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RESEARCH ARTICLE

A comparison of propofol induction dose requirement for induction in patient with supratentorial brain tumor and patients without intracranial tumor

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Abstract

Aim:-To compare the propofol induction dose requirement haemodynamic effects in patients having intracranial tumour with non intracranial tumour patients.

Method: - 100 patients in each group were taken in this prospective, randomized study. Either of a 4 dose of Propofol (0.5, 1, 1.5, or 2.0 mg/kg) was given in induction. After 2 minutes of propofol given, 10s, 50 HZ, 80 ma transcutaneous tetanic current was given to the ulnar nerve as a test for response to painful stimuli. Any abnormal body movements were noted as a positive response. Haemodynamic data were observed for 2 minutes.

Results:- Mean induction dose of propofol was required to abolish the tetanic painful stimuli was0.88+/- 0.51mg/kg in Group T and 1.92+/-3.66 mg/kg in Group C. Propofol dose was significantly less required in large tumour(>30mm) than smaller tumour patients. 55 (55%) patients with large tumor were induced with 1mg/kg in group T while it was 1% in Group C. Out of this 55 patients, 41(74.5%) were of large tumor and 14(24.5%) were small tumour patients. 33% of patients were induced with 1.5 mg/kg in Group T. In Group C, 84 patients were required large dose (2mg/kg) compared to 2 patients in Group T.

Conclusion: - There is a less dose requirement of Propofol during anaesthesia induction in patients of supratentorial mass lesion especially having a tumour of larger (>30mm) size.

INTRODUCTION

The anaesthetic drug requirement is decreased in animals with head injury (Matthews T .V. Chan, 1999). But there is no data regarding the effect of intracranial tumor on the potency for intravenous anaesthetics. The anaesthetic dose requirement for pentobarbital, Fentanyl citrate and Sufentanyl were decreased by 28% and 25-26% respectively, in male Sprague-Dawley rats with cryogenic brain injury (Archer DP 1991, Archer DP 1993).The effectiveness of anaesthetics agents has not been found in other brain pathological condition.

Intra-cranial tumor increases brain responsiveness to anaesthetics agents, although many surgical and anaesthetic factors may also delay emergence from anaesthesia.

Practically, patients with large brain tumors (>30mm) undergoing craniotomies for tumor excision are slower to emerge from anaesthesia compare to patients undergoing non cranial surgeries.

Therefore, this study was, designed to find a safe and effective anaesthesia induction dose of propofol and its effects on haemodynamic effects in patients with supratentorial tumors and to compare it patients without intracranial tumors.

METHOD:-

After obtaining institutional ethical board approval, written informed consent from 200 patients aged from 18-60 years from both sexes undergoing craniotomy equally divided in Group T(with supratentorial tumors) and Group C laminectomy (without intracranial tumors) for the study.

Patients were assessed pre operatively through history and clinical examination done. Investigations were carried out and analysed. Only patients belonging to ASA 1 and 2 were selected for the study.

We had excluded the patients having features like pregnancy, disoriented, known allergy to study drug, medical co-morbidities, and history of alcohol or opioids abuse.

All patients were fasted for 10 hrs and no pre anaesthetic medication was prescribed. Tab. Sodium Valproate 100mg and Tab. Dexamethasone 4mg was continued before surgery in all patients of group T.

On arrival in the operation theatre, patients were monitored with routine non-invasive blood pressure measurement, pulse oximeter and E.C.G and heart rate were recorded. Anaesthetic technique was identical in all the patients.

After securing large bore intravenous line, patients were given pre oxygenation 6lit/min for 5 minutes; non invasive blood pressure was recorded. Hundred patients in each group were randomly allocated in Group T (patient with supratentorial tumors) and in Group C (patient without intracranial tumors).

Four doses of Propofol 0.5,1,1.5,2mg/kg IV were given as induction dose in random fashion in both the groups. Propofol was injected over 10 sec via peripheral vein and was followed by a flush of 10 ml normal saline solution. A patient was undisturbed except for non-invasive measurement of arterial pressure. Heart rate and S.B.P., D.B.P., M.A.P. was recorded immediately before, at 1 min and 2 min after administration of propofol.

2minutes after the start of propofol injection patients were called by their names and were asked to open their eyes. . Patients who did not open their eyes were recorded as "no response or negative response to verbal command". These patients were then given a standard transcutaneous tetanic stimulus of (10sec, 15Hz 60 mA) by TOF-GUARD BIOMETER DENMARK to the ulnar nerve at the wrist delivered by a constant current peripheral nerve stimulator Any purposeful movement of the head, neck or limbs apart from the stimulated arm within 30 sec after the stimulus was considered a positive response. Absence of positive response was recorded as "No response to tetanic stimulus". Grimacing, bucking, swallowing and hyper ventilation were not considered as positive responses.

