Update on dexmedetomidine: use in nonintubated patients requiring sedation for surgical procedures

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Abstract: Dexmedetomidine was introduced two decades ago as a sedative and supplement to sedation in the intensive care unit for patients whose trachea was intubated. However, since that time dexmedetomidine has been commonly used as a sedative and hypnotic for patients undergoing procedures without the need for tracheal intubation. This review focuses on the application of dexmedetomidine as a sedative and/or total anesthetic in patients undergoing procedures without the need for tracheal intubation. Dexmedetomidine was used for sedation in monitored anesthesia care (MAC), airway procedures including fiberoptic bronchoscopy, dental procedures, ophthalmological procedures, head and neck procedures, neurosurgery, and vascular surgery. Additionally, dexmedetomidine was used for the sedation of pediatric patients undergoing different type of procedures such as cardiac catheterization and magnetic resonance imaging. Dexmedetomidine loading dose ranged from 0.5 to 5 µg kg⁻¹, and infusion dose ranged from 0.2 to 10 µg kg⁻¹·h⁻¹. Dexmedetomidine was administered in conjunction with local anesthesia and/or other sedatives. Ketamine was administered with dexmedetomidine and opposed its bradycardiac effects. Dexmedetomidine may be useful in patients needing sedation without tracheal intubation. The literature suggests potential use of dexmedetomidine solely or as an adjunctive agent to other sedation agents. Dexmedetomidine was especially useful when spontaneous breathing was essential such as in procedures on the airway, or when sudden awakening from sedation was required such as for cooperative clinical examination during craniotomies.

Keywords: dexmedetomidine, sedation, nonintubated patients

Introduction
Dexmedetomidine was introduced two decades ago as a sedative and supplement to sedation in the intensive care unit for patients whose trachea was intubated. However, since that time dexmedetomidine was quickly adapted by anesthesiologists in the operating room. Novel applications have created discussions in many anesthesiology journals, conferences and practices. However, there is still debate between those who approve these applications and those who do not.

More recently, dexmedetomidine has been used as a sedative and hypnotic for patients undergoing procedures without the need for tracheal intubation. This review will focus on the application of dexmedetomidine as a sedative and/or total anesthetic in patients undergoing procedures without the need for tracheal intubation. We have reviewed the literature on the use of dexmedetomidine, and we would like to emphasize that many of these references are case reports that involve only a small number of patients. This could be due to the fact that such applications of dexmedetomidine are new and have not
Dexmedetomidine has previously been used in the intensive care setting in patients that are undergoing mechanical ventilation for less than 24 hours; however, more recently it has been used for sedation and analgesia in adults and pediatric patients undergoing small and minimally invasive procedures.

This review focuses on using dexmedetomidine in patients undergoing different procedures without tracheal intubations. References were identified via MEDLINE (through to July 2009) with key words including ‘dexmedetomidine’, ‘sedation’, and ‘nonintubated’. References cited in the published articles were also reviewed for possible inclusion. Dexmedetomidine was used for sedation in monitored anesthesia care (MAC), airway procedures including fiberoptic bronchoscopy, dental procedures, ophthalmological procedures, head and neck procedures, neurosurgery, and vascular surgery. Additionally, the last section of this review focuses on using dexmedetomidine for the sedation of pediatric patients undergoing procedures which require sedation. We reviewed 15 prospective studies, 9 retrospective studies, and 10 case reports/series. Table 1 includes a summary of these studies and we suggest using it as a guide when reading each study.

Dexmedetomidine as a sedative
Sedation is commonly needed during procedures which do not require general anesthesia with tracheal intubation. Each class of sedative drugs has a different combination of anxiolytic, hypnotic, amnestic, and analgesic effects. Selection of the most appropriate medication for a specific patient requires consideration of many factors such as potential drug interactions and pharmacokinetics and pharmacodynamics of each drug. The ideal sedative is free of serious adverse effects; is not associated with significant drug interactions; does not accumulate with repeated dosing even in the presence of organ dysfunction; is easy to administer; has a quick and predictable onset and dissipation of effect; and is inexpensive.

Although no sedative is ideal, a number of agents have characteristics which make them useful. Benzodiazepines, opioids, and propofol have all been useful in the appropriate setting.\(^2\) Dexmedetomidine is a medication that appears to have great utility in areas of sedation. Dexmedetomidine, an imidazole, is a potent \(\alpha_2\)-adrenoceptor agonist that has eight times greater specificity for \(\alpha_2\) receptors than does clonidine.\(^3\) The actions of dexmedetomidine are thought to be mediated through post-synaptic \(\alpha_2\) receptors which activate pertussis toxin-sensitive G proteins; thus, increasing conductance through potassium ion channels.\(^4\)

Dexmedetomidine has gained popularity, or that approval by the Institutional Review Board for a randomized controlled study may be difficult because of the innovative applications and the lack of Food and Drug Administration (FDA) approval for dexmedetomidine use in nonintubated patients. We postulate that a combination of these reasons has led to the rarity of double-blinded, controlled, randomized, prospective studies describing the use of dexmedetomidine for patients undergoing procedures that do not require tracheal intubation. However, in late 2008, the FDA approved the use of dexmedetomidine for nonintubated patients requiring sedation prior to and/or during surgical and other procedures. We expect that more studies in this field will appear in the literature in the near future.

