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GUIDELINES

Safety in magnetic resonance units: an update

Association of Anaesthetists of Great Britain and Ireland

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This is a consensus document produced by expert members of a Working Party established by the Association of Anaesthetists of Great Britain and Ireland (AAGBI). It updates and replaces previous guidance published in 2002, and has been seen and approved by the Council of the AAGBI.

Summary

The number of anaesthetists who are involved in magnetic resonance (MR) units is increasing. Magnetic resonance systems are becoming more powerful and interventional procedures are now possible. This paper updates information relating to safety terminology, occupational exposure, reactions to gadolinium-based contrast agents and the risk of nephrogenic systemic fibrosis. Magnetic resonance examinations of patients with pacemakers are still generally contra-indicated but have been carried out in specialist centres under strictly controlled conditions. As availability of MR increases, so the education of anaesthetists, who are occasionally required to provide a service, must be considered.

Anaesthesia in MR units was first described in the 1980s. Guidelines on the provision of anaesthetic services in MR units were published by the Association of Anaesthetists of Great Britain and Ireland (AAGBI) in 2002 [1]. Since then, the number of hospitals with MR units, and hence the number of patients requiring anaesthesia for MR, has increased. While the issues relating to setting up anaesthetic services in MR have not changed, there have been a number of developments that warrant this update:

1. Safety terminology and guidelines have changed.
2. MR systems utilise higher magnetic-field strengths and more open designs are available.
3. Interventional and intra-operative MR are now routine in some centres.
4. Mobile MR scanners are increasingly used to reduce waiting lists.
5. Although still generally contra-indicated, some patients with pacemakers have been scanned under strictly controlled conditions in specialist centres.
6. 'MR safe' medical implants are now being produced.
7. New equipment is now available for use in MR.
8. Out-of-hours availability of MR investigations has increased.
9. Reports of allergic reactions to MR contrast media have increased.
10. Gadolinium based contrast agents (Gd-CAs) are associated with a varying degree of risk of nephrogenic systemic fibrosis in patients with impaired renal function.

Safety guidelines and legislation

In 2007 the Medicines and Healthcare products Regulatory Agency (MHRA) updated safety guidance as a Device Bulletin [2]. Three terms are now to be used as standard in an attempt to remove any ambiguity caused by the old *MR compatible* system. These terms are *MR conditional*, *MR safe* and *MR unsafe*. MR conditional refers to an item that has been demonstrated to pose no known hazards in a specified MR environment with specified conditions of use. Many items in the MR environment will now be marked as MR conditional, and the conditions under which they can be safely used must accompany the device. This change of terminology has come about because of reports of injuries and problems with MR compatible equipment [3]. Conditions that define the specified MR environment include main magnetic field strength, spatial magnetic field gradient, dB/dt (time rate of change of the magnetic field), radio frequency (RF) field strength, and specific absorption rate. Additional conditions, including specific configurations of the item of equipment, may be required.

Equipment is designated as MR safe if it presents no safety hazard to patients or personnel when it is taken into the MR examination room, provided that instructions concerning its use are correctly followed. This does not, however, guarantee that it will function normally and not interfere with the correct operation of the MR imaging equipment, with degradation of image quality.

New equipment, such as infusion pumps [4], warming mattresses and temperature probes are now available. It is important to understand the manufacturers' instructions of all equipment that is brought into the vicinity of the MR scanner.

It should be recognised that the supervising MR radiographer is responsible operationally for MR safety within the controlled area and that anaesthetic staff should defer to him/her in relation to MR safety matters, in particular control of access of staff and equipment into the controlled area. Where staff are given access codes or swipe-card access to the controlled area, they should not be shared with others, nor should they provide access to others unless specifically authorised to do so.

Inspired oxygen concentration

The use of 100% O_2 during anaesthesia should be reported to the reporting radiologist as this can produce an artefact in the form of an abnormally high signal in cerebrospinal fluid (CSF) spaces in the T2 weighted fluid attenuated inversion recovery (FLAIR) sequence.

Acoustic noise

The time-varying magnetic field gradients produce audible noise within the magnet interior. Since the guidelines were published by the AAGBI, the Control of Noise at Work Regulations have been updated [5]. This document introduced lower exposure limit values and action values in the working environment. When the noise level exceeds 80 dB (A), it is recommended that staff and others remaining in the scanning room should wear ear protection.

Other documents have been published by the Health Protection Agency relating to patient exposure guidance [6] and static field guidance [7]. The website of the British Association of MR Radiographers (BAMRR) remains an excellent resource for safety issues and provides links to many useful safety sites [8].

