Enhanced Perioperative Safety and Comfort During Airway-Related Surgeries and Procedures With Dexmedetomidine—A Brief Review and Clinical Practice Experience

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Dexmedetomidine, an α-2 adrenergic receptor agonist, provides analgesia, sedation, anxiolysis, sympatholysis and anesthetic-sparing effect, without inducing significant respiratory depression. Due to these properties, its clinical use is no longer limited to serving as a sedative agent in the intensive care unit. Proper airway management and the avoidance of cardiac and respiratory complications are common goals of everyday anesthesia practice. Ensuring airway safety is pivotal during the anesthesia stages of induction, maintenance and recovery. In this review, we focus on the advantages of dexmedetomidine in awake fiberoptic intubation (AFOI), diagnostic examinations and surgeries of patients with obstructed airways, and reducing emergence delirium effectively without causing further adverse events. With increasing implementation in different anesthetic scenarios, dexmedetomidine provides a favorable option to enhance patient safety and comfort.

Keywords: airway-related surgery, dexmedetomidine, DISE, intraoperative application, safety

Introduction

Dexmedetomidine, a highly selective α-2 adrenoreceptor agonist, plays an increasingly important role in anesthetic practice of recent years. It exhibits dose-dependent sedation, anxiolysis, sympatholysis, anesthetic-sparing effects, and analgesia (acting on spinal and supraspinal sites) with minimal or no respiratory depression.1 Our aim is to review contemporary articles on the applications of dexmedetomidine in awake fiberoptic intubation (AFOI), reducing emergence delirium in airway-related surgeries, obese patients undergoing general anesthesia, and diagnostic procedure of the obstructed airway, along with our own clinical experiences.

Pharmacodynamics

Dexmedetomidine acts via binding to G-protein coupled α-2 adrenergic receptors, which are found in the central, peripheral, and autonomic nervous systems, as well as vital organs and blood vessels of the body. Three subtypes of α-2 adrenergic receptors (α-2A, α-2B, α-2C) have been identified, which exhibit different pharmacological functions and activities.2

The sedative effects are comparable to natural sleep in terms of respiratory pattern and electroencephalogram (EEG) changes. Dexmedetomidine is thought to activate an endogenous pathway which promotes non-rapid eye movement (NREM) sleep.3 Stimulation of α-2A receptor in the locus ceruleus inhibits noradrenerg-
Dexmedetomidine Experience in Airway-Related Surgeries and Procedures

Pharmacokinetics

Dexmedetomidine has poor bioavailability due to its extensive first pass metabolism. As a result of unstable drug concentrations via oral intake, the intravenous route is preferred in perioperative and intensive care. When infused intravenously at a dose range of 0.2–0.7 mcg/kg/hr, it exhibits linear pharmacokinetics. It is rapidly distributed with an onset time of approximately 15 minutes and has an elimination half-life of 2 hours. The context sensitive half-time (t1/2CS) of dexmedetomidine during long-term infusion is increased with time (e.g. 10-minute infusion, t1/2CS 4 minutes; 8-hour infusion, t1/2CS 250 minutes). The context sensitive half-time of approximately 15 minutes and has an elimination half-life of 2 hours. The context sensitive half-time of approximately 15 minutes and has an elimination half-life of 2 hours. The context sensitive half-time of approximately 15 minutes and has an elimination half-life of 2 hours.

Anesthetic Sparing Effects

With increasing intraoperative use of dexmedetomidine, it has been found to reduce the dosage requirements of other anesthetic agents (both intravenous and inhaled agents) with an observed opioid sparing effect. Postoperative benefits have been reported with 25 to 54% reduction in the amount of “rescue” opioids used after surgery. Prolonged time for the first request of post-operative analgesics have also been seen when dexmedetomidine was used intraoperatively. Regardless of the methods of perioperative dexmedetomidine administration (i.e. as a bolus or continuous infusion), Bellon et al. found it still effectively reduced opioid consumption in the postoperative period.