Dexmedetomidine use during monitored anesthesia care
The safety and efficacy of dexmedetomidine in nonintubated patients requiring sedation for surgical and diagnostic procedures has been evaluated prospectively.\(^5\) More patients in the placebo group could not be sedated with midazolam alone and required additional sedation with propofol or general anesthesia to complete the surgical procedure. However, the design of the study favored the dexmedetomidine group. It was predicted that the group receiving dexmedetomidine would have a superior sedation effect when compared to the placebo group because patients received an extra sedative. The study would have been more convincing if another hypnotic that is commonly used during MAC, such as propofol at 50 to 75 \(\mu g\ kg^{-1} min^{-1}\), was used instead of saline for comparison. However, the findings of the study are important as they demonstrate that the use of dexmedetomidine for procedures requiring MAC is safe and superior to the combination of midazolam and fentanyl.

In another study, the cardio-respiratory effects of equivalent doses of dexmedetomidine and propofol for intraoperative sedation were evaluated in forty patients receiving nerve blocks for inguinal hernia and hip/knee procedures.\(^6\) Although the number of patients enrolled is small compared to the previous study, the study design is more appropriate and practical in our opinion. However, it could be that the low propofol dose used (38 \(\mu g\ kg^{-1} h^{-1}\)) as compared to that used in clinical practice for such cases (50 to 75 \(\mu g\ kg^{-1} min^{-1}\)) had a role in making dexmedetomidine provide a better sedation profile.

Dexmedetomidine use during airway procedures
The advantage of dexmedetomidine as a sedative and its respiratory profile make many anesthesiologists excited.
Table 1 Literature evaluating the efficacy and adverse effects of dexmedetomidine for sedation in nonintubated patients

