Challenges in the anesthetic management of ambulatory patients in the MRI suites

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Purpose of review
MRI is becoming an indispensable diagnostic tool. The need for prolonged motion-free periods has substantially increased the need for deep sedation or anesthesia in a challenging environment. This review summarises recent literature with respect to pharmacological sedative strategies, nonpharmacological alternative approaches, airway management and safety issues in the ambulatory setting.

Recent findings
Most literature researches the pediatric patient population. The American Society of Pediatrics published guidelines for monitoring and management of pediatric patients during sedation for diagnostic procedures. Dexmedetomidine is the most researched agent for sedation. It remains uncertain what the clinical implications are of the potential neurotoxicity of repeat sedation or anesthesia in young children. Airway strategies highlight the use of end-tidal carbon dioxide monitoring. Technical imaging advancement and nonpharmacological sedation alternatives allow for shorter procedures with a lower need for sedation.

Summary
The anesthetic management of ambulatory patients in the MRI environment has its specific challenges and safety issues. However, the implementation of safety guidelines, new pharmacological and alternative nonpharmacological sedation strategies offer interesting perspectives to tackle these challenges.

Keywords
anesthesia, dexmedetomidine, imaging, MRI, sedation

INTRODUCTION

MRI is one of the most important innovations of the last decades. Being noninvasive and radiation-free, MRI is an indispensable diagnostic tool. However, the MRI exam requires long motion-free periods. This is difficult to obtain in certain patient categories such as the anxious, claustrophobic or developmentally delayed adult and more specifically the pediatric patient population. The evolution of interventional procedures and growing sensitivity to pain and anxiety in children have increased the need for deep sedation or anesthesia outside the operating room. The specific nontraditional environment of the MRI suite poses certain challenges for the anesthetic management.

This article reviews recent literature concerning the anesthetic management of ambulatory patients in the MRI suite. Almost all publications focus on the pediatric patient and articles on adult patients are scarce. It highlights the literature on patient safety and sedation guidelines, airway management, pharmacological advances and nonpharmacological sedation alternatives.

PHARMACOLOGICAL ADVANCES

Over the past decade, the need for sedation outside of the operating room setting has increased significantly [1]. Sedation for MRI is challenging; one has to prevent patient's movements and to maintain hemodynamic and respiratory stability whereas MRI suite conditions, equipment and device features and the possible side-effects of the anesthetic agents increase patient risks [2].

Selection of appropriate drugs and dosage is therefore essential. For a long time, clinicians have been seeking agents that provide rapid onset of induction and recovery with low side-effects and minimally invasive routes of administration.

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KEY POINTS

- Dexmedetomidine, a selective alpha-two agonist, is shaping up as a strong adjunct for sedation in the MRI environment.
- The controversial potential neurotoxicity of repeat sedation and anesthesia in young children might increase interest in nonpharmacological sedation alternatives.
- The American Society of Pediatrics published guidelines for monitoring and management of sedation in pediatric patients for diagnostic procedures.
- End-tidal carbon dioxide monitoring should be used for deeply sedated patients because of the increased risk of airway compromise.

Historically common classes of agents for imaging procedures have been benzodiazepines, opioid analgesics, intravenous anesthetics (propofol, ketamine), inhalational anesthetics (e.g. sevoflurane), barbiturates (mainly pentobarbital) and hypnotics (e.g. chloral hydrate) [3].

Most recent publications focus on the use of dexmedetomidine (Dex) that is shaping up as a valuable adjunct for multiple indications within pediatric anesthesia [4▪▪].

