

Original Article

## Clinical Outcomes of Dexmedetomidine As An Anesthetic Adjuvant in Intracranial Surgery, An Experience from Irfan General Hospital Peshawar: A Prospective Case Series Study

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### ABSTRACT

**Objective:** Neuro anesthesia (most commonly general) is indicated in intracranial surgery, the goal of which is to maintain a stable hemodynamic environment. This study aimed at evaluating the effectiveness of Dexmedetomidine (DEX) when used as an adjuvant in intracranial surgery.

**Materials And Methods:** A prospective design was utilized and the data was collected at the Department of Neurosurgery Irfan General Hospital Peshawar in patients undergoing intracranial. All those patients having a score of 14 or 15 on the Glasgow Coma Scale, and I and II on the American Society of Anesthesiologists (ASA) undergoing intracranial surgery under general anesthesia were included in the study.

**Results:** The majority of patients were males 35 (66%) while 18 (34%) were females. 29(55%) patients were categorized as grade I while 24 (45%) as grade II according to the American Society of Anesthesiologists-Physical status. mean extubation time of our sample of patients undergoing craniotomy was  $6.21 \pm 2.16$  minutes while the time for rescue analgesia was  $41.23 \pm 23.15$  minutes. The heart rate values decreased significantly when noted at different intervals from the baseline.

**Conclusion:** Dexmedetomidine is an effective and safe anesthetic adjuvant when used in intracranial surgery and provides stable hemodynamics both intra and post-operatively. The neuro anesthetic drug also reduces the requirements of other opioids and rescue drugs.

**Keywords:** Anesthetic Adjuvant, Dexmedetomidine, Intracranial Surgery.

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### INTRODUCTION

Craniotomy consists of several neurosurgical

procedures performed for various neurological disorders including infections and tumors of the brain, fractures of the skull, vessel lesions (aneurysms, hematomas, or arteriovenous malformation), foreign objects, and implantation of electrodes.<sup>1</sup> Neuro anesthesia (most commonly general) is indicated in intracranial surgery, the goal of which is to maintain a stable hemodynamic environment along with smooth induction and optimum level of operative conditions such as maintenance of cerebral oxygenation and perfusion pressure and a relaxed brain.<sup>2</sup> Smooth emergence and rapid recovery are integral for the assessment of neurocognitive responses following craniotomy. To achieve these goals, the optimum selection of anesthetics is therefore a necessity.<sup>3</sup> There is no consensus regarding the anesthetic drugs and combinations which are optimum to be used in craniotomy. Opioids are associated with providing hemodynamic stability and effective analgesia but are also associated with adverse effects such as respiratory depression, postoperative nausea and vomiting, and delayed recovery.<sup>4</sup>

Dexmedetomidine (DEX), an  $\alpha_2$  adrenoreceptor agonist is a highly selective anesthetic drug and adjuvant having both analgesic and sedative effects with  $\alpha_2$ :  $\alpha_1$  adrenoreceptor ratio of 1600:1 which is 7 to 8 times higher than clonidine making it the sedative–anxiolytic.<sup>5</sup> Because of its central sympatholytic action, dexmedetomidine exhibits its dose-dependent effects of anxiolysis, sedation, and antinociception while also preventing intraoperative tachycardic and hypertensive episodes. A cooperative form of sedation is provided by dexmedetomidine, as the patient can easily wake up and comply with the early neurological assessment.<sup>6</sup> Dexmedetomidine (DEX), unlike short-acting opioids exhibits its function without causing any respiratory depression while also reducing perioperative opioid and anesthetic requirements.<sup>7</sup> Pharmacokinetic and pharmacodynamic properties of

dexmedetomidine make it the proper fit as an anesthetic adjunct in neurosurgical anesthesia and is associated with various advantages such as its patency during awake craniotomy, neuroprotection, minimum or no respiratory depression, preservation of neural function through minimal disruption of neurophysiological monitoring along with an unchanged intracranial pressure (ICP).<sup>8</sup> This study aimed at evaluating the effectiveness of Dexmedetomidine (DEX) when used as an adjuvant in intracranial surgery in terms of hemodynamic stability, the requirement of rescue drugs along with complications.

