IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 6 Ver. VI (Jun. 2015), PP 37-42
www.iosrjournals.org

Study to Assess the Role of Dexmedetomidine in Patients Undergoing Craniotomies and Laminectomies under General Anaesthesia

Dr. Priyamvada Gupta[1] Dr.Anshika Sharma[2] Dr. Sudhir Sachdeva[3]
Dr. Durga Jethava[4]

1. Associate Professor (Dept.of Anaesthesiology, Mahatma Gandhi Medical College/ Mahatma Gandhi University of Medical Science and Technology,Jaipur,Rajasthan, India),corresponding author,principal investigator.
2. Postgraduate student (Dept.of Anaesthesiology, Mahatma Gandhi Medical College/ Mahatma Gandhi University of Medical Science and Technology,Jaipur,Rajasthan, India)
3.Professor(Dept.of Anaesthesiology, Mahatma Gandhi Medical College/ Mahatma Gandhi University of Medical Science and Technology,Jaipur,Rajasthan, India)
4.PHOD(Dept.of Anaesthesiology, Mahatma Gandhi Medical College/ Mahatma Gandhi University of Medical Science and Technology,Jaipur,Rajasthan, India)

Abstract: *Dexmedetomidine a highly selective α-2 agonist has been shown to provide good perioperative haemodynamic stability and analgesia. It may provide neuroprotection and hence may be considered to be a suitable adjuvant during neurosurgical anaesthesia. This prospective randomized double-blind control study was designed to assess the perioperative effects of infusion of dexmedetomidine in patients with intracranial surgeries and laminectomies done under general anaesthesia. Sixty ASA grade I /II patients between 18-50 years of age were divided randomly into 2 groups of thirty each. Group A: Inj. Dexmedetomidine was given as a bolus dose of 1 mcg/kg by slow iv infusion over 20 minutes just before induction of anaesthesia followed by a maintenance infusion of 0.4 mcg/kg/hr. The infusion was discontinued at the completion of surgery. Group B: The patients received similar volumes of normal saline. Data were expressed as mean values ± standard deviation. p-value < 0.05 was considered to be statistically significant. We observed that heart rate and mean arterial blood pressure decreased in group A (dexmedetomidine group) more than group B (placebo group)(p<0.05). Although this was within physiological limits. Hence we conclude that dexmedetomidine maintained the haemodynamic stability and provided better surgical field.*

Keywords: *α-2adrenergicagonist, craniotomy, dexmedetomidine, haemodynamics, neuroprotection, laminectomy.*

I. Introduction

The perioperative course of patients undergoing craniotomies and laminectomies is frequently complicated by tachycardia and hypertensive episodes. Hence hypotensive anaesthesia is required for better surgical field. Dexmedetomidine, an alpha2receptor agonist has been shown to provide good perioperative haemodynamic stability due to the sympatholytic and antinociceptive properties.[1,2,3,4,5]. It also decreases intraoperative opioid requirements.□[6□] In addition, it has been shown to have neural protective effects and hence may be a suitable anaesthetic adjuvant to neurosurgical anaesthesia.□[7,8,9,10□]

Aims & Objectives: We designed this study to assess the efficacy of dexmedetomidine in controlling tachycardia and hypertensive responses in patients undergoing craniotomies for intracranial tumours and laminectomies. Complications if any were also studied.

II. Methods

2.1 Methodology

A randomized, double blind study was conducted at Mahatma Gandhi Medical College, Jaipur, Rajasthan in which sixty ASA grade I /II patients between 18-50 yrs of age with radiological evidence of intracranial tumour / intervertebral compression were selected . After taking informed consent, patients were classified randomly into two equal groups of thirty each. Routine monitoring was started viz. heart rate (ECG), non invasive blood pressure (NIBP), arterial oxygen saturation(SpO2) etc. Patients in group A received inj. dexmedetomidine as a bolus dose of 1 µg/kg slow infusion over 20 minutes just before induction of anaesthesia followed by a maintenance infusion of 0.4 µg /kg/hr. The infusion was discontinued on completion of the surgery.Patients in-group B received similar volumes of isotonic saline. Anaesthesia was standard for all the patients. The patients were premedicated with intravenous doses of inj. midazolam 0.02 mg/kg , inj. Fentanyl 2

