Therapeutics and Clinical Risk Management

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

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

This article was published in the following Dove Press journal:
Therapeutics and Clinical Risk Management
10 March 2010
Number of times this article has been viewed

Mohanad Shukry
Jeffrey A Miller

University of Oklahoma Health Sciences Center, Department of Anesthesiology, Children's Hospital of Oklahoma, Oklahoma City, OK, USA

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 by 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.[1] However 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

Correspondence: Mohanad Shukry, MD
Assistant Professor of Anesthesiology, University of Oklahoma Health Sciences Center, Department of Anesthesiology, Children's Hospital of Oklahoma, 750 North East 13th Street, Suite 200, Oklahoma City, OK 73104, USA
Tel +1 405 271 4351 Ext 55151
Fax +1 405 271 4015
Email mohanad-shukry@ouhsc.edu

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 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 α_2-adrenoceptor agonist that has eight times greater specificity for α_2 receptors than does clonidine.[3] The actions of dexmedetomidine are thought to be mediated through post-synaptic α_2 receptors which activate pertussis toxin-sensitive G proteins; thus, increasing conductance through potassium ion channels.[4]

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 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 equisedative 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

Design (number of patients)	Procedure	DEX and other sedatives dose	Efficacy	Adverse effects
Multicenter P R DB (326)[5]	MAC sedation for a broad range of procedures preceded by local anesthetic block	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	Patients in both DEX groups required significantly less supplemental medication and reported significantly higher overall satisfaction and less postoperative anxiety	Incidence of respiratory depression was similarly low in both DEX groups compared to placebo
R P (40)[6]	Inguinal hernia or hip/knee procedures with nerve blocks	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})	DEX resulted in more sedation, lower blood pressure, and improved analgesia during recovery No difference between groups in psychomotor performance or respiratory rate	Sedation was more rapid with propofol, but similar at 25 min after LD
P (14)[7]	Awake laryngeal framework procedures; local anesthesia	LD of 1 μg $kg^{-1}$and infusion of 0.2–0.7 μg kg^{-1} h^{-1}	Adequate sedation for a majority of the procedures	Minimal undesirable hemodynamic or respiratory effects
CR (3)[9]	Direct laryngoscopy and bronchoscopy	LD of 1 μg kg^{-1} and infusion up to 10 μg kg^{-1} h^{-1}	No variation in hemodynamic stability	No prolongation of recovery times
RE (4)[10]	Direct laryngoscopy and bronchoscopy	LD of 2–5 μg kg^{-1} in addition to topical anesthetic	Adequate surgical conditions and preservation of spontaneous breathing	Using local anesthetic was key factor with this technique
Multicenter P R DB (124)[11]	Elective awake fiberoptic intubation	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	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	Incidence of hypotension was greater in the DEX group Hypertension greater in the placebo group
P R DB (30)[12]	Fiberoptic intubation	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	All airways were successfully secured	More patients in DEX group required more overall attempts at intubation (62% vs 24%) Remifentanil group had lower oxygen saturation but not significant
Clinical report (20)[13]	Awake fiberoptic intubation	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)	Able to perform an awake post-intubation neurological exam	Bradycardia and hypotension

(*Continued*)

Table 1 (*Continued*)

