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Comparative Study Of Dexmedetomidine And Clonidine For Premedication And Haemodynamic Changes In Patients Undergoing Intracranial Tumour Surgery.

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ABSTRACT

Hemodynamic stability in the perioperative period is of prime importance while providing general anesthesia in cranial tumor surgeries. Profound surgical stimuli associated with craniotomy often result in sympathetic activation and marked changes in arterial bloodpressure, cerebral blood flow, and thereby changes in intracranial pressure and cerebral perfusion pressure. The goals during neurosurgical anesthesia are intraoperative hemodynamic stability with attenuation of sympathetic responses to avoid intracranial hemorrhage. And to allow immediate neurological evaluation upon emergence. The purpose of the study is to compare the effectiveness of intravenous dexmedetomidine or Clonidine in attenuating the hemodynamic response to intracranial tumour surgery.For the study,60 patients of the age group 20-45 years with bodyweight 50-70kgs, GCS 13 to15, belonging to ASA PS I and PS II were selected and divided into two groups D and C. The study design was a prospective randomized comparative study done in Government Vellore Medical College, Vellore, Tamil Nadu, India in the year 2019-2020. Based on standard dosing, 1mcg/kg of dexmedetomidine diluted to 100ml with 0.9% saline over 10 minutes was given before induction for patients in group D. Patients randomized to group C received intravenous clonidine 1µ/kg body weight 35mins prior surgery. Heart rate and mean arterial pressure were comparable between the two groups during the study and were recorded at the following intervals. We found that dexmedetomidine is more effective in controlling the hemodynamic response than Clonidine in during craniotomy. It was concluded that 1 mcg/kg of dexmedetomidine infused slowly over 10 minutes is superior when compared to clonidine in attenuating the hemodynamic response during craniotomy. By attenuating the hemodynamic response, brain edema, increased intracranial pressure and intracranial hemorrhage can be prevented.

Keywords: Hemodynamic, clonidine, Dexmedetomidine, Intracranial Tumour Surgery

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INTRODUCTION

The goals of neuroanaesthesia are to provide good operating conditions and to ensure stable cerebral haemodynamics without sudden increases in intracranial pressure or acute brain swelling.As we all know during craniotomy for intracranial tumour there is associated abrupt increase in heart rate and mean arterial pressure. These adverse effects can lead to brain edema, increased intracranial pressure, or hemorrhage [1]. Different techniques have been used to blunt these deleterious hemodynamic changes. The hemodynamic response consists of an autonomic response to noxious stimuli which increases the sympathetic tone and elevates the blood pressure and heart rate [2]. The sudomotor response consists of sweating whereas the hormonal response consists of the release of corticosteroids, glucagon, and catecholamines due to activation of the hypothalamic-pituitary axis due to surgical stress [3]. α_2-Adrenergic agonists have been introduced to clinical anaesthesia for their sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties [12, 13]. Dexmedetomidine with an elimination half-life of two to three hours is a highly selective and potent and specific alpha 2 agonist (1620:1 for alpha 2 to alpha 1) and is seven to ten times more selective for alpha 2 receptors compared to clonidine and has a shorter duration of action [4]. Dexmedetomidine is considered full agonist at alpha 2 receptors as compared to clonidine, as dexmedetomidine also attenuates the hemodynamic response, decreases plasma catecholamine concentration during anesthesia and decreases perioperative requirements of inhaled anesthetics.Alpha 2 agonists provides good perioperative haemodynamic stability with decreased intraoperative opioid requirements [14] and studies in animals suggest that it may have other beneficial effects in terms of neural protection [15], These characteristics make dexmedetomidine useful anesthetic adjunct during operation. Previous studies reported that intravenous use has a definitive role in postoperative analgesia through the reduction of opioid consumption [5]. Hence, in this study it has been attempted to compare the beneficial effect of alpha 2 agonist dexmedetomidine and clonidine in maintaining the perioperative hemodynamic parameters.