New MR systems

At the end of 2006, it was estimated that there were approximately 500 fixed MR scanners involved in human imaging, installed at some 350 sites across the UK [6]. The SI unit of magnetic field strength or magnetic flux density is the Tesla (T) and initially, most clinical MR systems were 0.5, 1.0 or 1.5 T. In 1992 there were two MR units in Northern Ireland. Today there are 16, of which, one is a 3-T system. Other regions will have experienced a similar expansion but, since the withdrawal of funding from MagNET, up-to-date information for the UK is difficult to obtain.

Magnets operating at 3 T appeared in the early 1990s and by 2007 it was estimated that 35 units had installed 3-T systems [5]. The benefits of the higher field strength systems include improved image quality and higher spatial resolution. While it is claimed that 3-T scans are quicker, more efficient and require less Gd-CAs, practically these statements are debatable. It is the responsibility of the equipment manufacturers to indicate the field strength at which their equipment is MR safe or MR conditional. It should not be automatically assumed that equipment that is MR conditional at 1.5 T remains MR conditional at 3 T. A smaller number of ultra-high field MR systems are in use in research institutions world wide and these produce static fields in the range 4.7–9.4 T [6]. Anaesthetists may wish to be aware of the potential implications of replacing a 1.5-T system by a 3-T system. In a magnetic field strength survey of a 1.5-T system all spot measurements taken at 1 m above the floor level were found to be below the 0.5-mT safety limit. A similar survey for a 3-T system indicated that there were areas outside the magnet room where levels exceeded the safety limit. Barriers and warning notices, which indicate the risk of pacemaker malfunction, should be in place to prevent inadvertent public access.

Open systems

The horizontal-bore cylindrical type of scanner is still the commonest, but technology constantly changes and magnets are available with wider bores, which are less claustrophobic. More open scanners have been developed and units now exist that allow the patient to stand upright thus reducing the feeling of claustrophobia. In a conventional MR system operating at 1.5 T, because of its more closed design, it is less likely that radiological and anaesthetic staff would be exposed to significant static and time varying fields.

Interventional procedures and intra-operative MR

Advances in technology mean MR image-guided surgery is now possible, providing the surgeon with dynamic high-resolution images during intricate stereotactic neurosurgery. Various MR systems have been configured for this application, including 'doughnut' shaped magnets permitting surgery with real-time concurrent imaging, and portable systems set up to allow easy and rapid interchange between scanning and surgery. All the hazards associated with diagnostic MR also apply to

interventional procedures. There are additional risks from patient repositioning, contamination of the sterile field, and the proximity of ferromagnetic surgical instruments, including scalpels, to the magnetic field. Incorporating MR technology into the operating room provides new challenges [9].

Occupational exposure

It is difficult to measure occupational exposure to the various electro magnetic fields in MR units routinely. Personal dosimeters have been developed but are not, as yet, widely available. Some studies have suggested that staff members can be exposed to higher than recommended levels of time-varying gradient fields [10, 11]. In 2004, the European Union adopted a directive restricting occupational exposure to electromagnetic fields, including those used in MR. Some of the exposure limits threatened to impact on the current use and future development of MR technology. Known adverse effects are adequately addressed in the international standard governing the manufacture of MR systems. Initially, unable to influence the regulatory agencies, the MR community began to lobby both the UK and European Parliaments. Implementation of the directive has been delayed until 30 April 2012 to allow a permanent solution to be found. However, the timescale is short given the political and scientific complexities of the issue. A range of possible outcomes is explored in a report for the Institute of Physics [12]. Each option has advantages and disadvantages, and a great deal of detailed discussion and negotiation will be needed over the next 2 years to ensure satisfactory resolution of the problem.

Pacemakers and medical implants

The MHRA safety guidance [2] still specifies that pacemakers are an absolute contraindication to MR and it therefore remains the mantra of radiology departments that any individual with a pacemaker should not enter the MR unit. This is due to the concern that the magnet field strengths in excess of 0.5 mT (5 Gauss) could cause a fatal malfunction of the pacemaker. Sudden deaths have been reported in patients with pacemakers during or shortly after MR investigations [13, 14]. However, both pacemaker and MR technology are continually developing and there are times when MR is needed to provide valuable clinical information in patients with pacemakers. There have been a small number of cases when a patient with a non-compatible pacemaker has required MR imaging.

Approximately two million Europeans have implanted pacemakers, but these patients are strongly discouraged from receiving MRI scans. According to estimates, 50–75% of patients world-wide with implanted cardiac devices are expected to need a MR scan during the lifetime of their device [15]. Editorials in the American and European literature concluded that the risk:benefit ratio for patients with pacemakers undergoing MR has shifted towards safety, if guidelines are followed [16, 17]. Discussion in the correspondence sections has been generated [18]. In summary, the presence of a permanent pacemaker no longer represents a strict contra-indication to MR in carefully selected clinical circumstances provided that specific strategies are followed [19].