Design (number of patients)	Procedure	DEX and other sedatives dose	Efficacy	Adverse effects
R P DB (60)[17]	Third molar surgery under local anesthetic	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	DEX provided predictable sedation. Similar pain and satisfaction scores Midazolam provided greater amnesia	Heart rate and blood pressure were lower with DEX Midazolam caused restlessness and disinhibition
P DB Crossover R (20)[18]	Significantly impacted third molar surgery under local anesthesia	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	Similar respiratory findings Midazolam group showed greater amnesia Patients significantly preferred DEX	Mean heart rate and blood pressure significantly lower in the DEX group Higher likelihood of a pain response in the midazolam group
P (15)[19]	Dental procedures	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	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	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)
P R (40)[20]	Cataract surgery under peribulbar block	LD of 1 μg kg^{-1} over 10 min. Additional doses of 5 μg were administered if necessary No sedation in control group	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	Lower intraoperative heart rate in DEX group with atropine needed in 5 patients Higher incidence of dry mouth in DEX group
P DB R (44)[21]	Cataract surgery under peribulbar block	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	DEX had slightly higher satisfaction scores; similar surgeon satisfaction scores in both groups	DEX group had overall lower blood pressure and heart rate and delayed readiness for discharge [45 (36–54) vs 21 (10–32) min, $P < 0.01$]
P R (50)[26]	Craniotomy for tumors located near the motor cortex	LD of 1 μg kg^{-1}, maintenance dose of 0.2–0.8 μg kg^{-1} h^{-1} General anesthesia with propofol and remifentanil	Total tumor excision was more likely and higher mean satisfaction scores in DEX group	
RE (18)[27]	Placement of spinal cord stimulator with local anesthesia	LD of 1 μg kg^{-1} and infusion of 0.2–1.7 μg kg^{-1} h^{-1} Non-DEX patients received propofol anesthesia	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	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})

P R DB (56)[28]	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 bradycardia 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
P R PC (55)[30]	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	Less than 50% of patients in DEX group required rescue medications All patients in placebo group required rescue mediation	
P R DB (46)[32]	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	DEX group required fewer dose adjustments Oxygen supplementation and pain scores were similar in both groups	Deep sedation was not encountered in any patient
RE (20)[37]	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	All patients completed sedation Blood pressure and heart rate were within 20% of baseline	12/20 patients required a propofol bolus at some point during the procedure due to patient movement
RE (16)[38]	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	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 Apnea was not noted	In 2 patients, bradycardia required decreasing the infusion at 12 min instead of 30 Two patients developed upper airway obstruction, which responded to repositioning of the airway
P R (44)[39]	Cardiac catheterization in spontaneously breathing patients	DEX + ketamine (group 1): LD over10 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 ketamine.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; $P < 0.01$)

(*Continued*)

Table 1 (*Continued*)

Design (number of patients)	Procedure	DEX and other sedatives dose	Efficacy	Adverse effects
RE (250)[41]	CT imaging	LD of 2 μg kg^{-1} over 10 min and infusion of 1 μg kg^{-1} h^{-1}	Provided appropriate sedation	Noticeable changes in heart rate and mean arterial blood pressure during bolus and infusion relative to awake values ($P < 0.001$)
RE (62)[42]	CT imaging	LD of 2 μg kg^{-1} over 10 min (mean 2.2 μg kg^{-1}) and infusion of 1 μg kg^{-1} h^{-1}	10 patients needed second LD	Noticeable changes in heart rate and mean arterial blood pressure 2 patients became agitated during LD
RE (747)[43]	MRI sedation	LD of o 3 μg kg^{-1} over 10 min, and infusion rate of 2 μg kg^{-1} h^{-1}	Rate of successful sedation (able to complete the imaging study) when using DEX alone was 97.6%	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
R RE (80)[44]	MRI sedation	LD of 1 μg kg^{-1} and infusion of 0.2 μg kg^{-1} h^{-1} Midazolam loading dose of 0.2 mg kg^{-1} and infusion of 6 μg kg^{-1} h^{-1} Midazolam or propofol for rescue	Better quality imaging, and greater rate of sedation in the DEX group The onset of sedation time was shorter in group M (<0.001)	No hemodynamic or respiratory effects. More need for rescue drugs in the midazolam group
R RE (60)[45]	MRI sedation	LD 1 μg kg^{-1} and infusion of 0.5 μg kg^{-1} h^{-1} Propofol loading dose of 3 mg $kg^{-1}$with infusion of 100 μg kg^{-1} min^{-1}	Onset of sedation, recovery, and discharge time significantly shorter in the propofol group	5/30 patients had inadequate sedation in the DEX group 3/30 patients had significant desaturation in the propofol group