MATERIALS AND METHODS

For this study, 60 patients of the age group 20-45 years with bodyweight 50-70kgs, GCS 13 to15, and belonging to ASA PS I and PS II were selected and divided into two groups C and D. Ethics committee approval was obtained. The study design was a prospective randomized double blinded study done in Government Vellore Medical College & Hospital, Vellore, Tamil Nadu, India, in the year 2019-2020.Patients randomized to group C received intravenous clonidine 1µ/kg body weightdiluted with 100ml with 0.9% saline wasgiven 35mins prior surgery. For patients belonging to group D,the timing of dexmedetomidine 1µ/kg body weightdiluted to 100ml with 0.9% saline was given 10 mins prior surgery.Parameters like systemic blood pressure, heart rate, Spo2, ETCO2 and ECG were recorded at regular intervals like

- P -prior to premedication
- I1 -prior to induction
- I2 -3 min after induction
- I3 - at time of incision
- I4 -every 15min thereafter
- EA -5 min after extubation

Exclusion Criteria

- Patients with Hypertension and on treatment with α-methyl dopa, clonidine or other α_2 adrenergic agonist.
- Ischemic heart disease
- Heart block
- Pregnancy or lactating mothers
- Signs and symptoms of raised intracranial pressure
- Previous craniotomy
- MoRbid obesity
- Tumors of hypophysis
- Head injury
- Patient not willing to participate.

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All patients were given general anaesthesia and were induced using intravenous thiopentone[5mg/kg dose],and Vecuronium bromide (0.1 mg. kg iv) and maintained with O2+N2O + isoflurane and vecuronium.

Statistical Analysis

Results for parametric data were reported as means+-SD. Demographic data were analyzed by student paired t-tests. Hemodynamic data were analyzed by independent t-test for differences between groups and paired t-test for differences within groups. For post-hoc comparison, Bonferroni test. A value of <0.05 was considered significant statistically.

OBSERVATION AND ANALYSIS

Demographic data were analyzed by Student t-tests. Hemodynamic data were analyzed by independent t-test for differences between groups and paired t-test for differences within groups. For post-hoc comparison, the Bonferroni test. A value of<0.05 was considered statistically significant.

While analyzing the age distribution, gender, and ASA PS, among the intervention groups using an unpaired t-test, the data was found to be statistically insignificant(p>0.05)

RESULTS

Table 1: Comparison Of Dose Of Fentanyl During Maintenance In 2 Groups

GROUP	MEAN DOSE [µg]	SD	p
GROUP C	185.4	16.23	0.00002
GROUP D	168.5	15.31	significant

Fentanyl dose for maintaince was reduced in group D which was significant.

Table 2: Comparison Of Dose Of Vecuronium During Induction 2 Groups

GROUPS	VECURONIUM		
	MEAN[mg]	SD	p
GROUP C	9.8	1.3	0.125
GROUP D	9.1	1.6	Not significant

Requirement of vecuronium for induction was almost comparable and p value was not significant in group D and C.

Table 3 : Heart Rate

HR	GROUP	N	MEAN	STD. DEVIATION	P VALUE BY "t" TEST
P -prior to premedication	D	30	80.97	5.25	0.924
	C	30	81.10	5.50	
I1 -prior to induction	D	30	81.50	5.01	0.920
	C	30	81.63	5.26	
I2 -3 min after induction	D	30	72.00	4.58	<0.001
	C	30	77.00	5.19	
I3 - at time of incision	D	30	71.87	4.11	<0.001
	C	30	76.87	4.82	
I4 -every 15min thereafter	D	30	72.90	4.04	<0.001

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	C	30	77.87	4.71	
EA -5 min after extubation	D	30	72.10	3.62	<0.001
	C	30	76.40	3.94	

The heart rate distribution among patients was done using unpaired t-test, it was observed that attenuation of heart rate in the group D was better than group C and results were found to be statistically significant ($p<0.05$).

Table 4: Systolic BP

SBP	GROUP	N	MEAN	STD. DEVIATION	P VALUE BY "t" TEST
P -prior to premedication	D	30	125.60	9.39	0.748
	C	30	126.40	9.79	
I1 -prior to induction	D	30	125.40	8.36	0.823
	C	30	125.90	8.90	
I2 -3 min after induction	D	30	114.80	6.71	0.002
	C	30	121.00	7.95	
I3 - at time of incision	D	30	115.70	6.92	0.084
	C	30	119.03	7.73	
I4 -every 15min thereafter	D	30	113.10	6.02	0.005
	C	30	117.80	6.40	
EA -5 min after extubation	D	30	111.47	5.14	<0.001
	C	30	117.20	5.90	

While analyzing the systolic BP distribution among patients,it was observed that attenuation of systolic BP in the group D was better than group C and results were found to be statistically significant ($p<0.05$).

Table 5: Diastolic BP

DBP	GROUP	N	MEAN	STD. DEVIATION	P VALUE BY "t" TEST
P -prior to premedication	D	30	79.10	6.21	0.157
	C	30	81.53	6.91	
I1 -prior to induction	D	30	79.70	4.65	0.288
	C	30	81.17	5.87	
I2 -3 min after induction	D	30	72.97	4.55	0.001
	C	30	77.53	5.48	
I4 -every 15min thereafter	D	30	72.80	4.48	0.012
	C	30	76.23	5.71	
EA -5 min after extubation	D	30	70.73	4.49	<0.001
	C	30	76.07	4.73	

While analyzing the diastolic BP distribution among patients,it was observed that attenuation of diastolic BP in the group D was better than group C and results were found to be statistically significant ($p<0.05$).