<table>
<thead>
<tr>
<th>Design (number of patients)</th>
<th>Procedure</th>
<th>DEX and other sedatives dose</th>
<th>Efficacy</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicenter P R DB (326)</td>
<td>MAC sedation for a broad range of procedures preceded by local anesthetic block</td>
<td>LD of 0.5 for first group and 1.0 µg kg⁻¹ for second group followed by infusion of 0.6–1 µg kg⁻¹ h⁻¹; Supplemental medications included: 0.5 mg midazolam and 25 mcg fentanyl in repeated doses</td>
<td>Patients in both DEX groups required significantly less supplemental medication and reported significantly higher overall satisfaction and less postoperative anxiety</td>
<td>Incidence of respiratory depression was similarly low in both DEX groups compared to placebo</td>
</tr>
<tr>
<td>R P (40)</td>
<td>Inguinal hernia or hip/knee procedures with nerve blocks</td>
<td>LD of 1 µg kg⁻¹ with infusion of 0.4–0.7 µg kg⁻¹ h⁻¹ (average 0.7 µg kg⁻¹ h⁻¹); Propofol loading dose 0.75 mg kg⁻¹ and infusion of 12.5–75 µg kg⁻¹ min⁻¹ (average 38 µg kg⁻¹ min⁻¹)</td>
<td>DEX resulted in more sedation, lower blood pressure, and improved analgesia during recovery; No difference between groups in psychomotor performance or respiratory rate</td>
<td>Sedation was more rapid with propofol, but similar at 25 min after LD</td>
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<tr>
<td>P (14)</td>
<td>Awake laryngeal framework procedures; local anesthesia</td>
<td>LD of 0.2–0.7 µg kg⁻¹ h⁻¹</td>
<td>Adequate sedation for a majority of the procedures</td>
<td>Minimal undesirable hemodynamic or respiratory effects</td>
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<tr>
<td>CR (3)</td>
<td>Direct laryngoscopy and bronchoscopy</td>
<td>LD of 1 µg kg⁻¹ and infusion up to 10 µg kg⁻¹ h⁻¹</td>
<td>No variation in hemodynamic stability</td>
<td>No prolongation of recovery times</td>
</tr>
<tr>
<td>RE (4)</td>
<td>Direct laryngoscopy and bronchoscopy</td>
<td>LD of 2–5 µg kg⁻¹ in addition to topical anesthetic</td>
<td>Adequate surgical conditions and preservation of spontaneous breathing</td>
<td>Using local anesthetic was key factor with this technique</td>
</tr>
<tr>
<td>Multicenter P R DB (124)</td>
<td>Elective awake fiberoptic intubation</td>
<td>LD of 1 µg kg⁻¹ and infusion of 0.7 µg kg⁻¹ h⁻¹; topical lidocaine; Patients received 0.2 mg to 0.5 mg kg⁻¹ of midazolam for rescue medication</td>
<td>Fewer patients in the study group required midazolam to achieve/maintain sedation; Mean total dose of midazolam was lower in the DEX group; Incidence of respiratory depression was similar in both groups</td>
<td>Incidence of hypotension was greater in the DEX group; Hypertension greater in the placebo group</td>
</tr>
<tr>
<td>P R DB (30)</td>
<td>Fiberoptic intubation</td>
<td>LD of 0.4 µg kg⁻¹ then infusion rate of 0.7 µg kg⁻¹ h⁻¹; Remifentanil bolus of 0.75 µg kg⁻¹ then infusion rate of 0.075 µg kg⁻¹ min⁻¹; Midazolam 2 mg and local airway lidocaine anesthesia for all patients</td>
<td>All airways were successfully secured</td>
<td>More patients in DEX group required more overall attempts at intubation (62% vs 24%); Remifentanil group had lower oxygen saturation but not significant</td>
</tr>
<tr>
<td>Clinical report (20)</td>
<td>Awake fiberoptic intubation</td>
<td>LD of 1 µg kg⁻¹ over 10–15 min and infusion of 0.7 µg kg⁻¹ h⁻¹; Fentanyl (50–150 µg) and midazolam (0.5–3 mg)</td>
<td>Able to perform an awake post-intubation neurological exam</td>
<td>Bradycardia and hypotension</td>
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<table>
<thead>
<tr>
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<tr>
<td>Third molar surgery under local anesthetic</td>
<td>LD (up to) 1 µg kg(^{-1}) or midazolam bolus (up to) 5 mg; DEX median dose of 0.88 µg kg(^{-1}) and midazolam median dose of 3.6 mg</td>
<td>DEX provided predictable sedation. Similar pain and satisfaction scores</td>
<td>Heart rate and blood pressure were lower with DEX. Midazolam caused restlessness and disinhibition</td>
</tr>
<tr>
<td>Significantly impacted third molar surgery under local anesthesia</td>
<td>DEX 4 µg kg(^{-1}) h(^{-1}) or midazolam 0.4 µg kg(^{-1}) h(^{-1}); infusions began 15 min prior to first operation; at the second operation the agents switched</td>
<td>Similar respiratory findings</td>
<td>Mean heart rate and blood pressure significantly lower in the DEX group. Higher likelihood of a pain response in the midazolam group</td>
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<tr>
<td>Dental procedures</td>
<td>LD of 1 µg kg(^{-1}) infused over 10 min, maintenance dose of 0.2–0.8 µg kg(^{-1}) h(^{-1}) to achieve a Ramsay Sedation Score of 2–5</td>
<td>Patient satisfaction on a score of 10 was (8.6 ± 2.3), and surgeons' satisfaction on a score of 5 was (3.9 ± 1.3); No statistical change in heart rate or respiratory rate from baseline</td>
<td>Significant difference in blood pressure and baseline. Recovery time was long (82.2 ± 24.3 min) related to the procedure time (14.6 ± 17.6 min)</td>
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<tr>
<td>Cataract surgery under peribulbar block</td>
<td>LD of 1 µg kg(^{-1}) over 10 min. Additional doses of 5 µg were administered if necessary; No sedation in control group</td>
<td>Higher patient and surgeon satisfaction in the dexmedetomidine group during the performance of peribulbar block; More sedation and slightly lower intraocular pressure in the DEX group</td>
<td>Lower intraoperative heart rate in DEX group with atropine needed in 5 patients. Higher incidence of dry mouth in DEX group</td>
</tr>
<tr>
<td>Cataract surgery under peribulbar block</td>
<td>LD 1 µg kg(^{-1}) over 10 min; followed by 0.1–0.7 µg kg(^{-1}) h(^{-1}) infusion; Midazolam 20 µg kg(^{-1}); followed by 0.5 mg boluses as required; Sedation was titrated to a Ramsay Sedation score of 3</td>
<td>DEX had slightly higher satisfaction scores; similar surgeon satisfaction scores in both groups</td>
<td>DEX group had overall lower blood pressure and heart rate and delayed readiness for discharge [45 (36–54) vs 21 (10–32) min, (P &lt; 0.01)]</td>
</tr>
<tr>
<td>Craniotomy for tumors located near the motor cortex</td>
<td>LD of 1 µg kg(^{-1}), maintenance dose of 0.2–0.8 µg kg(^{-1}) h(^{-1}); General anesthesia with propofol and remifentanil</td>
<td>Total tumor excision was more likely and higher mean satisfaction scores in DEX group</td>
<td>Patients receiving DEX required more fentanyl during the procedure (2.46 ± 1.78 µg kg(^{-1})) compared with 1.11 ± 0.41 µg kg(^{-1})</td>
</tr>
<tr>
<td>Placement of spinal cord stimulator with local anesthesia</td>
<td>LD of 1 µg kg(^{-1}) and infusion of 0.2–1.7 µg kg(^{-1}) h(^{-1}); Non-DEX patients received propofol anesthesia</td>
<td>DEX allowed for a rapid change in the level of sedation and analgesia without respiratory depression and also helped in keeping the patient cooperative during functional testing; Provided more postoperative analgesia</td>
<td></td>
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</table>
Carotid endarterectomy using regional anesthesia

DEX group: LD of 0.5 µg kg\(^{-1}\) over 10 min and infusion of 0.2–0.8 µg kg\(^{-1}\) h\(^{-1}\)

Control group: LD of 40 µg fentanyl and 1 mg midazolam. Additional bolus of 20 µg fentanyl and 0.5 mg midazolam as needed.

