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Study on the application of dexmedetomidine in general anesthesia in elderly patients

Zhakeer Zilihumaer[a], Hong Chen[b*]

Department of Anesthesiology, Fifth Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, 830000, China
[a]1356155656@qq.com, [b]380093045@qq.com
[*]Corresponding author

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Abstract: Dexmedetomidine is a highly selective a2-adrenergic agonist with sedative, anxiolytic, and anti-sympathetic properties as well as hemodynamic stabilization, and is widely used in all phases of the perianesthesia period without significant effects on patient respiration. In elderly surgical patients, because of their age, degenerative changes in the autonomic nervous system and more comorbidities, dexmedetomidine anesthesia can effectively slow down intestinal motility and prevent various postoperative symptoms, better protect patients' cardiovascular and cerebrovascular, reduce the incidence of cardiovascular and cerebrovascular adverse events, and stabilize patients' hemodynamics. Compared with traditional opioids, dexmedetomidine is safer and more effective. This study reviews the advantages and specifics of dexmedetomidine in the anesthesia of elderly patients.

1. Introduction

With the rapid growth of the elderly population in our country, the proportion of elderly patients who need surgery is also increasing. The autonomic nervous system of the elderly has degenerative changes, the ability to regulate the target organs is reduced, and there are more complications. The physiological reserve of the elderly is decreased or a variety of functional abnormalities lead to increased body vulnerability and decreased anti-stress ability, and higher and stricter requirements are put forward for the scientific and effective surgical treatment. Dexmedetomidine is a highly selective α2-adrenergic receptor agonist with sedative, analgesic, sympathomolysis and anti-anxiety properties [1].It is widely used as a perioperative anesthetic aid and as a sedative in intensive care units. Previous studies have reported that dexmedetomidine may be associated with a lower incidence of postoperative delirium compared to other sedatives [2], prevents delirium in the intensive care unit [3], attenuates the operative stress response [4], and reduces postoperative mortality by up to 1 year [5].In recent years, more and more related medical research reports have shown that dexmedetomidine hydrochloride can inhibit the excitability of sympathetic nerve and promote the enhancement of vagus nerve excitability. Its pharmacological properties include promoting slow heart rate, reducing blood pressure and myocardial oxygen consumption, sedation and analgesia, etc., so it has a relatively mild impact on patients' spontaneous breathing. By

collecting and sorting out relevant literature, this study summarized and concluded the research progress of dexmedetomidine for anesthesia in elderly patients, and is reported as follows.

2. Pharmacological Properties and progress of dexmedetomidine

Dexmedetomidine is an A2-adrenergic receptor agonist, which has sedative, anti-anxiety, sympathomolysis and analgesic effects, with minimal inhibition of respiratory function.It is potent and highly selective against a2 receptors, with a ratio of 1620:1 a2: a1.Hemodynamic effects, including transient hypertension, bradycardia, and hypotension, are due to the peripheral vascular constriction and sympatholytic properties of the drug.Dexmedetomidine exerts its hypnotic effect by activating the presynaptic and postsynaptic a2 receptors in the ventricular center of the brain, thereby inducing an unconscious state similar to natural sleep, producing natural, "wakeable" sleep [6-10], which is unique in that the patient remains easily refreshed and cooperative.Dexmedetomidine is rapidly distributed and is metabolized to inactive metabolites by the liver mainly through glucosylation and hydroxylation.Existing evidence shows that the perioperative application of dexmedetomidine can inhibit stress response and reduce the concentration of various stress modulators, namely catecholamines and cortisol, thus producing a more stable hemodynamic curve during stressful events such as surgery or anesthesia induction [11-13].It reduces sympathetic outflow from the central nervous system (CNS) in a dose-dependent manner, and its analgesic effect has been described as saving opioids.There is increasing evidence that it has organ protective effects on ischemic and hypoxic injury, including cardiac, neuroprotective and renal protection [14].

3. Dexmedetomidine is used in anesthesia.

3.1 Dexmedetomidine administration method and dosage issues

Dexmedetomidine can be administered intravenously, intramuscularly, subcutaneously, nasally, bucally, rectum and orally [15]. Dexmedetomidine has relatively low bioavailability when taken orally. Poor (about 15%), there are abundant blood vessels in the nose and good drug permeability. It is simple, convenient, non-invasive and can reduce the first-pass effect. Dexmedetomidine is used for pretreatment as it is a sedative, anxiolytic, analgesic, sympatholytic, and haemodynamically stable. It can reduce intraoperative (up to 8%) and postoperative (up to 17%) oxygen consumption [16]. The preoperative dose is 0.33-0.67 mcg/kg intravenously or 2.5 mcg/kg intramuscularly, given 15 minutes before surgery. When lower concentrations are used intraoperatively, the need for other anesthetics is reduced. Fewer interventions are needed to treat tachycardia. The incidence of myocardial ischemia is also reduced. However, side effects like hypotension and bradycardia may occur, requiring intervention. In patients older than 65 years, a higher incidence of bradycardia and hypotension was observed after taking dexmedetomidine. Dose reduction is therefore necessary and renal function should be monitored.

