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Original Article

Anesthesia Section

A Pilot Study of Cerebral and Hemodynamic Changes During Sedation with Low Dose of Thiopental Sodium or Propofol in Patients with Acute Brain Injury

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ABSTRACT

Background: One of the most important therapeutic maneuvers in head injury patients is to maintain Intracranial Pressure (ICP) and Cerebral Perfusion Pressure (CPP) within normal levels.

Aims: To compare the effects of low dose of thiopental sodium and propofol on reducing ICP and CPP in patients with head injury that scheduled for neurosurgical interventions.

Settings and Design: Using a randomized, crossover pilot study, we enrolled patients with head injury that scheduled for neurosurgical interventions admitted to ICU unit of a teaching hospital during 2010 to 2011.

Materials and Methods: In this pilot study, patients randomized into two equal groups. The first group received bolus injection of thiopental sodium 2 mg/kg and a maintenance dose of 2 mg/kg/h and the second group was given a bolus dose of propofol 0.5 mg/kg followed by propofol infusion 20 µg/kg/min. All of patients were given dexamethasone 8 mg at time of catheter insertion. ICP measurement catheter was inserted for each patient and ICP, CPP, SPO_2 and MAP were recorded hourly for a period of 6 hours.

Results: There was no significant difference in sex and age between the two study groups ($p>0.05$). The mean ICP, CPP, SPO_2 and arterial blood pressure were found to be similar with no significant difference between both groups ($p>0.05$).

Conclusion: Both propofol and thiopental sodium were equally effective in monitoring and maintaining CPP and MAP and eventually an ideal SPO_2.

Keywords: Head injury, ICP, Propofol

INTRODUCTION

Head injury is one of the most frequent injuries with high morbidity and mortality in young people. It is recommended to maintain CPP higher than 60 mmHg [1]. Patients with traumatic brain injury and a consciousness level of less than 8 GCS scores with abnormal findings (hematoma, contusion, oedema, compressed basal cisterns) in CT scan need a continuous monitoring of CPP and ICP [2]. Propofol is one of the most common drugs routinely used at ICU to sedate patients and to control elevated ICP and maintain CPP. The most significant benefit of propofol administration is the maintenance of cerebral auto-regulation and response to carbon dioxide within normal levels although adverse effects such as myoclonus, apnea, hypotension and rare occasions of local thrombophlebitis may occur [3-6]. However, administration of high doses of propofol for this intervention and the occurrence of complications in long-term infusion, emphasized on avoiding the recommendation of propofol for long duration [7,8]. Barbiturates, in addition to depressive effects on CNS metabolism, decrease the cerebral metabolic rate of O_2 ($CMRO_2$) and cause a reduction in ATP consumption in brain cells, leading to a dose-dependent neuroprotection. Moreover, thiopental sodium also causes a decline in the level of mean arterial blood pressure (MAP) although this reduction is not accompanied with a significant reduction in CPP [9]. The adverse effects of thiopental sodium include allergic reactions, local tissue irritation and necrosis, cardiovascular and respiratory complications [10]. The tight control of CPP is accompanied with an improvement in outcome, and also a high correlation between the severity of injury and increased ICP (>20 mmHg) and poor outcome is reported [11]. However, infusion of high dose of thiopental sodium and barbiturate coma induce is associated with serious adverse effects such as hypotension, azotemia, pneumonia, and electrolyte imbalance (hypernatremia, hypokalemia, hyperkalemia) [12-14]. Hung Shik An et al., declared that low dose barbiturate with BIS monitoring provided enough duration of barbiturate coma possible to control ICP [9].

We hypothezied that low dose of thiopental sodium could be a proper alternative to monitor the target cerebral and haemodynamic parameters in patients with traumatic head injury. The aim of the present study was to compare the effects of propofol and thiopental sodium on ICP and CPP in patients with severe head injury.

