and extubation. Also, the requirement of inhalational agent and opioid analgesia is decreased significantly with propofol infusion @100 µg/kg/min as well as @150 µg/kg/min during surgery however infusion @100 µg/kg/min provides better haemodynamic stability.Patients given propofol infusions were calm and cooperative during extubation with stable haemodynamics as compared to control group. Post extubation, patients were adequately sedated as assessed by Ramsay sedation score and early awakening was noted in them.Also we would like to comment that BIS has been an indispensable tool in assessing intraoperative awareness and decreasing the requirement of inhalational agent.

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