µg/kg, inj. glycopyrolate 0.2 mg and inj. ondansetron-4 mg. After completion of the loading dose of dexmedetomidine, induction was done with i/v propofol 2mg/kg. Intubation was facilitated by intravenous rocuronium 1mg/kg. Anaesthesia was maintained with nitrous oxide in oxygen 60:40% and isoflurane. Muscle relaxation was maintained with inj. vecuronium. Routine monitoring consisted of NIBP, ECG, SpO2, EtCO2 recorded at frequent intervals. Temperature was maintained at 32 degree celsius. Target mean arterial pressure (MAP) was 60-70 mm Hg and end tidal carbon dioxide (EtCO2) 30-32mmHg.On completion of surgery, the neuromuscular blockade was reversed with i/v Neostigmine0.05mg/kg and inj. glycopyrolate 0.01 mg/kg. The discontinuation time of dexmedetomidine infusion was recorded. Expected side effects with the use of dexmedetomidine are bradycardia,arrhythmias and hypotension.The measures to control these side effects were kept ready .

Inclusion criteria- Patients of ASA grade I /II, age 18-50 years and with radiological evidence of intracranial tumours / intervertebral compressions were selected . Exclusion criteria- ASA grade III/ IV ,age less then 18 years and more than 50 years,arrythmias, heart blocks, drug allergy, convulsions, those on antidepressants/alpha adrenergic agents/any other medication. Patients refusing to give consent for the study were also excluded.

2.2 Ethics: The study was conducted after due approval from the Institutional Ethics Committee. Proper written informed patient consent was taken before surgery. The patients were informed that they had a right to reject to participate in the study.

III. Indentations And Equations

3.1Statistics

Data were expressed as mean values ± standard deviation (SD). Quantitative data was analyzed using t-test and qualitative by chi square test using IBM SPSS statistics 20.0 software. Changes in haemodynamic variables from baseline and a comparison of means were analyzed by paired t-test for each time interval. Further analysis was carried out for intervals during which differences from the baseline were statistically significant. A p-value < 0.05 was considered to be statistically significant

IV. Results

Both the study groups were identical in terms of age, sex ratio, weight, ASA status of patients and duration of surgery. (TABLE 1).Baseline values of heart rate were identical in both the groups(p=0.455) .After intubation there was increase in heart rate in group B whereas group A depicted decrease from baseline values(p<0.0001).Similar trends were observed at the time of extubation (p<0.0001).In the intra operative period the reference value was taken as 30min after intubation and it was observed that patients in group A had lower heart rates than baseline as compared to group B(p<0.0001)(TABLE 2).Similar trends were observed for mean, systolic and diastolic blood pressures(TABLES 3,4,5 respectively).There were no incidence of complications in either group(TABLE 6).

V. Figures And Tables

Table 1.Demographic Characteristics

SNo	VARIABLE	GROUP A	GROUP B	P-VALUE
1.	Age (years)	35.12 ± 14.79	37.13 ± 11.22	0.761
2.	Gender (male/female)	18/12	17/13	0.432
3.	Weight (Kgs)	58.23 ± 11.47	52.23 ± 10.07	0.342
4.	ASA physical status(I/II)	12/18	15/15	0.453
5.	Duration of surgery(minutes)	132.56 ± 84.73	126.56 ± 12.83	0.756

Table 2.Heart Rate

SNo	TIME VARIABLE	GROUP A	GROUP B	P-VALUE
1.	Baseline	82.9 ± 9.09	84.4 ± 6.09	0.4558
2.	Just after completion of loading dose	65.4 ± 5.04	84.4 ± 6.09	□ 0.0001
3.	Just after intubation	73.4 ± 11.93	112 ± 12.04	□ 0.001
4.	10 mins after intubation	70.4 ± 8.38	98.4 ± 9.08	□ 0.001
5.	30mins after intubation	67.1 ± 9.64	88.2 ± 8.4	□ 0.001
6.	60minsafter intubation	72 ± 8.43	112.4 ± 11.2	□ 0.001
7.	End of surgery	78.2 ± 8.14	98.4 ± 5.52	□ 0.001
8.	Extubation	78.4 ± 4.24	110.2 ± 4.02	□ 0.001