MR compatible pacemakers are now available and have been implanted in some patients. One pacemaker manufacturer has received a Conformité Européenne (CE) Mark for its second-generation MR safe pacing system. However, approval has not yet been forthcoming from the Food and Drug Administration in the USA [20].

Programmable shunts

The pressure setting of programmable hydrocephalus shunts may be unintentionally changed by the magnetic field leading to over- or under-drainage of CSF. If these patients are to undergo an MR examination, a programmer and a trained clinician should be available to verify the correct setting and to reprogram the device, if required, immediately following the MR procedure. Advice must be given to the patient on how to recognise over- and under-drainage and whom to contact should these conditions develop [2].

Neurostimulators

A wide variety of neurostimulators are now in use. Concerns about MR safety relate to the RF and gradient fields that may interfere with the operation of these devices or cause thermal injury. It is recommended that patients implanted with neurostimulators should not undergo MR. However, some manufacturers are suggesting that MR examinations of specific devices may be safe if strict guidelines relating to scanning parameters, in particular to RF exposure, are followed [2].

Out-of-hours MR imaging

There are many indications for urgent MR imaging, but they can be grouped into two main areas: suspected spinal cord or cauda equina compression; and investigation of acute neurological conditions. Hospital trusts have faced litigation when treatment has been delayed due to lack of 24-h MR availability. Patients in intensive care units (ICUs) who require urgent MR will need to be accompanied by anaesthetic staff. Intensive care patients have additional sources of hazard including central lines and intracranial pressure transducers [21]. Screening

checklists have been adapted for use in intensive care. It should be remembered that the ultimate operational responsibility for safety issues remains with an appropriately trained MR Authorised Person (usually the supervising radiographer) and the MR radiologist [2].

Training

Training requirements for any staff entering the MR unit are detailed by the MHRA [2]. The responsibility for safety training lies with the MR Responsible Person who may be the clinical director, head of department, clinical scientist or MR superintendent radiographer. The unit's MR Safety Advisor should provide technical advice. The wide range of staff from differing disciplines who need access to the MR environment have been designated into categories. Anaesthetists fall into MHRA category B; that is, they may be present with a patient in the MR controlled area during scanning. They should be aware of safety aspects related to the main static magnetic fields, RF fields, gradient magnetic fields and electrical safety of equipment. They must understand the significance of the MR controlled area and the inner MR controlled area. They should be familiar with emergency procedures arising from causes other than equipment failure and should be aware of the need to evacuate the patient from the inner controlled area in order to deal with emergency resuscitation. Training also includes an understanding of the projectile effect and the influence of the magnetic field upon medical implants, prostheses and personal effects.

Anaesthetists should understand the consequences of quenching of super-conducting magnets, and be aware of the recommendations on exposure to MR and the need for ear protection.

How can these training requirements be met? The potential for e-learning should be considered. The Royal College of Anaesthetists includes the physics of MRI in its basic science syllabus [22]. Trainees who have completed an e-learning module and attended an elective MR list would then be certified as suitable to accompany ICU patients for MR imaging. Regular reviews of training status as well as updates and refresher courses will be required. Hospitals will wish to apply local rules regarding consultant supervision of anaesthetic trainees in MR units.

Contrast reactions

Gadolinium-based contrast agents are used in MR for demonstration of vascular structures or to improve contrast resolution of tissues. In comparison with other radiological contrast agents, Gd-CAs are relatively safe with a high therapeutic ratio and low incidence of anaphylaxis (approximately 1:100 000). The side-effects of Gd-CAs are generally mild and include headache, nausea and vomiting, local burning, skin wheals (2%), itching, sweating, facial swelling and thrombophlebitis [23]. More severe reactions have occurred and radiology staff should be familiar with guidelines related to the management of suspected anaphylaxis [24].

Nephrogenic systemic fibrosis

There has been recent attention to reports that patients with renal failure are at risk of developing a rare, potentially life-threatening condition with Gd-CAs called nephrogenic systemic fibrosis or nephrogenic fibrosing dermopathy (NSF/NFD). The glomerular filtration rate (GFR) should be estimated in all patients with kidney disease to identify those at risk of developing NSF/NSD. If the GFR is estimated at less than 30 $ml.min^{-1}$ per 1.73 m^{-2}, the risk of Gd-CAs should be balanced against benefit, and a minimal dose of Gd-CAs only administered if an unenhanced scan proves insufficient [25]. The Gd-CA should not be administered again for at least 7 days. Current evidence suggests that contrast agents may be classified as high-risk, e.g. gadopentelic acid, medium-risk, e.g. gadobenic acid, and low-risk e.g. gadoteridol [26]. The use of high-risk agents is contra-indicated in neonates and during the peri-operative period in patients undergoing liver transplantation. The Gd-Cas are not recommended in pregnancy unless absolutely necessary.