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 μg kg^{-1} and infusion rate of 0.5 μg kg^{-1} h^{-1}; at 30 minutes the infusion rate was increased to 3 μg 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 μg kg^{-1} over 10 minutes, and then infused in a dose of 0.2–0.7 μg 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 μg 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 μg kg^{-1}.[10] In this report, dexmedetomidine was administered as boluses of 0.5 μg 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 μg 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 ≥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 μg kg^{-1} h^{-1}) was compared to remifentanil (0.075 μg kg^{-1} min^{-1}) by a blinded operator performing AFOI.[12] The loading dose of dexmedetomidine in this study (0.4 μg kg^{-1}) is lower than the recommended loading dose of (1 μg 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[14] administered low dose of ketamine (15 mg kg^{-1} bolus and then infusion of 20 mg h^{-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[15] reported on the usefulness of dexmedetomidine to facilitate AFOI in four patients one of them did not receive topical anesthesia. Dexmeditomidine was administered as a bolus of 1 μg kg^{-1} over 10 minutes followed by infusion of 0.5 μg kg^{-1} h^{-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.[16] A randomized, double-blind study compared dexmedetomidine and midazolam for intravenous sedation during third molar surgery under local anesthesia.[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.[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.[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.[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.[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.[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.[23] 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.[22,24,25] 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.[24,25]

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.[26] In another study, dexmedetomidine also proved to be advantageous as a sedative in neurosurgical procedures done in the prone position.[27] 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.[28] 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.[29] 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.[30] 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.[31] 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[32] 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.[33] Although one of the earliest applications for dexmedetomidine in pediatric patients was to prevent/treat emergence delirium,[34] administering the drug for sedation during procedure with spontaneously ventilating children has increasingly been utilized.[35] Today, dexmedetomidine is used in pediatric patients for sedation in many diagnostic procedures and surgeries including awake craniotomies.[25]

Cardiac catheterization

Although dexmedetomidine has a great respiratory profile, it affects blood pressure, heart rate and cardiac output.[36] 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.[37] 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.[38] 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.[39] 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,[40] and its use in MRI and CT scan are becoming popular. Dexmedetomidine was successfully used in 250 patients for sedation for CT imaging.[41] This study was preceded by a pilot study on 62 patients that showed a mean recovery time of 32 ± 18 minutes.[42] The same authors have utilized a sedation protocol for MRI using dexmedetomidine.[43] 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.[44] 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.[45] 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 has the potential for an increasing role in anesthesia and sedation. Additionally, dexmedetomidine offers an alternative choice to propofol, opioids, and benzodiazepines for the sedation of patients whose trachea are not intubated during minimally invasive procedures.

Acknowledgments

The authors would like to thank James Mayhew, MD, Professor, Department of Anesthesiology, OUHSC for his editorial help in preparing the manuscript.

Disclosures

The authors declare no conflicts of interest.

References

1. Dyck JB, Shafer SL. Dexmedetomidine pharmacokinetics and pharmacodynamics. *Anaesthetic Pharmacology Review*. 1993;1:238–245.
2. Jacobi J, Fraser GL, Coursin DB, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med*. 2002;30:119–141.
3. Virtanen R, Savola JM, Saano V, Nyman L. Characterization of the selectivity, specificity, and potency of medetomidine as an α_2-adrenoceptor agonist. *Eur J Pharmacol*. 1988;150:9–14.
4. Salonen M, Reid K, Maze M. Synergistic interaction between alpha-2 adrenergic agonists and benzodiazepines in rats. *Anesthesiology*. 1992;76:1004–1011.
5. Candiotti K, Bergese S, Bokesch PM, Feldman M, Wisemandle W, Bekker A. Monitored anesthesia care with dexmedetomidine: a prospective, randomized, double-blind, multicenter trial. *Anesth Analg*. 2009 Aug 27. [Epub ahead of print].
6. Arain SR, Ebert TJ. The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. *Anesth Analg*. 2002;95:461–466.
7. Jense RJ, Souter K, Davis J, Romig C, Panneerselvam A, Maronian N. Dexmedetomidine sedation for laryngeal framework surgery. *Ann Otol Thinol Laryngol*. 2008;117:659–664.
8. Ohata H, Tanemura E, Dohi S. Use of high-dose dexmedetomidine infusion for anesthesia and sedation in a patient for microlaryngeal surgery maintained with spontaneous breathing. *Masui*. 2008;57:428–432.