## MATERIALS AND METHODS

### Study Design & Setting

A prospective design was utilized and the data was collected at the Department of Neurosurgery Irfan General Hospital Peshawar from patients undergoing intracranial surgery from February 2022 till February 2023. Ethical approval was granted by the Institutional Review Board and informed consent was taken from the included participants. Nonprobability convenience sampling was used.

### Inclusion Criteria

All those patients having scores of 14 or 15 on the Glasgow Coma Scale, and I and II on the American Society of Anesthesiologists (ASA) undergoing intracranial surgery under general anesthesia were included in the study.

### Exclusion Criteria

Pregnant females, with pre-operative heart rates less than 60 beats per minute and those having pre-existing cardiovascular, hepatic, or renal disease were excluded.

Demographic variables and perioperative data were collected. A total of 80 patients underwent craniotomy during the time frame out of which 53

patients were included according to the inclusion criteria. In those patients, Dexmedetomidine was administered as an adjuvant anesthetic.

### Administration of Dexmedetomidine

After shifting the patient in the operating room and before administering the anesthesia, the consciousness level, sedation score along with assessment of hemodynamic variables (Heart rate, systolic and diastolic blood pressure, mean arterial pressure, respiratory rate, and oxygen saturation) were assessed and documented. Dexmedetomidine infusion was given at about 20 minutes before administering anesthesia. At every 5 minutes interval, the hemodynamic variables were assessed during infusion. During surgery dexmedetomidine was administered at the rate of 1 microgram/kg for 10 minutes to achieve the plasma level and then a maintenance dose of 0.6 microgram/kg/hr. After the surgery, the immediate neurocognitive assessment was performed while the post-operative sedation level was assessed by the University of Michigan Sedation Scale (UMSS) values of which are given in Table 1.

**Table 1:** University of Michigan Sedation Scale<sup>9</sup>.

UMSS SCORE	
0	Awake and alert
1	Sleepy/responds appropriately
2	Somnolent/Arouses to stimulus of light
3	In deep sleep and arouses to deeper physical stimulus
4	Not arousable to stimulus

### Primary Outcome

The primary outcome assessed was to measure the intraoperative hemodynamic response and stability in terms of measuring heart rate, blood pressure, and respiratory rate at different intervals.

Hemodynamic values were recorded at different intervals such as baseline values (preoperative) T0, post-intubation T1, during the

pinning T2, at the time of incision T3 and after certain hours of incision (H1, H2, H3, H4), at the end of skin closure T-end and after first two hours from ICU admission (ICU H1 and ICU H2).

### Secondary Outcome

The secondary outcome of our study was to assess the need for other agents including propofol and fentanyl intraoperatively and nalbuphine postoperatively.

By incorporating the descriptive statistics, the analysis was carried out using the software SPSS version 26. For the data which was numerical i.e., age the mean and standard deviation were reported while for the categorical data, the percentages and frequencies were used.

## RESULTS

### Patient Characteristics and Perioperative Data

During the one-year time frame, a total of 53 patients undergoing craniotomy were administered Dexmedetomidine as an adjuvant.

### Age Distribution

The mean age of the participants was 42.3 ranging from 24 to 55.

### Gender Distribution

Males constituted the majority of the sample 35 (66%) as compared to females 18 (34%). 29 (55%) patients were categorized as grade I while 24 (45%) as grade II according to the American Society of Anesthesiologists-Physical Status. The results of demographic variables and

**Table 2:** Demographic variables and Peri-operative data:

Variables and Perioperative Data	Mean and Standard Deviation
Age (Years)	42.3(18.4)
Body Mass Index (kg/m <sup>2</sup> )	24.6 (6.9)

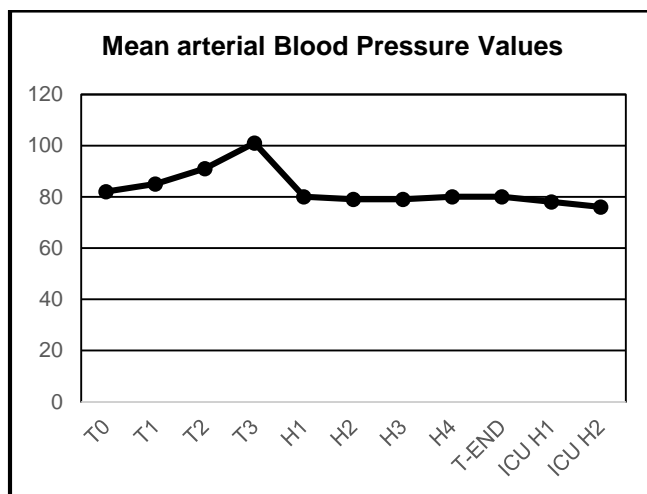
Duration of surgery (minutes)	240 (49.8)
Recovery time (minutes)	10 (3.1)

perioperative data are summarized in Table 2.