Conclusions

While some safety terminology has altered, the basic recommendations for provision of anaesthetic services in MR units have remained the same since first published in 2002 [1]. Anaesthetists who are involved with 3-T systems, open scanners or interventional and intra-operative procedures should remain acquainted with the constantly changing recommendations relating to occupational exposure. They should take all practical steps to minimise the risk from exposure. MR examinations of patients with pacemakers are no longer absolutely contra-indicated but may be carried out under strictly controlled conditions in exceptional cases. Increased requirements for MR imaging in intensive care and postoperative patients have increased the need for repeated training. The employment of e-learning modules may facilitate such training. There has been an increase in the number of allergic reactions to Gd-CAs and it is recognised that patients with renal failure are at risk of developing NSF.

References

1 Association of Anaesthetists of Great Britain and Ireland. *Provision of Anaesthetic Services in Magnetic Resonance Units*.

The Association of Anaesthetists of Great Britain and Ireland, 2002. http://www.aagbi.org/publications/guidelines/docs/mri02.pdf (accessed 08/12/2009).
2 Device Bulletin Safety Guidelines for Magnetic Resonance Imaging Equipment in Clinical Use DB2007(03) December 2007 http://www.mhra.gov.uk/Publications/Safetyguidance/DeviceBulletins/CON2033018 (accessed 08/12/2009).
3 Farling PA, McBrien ME, Winder RJ. Magnetic resonance compatible equipment: read the small print! *Anaesthesia* 2003; **58**: 86.
4 Bradley PG, Harding SG, Reape-Moore K, Abeygunaratne R, Menon DK. Evaluation of infusion pump performance in a magnetic resonance environment. *European Journal of Anaesthesiology* 2004; **21**: 729–33.
5 The Control of Noise at Work Regulations 2005. Statutory instrument 2005 N0.1643 http://www.opsi.gov.uk/si/si2005/20051643.htm (accessed 02/02/2010).
6 Protection of patients and volunteers undergoing MRI procedures. Advice from the Health Protection Agency. ISBN: 978-0-85951-623-5 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1222673275524 (accessed 8/12/2009).
7 Static Magnetic Fields. Health Protection Agency. 2008 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1211184025757 (accessed 9/12/2009).
8 British Society of MR Radiographers http://www.bamrr.org/content.aspx?Group=links&Page=links (accessed 08/04/2010).
9 Bergese SD, Puente EG. Anesthesia in the intra-operative MRI Environment. *Neurosurgery Clinics of North America* 2009; **20**: 155–62.
10 Vecchia P, Matthes R, Ziegelberger G, et al. (editors). Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz-300 GHz). International Commission on Non-Ionizing Radiation Protection, 2008. http://www.icnirp.de/documents/RFReview.pdf (accessed 09/12/2009).
11 Bradley JK, Nyekiova M, Price DL, Lopez LD, Crawley T. Occupational exposure to static and time-varying gradient magnetic fields in MR units. *Journal of Magnetic Resonance Imaging* 2007; **26**: 1204–9.
12 Keevil S, MRI and the Physical Agents (EMF) Directive. Reproduced by permission of the Institute of Physics. 2008. http://www.iop.org/activity/policy/Publications/file_32151.pdf (accessed 08/12/2009).
13 Ferris NJ, Kavnoudias H, Thiel C, Stuckey S. The 2005 Australian MRI safety survey. *American Journal of Roentgenology* 2007; **188**: 1388–94.
14 Bartsch CH, Irnich W, Risse M, Weller G. Unexpected sudden death of pacemaker patients during or shortly after magnetic resonance imaging (MRI). In *XIX Congress of International Academy of Legal Medicine*. Milan, Italy, 2003; 3–6. Abstract No 114.
15 Kalin R, Stanton MS. Current clinical issues for MRI scanning of pacemaker and defibrillator patients. *Pacing and Clinical Electrophysiolgy* 2005; **28**: 326–8.
16 Martin ET, Coman JA, Shellock FG, et al. Magnetic resonance imaging and cardiac pacemaker safety at 1.5 Tesla. *Journal of the American College of Cardiology* 2004; **43**: 1315–24.
17 Martin ET. Can cardiac pacemakers and magnetic resonance imaging co-exist? *European Heart Journal* 2005; **26**: 325–7.
18 Gimbel JR, Wilkoff BL, Kanal E, Rozner MA. Safe, sensible sagacious: resposible scanning of pacemaker patients. *European Heart Journal* 2005; **26**: 1683–91.
19 Shellock FG. MR Imaging and electronically activated devices. *Radiology* 2001; **219**: 294.
20 Press Release. http://wwwp.medtronic.com/Newsroom/NewsReleaseDetails.do?itemId=1245340154210&lang=en_US (accessed 29/01/2010).
21 Newcombe VF, Hawkes RC, Harding SG, et al. Potential heating caused by intraparenchymal intracranial pressure transducers in a 3-tesla magnetic resonance imaging system using a body radiofrequency resonator: assessment of the Codman MicroSensor Transducer. *Journal of Neurosurgery* 2008; **109**: 159–64.
22 Royal College of Anaesthetists http://www.rcoa.ac.uk/docs/eLA-Curriculum.pdf (accessed 29/01/2010).
23 Li A, Wong CS, Lee CM, Au Yeung MC. Acute adverse reactions to magnetic resonance contrast media – gadolinium chelates. *British Journal of Radiology* 2006; **79**: 368–71.
24 Harper NJN, Dixon T, Dugue P, et al. Guidelines: suspected anaphylactic reactions associated with anaesthesia. *Anaesthesia* 2009; **64**: 199–211.
25 Shellock FG, Spinazzi A. MRI safety update 2008: part 1, MRI contrast agents and nephrogenic systemic fibrosis. *American Journal of Roentgenology* 2008; **191**: 1129–39.
26 Drug Safety Update 2010; **3**: 3–5 http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON068297 (accessed 15/02/2010).