9. Ramsay MA, Luterman DL. Dexmedetomidine as a total intravenous anesthetic agent. *Anesthesiology*. 2004;101:787–790.
10. Shukry M, Kennedy K. Dexmedetomidine as a total intravenous anesthetic in infants. *Pediatr Anesth*. 2007;17:581–583.
11. Bergese SD, Candiotti K, Zura A, Bokesch PM, Bekker AY. Dexmedetomidine for sedation during elective awake fiberoptic intubation: A multicenter trial. *Anesthesiology*. 2008;109:A-186.
12. Hagberg CA, Lam NC, Abramson SI, Vahdat K, Craig J. Dexmedetomidine vs remifentanil for sedation in awake intubation-a randomized, double-blind trial. *Anesthesiology*. 2008;109:A-14.
13. Avitsian R, Lin J, Lotto M, Ebrahim Z. Dexmedetomidine and awake fiberoptic intubation for possible cervical spine myelopathy: a clinical series. *J Neurosurg Anesthesiol*. 2005;17:97–99.
14. Scher CS, Gitlin MC. Dexmedetomidine and low-dose ketamine provide adequate sedation for awake fiberoptic intubation. *Can J Anesth*. 2003;50:607–610.
15. Bergese SD, Khabiri B, Roberts WD, Howie MB, McSweeney TD, Gerhardt MA. Dexmedetomidine for conscious sedation in difficult awake fiberoptic intubation cases. *J Clin Anesth*. 2007;19:141–144.
16. Ogawa S, Seino H, Ito H, Yamazaki S, Ganzberg S, Kawaai H. Intravenous sedation with low-dose dexmedetomidine: its potential for use in dentistry. *Anesth Prog*. 2008;55:82–88.
17. Cheung CW, Ying CLA, Chiu WK, Wong GTC, Ng KFJ, Irwin MG. A comparison of dexmedetomidine and midazolam for sedation in third molar surgery. *Anaesthesia*. 2007;62:1132–1138.
18. Ustun Y, Gunduz M, Erdogan O, Benlidayi ME. Dexmedetomidine versus midazolam in outpatient third molar surgery. *J Oral Maxillofac Surg*. 2006;64:1353–1358.
19. Makary LF, Vornik VD, Finn R, Lenkovsky F, Thurmon JJ. Dexmedetomidine as a sole sedative agent in office based dental procedures. *Post Graduate Assembly in Anesthesiology, New York*. 2008:P-9095.
20. Ayoglu H, Altunkaya H, Ozer Y, et al. Dexmedetomidine sedation during cataract surgery under regional anesthesia. *Br J Anaesth*. 2007;99:448.
21. Alhashemi JA. Dexmedetomidine vs midazolam for monitored anaesthesia care during cataract surgery. *Br J Anaesth*. 2006;96:722–726.
22. Bernardini DJ, Shapiro FE. Dexmedetomidine during TIVA: a unique approach to intraoperative wake up test. *Post Graduate Assembly in Anesthesiology, New York*. 2006:P-9021.
23. Plunkett AR, Shields C, Stojadinovic A, Buckenmaier CC. Awake thyrodiectomy under local anesthesia and dexmedetomidine infusion. *Mil Med*. 2009;174:100–102.
24. Maurtua MA, Cata JP, Martirena M, et al. Dexmedetomidine for deep brain stimulator placement in a child with primary generalized dystonia: case report and literature review. *J Clin Anesth*. 2009;21:213–216.
25. Ard J, Doyle W, Bekker A. Awake craniotomy with dexmedetomidine in pediatric patients. *J Neurosurg Anesthesiol*. 2003;15:263–266.
26. Chan MT, Chan DT, Poon WS, Gin T. Awake craniotomy is preferred for removal of tumors located at or near motor cortex. *Anesthesiology*. 2008;109:A-472.
27. Visoiu M, Tahbaz AA, Bendo A. Dexmedetomidine is effective for spinal cord stimulator placement and postoperative pain control. *Anesthesiology*. 2008;109:A-1666.