Dexmedetomidine

Dexmedetomidine, a selective alpha 2 adrenoceptor agonist, is a relatively recently used drug with sedative, anxiolytic, sympatholytic and analgesic properties [4▪▪]. It is painless, odorless, tasteless and may be administered by oral, buccal, nasal, rectal, subcutaneous, intramuscular and intravenous routes [2,4▪▪]. It has raised great interest because of its sedative property and very well tolerated therapeutic window with respect to respiratory depression. [1] It is currently approved by the US Food and Drug Administration (FDA) for only to be used in adults [5] but is increasingly used off-label inside and outside Europe in the pediatric setting for a variety of indications and seems very well suited for painless procedures that require a motionless patient [4▪▪]. Sulton *et al*. documented pediatric procedural sedation with Dex in the USA ($n = 13.072$). They reported a very high success rate (99.7%) and quantified adverse event rates (3.6%) with airway obstruction as the most frequent one (0.27%) [5]. Another publication investigated the efficacy and safety of a high dose of Dex (2 μg/kg i.v., followed by 1/μg/kg/h i.v. infusion) as a sole sedative agent in 544 children undergoing MRI [1]. Dex was effective in 78.5% of cases, and in 21.5%, additional medication was needed. Bradycardia can be encountered with Dex, especially in young children [1,6]. The use of a prophylactic anticholinergic (atropine or glycopyrrolate) prior to Dex to prevent bradycardia in pediatric imaging was recently investigated but other than a transient insignificant increase in heart rate and blood pressure, no advantage was demonstrated [6].

Recovery and discharge times are important in the outpatient MRI setting. A recent meta-analysis compared the clinical efficacy of propofol that is by many considered as the gold standard sedative agent versus Dex in children undergoing MRI and reported similar duration of sedation but increased recovery times with Dex [7]. Two studies reported discharge times of 92 and 79–101 min, respectively [1,8] after high doses of Dex (2 μg/kg i.v. over 10 min followed by a continuous i.v. of 1–1.5 μg/kg/h) that are longer than previously reported. However, this does not diminish its usefulness and it appears to be a good alternative for intravenous sedation in children with propofol, especially because of the lower incidence of adverse effects [1,7]. Loh *et al.* [9] investigated the efficacy of sedation with Dex compared with Propofol in 30 claustrophobic adults undergoing MRI. They reported both agents effectively reduce anxiety levels but Dex took longer to induce to anxiolysis and sleep with more frequent hemodynamic changes and possible lower image quality.

Administration of Dex before emerging from inhalation anesthesia for MRI does not reduce the incidence or severity of emergency delirium [10].

Dex can be administered to children through the nasal route where it is rapidly absorbed through vascular membranes [2]. The popularity of this route increases because of the ease of administration, the effectiveness and possibility to apply further rescue doses [4▪▪]. One prospective study compared two different intranasal doses (3 and 4 μg/kg) of Dex in 60 children, aged 1–10 years for MRI sedation and reported comparable results for onset and duration of sedation and recovery time. However, 4 μg/kg of intranasal Dex was found to be more efficient, required less rescue doses, resulted in better parental separation mood and had lower BIS values [2]. Zhang *et al.* [11] reported the ED50 of intranasal Dex as rescue sedation in children undergoing MRI increases with age during the first 3 years of life, from 0.4 μg/kg in children aged 1–6 months to 1.0 μg/kg in children aged 25–36 months.

Chloral hydrate

Chloral hydrate is a nonopiate, nonbenzodiazepine drug that is known to induce sleep with no major hemodynamic or respiratory effects whenever

administered orally in doses of 50–75 mg/kg [12]. However, it has been associated with side-effects as prolonged sedation, paradoxical excitement, delirium, airway obstruction, respiratory depression and has an unpleasant bitter taste [12]. Delgado *et al.* retrospectively evaluated the use, effectiveness and safety of chloral hydrate administered by radiologists for the sedation of children ($n = 1703$) who require MRI procedures [13]. Moderate-to-deep sedation was achieved in 95% of the patients. A single oral dose of 40–60 mg/kg was administered in 86.7% of the patients, whereas 13.3% required an additional dose of 10–20 mg/kg. The authors also reported that the highest failure rate was noticed in the neonates group. In the same age group, intranasal Dex was studied as rescue medication in 150 infants (1–6 months) who were not adequately sedated for MRI after an initial oral dose of 50 mg/kg of chloral hydrate in a prospective, double-blind, randomized controlled trial [12]. Intranasal Dex was administered in a dosage of 1 or 2 μg/kg. Fifty infants received a second oral dose of chloral hydrate (25 mg/kg). The authors concluded that intranasal Dex induced satisfactory rescue sedation and appeared to cause sedation in a dose-dependent manner.