3.2 Application of dexmedetomidine in regional anesthesia in elderly surgical patients

Dexmedetomidine is highly lipophilic and therefore rapidly distributed in neural tissue. When used on the neuraxis, it produces anti-pain effects by binding to α-2 receptors in the dorsal horn of the spinal cord [17]. Epidural dexmedetomidine, as an adjuvant to local anesthesia, prolongs the duration of sensory and motor block, makes the motor block more intense, and has good postoperative analgesia. [18] Epidural dexmedetomidine, used as an adjunct to local anesthetics along with general anesthesia, has been shown to reduce intraoperative anesthesia requirements,

improve oxygenation, and prolong postoperative analgesia. [19] In epidural anesthesia, dexmedetomidine, as an auxiliary drug to ropivacaine, has better effects than clonidine and fentanyl [20, 21]. Adding dexmedetomidine to local anesthetics can enhance sensory blockade, produce stronger motor blockade, and prolong postoperative analgesia, thereby reducing the dosage of local anesthetics. In peripheral nerve blocks, dexmedetomidine has also shown efficacy in prolonging sensory blockade and prolonging postoperative analgesia when used with local anesthetics. Animal studies have demonstrated no neurotoxicity when applied directly to neural models [22, 23]. In addition, dexmedetomidine has been compared with lonidine as an adjuvant to local anesthetics in peripheral nerve blocks such as supraclavicular brachial plexus block, and it was found that dexmedetomidine can prolong the duration of sensory and motor blockade, and prolongs the need for rescue analgesics [24]. In venous regional blocks, the addition of dexmedetomidine to lidocaine has been shown to improve block quality, reduce tourniquet pain, and prolong postoperative analgesia with minimal side effects [25-26].

3.3 Application of dexmedetomidine in general anesthesia in elderly surgical patients

Due to its anxiolytic, analgesic, sympatholytic, and sedative properties, dexmedetomidine has been found to be useful in preconditioning, preventing laryngoscopy stress reactions, and preventing the development of delirium. The effects of dexmedetomidine on blood pressure are biphasic, with an initial transient increase in blood pressure and a reflex decrease in heart rate due to stimulation of alpha-2B subtype receptors in vascular smooth muscle. The subsequent decrease in blood pressure and heart rate is due to the inhibition of central sympathetic outflow and stimulation of presynaptic α-2 receptors, resulting in reduced release of norepinephrine, resulting in a further decrease in blood pressure. [27, 28] However, these hemodynamic effects may be harmful in patients with fixed stroke volume, patients using deceleration drugs such as β-blockers, digitalis, etc., and patients with hypovolemia. Dexmedetomidine causes a decrease in cerebral blood flow and cerebral oxygen metabolism requirements, as well as a slight decrease in intracranial pressure. It has neuroprotective effects by reducing catecholamines in the circulation and brain; thus, reducing excitability and improving blood supply to ischemic brain tissue. It also reduces levels of glutamate, which has been found to enhance cellular brain damage, particularly in subarachnoid hemorrhage [29]. Dexmedetomidine does not have any depressive effect on respiratory function and does not impair ventilation or gas exchange even at higher doses; however, it may produce mild hypercapnia.

3.4 Application of dexmedetomidine during anesthesia in elderly surgical patients

The body has a strong stress response during the perianesthesia period. This phenomenon occurs due to indwelling endotracheal tubes, pain, etc., resulting in patients with faster heart rates, higher blood pressure, and unbalanced myocardial oxygen supply and demand. On the one hand, it has promoted a significant increase in the occurrence of cardiovascular accidents and other complications in elderly patients with hypertension, such as arrhythmia, myocardial ischemia, etc.; on the other hand, it has further increased the occurrence of cardiovascular accidents and other complications in elderly patients without underlying diseases. Due to its sympathetic effects, dexmedetomidine can attenuate the hyperdynamic response to laryngoscopy and surgery and maintain a stable hemodynamic state [30-31]. It has also been found to potentiate the effects of all anesthetics (i.e., intravenous and inhaled) and to have an opioid-sparing effect, thereby reducing the dose required [32-35]. It can also help reduce the body's oxygen demand and Helps prevent intraoperative myocardial ischemia [36-37]. Dexmedetomidine has been reported to reduce the requirement for rocoulan during sevoflurane anesthesia, an effect that may be due to dexmedetomidine altering the pharmacokinetics of rocoulan [38]. More recently, dexmedetomidine