Adverse Effects

The most common adverse effects include hypotension (vasodilatation or diuresis from increased glomerular filtration), hypertension (transient), bradycardia, and complaints of dry mouth (decrease of salivation). Other miscellaneous effects such as fever, rigors, cyanosis, hyperglycemia, electrolyte imbalances, are extremely rare. Worth noting is that there have been few reports of dexmedetomidine causing arrhythmias, atrioventricular (AV) blocks, and even cardiac arrests. The mechanisms of the cardiac events are still now clear; there are few suggestions, for examples, dose-related intolerance, modulated vagal activity, depressive effect on sinoatrial and AV nodal function, inhibitory effect on cardiac pacing autoregulation and central sympathetic outflow (decreasing of norepinephrine release). Thus, patients with cardiac diseases or preexisting arrhythmias using
Intraoperative Applications

Facilitating AFOI

AFOI is widely accepted as the gold standard in management of known difficult airway, but it can be a terrible experience for the patient. Even with perfect airway nerve blockade, patients will go through horrific choking-like sensations and have violently uncontrolled reflex behaviors. These dangerous movements not only hurt themselves, but also disrupt proper airway management. A major challenge is how to provide adequate anxiolysis, whilst ensuring spontaneous ventilation. Conventional sedatives, like benzodiazepines, opioids, and propofol, may cause respiratory depression at higher doses or even lower doses due to inter-individual variation.

Dexmedetomidine’s properties make it an ideal solution to this problem, through providing a minimal respiratory inhibition and a relatively dry fibroscopic field for anesthesiologists due to its antisialogogue effect. Tsai et al. in 2010 compared dexmedetomidine (loading dose 1 mcg/kg over 10 min), with propofol (Ce 3 mcg/mL), and found that patients in the dexmedetomidine group showed better tolerance, lower incidences of hypoxia, and more cooperation. Their results revealed that a loading dose of dexmedetomidine (1 mcg/kg/hr) resulted in 50% of patients recalling the endoscopy insertion but only 5% recalling intubation. It showed higher levels of patient satisfaction than usual awake intubation without sedation. Zhou et al. in 2016 indicated that dexmedetomidine provides better sedation with similar success rates for intubation when compared to other conventional sedatives. Both studies stated that more local anesthetics must be applied in order to minimize cough reflex during fiberoptic intubation due to preservation of airway protection reflex. The higher risks of bradycardia and hypotension, can easily be managed with atropine and vasoactive agents. In a more recent study, it showed that a combination of dexmedetomidine with airway nerve blockade enhanced patient’s tolerance and comfort during awake intubation. In our own clinical practice, intravenous infusion of dexmedetomidine at a rate of 0.5–0.8 mcg/kg/hr for at least 20 minutes plus topical blocks can create optimal conditions for fiberoptic endotracheal intubation with less post-traumatic stress disorder (PTSD)-like memory recall.

However, dexmedetomidine did not provide better results when compared with remifentanil in several studies. For example, it takes longer time to adequate sedation level and decreased first success attempt rate. There was no significant difference in hemodynamic changes, adverse events, or patient’s tolerance. In a recent review, there is no strong evidence supporting that dexmedetomidine is the primary choice in AFOI, but is an additional option among other sedatives. The above descriptions are shown in the Table 1.

Reducing Incidences of Emergence Delirium in Airway-Related Surgeries

Generally, ear, nose, and throat (ENT) operations and other oral cavity surgeries under general anesthesia are associated with higher incidences of emergence agitation, which increases risks of self-extubation (causing hypoxia and aspiration pneumonia), negative pressure pulmonary edema, self-injury airway trauma, or injury of attending medical staffs. Other contributing risk factors are male gender, inhalational anesthesia, inadequate analgesia, and presence of urinary catheter or endotracheal tube. Meng et al. have demonstrated preventive effects of dexmedetomidine on emergence agitation and smooth extubation in the pediatric population undergoing tonsillectomy. In adults undergoing minor surgical procedure such as septoplasties, dexmedetomidine exhibits shorter time to extubation, and similar hemodynamic and recovery profile in comparison with remifentanil.