Patients who responded to verbal command were not given tetanic stimulus and were recorded as positive response to tetanic stimulus. These patients were given rescue Inj. propofol in the incremental dose of 0.5mg/kg at 2minutes interval till they do not respond verbally and followed by tetanic stimuli. Now patients were induced routinely with Inj.Fentanyl citrate 4mcg/kg.

Patients were ventilated for 3 minutes following Inj. Vecuronium bromide injection 0.5 mg/kg. After 90 seconds of muscle relaxant given, patients were intubated orally with cuffed endotracheal tube of appropriate size. Endotracheal tube was fixed and secured.

Anaesthesia was maintained with O_2 (50%) + N_2O (50%) + Sevoflurane (1%-3%) and infusion dose of Inj. Vecuronium bromide 5 -12 mcg/kg/min. Ventilation was controlled mechanically and adjusted to maintain an end tidal CO_2 concentration between 30-35 mm of Hg. All the parameters including heart rate, systolic arterial pressure and diastolic arterial pressure were recorded at following intervals. Before propofol injection (BF), 1minute after propofol induction ($P_{1)}$, 2 minute after propofol induction (P_2).

We had defined following parameters for study like hypotension as SBP < 25% of baseline value or 90 mm of Hg, whichever was lower. Hypertension was defined as SBP >25 % of baseline value or 150 mm of Hg, whichever was greater. Tachycardia was defined as HR > 25 % of baseline value and bradycardia was defined as HR <50 beats per minute. An arrhythmia was defined as any ventricular or supraventricular premature beat or any rhythm other than sinus rhythm. Incidences of all these parameters were recorded in all the groups.

After completion of surgery patients were reversed with Inj. Glycopyrrolate (8 mcg/kg) and Inj. Neostigmine bromide (50 mcg/kg) extubated following conformation of tone power and consciousness return and then shifted to post-operative ward.

RESULTS:-

There was no significant difference in the demographic parameters mentioned above in both the groups.

Propofol dose per kg requirement was significantly low (p value 0.0054) in patients having large tumour in group T (Table I) compared to group C. In Group T, 33 patients with brain tumors required 1.5mg/kg, 55 patients required propofol dose of 1mg/kg, and 10 patients required 0.5mg/kg for loss of verbal command and no response to tetanic stimuli. Majority of patients (85%) of patients of group C needed induction dose of 2mg/kg while contrast to these only 2 patients of group T needed this large induction dose.

Mean induction dose of propofol required is 0.88+/- 0.51mg/kg in Group T (with supratentorial tumor) in comparison of Group C (without intracranial surgery) patients required mean effective dose of 1.92+/-3.66 mg/kg for loss of verbal command and no response to tetanic stimuli which is statically significant.(Table II)

The maximum decrease in SBP and diastolic BP noted was in group T patients at 2 minutes interval (Table III and Table IV).Table V shows that, the heart rate was not significantly decreased in both groups at 2 minute interval.

Only two of our patients in Group T had developed hypotension and bradycardia following administration of 2mg/kg dose and was treated by infusing crystalloids and Inj. Atropine Sulphate 0.6mg IV for bradycardia. No other side effects have reported in any other patients in both the groups namely, hypertension or arrhythmias.

Table I
Different induction doses of Propofol requirement

PROPOFOL	*GROUP T*	*LARGE TUMOR*	*SMALL TUMOR*	*GROUP C*
0.5 MG/KG	10	9	1	0
1MG/KG	55(55%)	41(74.5%)	14(25.45%)	1
1.5MG/KG	33(33%)	29(87%)	4(12.12%)	15(15%)
2MG/KG	2	0	2	84(84%)

Propofol induction dose requirement to abolish verbal command and tetanic stimuli was 1mg/kg in 41 patients (74.5%) of large tumor and 14(25.45%) in group T while it was only in 1 (2%) patient.