Placebo infusion

Sedation was titrated to a Ramsay Sedation Score of 2–4 in both groups

No difference in the need of hemodynamic interventions. DEX was less likely to need treatment for hypertension/tachycardia (DEX 40% vs STD 72%; P = 0.03) No difference in the need to treat hypotension or brady- cardia when undergoing intra-arterial shunting. DEX group had significantly better pain control in the PACU

DEX group had more episodes of hypotension in the PACU

Vascular procedures such as stents and fistula with local anesthesia

DEX groups: LD of 0.5 or 1 µg kg\(^{-1}\) over 10 min and infusion of 0.6–1.0 µg kg\(^{-1}\) h\(^{-1}\)

Rescue with midazolam 0.5 mg and 25 µg fentanyl as needed for both groups

DeX group required fewer dose adjustments

Deep sedation was not encountered in any patient

Extracorporeal shockwave lithotripsy in spontaneously breathing patients

DEX: LD of 1 µg kg\(^{-1}\) over 10 min followed by infusion of 0.2 µg kg\(^{-1}\) h\(^{-1}\)

Propofol: LD of 1 mg kg\(^{-1}\) for 10 min followed by 2.4 mg kg\(^{-1}\) h\(^{-1}\) during the procedure

Fentanyl 1 µg kg\(^{-1}\) was administered to all patients 10 min before ESWL

Using visual analogue scale, pain intensity was evaluated at 5-min intervals

All patients completed sedation scores were similar in both groups

All patients required rescue medications

Deep sedation was not encountered in any patient

Cardiac catheterization in spontaneously breathing patients

LD of 1 µg kg\(^{-1}\) and infusion of 1–2 µg kg\(^{-1}\) h\(^{-1}\) (mean of 1.15 µg kg\(^{-1}\) h\(^{-1}\) )

Midazolam PO (0.75 µg kg\(^{-1}\) ) for all patients

Midazolam PO (0.75 µg kg\(^{-1}\) ) for all patients

Blood pressure and heart rate were within 20% of baseline

No clinically significant changes in blood pressure or respiratory rate; no apnea; no patient responded to placement of arterial and venous cannula

Three patients required a supplemental dose of ketamine (1 mg kg\(^{-1}\) ) during the procedure

Ketamine was not noted

Cardiac catheterization in spontaneously breathing patients

LD of ketamine (2 mg kg\(^{-1}\) ) and DEX (1 µg kg\(^{-1}\) ) administered over 3 min followed by infusion of DEX (2 µg kg\(^{-1}\) h\(^{-1}\) for the initial 30 min then 1 µg kg\(^{-1}\) h\(^{-1}\) for the duration of the case)

Ketamine (1 mg kg\(^{-1}\) ) for rescue

All patients completed sedation

Blood pressure and heart rate were within 20% of baseline

No clinically significant changes in blood pressure or respiratory rate; no apnea; no patient responded to placement of arterial and venous cannula

Three patients required a supplemental dose of ketamine (1 mg kg\(^{-1}\) ) during the procedure

Ketamine was not noted

Cardiac catheterization in spontaneously breathing patients

DEX + ketamine (group 1): LD over 10 min of 1 µg kg\(^{-1}\) of DEX and ketamine (1 mg kg\(^{-1}\) )

Then infusion of 0.7 µg kg\(^{-1}\) h\(^{-1}\) of DEX and 1 mg kg\(^{-1}\) h\(^{-1}\) of ketamine for maintenance

Propofol + ketamine (group 2): LD of 1 mg kg\(^{-1}\) of propofol and 1 mg kg\(^{-1}\) of ket- amine. Then 100 µg kg\(^{-1}\) min\(^{-1}\) of propofol and 1 mg kg\(^{-1}\) h\(^{-1}\) of ketamine. Additional doses of ketamine, 1 mg kg\(^{-1}\), were administered when a patient showed discomfort in both groups

Ketamine consumption for maintenance of sedation in group 1 was significantly more than in group 2 (2.03 mg kg\(^{-1}\) h\(^{-1}\) vs 1.25 mg kg\(^{-1}\) h\(^{-1}\) ) (P < 0.01)