However, a randomized control trial with patients undergoing orthognathic surgeries did not show a significant difference in emergence agitation compared with the control group; in this trial,

Table 1. Advantages and disadvantages of dexmedetomidine in awake fiberoptic intubation

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Minimal respiratory</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>depression</td>
<td>Longer operating time (longer time to optimal sedation)</td>
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<tr>
<td>Analgesic</td>
<td></td>
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<tr>
<td>Xerostomia</td>
<td>Higher rate of recall of topical anesthesia and endoscopy</td>
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<tr>
<td>Sedative</td>
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<tr>
<td>Higher patient satisfaction</td>
<td></td>
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<tr>
<td>rate</td>
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<tr>
<td>Better patient tolerance</td>
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Dexmedetomidine was only given in a bolus dose (1 mcg/kg/hr) for 10 minutes at the end of surgery. The inadequate onset time was probably the reason for poor prophylactic result. Hence, several others have reported less emergence agitation with the use of dexmedetomidine (0.4 mcg/kg/hr) perioperatively in nasal surgery and in the elderly population receiving orthopedic surgery.\(^{28,30-32}\) Polat et al. compared remifentanil with dexmedetomidine and found significantly reduced incidences of emergence agitation in both groups (3.3 and 20%, respectively) compared with the placebo group (46.7%; \(p < 0.001\)).\(^{31}\) In order to reduce postoperative complications of emergence agitation, preventive use of dexmedetomidine has the potential to achieve the balance between providing sufficient sedation while preserving respiratory drive. In our experiences, continuous infusion of dexmedetomidine should be started immediately after anesthetic induction at a rate between 0.4–0.7 mcg/kg/hr. Due to less respiratory depression, dexmedetomidine can be continuously given until successful extubation. This facilitates a calm and comfortable experience for patients during transportation and in the post-anesthesia care unit. Physical restraint-related injuries can potentially be avoided.

One needs to keep in mind that post-surgical pain, endotracheal intubation, and inserted catheters also contribute to emergence agitation.\(^{26}\) Although dexmedetomidine exhibits opioid-sparing effect, some studies did not observe anti-delirium effects possibly due to the existence of other delirium-contributing factors.\(^{33}\) Thus, though dexmedetomidine can be used to reduce the risk of agitation, adequate pain control and early removal of foreign catheters are also important factors to ensure a comfortable and safe postoperative recovery in the post-anesthesia care unit.

### Minimizing Risks of Adverse Respiratory Events in Obese Patients

When planning the anesthesia of obese patients, extra attention should be placed on obstructive sleep apnea (OSA), hypoventilation syndrome, and postoperative atelectasis. In the postoperative period following anesthesia, obese patients are prone to develop adverse respiratory events, referred to as critical respiratory events (CRE). Since dexmedetomidine experiences less respiratory depression, it can be utilized as a sedative agent in morbidly obese patient, as well as an anesthetic adjuvant during general anesthesia.\(^{33}\)

In several studies, dexmedetomidine attenuates cardiovascular responses to noxious stimuli (such as intubation or surgical manipulations), along with a reduction of required dosage of opioid and volatile agents. Less opioid usage thereby lowers the incidence of postoperative nausea and vomiting (PONV).\(^{10,34-36}\) Abu-Halaweh et al. demonstrated that postoperative initiation of dexmedetomidine use (at a dosage of 0.3 mcg/kg/hr) reduced the mean total consumption of morphine following laparoscopic bariatric surgery.\(^{37}\) A meta-analysis by Singh et al.\(^{38}\) concluded that obese patients who receive perioperative dexmedetomidine had nearly one-third less opioids consumption in comparison with the controls and 25% reduction in the pain score. Most of the trials in this analysis used a dexmedetomidine infusion dose of 0.4 mcg/kg/min. The timing of the given dose on the opioid-sparing effect was higher when the infusions used in the postoperative phase in comparison with intraoperative phase alone. However, continuous infusion dexmedetomidine from intraoperative through postoperative phase was not compared by any presently studies. The incidence of PONV was reduced by 76% in comparison with controls, which is a clinical significant reduction without additional antiemetic drugs being used.\(^{39}\) This not only increased clinical safety but also likely to have better patient satisfaction. Although timing and dosing of dexmedetomidine is still controversial,\(^{36}\) in our clinical practice, intravenous infusion of dexmedetomidine (0.5 mcg/kg/hr) will be given 30 minutes before the end of surgery for obese patients with OSA who are at increased risks of compromised airway. Smooth extubation and maintenance of adequate respiratory drive are vital to ensure airway management safety in these high-risk patients. This result is comparable with a prospectively randomized-controlled trial by Tufanogullari et al. of recovery outcomes of bariatric surgeries. They found out that the time to tracheal extubation did not differ when comparing patients with and without dexmedetomidine infusion. In addition, the duration of post-anesthetic care unit (PACU) stay was significantly shorter in those with dexmedetomidine use intraoperatively.\(^{36}\)

### Enhancing Safety of Procedural Sedation of Drug-Induced Sleep Endoscopy (DISE)

In many recent reviews, dexmedetomidine has seen extensive use in non-intubated surgeries and other non-intubated procedures. It has been demonstrated...
able to be safely used in bronchoscopies, transesophageal echocardiographies, shockwave lithotripsies, vitreoretinal surgeries, tonsillectomies of pediatric patients, etc. We implement the routine use of dexmedetomidine to provide sedation for DISE, a dynamic airway evaluation exam for patients suffering from OSA.