Table 3.Mean Bloodpressure

S.No.	TIME VARIABLE	GROUP A	GROUP B	P-VALUE
1.	Baseline	82.9 ± 4.08	85.4 ± 6.20	0.070
2.	Just after completion of loading dose	70.2 ± 5.04	84.2 ± 4.20	□ 0.001
3.	Just after intubation	74.4 ± 6.05	120.0 ± 5 4.0	□ 0.001
4.	10mins after intubation	72.4 ± 4.04	100.2 ± 4.20	□ 0.001
5.	30mins after intubation	64.2 ± 3.04	97.4 ± 4.20	0.001
6.	60mins after intubtion	62.0 ± 4.04	90.4 ± 3.34	□ 0.001
7.	End of surgery	64.2 ± 2.06	96.2 ± 2.03	□ 0.001
8.	Extubation	68.2 ± 4.02	110.2 ± 2.04	□ 0.001

Table 4.Systolic Bloodpressure

S. No.	TIME VARIABLE	GROUP A	GROUP B	P-VALUE
1.	Baseline	124.3 ± 12.46	122.5±10.24	0.499
2.	Just after completion of loading dose	108.0 ± 8.24	120.1 ± 8.62	□ 0.001
3.	Just after intubation	98.4 ± 9.08	136.5 ± 6.23	□ 0.001
4.	10 min after intubation	94 ± 12.04	112 ± 12.04	□ 0.001
5.	30 min after intubation	100 ± 8.68	122.8 ± 8.41	□ 0.001
6.	60 min after intubation	98.2 ± 9.20	125.81 ± 6.66	□ 0.001
7.	End of surgery	100.1 ± 7.76	132.5 ± 8.24	□ 0.001
8.	Extubation	98.8 ± 8.01	148.32 ± 5.89	□ 0.001

Table5.Diastolic Blood Pressure

S. No.	TIME VARIABLE	Group A	Group B	P-Value
1.	Baseline	80.4 ± 10.46	84.2±8.24	0.124
2.	Just after completion of loading dose	68.2 ± 8.24	82.4 ± 6.81	□ 0.001
3.	Just after intubation	68.24 ± 12.48	88.4 ± 9.04	□ 0.001
4.	10 min after intubation	70.2 ± 10.2	86.3 ± 9.08	□ 0.001
5.	30 min after intubation	60.2 ± 9.08	75.4 ±12.23	□ 0.001
6.	60 min after intubation	56.4± 8.33	72.4 ± 10.04	□ 0.001
7.	End of surgery	60.0 ±7.87	81.5 ± 9.22	□ 0.001
8.	Extubation	68.4 ± 7.68	88.6 ± 11.03	□ 0.001

Table6. Complications

S.No	VARIABLE	GROUP A	GROUP B
1.	Respiratory depression	none	none
2.	Bradycardia	1	none
3.	Arrythmias	none	none
4.	Convulsions	none	none

VI. Conclusions

Dexmedetomidine is a highly selective α2 agonist. It has potent sympatholytic, anxiolytic, sedative and analgesic properties mediated through α2-adrenoreceptors in the central and peripheral nervous system[11,12,13]. Dexmedetomidine-induced sedation qualitatively resembles normal sleep from which patients can be easily aroused. This type of sedation is termed as conscious sedation unlike that caused by drugs acting on gamma-amino butyric acid receptors such as benzodiazepines or propofol[14,15]. It causes a dose-dependent decrease in arterial blood pressure and heart rate associated with a decrease in serum norepinephrine concentrations[4].The effect of α2-agonists on haemodynamics is biphasic: an immediate increase in systemic arterial pressure (mediated by stimulation of peripheral α2 adrenoceptors) followed by a longer lasting reduction