MATERIALS AND METHODS

This was a randomized, crossover pilot study on head injury patients who were admitted to Shahid Rajaei teaching hospital during 2010-2011 that scheduled for neurosurgical interventions. Inclusion criteria were the level of consciousness less than 8 according to the Glasgow Coma Scale (GCS), the presence of head trauma without any trauma to other vital organs and the age between 15-45 years. Exclusion criteria included the previous history of diseases such as convulsion, diabetes, hypertension, high or low body temperature, ICP greater than 25 and also the patients who suffered high arterial blood pressure during their hospitalization period at a level which made the therapeutic intervention inevitable. Patients were randomly assigned in chronological order into two groups by even thiopental sodium group and propofol group. For each patient before the inclosing of the dura, an ICP measurement catheter was inserted by neurosurgical surgeon. The catheter is inserted through the brain into the lateral ventricle. All of patients was given dexamethasone 8

mg at time of catheter insertion. The patients of the thiopental group in the ICU received a bolus injection of thiopental sodium 2 mg/kg and a maintenance dose of 2 mg/kg/h and the propofol group was given a bolus dose of propofol 0.5 mg/kg followed by propofol infusion 20 µg/kg/min.

ICP, CPP, SPO_2 and MAP were recorded hourly for a period of 6 hours. In case of an ICP greater than 25 mmHg, 100 ml mannitol was injected and the patient excluded from the study. The determination sample size of this study was based on the previous studies [9,10] and also the total number of patients with head trauma that scheduled for neurosurgical interventions during two years ago. Data were analysed in SPSS by t-test and Chi-square test. A p-value <0.05 was taken as the level of significance.

RESULTS

There was no significant gender difference between the two groups. The distribution of 'males' and 'females' in both groups was similar, though the number of men was higher than women in two groups. (p=0.74). The mean age of patients in thiopental sodium group was 32.7±8.9 years and in propofol group 36.1±5.8 years, indicating a lack of significant difference between the two groups revealed by t-test (p=0.19). The cerebral perfusion pressure in the propofol group was 2 mmHg higher than the thiopental sodium group yet the difference between the two groups was found to be insignificant, statistically (p=0.53). Also, the intracranial pressure in the thiopental sodium group was higher than the propofol group but statistically no significant difference between the two groups was found (p=0.13). Furthermore, both groups showed acceptable levels of mean arterial blood pressure and arterial oxygen saturation with no significant difference between the two groups (p>0.05) [Table/Fig-1].

Group → / Variable ↓	Thiopental sodium n=20	Propofol n=20	p-value
CPP (mmHg) [average]	75/9±2/2	77/9±2/2	0.53
At time of catheter insertion	78/8±14/1	79/8±15/4	
1 h	78±12/1	82/5±15/8	
2h	74/9±11/8	77/9±14/2	
3h	74/4±9/5	74/4±11/6	
4h	74/4±10/5	76/5±10	
5h	76/8±13/2	79/1±13/2	
6h	74/1±10	75±9/6	
ICP (mmHg)) [average]	11/3±0/4	10/4±0/40	0.13
At time of catheter insertion	13/4±2/4	13/2±3	
1 h	11/3±2/6	10/6±3/1	
2h	11/8±2/6	9/9±2/3	
3h	10/9±2/8	9/8±2/2	
4h	10/6±2/3	9/5±2	
5h	10/6±3	9/8±2/1	
6h	10/3±1/8	9/9±2/3	
MAP (mmHg))[average]	87/3±2/1	88/2±2/1	0.76
At time of catheter insertion	92/2±13/1	93/1±16/7	
1 h	89/8±11/8	93/2±15/7	
2h	86/7±12/2	87/8±14/2	
3h	85/3±9/3	83/6±11/3	
4h	85/1±10/3	86/1±9/7	
5h	88±11/4	89±13/3	
6h	84/2±9/3	84/8±10/4	
SPO_2 (mmHg))[average]	97/1±0/2	96/9±0/2	0.65
At time of catheter insertion	97/3±1/3	96/9±1/7	
1 h	97±1/2	96/6±1/9	
2h	96/4±1/4	97/2±1/6	
3h	97/3±1/2	97±1/4	
4h	97/5±1/9	96/6±2	
5h	97/2±1/5	97±1/6	
6h	96/9±1/2	97/2±1/3	

[Table/Fig-1]: Comparison of mean CPP, ICP, SPO_2 and MAP in two study groups. Data are presented as mean±SD, h=hour. p-value is from Repeated measure analysis

DISCUSSION

The findings of the present study demonstrated that both propofol and thiopental sodium produced similar effects on ICP, CPP, MAP, and SPO_2 in two study groups with no significant difference between the two groups.