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Anesthesia for MRI in the pediatric patient

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The magnetic resonance imaging suite is a challenging environment for the anaesthesiologists, and carries inherent risks. Several factors account for this, including the remote location, the unique features of the magnetic resonance imaging scanner and patient-related factors. A systematic approach, similar to that of anesthesia provided in the operating room (*i.e.* proper fasting, informed consent, focused airway examination, medical and surgical history, family history, previous sedation experiences) is mandatory. Understanding the implications of the magnetic resonance imaging environment will facilitate ensuring the safety of the patient. A well-equipped anesthesia machine, standard monitoring (electrocardiogram, oxygen saturation and non-invasive blood pressure), trained personnel and adequate planning should be standard for all out of the operating room procedures. Finally, rigorous discharge criteria are recommended to detect residual sedation.

Key words: **Magnetic resonance imaging - Sedation - Anesthesia, general - Child - Discharge criteria - Fasting guidelines.**

The goal of anesthesia for magnetic resonance imaging (MRI), painless procedure that offers the distinct advantage over other modalities of using non-ionizing radiation, is to provide immobility, safety and comfort for the patient while achieving the best diagnostic study.[1]

The duration varies from 30 to as long 90 minutes and may even require movement of the patient during coil changes when both brain and spine imaging are done during the same sitting.[2]

In addition, the required intense magnetic fields create unique problems with the use of physiologic monitors, standards anesthesia machines and ventilators.[1]

The literature about the pediatric patient's sedation

Until 1985 there were no guidelines for pediatric sedation. Unfortunate adverse events in dental offices heightened awareness of the hazards of pediatric sedation.[3] This led the American Academy of Pediatrics (AAP) to develop guidelines for the elective use of sedation and general anesthesia.[4] Unfortunately the first guidelines adapted language from the National Institute of Health regarding dental sedation, especially the misnomer "conscious sedation", an oxymoron in the pediatric population.

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TABLE I.—*Definition of general anesthesia and levels of sedational analgesia.*

	Minimal sedation (Anxiolysis)	Modrrate sedation/analgesia (Conscious sedation)	Deep sedation	General anesthesia
Responsiveness	Normal response to verbal stimulation	Purpoeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable, even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often re-quired
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

The AAP later revised the guideline. Pulse oximetry was required for all sedated children and a systematic approach similar to that used by anaesthesiologists was developed, *i.e.*:

— proper fasting time
— informed consent
— focused airway examination
— medical/surgical history
— previous sedation experiences
— recommended equipment and medication
— proper monitoring and documentation during and after the procedure
— strict discharge criteria.

During the following years the American Association of Anaesthesiologists (ASA) become involved with the sedation safety, in part because the Joint Commission on Accreditation of HealthCare Organisations (JCAHO) modified their regulations in such a way that made departments of anaesthesiology responsible for developing "within institution" sedation guidelines.

The first ASA iteration succeeded in changing the terminology from the oxymoron "conscious sedation" to the more appropriate term "sedation/analgesia".

In 2002, the ASA published revised sedation guidelines that address all depths of sedation.[5] The ASA, working closely with JCAHO, also developed new language to describe the sedation's process, which was later incorporated by the JCAHO.[6] Now, three stages of sedation and general anesthesia are described:

— minimal sedation
— moderate sedation
— deep sedation
— general anesthesia.