in pressure caused by stimulation of α2-adrenoceptors in the central nervous system[5]. These actions may have contributed to the findings in the haemodynamic profile in patients who received dexmedetomidine in our study. In some earlier reports, premedication with oral clonidine, another α-2 agonist , provided attenuation of the haemodynamic responses to laryngoscopy and intubation[16,17]. In our study, a loading dose of 1 μg/kg dexmedetomidine was given over 20 minutes, followed by a continuous infusion of 0.4 μg/kg/hour. The following conclusions were drawn:-

- dexmedetomidine blunted pressor response to intubation and extubation
- better haemodynamic stability in the perioperative period with use of dexmedetomidine
- an acceptable recovery profile of the patients in dexmedetomidine group.

In patients undergoing general or gynaecological surgery, numerous studies have shown that dexmedetomidine blunts the cardiovascular responses to intubation[18,19]. Our findings were in accordance with them. In addition to this beneficial property of alpha2-agonists, they have also been reported to increase the risk of hypotension and bradycardia. These effects have most often been seen in young healthy volunteers or after rapid bolus administration[19,20]. In our study there was no difference between the groups in the occurrence of bradycardia or hypotension.This was probably because we used low bolus and maintenance doses; and bolus doses were also administered slowly. Numerous studies have shown that dexmedetomidine reduces the analgesic and anaesthetic requirements in the perioperative period.[21,22,23] We observed the same though statistical analysis was not done since it was not a part of our study. inj. fentanyl 50 mcg iv was given as rescue analgesic. It has also been shown that dexmedetomidine potentiates analgesia caused by fentanyl in animals [24,25] and reduces its dose requirements in humans during surgery.

The haemodynamic responses to intracranial and spinal surgery are most often seen at the start or the end of the surgery and during the manipulation of certain structures within the brain. After surgery the hypertension may lead to postoperative intracranial haematomas.[26]Hence it is mandatory to maintain haemodynamic stability throughout the peri operative period. The haemodynamic responses to emergence from anaesthesia and extubation were also blunted with dexmedetomidine and the centrally mediated sympatholytic effect has continued well into the postoperative period.[27]

Expected side effects with the use of dexmedetomidine are arrythmias, bradycardia, hypotension and convulsions. The measure to control these side effects were ready with us. In our study none of the side effects was observed. This again may be attributed to the use of lower doses. Only one patient had bradycardia which subsided with discontinuation of dexmedetomidine. No pharmacological intervention was required. It has been shown to have minimal effects on respiration and tracheal extubation has been successfully carried out in critically ill patients under continuing dexmedetomidine sedation.[28,29]

Dexmedetomidine has been used in neurosurgical procedures involving neurophysiologic monitoring and it was observed that cortical evoked potential, amplitude and latencies were minimally affected.[30]The golden standard of neuroanaesthesia includes maintenance of anaesthesia with isoflurane or propofol with fentanyl.[31] Recently, new agents, such as sevoflurane, desflurane and remifentanil, have been added to this. High concentrations of volatile anesthetics can blunt the carbon dioxide response and render CBF pressure passively.[32] Even with low concentrations, hyperventilation is needed to counteract the vasodilatation caused by the volatile anaesthetics, to avoid increases in the intracranial pressure in patients with mass occupying lesions. In dogs, administration of dexmedetomidine significantly attenuated isoflurane- and sevoflurane-induced dilation of cerebral arterioles.[33] In the present study, we administered isoflurane, and moderate hyperventilation was used so as to maintain EtCO2 around 32 mm Hg.