has been used to facilitate awake fiberoptic intubation in patients with compromised airways due to upper respiratory anatomy distortion and infection. It provides good sedation and analgesia with little respiratory depression and no impact on airway reflexes, keeping the patient calm and minimizing the chance of aspiration. [39-41] More recently, it has been used for awake fiberoptic intubation without local anesthesia of the upper respiratory tract and as the sole sedative in patients with documented hypersensitivity to local anesthetics [42]. Dexmedetomidine has both sympathetic and anesthetic effects, making it an ideal tool for inducing and maintaining controlled hypotension during a variety of surgeries, minimizing blood loss, and providing a useful tool for spinal fusion surgery, Endoscopic sinus surgery, sinus surgery, and maxillofacial surgery provide optimal conditions [43-44].

3.5 Dexmedetomidine for difficult airway

Awake fiberoptic intubation in patients with difficult airways is known to cause discomfort. This issue is problematic because the anesthesiologist hopes to maintain a patent airway through spontaneous ventilation to avoid the complications of respiratory depression and pulmonary aspiration. However, the patient must feel adequately comfortable during the procedure. A number of drugs have been described to facilitate this process, including benzodiazepines, local anesthetic infusions, and opiate agonists. Dexmedetomidine provides an ideal solution to this problem, in addition to creating a dry field for the anesthetist, as it is an antiparasitic agent. In a recent investigation of seven patients undergoing intravenous sedation with dexmedetomidine and an oropharyngeal local anesthetic [45], no patient experienced changes in saturation, all patients had successful fiberoptic cannulation, and no patient experienced any breathing Evidence for suppression of end-tidal carbon dioxide [46].

3.6 Effect of dexmedetomidine on postoperative delirium and cognitive dysfunction in elderly patients

Post-anesthesia cognitive dysfunction is a common clinical manifestation of postoperative mental disorders and has gradually become the focus of attention. [47-48] This often occurs after cardiac surgery, hip replacement, mandibular fractures, and other major surgeries. Preoperative dexmedetomidine sedation has been reported to reduce the incidence of postoperative acute delirium. Dexmedetomidine reduces cerebral blood flow in a dose-dependent manner. However, CO2 responsiveness and cerebrovascular autoregulation remained unchanged. Animal experiments show that dexmedetomidine has a protective effect on the brain. It acts on a2A receptors to reduce the area of gray and white matter damage caused by perioperative excitotoxins. In rats lacking a2A receptors, dexmedetomidine did not protect white matter from damage. In addition, white matter lesions were relatively severe. In terms of local effects, dexmedetomidine can improve neuronal cell survival after global cerebral ischemia and ischemia/reperfusion. The mechanism of brain protection can be summarized as: reduction of norepinephrine release in brain tissue, regulation of the balance of apoptotic proteins and anti-apoptotic proteins, reduction of excitatory neurotransmitter release in the brain, phosphorylation of heat shock protein 27 The reduction of caspase-3 expression in chemical and brain tissues and the activation of extracellular signal-regulated protein kinase 1/2 produce neuroprotective effects. In addition, preoperative dexmedetomidine sedation has also been reported to reduce the incidence of postoperative acute delirium. However, there are currently no studies reporting on the effect of dexmedetomidine on postoperative cognitive function in elderly patients.

4. Conclusion

Dexmedetomidine is a potent, highly selective alpha-2 adrenergic receptor agonist with sedative, analgesic, anxiolytic, sympatholytic, and opioid properties. It provides a unique type of sedation known as "conscious sedation," in which the patient appears sleepy but is easily aroused, cooperative, and communicative when stimulated. Its rapid onset of action and relatively short onset of action make dexmedetomidine suitable for intensive care units, postoperative cardiac and non-cardiac patients, and invasive and non-invasive procedures, as it can be easily titrated. Some studies suggest that short-term sedation is safe, although hypotension and bradycardia are the most significant side effects. Furthermore, it appears to have minimal respiratory depression and, therefore, it can be used safely in both mechanically ventilated and naturally breathing patients. These properties make dexmedetomidine an effective drug for current early extubation and fast track post-operative cardiac patients. Overall, dexmedetomidine has unique properties that make it an ideal drug for anesthesiologists and intensivists. It is an excellent sedative and analgesic with opioid-sparing properties and minimal respiratory depression; does not reduce intestinal motility; prevents postoperative nausea, vomiting, and tremors; and is neuroprotective, cardioprotective, and renal Conservation has potential benefits. As mentioned above, it can be used extensively and requires vigilance during use. The use of intraoperative dexmedetomidine may be considered warranted as part of an overall strategy to enhance recovery after surgery in the elderly.

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