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Table 6: Mean Arterial Pressure

MAP	GROUP	N	MEAN	STD. DEVIATION	P VALUE BY "t" TEST
P -prior to premedication	D	30	94.60	6.56	0.309
	C	30	96.49	7.64	
I1 -prior to induction	D	30	94.33	5.54	0.273
	C	30	96.08	6.63	
I2 -3 min after induction	D	30	86.20	4.79	<0.001
	C	30	92.02	6.08	
I3 - at time of incision	D	30	87.10	4.94	0.022
	C	30	90.50	6.16	
I4 -every 15min thereafter	D	30	88.23	4.96	0.017
	C	30	91.64	5.79	
EA -5 min after extubation	D	30	84.31	4.11	<0.001
	C	30	89.78	4.70	

While analyzing the mean arterial pressure distribution among patients using unpaired t-test, it was observed that attenuation of mean arterial pressure in the group D was better than C and results were found to be statistically significant ($p<0.05$)

DISCUSSION

Different modalities have been experimented with to reduce the hemodynamic response to Intracranial Tumour Surgery [6]. The concept of neuroanaesthesia includes several principles, the haemodynamic stability perioperatively being one of utmost importance. During surgery, abrupt increases in arterial blood pressure may cause bleeding or oedema in the operating field. Low arterial pressures on the other hand predispose the patients to cerebral ischaemia, because autoregulation of the cerebral blood flow (CBF) is often impaired near tumours or traumatized areas [7, 8]. Dexmedetomidine, a selective alpha 2 adrenoreceptor agonist has a sedative, analgesic, and anesthetic sparing effect [9]. Thus it was found that dexmedetomidine is more effective in controlling the hemodynamic response than Clonidine. Despite dexmedetomidine having side effects such as hypotension and bradycardia which can be detrimental in neurosurgical patients, we did not observe any such side effects when dexmedetomidine was slowly infused over 10 minutes in a dose of 1mcg/kg.

It has also been shown tha dexmedetomidine potentiates analgesia caused by fentanyl and reduces its dose requirements in humans during surgery [17]. Fentanyl dose for maintaince was reduced in dexmedetomidine group which was significant in our study. Requirement of vecuronium for induction was almost same in both groups.Both decreased haemodynamic responses to various noxious stimuli and attenuated the emergence from anaesthesia by decreasing the immediate haemodynamic response.

More significant haemodynamic stability with dexmetomidine was noticed. Mean arterial pressure, pulse are reduced in both group but more so with dexmetomidine. In our study we found that heart rate and mean arterial pressure were significantly lower in dexmedetomidine group when compared to the clonidine group in accordance to other study [11]. We used a lower dose of dexmedetomidine and clonidine anticipating untoward effects. However, a dose response curve is required to ascertain the role of above two drugs, which could not be done in the present study [10].

Limitations

Estimating the anaesthetic depth by changes mediated by autonomic nervous system (e.g. increases in arterial pressure and HR) is difficult as dexmedetomidine and clonidine increases haemodynamic stability.This study does not allow us to make any conclusions about possible neuroprotective or cerebral vasoconstrictive effects

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CONCLUSION

Dexmedetomidine is a useful sedative agent with analgesic properties, hemodynamic stability, and the ability to recover respiratory function in mechanically ventilated patients facilitating early weaning. Besides being a new modality of sedation and analgesia in ICU patient management, it has been studied in several other perioperative setting. Both dexmedetomidine and clonidine decreased haemodynamic responses to various noxious stimuli and attenuated the emergence from anaesthesia by decreasing the immediate haemodynamic response. More significant haemodynamic stability with dexmetomidine was noticed.Mean arterial pressure, pulse rate are reduced in both group but more so with dexmetomidine. It was concluded that 1 mcg/kg of dexmedetomidine infused slowly over10 minutes is superior when compared to clonidine in attenuating the hemodynamic changes during Intracranial Tumour Surgery **.**The possible limitations of the study were the low dose of drugs used, small sample size, inability to monitor the serum concentration of the drugs. Also this study does not allow us to make any conclusions about possible neuroprotective or cerebral vasoconstrictive effects. So further studies are required for assessing these effects of alpha 2 agonists.

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