Recently, the AAP adopted the ASA definitions for their sedation guidelines.[7] Now the AAP, ASA and JCAHO are speaking the same language. In addition, the JCAHO introduced the essential concept of rescue, *i.e.* the practitioner must have the skills to rescue should the patient progress to a deep level of sedation than intended.

The Neuroanesthesia and Neurointensive Study Group of the Italian Society of Anesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI) with the Italian Society of Neonatal and Pediatric Anaesthesia and Resuscitation (SARNePI) have been published in 2004 the SIAARTI-SARNePI Guidelines for sedation in pediatric neuroradiology.[8]

Definitions

When the sedation guidelines of the AAP were first reported, a distinction was made between conscious sedation, deep sedation and general anesthesia. Those guidelines have since undergone refinement. The term "conscious sedation" was considered impractical for young children,[9] and was changed to

"moderate sedation". The new terminology promoted by JCAHO describes the following: minimal sedation (anxiolysis), moderate sedation/analgesia (conscious sedation), deep sedation and general anesthesia (Table I).

Obviously the transition from moderate sedation to general anesthesia progress through a *continuum*: one can pass from the preservation of protective reflexes and the ability to maintain a patent airway to the inability to breath spontaneously. If this occurs without adequate vigilance or monitoring, severe adverse events may occur, including cardio circulatory arrest.[8]

Anaesthetic management

Safety considerations

There are a number of potential risks associated with the MRI environment. The major risk encountered deals with ferromagnetic objects or equipment and their projectile capabilities in the MRI scanner room.

The MRI setting creates also an unavoidable distance between the patient and the anaesthesiologist. The major problems are a lack of visibility and a lack of access to the patient. Undoubtedly, these factors will have an impact on anesthesia management. In many institutes, a video system is available that permits visual contact with the patient throughout the scanning process.[10]

Moreover, the patients who require anesthesia in the MRI suite must be provided with the same level of safety and monitoring as in the operating room. Deep sedation and general anesthesia are equivalent and require the same monitor. MRI-compatible physiological monitors and anesthesia machines, commercially available and preferable, must be equipped with "standard monitors", including an electrocardiogram, fiberoptic cabled pulse oximetry, non-invasive blood pressure, capnography.

Patient considerations

Before sedation, the patient's health history and physical examination should be obtained, including vital signs, auscultation of the heart and lungs, and evaluation of the respiratory tract.

There is no indication for routine ECG, chest X-ray or blood chemistry analyses in ASA I or II patients. Diagnostic and laboratory studies should be directed towards concomitant illness.[8] Fasting rules for elective and sedation anesthesia are listed in Table II.

TABLE II.—*Fasting rules.*

Ingested material	Minimum fasting period
Clear liquids	2 h
Breast milk	4 h
Infant formula	6 h
Non-human milk	6 h
Light meal	6 h

Anaesthetic techniques

The choice of anaesthetic technique for MRI will depend on patient's related factors and the duration of the study. Various techniques have been employed which include anxiolysis, total intravenous anesthesia (TIVA), volatile-based anesthesia.

A host of drug, both oral and intravenous agents have been used to achieve sufficient depth of sedation with varying degrees of success.[11-13] The drugs commonly used in pediatrics are listed in Table III.

Since even the lightest movement cause artefacts in imaging and the child can not be directly controlled, deep sedation or general anesthesia is often induced.

No data exist on whether a specific anaesthetic technique is superior for MRI. However, Usher and Kearney [14] recently conducted a survey of pediatric anesthesia departments in 11 Canadian medical institutes, and reported more than 50% use of TIVA with propofol for MRI.

A recent study of Usher [15] demonstrated good preservation of upper airway patency and rapid recovery using general anesthesia doses of propofol in children.

Although the guidelines of foreign scientific societies do not list halogenated agents for sedation in pediatric patients, these drugs are widely used, not only in Italy.

Recently, Suy [16] and DeSanctis [17] demon-

TABLE III.—*Drugs for sedation and antagonist.*

Drug	Route	Dose	Onset (min)	Duration (min)
Chloral hydrate	po	25/100 mg/kg	15-30	60-120
Fentanil	iv, im	0.5-1 m/kg	2-4	30-60
Ketamine	im	3-5 mg/kg	3-6	30-180
Meperidine	iv, im	0.2-0.5 mg/kg	4-8	60-90
Midazolam	po	0.5-1 mg/kg (max 15 mg)	20-30	60-90
Midazolam	in, rect	0.2-0.5 mg/kg	10-30	50-75
Midazolam	im	0.1-0.2 mg/kg	10-15	60-90
Midazolam	iv	0.02-0.1 mg/kg	5-10	30-60
Morphine	iv, im	0.05-0.1 mg/kg	5-10	45-120
Pentobarbital	po, rect	2-4 mg/kg (max 100 mg)	20-60	60-240
Pentobarbital	iv	1-2 mg/kg	3-5	20-40
Propofol	iv	Initial bolus: 1-2 mg/kg	1-2	5-15
Propofol	iv	Infusion: 50-250 m/kg/min	—	—
Flumazenil	iv	0.01-0.02 mg/kg	1-2	30-60
Naloxone	im	0.1 mg/kg	10-15	60-90
Naloxone	iv	0.1 mg/kg	2-4	30-40