Controversy exists about the neuroprotective effects of dexmedetomidine. This effect has been related to reduced sympathetic outflow, and it has been shown that a reduction in circulating catecholamines rather than cerebral catecholamine concentrations mediate neuroprotection after cerebral ischaemia[34] On the other hand dexmedetomidine is a direct cerebral vasoconstrictor that may override the cerebral pressure autoregulation.[35] In a recent study using positron emission tomography dexmedetomidine decreased global CBF in human volunteers while at the same time decreasing systemic arterial pressure and cardiac output.[36] This may predispose to cerebral ischemia, although in animal studies the vasodilatory response to hypoxia has been preserved.[37] Dexmedetomidine has been successfully used for sedation during awake craniotomy.[38]

This study protocol does not allow us to make any conclusions about possible neuroprotective or cerebral vasoconstrictive effects of dexmedetomidine. We have however demonstrated the safety and feasibility of dexmedetomidine in these patients in terms of cardiorespiratory stability which may in turn have beneficial

neurophysiological effects. More such studies on neuroprotection are warranted in clinical settings. We could have done intracranial pressure monitoring and cMRO2 studies, but it was not available with us.

Conflict of interest: None
Acknowledgements: Nil
Source of support: Nil

References

[1]. Kamibayashi T, Maze M. Clinical uses of alpha2-adrenergic agonists. Anesthesiology. 2000;93(11)1:57-69
[2]. Farber NE,Samso E, Staunton M, Schwabe D, Schmeling WT. Dexmedetomidine modulates cardiovascular responses to stimulation of central nervous system pressor sites. Anesth Analg 1999;889(4):617-24
[3]. Basar H, Akpinar S, Doganci N, et al. The effects of preanesthetic, single-dose Dexmedetomidine on induction, hemodynamic and cardiovascular parameters. J ClinAnesth. 2008;20(6):431-436.
[4]. Kallio A, Scheinin M, Koulu M, et al. Effects of dexmedetomidine, a selective alpha 2adrenoceptor agonist, on hemodynamic control mechanisms. Clin Pharmacol Ther 1989;46(6):3342.
[5]. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology 1992;77(6):1134-42.
[6]. Cottrell JE, Smith DS,Sakabe T, Nakakimura K. Effects of anesthetic agents and other drugs on cerebral blood flow, metabolism, and intracranial pressure. In: Cottrell JE, Smith DS, editors. Anesthesia and Neurosurgery. 4th Edn. St Louis: Mosby; 2001:129-43.
[7]. Hoffman WE, Kochs E, Werner C, Thomas C, Albrecht RF. Dexmedetomidine improves neurologic outcome from incomplete ischemia in the rat. Reversal by the alpha 2-adrenergic antagonist atipamezole. Anesthesiology 1991;75:328-32.
[8]. Maier C, Steinberg GK, Sun GH, Zhi GT, Maze M. Neuroprotection by the alpha 2adrenoreceptor agonist dexmedetomidine in a focal model of cerebral ischemia. Anesthesiology 1993;79:306-12.
[9]. Prielipp RC, Wall MH, Tobin JR, et al. Dexmedetomidine-induced sedation in volunteers decreases regional and global cerebral blood flow. Anesth Analog 2002;95:1052-9.
[10]. Gurbert A, Mogol EB, Turker G, et al. Intraoperative infusion of Dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth. 2006;53(7):646-652.
[11]. Yazbek-Karam VG, Aquad MM. Perioperative uses of Dexmedetomidine. Middle East J Anesthesiol.2006;18(6):1043-1058.
[12]. Hall JE, Uhrich TD, Barney JA, et al. Sedative, amnesic, and analgesic properties of small-dose Dexmedetomidine infusions.Anesth Analg. 2000;90(3):699-705.
[13]. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth 1992;68:126-31.
[14]. Hudes ET, Marans HJ, Shine K, Scott AC, Hirano GM. A comparison of morphine-perphenazine and midazolam on preoperative sedation and arterial oxygen saturation. Can J Anaesth 1991;38:187-90. intramuscular