Heart rate in DEX group was significantly lower than group 2

The recovery time was also longer in group 1 than in group 2 (49.54 vs 23.16 min, respectively; P < 0.01)
<table>
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<tbody>
<tr>
<td>RE (250)&lt;sup&gt;a1&lt;/sup&gt;</td>
<td>CT imaging</td>
<td>LD of 2 µg kg&lt;sup&gt;-1&lt;/sup&gt; over 10 min and infusion of 1 µg kg&lt;sup&gt;-1&lt;/sup&gt; h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Provided appropriate sedation</td>
<td>Noticeable changes in heart rate and mean arterial blood pressure during bolus and infusion relative to awake values (P &lt; 0.001)</td>
</tr>
<tr>
<td>RE (62)&lt;sup&gt;a2&lt;/sup&gt;</td>
<td>CT imaging</td>
<td>LD of 2 µg kg&lt;sup&gt;-1&lt;/sup&gt; over 10 min (mean 2.2 µg kg&lt;sup&gt;-1&lt;/sup&gt;) and infusion of 1 µg kg&lt;sup&gt;-1&lt;/sup&gt; h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>10 patients needed second LD</td>
<td>Noticeable changes in heart rate and mean arterial blood pressure 2 patients became agitated during LD</td>
</tr>
<tr>
<td>RE (747)&lt;sup&gt;a3&lt;/sup&gt;</td>
<td>MRI sedation</td>
<td>LD of 3 µg kg&lt;sup&gt;-1&lt;/sup&gt; over 10 min, and infusion rate of 2 µg kg&lt;sup&gt;-1&lt;/sup&gt; h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Rate of successful sedation (able to complete the imaging study) when using DEX alone was 97.6%</td>
<td>Decreases in heart rate and blood pressure outside the established 'awake' norms, the deviation was generally within 20% of norms, and was not associated with adverse sequelae</td>
</tr>
<tr>
<td>R RE (80)&lt;sup&gt;a4&lt;/sup&gt;</td>
<td>MRI sedation</td>
<td>LD of 1 µg kg&lt;sup&gt;-1&lt;/sup&gt; and infusion of 0.2 µg kg&lt;sup&gt;-1&lt;/sup&gt; h&lt;sup&gt;-1&lt;/sup&gt; Midazolam loading dose of 0.2 mg kg&lt;sup&gt;-1&lt;/sup&gt; and infusion of 6 µg kg&lt;sup&gt;-1&lt;/sup&gt; h&lt;sup&gt;-1&lt;/sup&gt; Midazolam or propofol for rescue</td>
<td>Better quality imaging, and greater rate of sedation in the DEX group The onset of sedation time was shorter in group M (&lt;0.001)</td>
<td>No hemodynamic or respiratory effects. More need for rescue drugs in the midazolam group</td>
</tr>
<tr>
<td>R RE (60)&lt;sup&gt;a5&lt;/sup&gt;</td>
<td>MRI sedation</td>
<td>LD 1 µg kg&lt;sup&gt;-1&lt;/sup&gt; and infusion of 0.5 µg kg&lt;sup&gt;-1&lt;/sup&gt; h&lt;sup&gt;-1&lt;/sup&gt; Propofol loading dose of 3 mg kg&lt;sup&gt;-1&lt;/sup&gt; with infusion of 100 µg kg&lt;sup&gt;-1&lt;/sup&gt; min&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Onset of sedation, recovery, and discharge time significantly shorter in the propofol group</td>
<td>5/30 patients had inadequate sedation in the DEX group 3/30 patients had significant desaturation in the propofol group</td>
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</table>

Abbreviations: CR, case report; DB, double blinded; DEX, dexmedetomidine; LD, loading dose; P, prospective; PC, placebo-control; R, randomized; RE, retrospective.
about using it to anesthetize patients for surgery on the airways when maintaining spontaneous ventilation is necessary. Since dexmedetomidine does not negatively affect the respiratory rate or depth compared to other sedatives, it has proven to be advantageous for such procedures. Dexmedetomidine, coupled with local anesthesia, provided excellent sedative and operative conditions for awake laryngeal framework procedures.\(^7\) Dexmedetomidine produced virtually minimal undesirable hemodynamic or respiratory effects, while allowing for adequate sedation the majority of the time.

Ohata and his colleagues\(^8\) reported their experience with the anesthetic management using high-dose dexmedetomidine for microlaryngeal surgery on a patient maintaining spontaneous breathing. Anesthesia was maintained with a dexmedetomidine infusion (loading dose of 1.0 \(\mu\)g kg\(^{-1}\) and infusion rate of 0.5 \(\mu\)g kg\(^{-1}\) h\(^{-1}\); at 30 minutes the infusion rate was increased to 3 \(\mu\)g kg\(^{-1}\) h\(^{-1}\)), intermittent small doses of fentanyl, and topical application of lidocaine on the tongue, pharynx and larynx. Although end tidal CO\(_2\) remained normal, hypotension occurred resulting in the need for small doses of ephedrine. The authors emphasized the importance of adequate topical anesthesia as essential for procedural sedation with dexmedetomidine.

The two previous reports described dexmedetomidine administration in different doses. To avoid hemodynamic instability, it is recommended that dexmedetomidine be administered as a loading dose of 1 \(\mu\)g kg\(^{-1}\) over 10 minutes, and then infused in a dose of 0.2–0.7 \(\mu\)g kg\(^{-1}\) h\(^{-1}\). However, many clinicians are finding this range inadequate for sedation when performing procedures, especially on the airways. Ramsay and Luterman\(^9\) described the administration of dexmedetomidine in doses up to 10 \(\mu\)g kg\(^{-1}\) h\(^{-1}\) when using it as the sole sedative for procedures on the airways. Three patients were hemodynamically stable during the procedures and recovery times were not prolonged compared to conventional anesthetic. Additionally, one of the authors (MS) has reported administering dexmedetomidine as a total anesthetic for four infants undergoing direct laryngoscopy and bronchoscopy with doses ranging of 2 to 5 \(\mu\)g kg\(^{-1}\).\(^{10}\) In this report, dexmedetomidine was administered as boluses of 0.5 \(\mu\)g kg\(^{-1}\) every few minutes.

