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Review Paper

Use of dexmedetomidine in neurosurgical procedures

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ABSTRACT:
Dexmedetomidine, a highly selective alpha-2 adrenergic receptor agonist, is gaining prominence in neurosurgery due to its unique sedative, analgesic, and neuroprotective properties. This review explores its pharmacodynamics, including its effects on cerebral blood flow and metabolism, and its clinical applications in deep brain stimulation, awake craniotomy, awake fiberoptic intubation, and as an adjunct to general anesthesia. With an arousable sedation profile and minimal respiratory depression, dexmedetomidine enhances patient cooperation and hemodynamic stability. Emerging evidence suggests potential benefits in neuroprotection and delirium prevention, though further research is needed to optimize dosing and confirm these effects in neurosurgical settings.

Keywords: Dexmedetomidine, neurosurgery, sedation, neuroprotection, awake craniotomy, deep brain stimulation, delirium prevention.

INTRODUCTION:

Dexmedetomidine a highly selective alpha 2 adrenergic receptor agonist, has emerged as a versatile sedative and analgesic agent with significant potential in neurosurgical settings.This review synthesizes current evidence on dexmedetomidine's role in neurosurgery ,focusing on its pharmacodynamic properties clinical applications and emerging areas of interest ,drawing from recent studies and clinical trials.

PHARMACODYNAMIC PROFILE:

Dexmedetomidine possess an alpha2:alpha 1 selectivity ratio of 1620:1; making it 8 times more selective for the alpha 2 adrenergic receptor. By activating pre and post synaptic alpha 2 adreno receptors within the CNS ,it hyperpolarises noradrenergic neurons ,induces an inhibitory feed back loop and reduces norepinephrine release there by resulting in a sympatholytic effect .[2]

Dexmedetomidine has biphasic effect on BP with modest decline in heart rate and BP with lower doses ;and potential bradycardia or transient hypertension at higher doses or rapid infusions.

Bradycardia is induced via vagomimetic action and blocked cardio accelerator nerves. Transient hypertension with bolus injection or during a loading dose is the result of smooth muscle contraction due to peripherally located alpha 2 adrenoreceptor on blood vessels.[1]

Dexmedetomidine induces sedation by decreasing activity of noradrenergic neurons in locus cereleus in the brain stem there by increasing the downstream activity of inhibitory GABA neurons in the ventrolateral preoptic nucleus .The sedative effects resemble natural sleep specifically stage -2 Non rapid eye movement sleep(NREM) as demonstrated by EEG studies.

Analgesic effects are produced by actions of alpha 2 adrenoreceptor in the spinal cord as well as supraspinal and peripheral sites.[4]

Studies have shown that dexmedetomidine reduces CMRO2(Cerebral Metabolic Rate of Oxygen) and CBF(Cerebral Blood Flow) .Alpha 2 adrenergic agonist also have shown to attenuate global and focal cerebral ischemic events .By reducing catecholamine production dexmedetomidine can potentially reduce neuronal injury .Neuroprotective effects of dexmedetomidine may also be due to enhanced production on epidural growth factor and brain derived neurotrophic factors.[4]

DOSAGE AND ADMINISTRATION:

Dexmedetomidine dosing varies by indication (Table 1). For procedural sedation and as an anesthetic adjunct, a loading dose of 0.5–1.0 μg/kg over 10 minutes is followed by an infusion of 0.3–1.0 μg/kg/hr or 0.3–0.5

μg/kg/hr, respectively. Intranasal administration for premedication ranges from 0.5–2 μg/kg, with effects onset within 15–20 minutes [31]. Rapid administration should be avoided to prevent hypertension and bradycardia, and lower doses are advised in the elderly or those with cardiovascular comorbidities.

Table 1: Dosages and Infusion Rates for Dexmedetomidine[2]

Dexmedetomidine Administration	Loading Dose (μg/kg)	Infusion Rate (μg/kg/hr)
Procedural Sedation	0.5–1.0 (over 10 min)	0.3–1.0
Anesthetic Adjunct	0.5–1.0 (over 10 min)	0.3–0.5
Intranasally	0.5–2	-

Safety and Limitations:

While dexmedetomidine is generally well-tolerated, its hemodynamic effects (e.g., bradycardia, hypotension) require careful monitoring, particularly in hypovolemic patients or those with conduction abnormalities [32]. The small sample sizes and variability in surgical durations in some studies limit generalizability, and further research is needed to optimize dosing and confirm neuroprotective and delirium-prevention effects [33].