Iv: intravenous; im: intramuscular; po: oral; in: intranasal

strated that sevoflurane is an ideal agent for this type of diagnostic procedure in newborns and infants. The authors emphasize the strict observation of recommendations, which include the practical experience and up-to-date specialized training of the anaesthesiologists carrying out sedation procedures in children.

One question that must be made relates to what "depth" of sedation or anesthesia will be provided for MRI in children. In particular, one must address the question as to whether there is a significant advantage to providing anesthesia for this procedure, or is moderate sedation sufficient. The answer must take into account an acceptable rate of "failed" sedation and the expectations of the patients and family who are being served. When sedation fails it is impossible to carry out the procedure (the child is crying, struggling and requires significant restraint.

Adverse sedation events in pediatrics

The most important study performed about the adverse sedation events in pediatrics is an analysis of medication used for sedation by Cotè.[18] The study showed 95 adverse events with 51 deaths and 9 permanent neurological injury. The review indicated that there was no relationship between outcome and drug class (opioids, benzodiazepines, barbiturates, sedatives, antihistamines, local, intravenous or inhalation anaesthetics) or route of administration (oral, nasal, rectal, intramuscular, intravenous, local infiltration and inhalation). Negative outcomes (deaths or permanent neurological injury) were often associated with drug overdose (n=28), with the use of 3 or more sedating medications compared with 1 or 2 medications (18/20 *vs* 7/70). Nitrous oxide in combination with any other class of sedating medications was frequently associated with adverse outcomes (9/10).

Moreover negative outcomes following administration of sedation occurred more commonly in environments in which rescue capability and monitoring standards were not met. Negative outcomes also correlated with drug overdose and drug combinations and interactions. Another negative outcome was administration of a sedative at home.

The majority of events presented with an adverse effect on respiration or oxygenation; however, a large fraction progressed to cardiac arrest, indicating the lack of skills to rescue the patient once a problem developed. These adverse outcomes were clearly preventable, and it was not the drug or route of administration, but rather the practitioner's lack of rescue skills and inadequate recovery.

Discharge criteria

Several critical incidents have been described when children are discharged while sedated and subsequently experience airway obstruction when positioned in a car seat.[18]

In order to clarify how different discharge criteria correlate with a "return to baseline mental status", Malviya [19] recently compared bispectral index score (BIS) with two sedation scales (UMSS and MMWT) in assessing children after sedation for echocardiographic examination. The authors found that when specific criteria were put in place there was a much higher percentage of patients who were back to their baseline consciousness (BIS >90) at the time of discharge when compared with traditional subjective assessment.

Conclusions

The progression from mild sedation to general anesthesia is not easily divided into discrete stages. The ASA consider sedation part of a continuum. This continuum is not drug specific, as various states, from mild sedation to general anesthesia can essentially be achieved with all sedative agents.

The most important goal of pediatric sedation is safety. As children are particularly vulnerable to the adverse effects of sedation and anesthesia,[18] the anaesthetist must have both the experience and equipment necessary to deal with sedated patient. In the deep sedation, and more in general anesthesia, the ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway and spontaneous ventilation may be inadequate. The role of the anaesthetist is critical for the patient's security.

In Europe the FEAPA [20] reports the need for the anaesthesiologist working with children to offer adequate, up-to-date training and continuous practical experience for this specific kind of patient.

The MRI environment creates challenges for the anaesthesiologist who work there. However, proper training and knowledge will ensure the safety of patients.

Silbert *et al.*[21] and Auroy *et al.*[22] have shown that greater experience reduces the risk of anaesthetic complications. Hoffmann *et al.*,[23] in an important analysis, assessed risk reduction in pediatric procedural sedation by application of the AAP/ASA guidelines. In that recent review, 960 patients were studied and the overall complication rate was found to be 4.2%. Those authors concluded that the AAP/ASA guidelines could reduce the risk for adverse events with pediatric procedural sedation.

Finally, discharge criteria for children who have been sedated should advance along with the drugs and techniques used for sedation during a procedure. The application of specific criteria in this realm is a significant improvement over subjective measures that have been used in the past.