It is important to note that when using dexmedetomidine for airway procedures, adding local anesthetic is essential. Additionally, many clinicians use what is considered high doses of dexmedetomidine, such as up to 10 \(\mu\)g kg\(^{-1}\) h\(^{-1}\) used in Ramsay’s report,\(^9\) in order to complete the procedure. Such high doses could affect the hemodynamics in a sedated patient without invasive surgeries. However, airway surgeries are very stimulating and this could explain the normal heart rate and blood pressure in patients undergoing these surgeries with high doses of dexmedetomidine.

### Dexmedetomidine use during fiberoptic bronchoscopy

Dexmedetomidine has been used extensively for flexible fiberoptic tracheal intubation alone or in combination with other drugs. In a multicenter randomized, double-blind study, the safety and efficacy of dexmedetomidine for sedation during elective awake fiberoptic intubation (AFOI) was evaluated.\(^{11}\) Following topical anesthesia with lidocaine and achieving a Ramsay Sedation Scale score \(\geq\)2, nasal or oral intubation using a flexible fiberoptic bronchoscope was performed. Fewer dexmedetomidine patients required rescue midazolam to achieve and/or maintain targeted sedation (47.3\% vs 86.0\%, \(P < 0.001\)). The mean total dose of rescue midazolam was lower with dexmedetomidine vs placebo (1.07 mg vs 2.85 mg, \(P < 0.001\)). No patients in the dexmedetomidine group required additional medication other than midazolam to complete the procedure while 4 placebo patients required supplemental fentanyl or propofol. The incidence of respiratory depression was similar in both groups. Not surprisingly, the most common adverse events were hypotension (27.3\%) with dexmedetomidine and hypertension (28.0\%) and tachycardia (24.0\%) with placebo. The hemodynamic stability composite endpoint score was similar between dexmedetomidine and placebo groups (0.12 vs 0.14). Dexmedetomidine in this study did not prove to provide a favorable respiratory profile.

In another study, sedation with dexmedetomidine (0.7 \(\mu\)g kg\(^{-1}\) h\(^{-1}\)) was compared to remifentanil (0.075 \(\mu\)g kg\(^{-1}\) min\(^{-1}\)) by a blinded operator performing AFOI.\(^{12}\) The loading dose of dexmedetomidine in this study (0.4 \(\mu\)g kg\(^{-1}\)) is lower than the recommended loading dose of (1 \(\mu\)g kg\(^{-1}\)) and this could explain the more attempts at intubation needed in the dexmedetomidine group. In another retrospective report, dexmedetomidine was successfully administered in conjunction with midazolam and fentanyl to facilitate AFOI in twenty patients with cervical spine myelopathy.\(^{13}\) The advantage of dexmedetomidine in these patients was the ability to perform an awake post-intubation neurological exam. However the disadvantages included the bradycardia and hypotension which developed in 13 patients. To counteract the bradycardia and hypotension effects of
Dexmedetomidine, Scher and Gitline\textsuperscript{14} administered low dose of ketamine (15 mg kg\textsuperscript{-1} bolus and then infusion of 20 mg h\textsuperscript{-1}) in conjunction with dexmedetomidine when performing AFOI for a 52-year-old male with history of failed direct tracheal intubation. Using dexmedetomidine, ketamine, and airway nerve blocks, the patient was comfortable, sedated and tolerated the procedure. In another report, Bergese and colleagues\textsuperscript{15} reported on the usefulness of dexmedetomidine to facilitate AFOI in four patients one of them did not receive topical anesthesia. Dexmedetomidine was administered as a bolus of 1 µg kg\textsuperscript{-1} over 10 minutes followed by infusion of 0.5 µg kg\textsuperscript{-1} h\textsuperscript{-1}. This is the only report that used dexmedetomidine for AFOI without using local anesthesia.

**Dexmedetomidine use during dental procedures**

Due to its significant properties as sedative and analgesic and safe respiratory profile, coupled with its ease of use and antisialagogue properties, dexmedetomidine was thought to be very useful in dental/oral procedures.\textsuperscript{16} A randomized, double-blind study compared dexmedetomidine and midazolam for intravenous sedation during third molar surgery under local anesthesia.\textsuperscript{17} The study proved that dexmedetomidine sedation was acceptable to patients and comparable to midazolam with more predictability, as patients receiving dexmedetomidine did not have any restlessness or disinhibition. Dexmedetomidine, due to its respiratory profile, is safer than midazolam or the combination of midazolam and fentanyl when used by nonanesthesiologists. In another interesting study, dexmedetomidine was compared to midazolam for sedation in patients with symmetrically impacted mandibular third molars.\textsuperscript{18} In this unique design each patient served as a control for him/herself. The study revealed that dexmedetomidine may be a better alternative to midazolam for intravenous sedation in oral procedures not only because of its reliability and safety, but because of its analgesic effect providing a satisfactory sedation level without any serious side effects. However, dexmedetomidine did not provide reliable amnestic effects. In another prospective study dexmedetomidine was used as the sole sedative in fifteen patients undergoing dental procedures.\textsuperscript{19} Patients recommended this sedation 86% of the time although 26% of them stated that they remembered initial local anesthetic injection.