Propofol

Propofol seems to be an ideal agent with a rapid onset and short duration of action, although a wide therapeutic range in some groups of children has been described [14]. Additionally, it has been associated with side-effects such as hypotension, respiratory depression and apnea.

One recent publication investigated whether children ($n = 258$) with attention-deficit hyperactivity disorder (ADHD) required larger doses of propofol for MRI sedation. The average sedative dose for all patients was 2.8 mg/kg (95% CI 2.62–2.94) and the authors concluded that children with ADHD do not have higher sedative requirements [14].

ALTERNATIVE NON-PHARMALOGICAL SEDATION TECHNIQUES

A multitude of nonpharmacological interventions such as simulation and play preparation, video and audio technologies have been developed and used with success in the past. In children younger than 6 months, strategies whereby natural sleep is induced after feeding and swaddling are generally sufficient to obtain diagnostic images [15]. In children between 1 and 6 years, sedation is often needed due to lack of cooperation [16]. Törnqvist *et al.* [17], however, examined if children aged 3–9 years could undergo a MRI awake if age-adjusted routines were used. These included a booklet and story book, a model of the MRI scanner with MRI sound and a DVD film during the exam. A majority of the children ($n = 30/33$) had their exam awake with adequate image quality. Another study in 79 children (4–10 years) evaluated the effectiveness of play therapy on the need for sedation intervention [18]. The interventions involved a MRI model, listing the steps of the scan, training the child to stand still and conducting dry runs with a doll or toy. The relative risk of sedation decreased by 49% compared with a control group ($P = 0.04$). Nordahl *et al.* [19] conducted a study in which children (9–13 years) with autism spectrum disorder and intellectual impairment underwent a MRI without the need for sedation. Behavioural strategies, visual support material and a mock MRI were used to aide in a breakdown process. All the 17 children were able to lie still and to complete a MRI sequence.

One could argue that such strategies are usually unnecessary, time-consuming and require a lot of resources. On the other hand, general anaesthesia can increase the cost of a MRI scan up to 33% [16].

SAFETY

The recent FDA safety warning about possible neurotoxicity of sedation drugs in children [20,21▪], the updated 2016 guidelines for monitoring and management of sedation in pediatric patients for diagnostic procedures by the American Academy of Pediatrics [22▪▪] and the specific safety issues of MRI such as the strong electromagnetic field, are challenging issues for everyone involved in sedating or anesthetising patients for MRI.

Safety of anesthetic agents

In December 2016, the FDA issued a 'Drug Safety Communication' (www.fda.gov/Drugs/ DrugSafety/ ucm532356.htm) that stated that the repeated or prolonged (more than 3 h) use of sedation drugs and general anesthesia in children less than 3 years old could 'affect the development of children's brains'. Experimental studies have shown that a variety of anesthetics including all anesthetic gases and the intravenous agents propofol, barbiturates, benzodiazepines and ketamine may cause neurodegeneration in the developing brain. However, the clinical extent to which these findings in rodents and primates can be generalized to the pediatric population remains unclear and studies have shown controversial results [20,21▪]. A consensus statement of the European Society of Anaesthesiology, the European Society for Paediatric Anaesthesiology and the

European Association of Cardiothoracic Anaesthesiology stated that the evidence to support the FDA warning is currently insufficient and incomplete and therefore it is not shared by the listed European Societies [21▪].

Specific safety issues

An extensive review by Tocchio *et al.* [23] concludes that MRI scanning with the latest more powerful devices does not harm the fetus or young children whenever operated within FDA regulations. As the energy that is absorbed by the body can cause tissue heating, MRI machines stop whenever the maximum amount of energy is reached. The FDA regulations state that maximal sound level for adults is 140 dB. Although there are no specific guidelines, passive hearing protection should be used in all children.