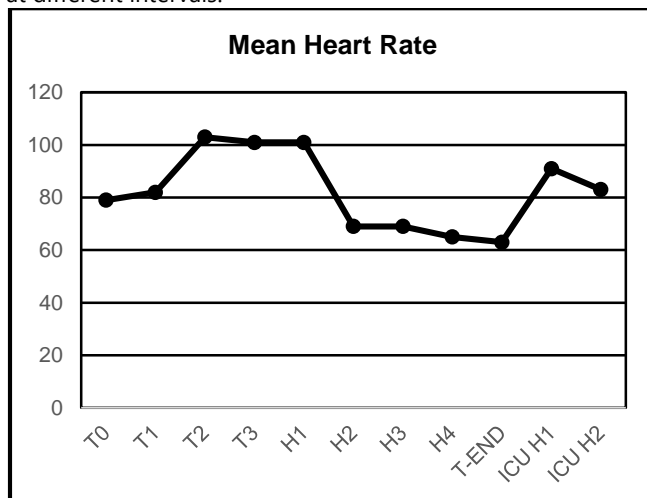
## Hemodynamic (Mean Arterial Blood Pressure, Heart Rate)

Mean arterial blood pressure as a measure of hemodynamic stability showed no significant increase in mean arterial blood pressure values recorded at different intervals compared to the baseline as shown in Figure 1.

The heart rate values decreased significantly when noted at different intervals from the



**Figure 1:** Follow-up values of Mean arterial blood pressure at different intervals.



**Figure 2:** Mean Heart Rate Values at different intervals.

baseline as is evident from Figure 2.

Requirements of rescue drugs used intraoperatively and postoperatively are highlighted in Table 2.

**Table 2:** Requirements of fentanyl/propofol and nalbuphine.

Total intraoperative fentanyl ( $\mu\text{g}$ )	120 (24.9)
Total intraoperative propofol ( $\text{mg}$ )	16 (35.1)
Total postoperative nalbuphine ( $\text{mg}$ )	7.2 (1.5)

The results of our study illustrate that the mean extubation time of our sample of patients undergoing craniotomy was  $6.21 \pm 2.16$  min while the time for rescue analgesia was  $41.23 \pm 23.15$  min. Sedation score was measured at the time of extubation and after 1 and 2 hours of extubation, results of which showed that the majority of patients had low scores indicating a good state of arousal (Table 3).

**Table 3:** University of Michigan sedation score at different intervals

The University of Michigan Sedation Score	Frequency/Percentages
<b>H0<sup>a</sup></b>	
1	37 (70%)
2	16 (30%)
<b>H1<sup>b</sup></b>	
0	30 (56%)
1	22 (41%)
2	2 (3%)
<b>H2<sup>c</sup></b>	
0	37 (69%)
1	16 (31%)

H0<sup>a</sup>: At the time of admission to ICU

H1<sup>b</sup>: After one-hour

H2<sup>c</sup>: After 2 hours

Perioperative complications were reported in a smaller proportion of patients, of which atropine was administered for bradycardia in 7 (13%) while Mephentermine was given for hypotension in 10 (18%) patients.

## DISCUSSION

Certain hemodynamic parameters such as blood pressure, heart rate, and respiratory rate should be maintained at an optimum level during intracranial surgery and are of paramount importance. Increased blood pressure during intracranial surgery can cause hemorrhage and vasogenic edema while hypotension leads to cerebral ischemia. During emergence from anesthesia, hypertension can cause intracranial hemorrhage.<sup>2</sup> These findings indicate that hemodynamic stability should be maintained not only intraoperatively but also postoperatively and at the time of emergence.

Dexmedetomidine, an alpha 2 agonist has been used as an anesthetic adjuvant and is associated with decreasing the amount of opioid, inhalational, and intravenous anesthetics requirements along with maintaining hemostatic stability.<sup>10</sup> The current study aimed to evaluate the clinical outcomes associated with the use of dexmedetomidine as an anesthetic adjuvant.