The literature reveals that dexmedetomidine is now recommended as a sedation agent for dental procedure especially in patients with high risk for respiratory depression and airway obstruction such as obese and a history of sleep apnea.

**Dexmedetomidine use during ophthalmology and other head and neck surgeries**

The efficacy of dexmedetomidine has been investigated during cataract surgery.\textsuperscript{20} During retrobulbar block, both patients and surgeon satisfaction scores (maximum 5) were lower in control group [1.9 (0.5)] compared with dexmedetomidine group [3.9 (0.6)] ($P$ = 0.016). After the dexmedetomidine loading dose, intraocular pressure was significantly decreased [12.3 (1.0) mmHg] compared to the preoperative value [16.1 (0.8) mmHg] ($P < 0.05$). There were no differences in Aldrete Scores or surgeon satisfaction scores between the two groups during the procedure. Two patients in dexmedetomidine group needed additional doses of 5 µg of dexmedetomidine after the loading dose, with one requiring two doses. The results of this study are not surprising as the control group did not receive any sedation. Although patients' satisfaction was higher in dexmedetomidine group while compared to saline, the results may differ if a continuous infusion of dexmedetomidine following the loading dose was used.

In a double-blind study of patients undergoing cataract surgery under peribulbar anesthesia, sedation with dexmedetomidine was compared to that of midazolam.\textsuperscript{21} Forty-four patients randomly received either. The author concluded that compared with midazolam, dexmedetomidine did not appear to be better for sedation than midazolam in patients undergoing cataract surgery due to cardiovascular depression and a delay recovery room discharge.

In facial surgeries, dexmedetomidine proved to be an excellent agent for sedation especially when the use of oxygen increases the risk of combustion.\textsuperscript{22} Dexmedetomidine was used as one of the primary anesthetic agents for spontaneously breathing patients undergoing constructive facial surgeries without supplemental oxygen. Dexmedetomidine permitted the surgeon to evaluate his surgical correction of a right-sided ptosis during bilateral upper blepharoplasty immediately prior to beginning a rhytidectomy. The patient was able to open and close her eyelid upon request permitting the surgeon to assess the adequacy of the corrected ptosis.

In a case report, dexmedetomidine was used in conjunction with local anesthetic and fentanyl to sedate a patient with obstructive sleep apnea, severe obstructive pulmonary disease,
and congestive heart failure undergoing thyroidectomy. A loading dose of 1 µg kg⁻¹ and infusion of 0.2 to 1 µg kg⁻¹ h⁻¹ were used with supplemental fentanyl. The patient tolerated the procedure very well and was able to cooperate with simple commands throughout the procedure.

**Dexmedetomidine use during neurosurgeries**

Another advantage of dexmedetomidine is its short action, which provides the ability to conduct a wake up test during a procedure. Dexmedetomidine in therapeutic doses is very effective in surgeries that require awake and communicative patients. Dexmedetomidine is especially useful during cortical mapping and when communication with the patient is necessary. In a randomized controlled study on craniotomies for tumors located near motor cortex, an awake technique using dexmedetomidine was compared to a general anesthetic technique. In another study, dexmedetomidine also proved to be advantageous as a sedative in neurosurgical procedures done in the prone position. These studies emphasized the ability to quickly awaken the patients when using dexmedetomidine, which is a great safety benefit in neurosurgical procedures.

**Dexmedetomidine use during vascular surgeries**

In 56 patients undergoing carotid endarterectomy using regional anesthesia, sedation with dexmedetomidine was compared to sedation using midazolam and fentanyl. Dexmedetomidine provided an acceptable alternative, without superiority to standard techniques for sedation during awake carotid endarterectomy. In another retrospective review the incidence of myocardial infarction, stroke, TIA and restenosis two years following carotid endarterectomy repair were similar between patients underwent general anesthesia and patients sedated with dexmedetomidine. Additionally, dexmedetomidine in 2 different loading doses (1 and 0.5 µg kg⁻¹) was efficacious for sedation in patients undergoing vascular procedures such as stent and fistula with local anesthesia. In the groups receiving dexmedetomidine at 0.5 µg kg⁻¹ and 1 µg kg⁻¹, 50% and 57% respectively did not require any rescue dose of midazolam, while all patients in placebo group did. This study shows that dexmedetomidine is safe and efficacious for these procedures. However, it does not show any superiority of sedation with dexmedetomidine over another type of sedatives as dexmedetomidine was compared to placebo. In another case report, dexmedetomidine, in conjunction with local anesthesia, provided adequate sedation for a patient for axillofemoral bypass graft with complicated medical history and difficult to manage airway.

Dexmedetomidine was administered as a loading dose of 1 µg kg⁻¹, then infused at 0.2–0.7 µg kg⁻¹ h⁻¹. Kaygusus et al evaluated the utility of dexmedetomidine when compared with propofol during extracorporeal shock-wave lithotripsy (ESWL) procedures in spontaneously breathing patients. The combination of dexmedetomidine with small dose of fentanyl was used safely and effectively for sedation and analgesia during ESWL. The design of this study was excellent in the way that dexmedetomidine was compared to propofol and not a placebo. Dexmedetomidine sedation was proved to be safe and efficacious compared to a normally practiced sedation with propofol.