Riassunto

L'anestesdia e la risonanza magnetica nucleare nei pazienti pediatrici

L'ambiente per RMI presenta, per l'anestesista dei rischi specifici. Numerosi sono i fattori che determinano tali rischi, in particolare la situazione logistica di lontananza dal paziente, la tecnologia unica dello scanner d'immagini, i fattori legati al paziente. E' sicuramente indispensabile adottare un approccio rigoroso, simile a quello utilizzato per l'esecuzione di anestesia nella sala operatoria (ad esempio, un periodo di digiuno adeguato, la raccolta di anamnesi familiare, precedenti esecuzioni di sedazione). La conoscenza delle implicazioni dell'ambiente di risonanza magnetica potrà, più facilmente, garantire la sicurezza del paziente. Una macchina d'anestesia di adeguate prestazioni, un monitoraggio standard (ECG, pulsossimetro e pressione arteriosa non-invasiva), la presenza di personale istruito e formato e una opportuna pianificazione delle procedure devono costituire lo standard per l'esecuzione di tutte le procedure al di fuori della sala operatoria. E' inoltre raccomandata l'adozione di rigorosi criteri di dimissione al fine di rilevare un'eventuale sedazione residua.

Parole chiave: Risonanza magnetica - Sedazione - Anestesia generale - Età pediatrica - Criteri di dimissione - Linee guida per il digiuno.

References

1. Osborne IP. Magnetic resonance imaging: new challenge and techniques. Curr Opin Anaesth 2002;15: 443-8.

2. Agnes NG. Sevoflurane sedation in infants-a fine line between sedation and general anesthesia. Pediatr Anesth 2005;15:1-2.
3. Smellman B. Pediatric sedation: can it be safely performed by non-anesthesiologists? Curr Opin Anaesth 2002;15:455-9.
4. American Academy of Pediatrics, Committee on Drugs. Guidelines for the elective use of conscious sedation, deep sedation and general anesthesia in pediatric patients. Pediatrics 1985;76:669-71.
5. ASA Task Force on sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96:1004-17.
6. Available at the Commission of Accreditation of Healthcare Organisations. Website: http://www.jcaho.org/, August 30/2003.
7. Committee on Drugs, American Academy of Pediatrics: Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: Addendum. Pediatrics 2002;110:836-8.
8. Levati A. SIAARTI-SARNePI guidelines for sedation in pediatric neuroradiology. Minerva Anesthesiol 2004;70:675-715.
9. Coté CJ. "Conscious sedation": time for this oxymoron to go away! Invited commentary. J Pediatr 2001;139:15-7.
10. Gooden CK. Anesthesia for magnetic resonance imaging. Curr Opin Anaesth 2004;17:339-42.
11. Hasler G. Anesthesia with midazolam and S-(+)-Ketamine in spontaneously breathing pediatric patients during magnetic resonance imaging. Paediatr Anaesth 2000;10:513-9.
12. Malviya SV. Pentobarbital *vs* Chloral Hydrate for sedation of children undergoing MRI: efficacy and recovery characteristics. Paediatr Anaesth 2004;14:589-95.
13. Sury MRJ. Development of a nurse-led sedation service for pediatric magnetic resonance imaging. Lancet 1999;353:1667-71.
14. Usher AG, Kearney RM. Anesthesia for MRI in children: a survey of Canadian pediatric centers. Can J Anaesth 2003;50:425.
15. Usher AG, Kearney RA, Tsui BCH. Propofol intravenous anesthesia for MRI in children. Pediatr Anesth 2005;15:23-8.
16. Sury MRJ, Harker H, Thomas M. Sevoflurane sedation in infants undergoing MRI: a preliminary report. Pediatr Anesth 2005;15:16-22.
17. DeSanctis Briggs V. Magnetic Resonance Imaging under sedation in newborns and infants: a study of 640 cases using sevoflurane. Pediatr Anesth 2005;15:9-15.
18. Coté CJ, Karl HW, Nottermann DA. Adverse sedation events in pediatrics: analysis of medications used for sedation. Pediatrics 2000;106:633-44.
19. Malviya SV. Can we improve the assessment of discharge readiness? A comparative study of observational and objective measures of depth of sedation in children. Anesthesiology 2004;100:218-24.
20. Available at the FEAPA Website: http://free.med.pl/feapa/
21. Silber ICH. Anesthesiologist board certification and patient outcomes. Anesthesiology 2002;96:1004-52.
22. Auroy Y, Ecoffey C, Messiah A. Relationship between complications of pediatric anesthesia and volume of pediatric anesthetics. Anesth Analg 1997;84:234-5.
23. Hoffmann GM. Risk reduction in pediatric procedural sedation by application of an AAP/ASA process model. Pediatrics 2002;109:236-43.

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REVIEW

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 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

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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.

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Disclosures

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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.