Table II

Propofol dose requirement

	Group T		Group C
	Group large	Group small	
Mean (mg/kg)	0.88	1.14	1.92
SD	0.51	1.12	3.66
P value	0.0054 very sig Large v/s control	0.0359sig Large v/s small tumour	0.0429 sig Small v/s control

Mean dose of Propofol was significantly less in Group T and especially in large tumor patients

Table III
Systolic BP

	GROUP T	*GROUP C*	*P value*	*95%CI*
Baseline	*118.6±9*	*116.32±8.9*	*0.07 not sig*	*95% CI* *-0.2161 to 4.7761*
1 min after *(p1)*	*102.6±12.2*	*105.6±5.8*	*0.02 sig*	*-5.664 to -0.336*
2min after (p2)	*102.4±4.2*	*100+/-7.2*	*0.03sig*	*0.156 to 3.444*

Hypotension was observed at 2minutes after propofol given n Group T inspite of lesser dose of propofol.

Table IV
Diastolic BP

	GROUP T	GROUP C	P value	95%CI
Baseline	77.98±5.1	78.2±4.2	0.7 not sig	-1.5229 to 1.0829
1mins after propofol(p1)	69.18±4.8	67.76±4.8	0.037 sig	0.08135 to 2.75865
2 mins after propofol(p2)	70.64±5.4	69.7±2.9	0.037 sig	0.0587 to 1.8213

Significant downward changes in diastolic BP at minutes in group T even thought lesser induction dose of propofol.

Table V
Pulse

	GROUP T	*GROUP C*	*P Value*	*95% CI*
Baseline	*85.38±9.1*	*86.84±6.2*	*0.1864 not sig*	*-3.6315 to 0.7115*
1mins after propofol (p1)	*83.36±7.08*	*85.94±4.9*	*0.5150 not sig*	*-2.3334 to 1.1734*
2 mins after propofol(p2)	*84.33±5.9*	*83.08±3.2*	*0.0640 not sig*	*--0.0736 to 2.5736*

Pulse rate was remain stable in both the study groups.

DISCUSSION:-

There is a definite correlation of intracranial tumour size and propofol induction dose requirement. In patients with large intracranial supratentorial tumors (more than 30 mm) the induction dose of propofol required to abolish response to verbal command and tetanic stimulus were less compared with doses needed in the control group.

The patients with large supratentorial tumors are more sensitive to propofol and that the exhibits increased response to anaesthetics may contribute to slower recovery in patients undergoing craniotomy for excision of large tumors.

M T Chan et al believed that in patients having large brain tumour needs less propofol, it is due to greater drug effect and increased sensitivity to propofol in large brain tumor. In our study propofol required was also low in large tumour patients.

In this study, we measured responses at two end points. Testing patients to verbal commands is commonly noticed and is applicable in our daily practice. However use of transcutaneous tetanic electric current as a supramaximal noxious stimulus has also been used.

Baseline haemodynamic parameters were stable in both groups. In Group T, even though majority of patients required lower induction dose of propofol, there is hypotension at 2 minutes which is statically significant (Table III).

Kazama et al reported the ED 50 of propofol to abolish movement to a tetanic electric stimulus was similar to that required for laryngoscopy and standard skin incision. The result suggested that the stimulus intensity of transcutaneous tetanic current is similar to skin incision. Nonetheless tetanic stimuli are non-invasive, repeatable in each individual and give reproducible results.

The change in propofol induction dose requirement may be as a result of pharmacokinetic and pharmacodynamics differences between tumor patients and the control groups. Pharmacokinetic changes alter the effect site concentration after a given dose of propofol; the cerebral effects may be markedly different between groups at the time of assessment.

We believe that the lower propofol requirements in patients with large brain tumors is mainly as a result of the greater drug effect that is associated with an increased sensitivity to propofol.

Larger propofol induction dose required of 2mg/kg in 84% in Group C while it was 2% in Group T. In Group T 55% of patients of large tumour (>30mm) patients induced with 1mg/kg propofol and it was only in one patient in group C.

Inspite of lowest induction propofol dose needed in large sized tumour patients in Group T blood pressure and pulse rate data were significantly reduced. This confirms that increased drug sensitivity in large sized tumour. Induction dose of propofol was statically significantly lower in large size tumor patients than small size tumor (Table II)

Blood pressure was significantly reduced from baseline at 2 minutes interval in large and small cranial tumour v/s control group having no tumour. We excluded the patients who were somnolent preoperatively because baseline sedation would be expected to enhance the response to propofol.

Interaction with concurrent drug administration may also affect the cerebral effects of propofol. All of our patients with brain tumors received Dexamethasone, Valproate as a standard practice in our neurosurgical unit although there is no data regarding the effect of these drugs on anaesthetic requirement.

CONCLUSION

The induction dose of propofol required for obtaining negative response to verbal command and that of tetanic stimulus was less in patients with large brain tumors(>30mm) compared with non cranial tumor patients. However propofol dose requirement was significantly less in large size tumour than small size tumor.

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