**Dexmedetomidine use in procedures performed on pediatric patients**

Dexmedetomidine has been used off-label as an adjunctive agent for sedation and analgesia in pediatric patients in the critical care unit and for sedation during noninvasive procedures in radiology. Although one of the earliest applications for dexmedetomidine in pediatric patients was to prevent/treat emergence delirium, administering the drug for sedation during procedure with spontaneously ventilating children has increasingly been utilized. Today, dexmedetomidine is used in pediatric patients for sedation in many diagnostic procedures and surgeries including awake craniotomies.

**Cardiac catheterization**

Although dexmedetomidine has a great respiratory profile, it affects blood pressure, heart rate and cardiac output. Because of this; utilizing dexmedetomidine during cardiac catheterization is not advised. Both bradycardia and hypotension may change the pressure measurements needed by the cardiologists during cardiac catheterization. However, the literature does contain few studies regarding using dexmedetomidine in spontaneously breathing children undergoing cardiac catheterization.

In a retrospective report which included 20 children undergoing cardiac catheterization with spontaneous ventilation, dexmedetomidine was used as the sole anesthetic for the procedure. Dexmedetomidine sedation was not sufficient by itself in 12/20 patients and propofol had to be used. Another retrospective analysis of 16 infants and children showed that a combination of ketamine and dexmedetomidine provided effective sedation for cardiac catheterization in infants and children without significant effects on cardiovascular or
ventilatory function. The efficacy of sedation was judged by the need for supplemental ketamine doses (1 mg kg⁻¹). However, in two patients, the dexmedetomidine infusion was decreased from 2 to 1 µg kg⁻¹ h⁻¹ at 12 to 15 minutes instead of 30 minutes due to bradycardia. As ketamine causes tachycardia, its combination with dexmedetomidine seems to reverse the bradycardia effects of dexmedetomidine.

The effects of dexmedetomidine-ketamine and propofol-ketamine combinations on hemodynamics, sedation level, and the recovery period in pediatric patients undergoing cardiac catheterization was evaluated. The dexmedetomidine-ketamine combination was not superior to a propofol-ketamine combination due to insufficient sedation and analgesia and a longer recovery time. Again, the literature does not support any superiority of dexmedetomidine’s application in cardiac catheterization in pediatric patients.

CT and MR imaging
Dexmedetomidine has been used solely to sedate children for procedures without stimulation, and its use in MRI and CT scan are becoming popular. Dexmedetomidine was successfully used in 250 patients for sedation for CT imaging. This study was preceded by a pilot study on 62 patients that showed a mean recovery time of 32 ± 18 minutes. The same authors have utilized a sedation protocol for MRI using dexmedetomidine. In their review of their sedation protocol, they found that utilizing a higher doses of dexmedetomidine was associated with higher completion of imaging without the need to administer other sedative. It is an interesting finding that the higher dose of dexmedetomidine (bolus of 3 µg kg⁻¹ and infusion of 2 µg kg⁻¹ h⁻¹) was associated with shorter recovery time (24.8 ± 19.5 min). This was due to the lower use of barbiturates for rescue due to lower failure of sedation with dexmedetomidine alone. In another study, the sedative, hemodynamic and respiratory effects of dexmedetomidine were evaluated and compared with those of midazolam in children undergoing MRI. Patients in dexmedetomidine group had a higher rate of imaging completion without the need to add another sedative (80% compared with 20% in the midazolam group). The same authors compared the sedative, hemodynamic, and respiratory effects of dexmedetomidine and propofol in children undergoing MRI. In our experience, propofol provides a faster onset and offset, more reliable, and predictable anesthetic agent during MRI sedation. Dexmedetomidine may be an alternative to propofol for nonanesthesiologists or when the patient is at risk for desaturation or airway collapse. The literature also reveals that in order to increase the success of using dexmedetomidine as the sole agent of sedation in MRI, providers must increase the doses required for bolus and infusion (2 to 3 µg kg⁻¹ and 2 µg kg⁻¹ h⁻¹ respectively).

In Summary, the efficacy of dexmedetomidine to provide sedation for patients undergoing procedures and surgeries varied depending on the clinical situation: efficacy in pediatric patients was greatest during noninvasive procedures, such as magnetic resonance imaging, and lowest during invasive procedures, such as cardiac catheterization. Efficacy in the adult patients was best when local anesthesia was used. Dexmedetomidine is relatively unique in its ability to provide sedation without causing respiratory depression. It enables anesthesiologists to facilitate a rapid patients wake up during procedures, especially neurosurgical ones. We conclude that dexmedetomidine has no deleterious clinical effects on respiration when used in adequate doses and provides adequate sedation and effective analgesia. We ascertain that dexmedetomidine offers an alternative choice to propofol, opioids, and benzodiazepines for the sedation of patients whose trachea are not intubated during minimally invasive procedures.

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References