The results of our study indicating that the administration of propofol modulate the level of intracranial pressure with no negative effect on the mean CPP which was 77.9 mmHg, a value within the normal range (50-150 mmHg). In a study by Girard et al., the effect of propofol on the levels of ICP and CPP in two target and control groups was compared and it was shown that the mean ICP in both groups was similar (13 versus 15 mmHg) while the CPP level in the propofol group was significantly lower than that found in control group [15].

In the present study, the mean ICP in the propofol group was lower than the thiopental sodium group whereas the mean CPP was higher in propofol group compared to the thiopental sodium group, however, the difference found to be insignificant, statistically. In Santra and Das's study reported from India, the effect of propofol and thiopental sodium on ICP, CPP and haemodynamic changes in patients who were candidates for elective craniotomy was investigated during induction and intubation [16]. The authors found a decreased level of CSF pressure in both groups following the induction of anaesthesia. The changes in MAP were noticeable in the propofol group; as a result CPP was significantly less in Group propofol than in Group thiopental [16]. However, in our study, as mentioned earlier, no significant difference in the level of CPP between the two study groups was revealed. Also, similar mean values for MAP and SPO_2 were demonstrated in both groups. The selected dose of thiopenthal sodium in current study was based on according to study by Hung-Shik An et al., which declared that low dose barbiturate with BIS monitoring provided enough duration of barbiturate coma possible to control ICP [9]. Furthermore we assumed that sedation dose of this agent may be improved cerebral and haemodynamic variables [10]. However, for refractory elevated ICP in severe TBI, sedative agents play a key role in the escalating tiers of therapy to reduce ICP [17,18].

On the contrary, Albouyeh et al., [19] showed that propofol compared to thiopental sodium causes less changes in haemodynamic signs because propofol is one of the hypnotic drugs with extra-hepatic metabolism that produces much less concentration, in comparison with thiopental sodium, following repeated administrations. Furthermore, propofol, due to its vagotonic effect, prevents the occurrence of haemodynamic changes in response to stimulations of the autonomic nervous system. However, these apparently controversial findings may be due to either the difference in dosage of thiopental sodium, population or using of dexamethasone. Nevertheless, among the different protocols used to lower ICP, propofol and thiopental sodium are known as the drugs with strong vasoconstriction effect on cerebral vessels and the ability to reduce cerebral blood volume (CBV), cerebral blood flow (CBF) and ICP.

Although some studies suggested that steroids have not been found to be useful and may be detrimental in ischemic lesions, cerebral injury [20] and also they are not routinely indicated in individuals with traumatic brain injury [21]. With respect to glucocorticoids they are effective in ameliorating the vasogenic oedema that accompanies tumours, inflammatory conditions, infections and other disorders associated with increased permeability of blood brain barrier, including surgical manipulation [20,21], we used low dose of

dexamethasone. We assumed that the combination of low dose dexamethasone-hypnotics (propofol or thiopental sodium) may be have the synergesic effect lead to better cerebral protection without additional side effects. Further studies are needed to evaluate the cerebral and haemodynamic changes during sedation with low dose of thiopental sodium or propofol without use of dexamethasone.

CONCLUSION

According to our findings, both propofol and thiopental sodium were equally effective in monitoring and maintaining CPP and MAP and eventually an ideal SPO_2. Although the decrease in the level of ICP in propofol group, compared to thiopental sodium, was to some extent more obvious yet the difference between the two study groups was insignificant and therefore, based on the specific conditions of patients, if the administration of propofol cannot be justified due to some possible complications, thiopental sodium at concentrations mentioned earlier, could be a proper alternative to monitor the target parameters in patients with traumatic head injury.

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