The sedative agent used in DISE is to achieve rapid-eye movement stage of sleep, which is known to induce several levels of upper airway obstruction. Propofol and dexmedetomidine are the most used agents for this procedure. Generally, dexmedetomidine provides a better control of hemodynamic profile and bispectral index (BIS) value, has lesser degree of airway obstruction, pain level and desaturation. On the other hand, propofol has its own advantages, including it is more effective in rapid sedation, shorter half-life, and inducing greater degree of tongue obstruction, but has higher incidence of oxygen desaturation and inhibiting respiratory drive. Nevertheless, both dexmedetomidine and propofol could achieve similar patterns of airway obstruction and hemodynamic stability when the depth of sedation is controlled with BIS monitoring.

In our clinical practice, a loading dose of 1 mcg/kg is given intravenously over 10 minutes to 15 minutes. The patients would fall asleep within a few minutes and the diagnostic endoscopic examination would begin. If the patient remains awake, an additional 5 minutes waiting time or extra rescue sedation, for example propofol 30–50 mg intravenously, will work to reach satisfactory anesthetic level for endoscopic examination. The most commonly observed adverse effects during DISE procedures are bradycardia and hypotension. In the absence of contraindications, atropine 0.1 mg/10 kg or glycopyrrolate 0.2 mg will be given intravenously. Even after the examination, profound bradycardia with hypotension can sometimes still occur in the post-anesthesia recovery room. Therefore, adequate hydration and increased staff alertness are necessary for perioperative care, with preparation of readily available inotropic agents.

### Conclusion

The new \( \alpha-2 \) adrenergic receptor blocker dexmedetomidine is a promising drug with favorable anesthetic properties and potential for numerous clinical applications, beyond what we mentioned here (Table 2). Although there is a significant sympatholytic effect during dexmedetomidine infusions, hemodynamic changes can be safely managed and controlled with adequate fluid hydration and catecholamine use as indicated. With less respiratory depression, smoother emergence and generally more stable hemodynamic profile, dexmedetomidine not only provides a safer

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<thead>
<tr>
<th>Characteristics of dexmedetomidine</th>
<th>Suitable population</th>
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<tr>
<td>No respiratory depression</td>
<td>• Patient undergoing airway-related surgeries or DISE</td>
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<tr>
<td></td>
<td>• OSA</td>
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<td></td>
<td>• Obesiy</td>
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<td>• Patient with difficult airway</td>
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<tr>
<td>Analgesia</td>
<td>• Patient with difficult airway</td>
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<td></td>
<td>• High risk of PONV</td>
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<td></td>
<td>• Obesity</td>
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<td></td>
<td>• OSA</td>
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<tr>
<td>Sparing effect of anesthetics</td>
<td>• High risk of PONV</td>
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<tr>
<td></td>
<td>• Obesity</td>
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<td></td>
<td>• OSA</td>
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<tr>
<td>Decrease incidence of postoperative delirium</td>
<td>• Patient undergoing airway-related surgeries</td>
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<tr>
<td></td>
<td>• Previous postoperative delirium</td>
</tr>
<tr>
<td>Improvement of hemodynamic stability</td>
<td>• Patient undergoing airway-related surgeries</td>
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<tr>
<td></td>
<td>• Patient with difficult airway</td>
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<td></td>
<td>• Surgery tends to bleeding</td>
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</tbody>
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DISE: drug-induced sleep endoscopy; OSA: obstructive sleep apnea; PONV: postoperative nausea and vomiting.
and more pleasant condition to perform procedures or surgeries involving difficult airway management, but also, improves overall quality of our perioperative anesthetic practice. Further novel uses of dexmedetomidine are constantly being developed, awaiting additional researches and randomized control trials to validate the results.

References


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