[15]. Dyck JB, Maze M, Haack C, et al. The pharmacokinetics and hemodynamic effects of intravenous and Dexmedetomidine hydrochloride in adult human volunteers.Anesthesiology. 1993;78(5):813-820.
[16]. Chadha R, Padmanabhan V, Joseph A, Mohandas K. Oral clonidine pretreatment for haemodynamic stability during craniotomy. Anaesth Intensive Care 1992;20:341-4.
[17]. Costello TG, Cormack JR. Clonidine premedication decreases hemodynamic responses to pin head-holder application during craniotomy. Anesth Analg 1998;86:1001-4.
[18]. Aho M, Lehtinen AM, Erkola O, et al. The effect of intravenously administered Dexmedetomidine on perioperative hemodynamics and Isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology. 1991;74(6):997-1002
[19]. Lawrence CJ, De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. Anaesthesia 1997;52:736-44.
[20]. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382-94.
[21]. Khan ZP, Munday IT, Jones RM, Thornton C, Mant TG, Amin D. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. 1: Pharmacodynamic and pharmacokinetic interactions. Br J Anaesth 1999;83:372-80.
[22]. Frölich MA, Arabshahi A, Katholi C, et al. Hemodynamic characteristics of Midazolam, Propofol, and Dexmedetomidine in healthy volunteers. J Clin Anesth. 2011;23(3):218-223.
[23]. Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. Anesthesiology 1997;86:1055-60.
[24]. Salmenperä MT, Szlam F, Hug CC Jr. Anesthetic and hemodynamic interactions of dexmedetomidine and fentanyl in dogs. Anesthesiology 1994;80:837-46.
[25]. Meert TF, De Kock M. Potentiation of the analgesic properties of fentanyl-like opioids with alpha 2-adrenoceptor agonists in rats. Anesthesiology 1994;81:677-88.
[26]. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. Anesthesiology 2000;93:48-54.
[27]. Talke P, Chen R, Thomas B, et al. The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. Anesth Analg 2000;90:834-9.
[28]. Shehabi Y,Ruettimann U, Adamson H, Innes R, Ickeringill M. Dexmedetomidine infusion for more than 24 hours in critically ill patients: sedative and cardiovascular effects. Intensive Care Med 2004;30:2188-96.
[29]. Hsu YW, Cortinez LI, Robertson KM, et al. Dexmedetomidine pharmacodynamics: Part 1 Crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology 2004;101:1066-76.
[30]. Bekker A, Sturaitis MK: Dexmedetomidine for neurological surgery. Neurosurgery 57:1-10, 2005.
[31]. Todd MM, Warner DS, Sokoll MD, et al. A prospective, comparative trial of three anaesthetics for elective supratentorial craniotomy. Propofol/fentanyl, isoflurane/nitrous oxide, and fentanyl/nitrous oxide. Anesthesiology 1993;78:1005-20.
[32]. McPherson RW, Brian JE, Traystman RJ. Cerebrovascular responsiveness to carbon dioxide in dogs with 1.4% and 2.8% isoflurane. Anesthesiology 1989;70:843-50.
[33]. Ohata H, Iida H, Dohi S, Watanabe Y. Intravenous dexmedetomidine inhibits cerebrovascular dilation induced by isoflurane and sevoflurane in dogs. Anesth Analg 1999;89:370-7.
[34]. Engelhard K, Werner C, Kaspar S, et al. Effect of the alpha2-agonist dexmedetomidine on cerebral neurotransmitter concentrations

during cerebral ischemia in rats. Anesthesiology 2002;96:450-7.
[35]. Ganjoo P, Farber NE, Hudetz A, et al. In vivo effects of dexmedetomidine on laser-doppler flow and pial arteriolar diameter. Anesthesiology 1998;88:429-39.
[36]. Prielipp RC, Wall MH, Tobin JR, et al. Dexmedetomidine-induced sedation in volunteers decreases regional and global cerebral blood flow. Anesth Analg 2002;95:1052-9.
[37]. Takenaka M, Iida H, Iida M, Dohi S. Intrathecal dexmedetomidine attenuates hypercapnic but not hypoxic cerebral vasodilation in anesthetized rabbits. Anesthesiology 2000;92:1376-84.
[38]. Mack PF, Perrine K, Kobylarz E, Schwartz TH, Lien CA. Dexmedetomidine and neurocognitive testing in awake craniotomy. J Neurosurg Anesthesiol 2004;16:20-5.