Several randomized control trials are conducted to evaluate the effectiveness of dexmedetomidine when used as an anesthetic adjuvant. A meta-analysis conducted in China illustrated that patients who were treated with DEX showed improved clinical outcomes as compared to placebo or other drugs. Those treated with DEX had lesser requirements for rescue agents and pharmacological interventions to control blood pressure abnormalities or other hemostatic factors.<sup>11</sup> Another systematic review and meta-analysis carried out In 2018 depicted the same findings and demonstrated that as compared to placebo or other drugs, the dexmedetomidine reduced post-operative pain, nausea, and vomiting to a greater extent along with maintaining the hemostatic variables at an optimum level.<sup>12</sup> Meta-analysis results are per our study as values of blood pressure and heart rate were recorded at different intervals from the baseline and the results were satisfactory in terms

of hemostatic stability intra and postoperatively and requirements of rescue agents.

Our study results reported that the requirements of Fentanyl and Propofol preoperatively were 120 ( $\mu\text{g}$ ) and 16 ( $\mu\text{g}$ ) while it was 7.2 ( $\mu\text{g}$ ) for Nalbuphine postoperatively. Results of another randomized control trial were in accordance with our study which illustrated that the treatment group in which dexmedetomidine was administered as anesthetic adjuvant showed decreased requirements of different drugs for hemodynamic stability as the intraoperative values of Fentanyl and Propofol reported in the study were 132 ( $\mu\text{g}$ ) and 14 ( $\mu\text{g}$ ) respectively while for post-operative requirements of Nalbuphine, the study reported requirements of 7.4 ( $\mu\text{g}$ ) and these values were reported to be higher in control group (Fentanyl: 260 ( $\mu\text{g}$ ), Propofol: 534.4 ( $\mu\text{g}$ ), Nalbuphine: 7.4 ( $\mu\text{g}$ )).<sup>13</sup> These findings illustrate the effectiveness of Dexmedetomidine in terms of the amount of rescue drugs required.

By administering DEX, initially, there is a rise in mean arterial blood pressure due to  $\alpha 2B$  postsynaptic receptors activation followed by a decrease in mean arterial blood pressure and heart rate as  $\alpha 2A$  receptors get activated in Central Nervous System.<sup>14</sup> Initial spike in arterial blood pressure was also noted in our study which can be prevented by avoiding the bolus dose. Minor perioperative complications were observed in our study in a smaller proportion of patients. These were hypotension 10 (18%) and bradycardia 7 (13%). These findings are consistent with a study conducted in Norway to evaluate pain after the surgical procedure of craniotomy administered with dexmedetomidine, the results of which reported that DEX was associated with less post-operative pain but was also associated with hypotension bradycardia at different intervals during surgery.<sup>15</sup> Complication of hypotension and bradycardia is attributed to the sympatholytic effects of the drug on the central nervous system.



The small size of our sample may be attributed to one of the limitations of the study along with the study design. Future studies of longer duration should be carried out along with comparing the effects of dexmedetomidine with a control group which would further clarify the hypothesis.

## CONCLUSION

Dexmedetomidine is an effective and safe anesthetic adjuvant when used in intracranial surgery and provides stable hemodynamics both intra and post-operatively. The neuroaesthetics drug also reduces the requirements of other opioids and rescue drugs. However, it also carries the risk of hypotension and bradycardia attributed to the sympatholytic action of dexmedetomidine.

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## Additional Information

**Disclosures:** Authors report no conflict of interest.

**Ethical Review Board Approval:** The study was conformed to the ethical review board requirements.

**Human Subjects:** Consent was obtained by all patients/participants in this study.

**Conflicts of Interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Financial Relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

**Other Relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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## AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Shahid Mabood, Asad Khan, Javed Iqbal & Fahad Mehmood	1. Study design and methodology.
2.	Shahid Mabood & Javed Iqbal	2. Paper writing.
3.	Abdul Haseeb Sahibzada & Javed Iqbal	3. Data collection and calculations.
4.	Shahid Mabood & Abdul Haseeb Sahibzada	4. Analysis of data and interpretation of results.
5.	Shahid Mabood & Asad Khan	5. Literature review and referencing.
6.	Abdul Haseeb Sahibzada	6. Editing and quality insurer.