28. McCutcheon CA, Orme RM, Scott DA, Davies MJ, McGlade DP. A comparison of dexmedetomidine versus conventional therapy for sedation and hemodynamic control during carotid endarterectomy performed under regional anesthesia. *Anesth Analg*. 2006;102:668–675.
29. Gallagher MP, Newman KB, Shutze WP, Ramsay MA, Hein HA. Dexmedetomidine and cervical block is as safe as general anesthesia in carotid endarterectomy. *Anesthesiology*. 2008;109:A-1098.
30. Huncke TK, Candiotti K, Bergese S, Kim S, Bekker A. Prospective, randomized, placebo-controlled study: Dexmedetomidine sedation in vascular procedures. *Anesthesiology*. 2008;109:A-449.
31. Rich JM. Dexmedetomidine as a sole sedating agent with local anesthesia in a high-risk patient for axillofemoral bypass graft: A case report. *AANA J*. 2005;73:357–360.
32. Kaygusuz K, Gokce G, Gursoy S, Ayan S, Mimaroglu C, Gultekin Y. A comparison of sedation with dexmedetomidine or propofol during shockwave lithotripsy: a randomized controlled trial. *Anesth Analg*. 2008;106:114–119.
33. Phan H, Nahata MC. Clinical uses of dexmedetomidine in pediatric patients. *Pediatr Drugs*. 2008;10:49–69.
34. Shukry M, Clyde MC, Kalarickal PL, Ramadhyani U. Does dexmedetomidine prevent emergence delirium in children after sevoflurane-based general anesthesia? *Pediatr Anesth*. 2005;15:1098–1104.
35. Berkenbosch JW, Wankum PC, Tobias JD. Prospective evaluation of dexmedetomidine for noninvasive procedural sedation in children. *Pediatr Crit Care Med*. 2005;6:435–439.
36. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology*. 2000;93:382–394.
37. Munro HM, Tirotta CF, Felix DE, et al. Initial experience with dexmedetomidine for diagnostic and interventional cardiac catheterization in children. *Pediatr Anesth*. 2007;17:109–112.
38. Mester R, Easley B, Brady KM, Chilson K, Tobias JD. Monitored anesthesia care with a combination of ketamine and dexmedetomidine during cardiac catheterization. *Am J Ther*. 2008;15:24–30.
39. Tosun Z, Akin A, Fuler G, Esmaoglu A, Boyaci A. Dexmedetomidine-ketamine and propofol-ketamine combinations for anesthesia in spontaneously breathing pediatric patients undergoing cardiac catheterization. *J Cardiothorac Vasc Anesth*. 2006;20:515–519.
40. Shukry M, Ramahdyani R. Dexmedetomidine as the primary sedative agent for brain radiation therapy in a 21-month old child. *Pediatr Anesth*. 2005;15:241–242.
41. Mason KP, Zgleszewski SE, Dearden JL, et al. Dexmedetomidine for pediatric sedation for computed tomography imaging studies. *Anesth Analg*. 2006;103:57–62.
42. Mason KP, Zgleszewski SE, Prescilla R, Fontaine PJ, Zurakowski D. Hemodynamic effects of dexmedetomidine sedation for CT imaging studies. *Pediatr Anesth*. 2008;18:393–402.
43. Mason KP, Zurakowski D, Zgleszewski SE, et al. High dose dexmedetomidine as the sole sedative for pediatric MRI. *Pediatr Anesth*. 2008;18:403–411.
44. Koroglu A, Demirbilek S, Teksan H, Sagir O, But AK, Ersoy OM. Sedative, haemodynamic and respiratory effects of dexmedetomidine in children undergoing magnetic resonance imaging examination: preliminary results. *Br J Anaesth*. 2005;94:821–824.
45. Koroglu A, Teksan H, Sagir O, Yucel A, Toprak HI, Ersoy OM. A comparison of the sedative, hemodynamic, and respiratory effects of dexmedetomidine and propofol in children undergoing magnetic resonance imaging. *Anesth Analg*. 2006;103:43–48.