CLINICAL APPLICATIONS IN NEUROSURGERY:

Deep Brain Stimulation (DBS) Electrode Implantation:

DBS is a standard treatment for Parkinson's disease, dystonias, and other movement disorders, requiring precise electrode placement guided by intraoperative neurophysiologic testing, including microelectrode recordings (MERs) and test stimulations [9]. General anesthesia or sedatives that impair patient responsiveness or interfere with MERs are contraindicated. Dexmedetomidine offers a unique advantage with its arousable sedation, allowing patients to cooperate with clinical assessments while minimizing interference with electrophysiological recordings [10]. Studies have demonstrated that dexmedetomidine, administered at a loading dose of 0.5–1.0 μg/kg over 10 minutes followed by an infusion of 0.3–1.0 μg/kg/hr, provides effective sedation without significant suppression of neuronal firing rates [11, 12]. This approach also improves hemodynamic stability, reducing the need for antihypertensive drugs and enhancing patient satisfaction [13].

Awake Craniotomy:

Awake craniotomy is employed for surgeries near eloquent brain areas (e.g., speech or motor centers) or for epilepsy focus mapping, necessitating patient cooperation during neurocognitive testing [14]. Dexmedetomidine's ability to induce a sleep-like, arousable sedation state is highly beneficial, enabling patients to perform complex tasks while remaining comfortable [15]. The procedure typically involves three phases: sedation or general anesthesia during cranial access and closure, and an awake phase for testing. Dexmedetomidine, often combined with low-dose remifentanil for analgesia, is administered at similar doses as in DBS (0.5–1.0 μg/kg loading dose, 0.1–0.7 μg/kg/hr infusion), with reduced rates during testing (0.1–0.2 μg/kg/hr) [16]. Its minimal respiratory depression reduces the risk of hypercapnia-induced cerebral swelling, a critical consideration in this population [17].

Awake Fiberoptic Intubation (AFOI):

In neurosurgical patients with unstable cervical spines or difficult airways, AFOI requires sedation to alleviate discomfort while preserving spontaneous ventilation. Dexmedetomidine's anxiolytic and sedative effects, coupled with its anti-sialogue properties, make it a promising agent [18]. Clinical studies using the standard DBS dosage regimen have shown favorable outcomes, though further research is recommended to establish its efficacy definitively [19, 20].

Premedication and Sedation in Neurologically Impaired Patients:

For neurosurgical patients with intellectual disabilities or severe anxiety (e.g., those undergoing shunt revisions), intranasal dexmedetomidine (0.5–2 μg/kg) provides effective premedication, particularly in children or uncooperative adults without intravenous access [21]. However, a high incidence of hypotension has been noted in elderly patients, necessitating cautious dosing [22]. Dexmedetomidine is also widely used for sedation during diagnostic imaging or EEG recordings in pediatric neurosurgical patients, with good tolerability [23].

Adjunct to General Anesthesia:

As an off-label adjunct, dexmedetomidine enhances general anesthesia in neurovascular and intracranial tumor surgeries by promoting hemodynamic stability and potentially offering neuroprotection, though further research is needed [24]. In intraoperative neuromonitoring (IONM) during spinal surgery, dexmedetomidine facilitates "propofol-sparing" techniques by potentiating propofol's effects while minimally affecting transcranial motor evoked potentials (TcMEPs) and somatosensory evoked potentials (SSEPs) [25]. A typical regimen includes a 0.5–1.0 μg/kg loading

dose over 10 minutes, followed by a 0.3–0.5 μg/kg/hr infusion [26].

Emerging Roles: Neuroprotection and Delirium Prevention:

Preclinical studies suggest dexmedetomidine's neuroprotective potential, particularly in neonatal models of intracranial hemorrhage and cerebral ischemia, possibly by reducing catecholamine-mediated neuronal injury [27]. However, perioperative neuroprotection remains unconfirmed in humans. Similarly, dexmedetomidine's use in ICU sedation has been linked to a reduced incidence of delirium compared to GABAergic agents [28], but intraoperative benefits in neurosurgical patients require further investigation [29, 30].

CONCLUSION:

Dexmedetomidine's unique profile,arousable sedation, minimal respiratory depression, and hemodynamic stability,positions it as a valuable tool in neurosurgery, particularly for DBS, awake craniotomy, AFOI, and IONM. Its potential in neuroprotection and delirium prevention warrants further exploration. With appropriate dosing and monitoring, dexmedetomidine enhances patient outcomes and supports the evolving demands of neurosurgical care.

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