Prompted by two cases of hypothermia in infants, Dalal *et al.* [24] measured the temperature of 164 infants undergoing an MRI. They found that younger children and especially those admitted to a neonatal intensive care unit, were at greater risk of developing hypothermia. Propofol sedation was also associated with hypothermia, probably to its vasodilatory properties. The authors implemented a new temperature protocol using a vacuum mattress to immobilize the infant, thereby reducing the need for sedation. Whenever general anaesthesia was necessary, active warming measures were taken. After the implementation of this protocol, no more children were hypothermic.

The use of gadolinium-based contrast agents (GBCA) can enhance tissue contrast, but has possible side-effects. Nephrogenic systemic fibrosis is a rare toxic reaction to GBCA in patients with kidney insufficiency and therefore dose reduction in kidney insufficiency is primordial [25]. Acute allergic reactions are rare (0.1%) with 7–20% considered severe.

Safety guidelines for (deep) procedural sedation and anesthesia

In 2016 the American Academy of Pediatrics and Pediatric Dentistry published guidelines for monitoring and management of pediatric patients before, during and after sedation for diagnostic and therapeutic procedures [22▪▪]. The article offers a systematic approach that intends to improve safety and outcomes of the deep sedation or general anesthesia that are usually required for a MRI and which are both associated with serious risks.

The above-said approach includes:

(1) No sedation without appropriate medical supervision.
(2) A thorough presedation evaluation for underlying conditions.
(3) Special attention for the evaluation of the airway for potential causes of airway obstruction.
(4) That every patient has to be fasted according to the fasting guidelines (for elective procedures).
(5) The presence of the necessary equipment for airway management and staff properly trained and skilled in airway management.
(6) Staff should be sufficient to carry out the procedure and to monitor the patient. The contribution and function of each sedation provider are important. [26]
(7) The presence of all appropriate medication and a clear understanding about its effects and interactions by the staff.
(8) Proper MRI compatible monitoring including oxygen saturation, ECG and end-tidal carbon dioxide monitoring.
(9) A properly equipped and staffed recovery area.
(10) Appropriate discharge instructions.
(11) Proper documentation before, during and after the procedure and continuous quality improvement with maintaining records of adverse events.

Grunwell *et al.* [27] researched the effect of the implementation of a pediatric procedural sedation guide for referral to general anesthesia for MRI studies. Following implementation of the guide, they reported a significant increase in referrals to general anesthesia ($P < 0.001$) and no decrease in serious adverse events ($P = 0.874$). The authors offer several possible reasons for these results and suggest that future work should focus on designing a multicenter study.

AIRWAY

Deep sedation or general anaesthesia can cause loss of protective airway reflexes and lead to obstructive respiratory events. Thorough screening before the procedure and intra-operative monitoring are essential [22▪▪]. Capnography and end-tidal carbon dioxide monitoring are fast becoming indispensable in the dark MRI suite, as they can detect airway obstruction before hypoxia ensues [28▪]. Head repositioning, jaw-thrust, chin-lift and neck extension can solve most airway obstructions and all sedation providers should be familiar with these basic techniques [22▪▪]. Airway devices may have a deleterious effect on the image quality. Ucisik-Keser *et al.* [29] evaluated the relationship between the use of an airway device and MRI image quality and concluded that supraglottic airway (SGA) devices were superior

to no airway devices. There was no interference of the SGA on the MRI scan whenever the pilot balloon was taped outside of the MRI plane. A study by Moustafa *et al.* [30] investigated the effect of a soft neck collar on upper airway size in sedated children during MRI and reported the collar could maintain a forward position of the mandible and neck extension without discomfort or requiring deep sedation. MRI imaging showed that the collar increased the cross-sectional area of the airway at the level of the soft palate and tongue, but decreased it at the level of the epiglottis [30]. Bosemani *et al.* [31] evaluated the patency of upper airway and associated risk factors in spontaneously breathing neonates and infants undergoing a head MRI and reported that a significant proportion of the study participants showed airway obstruction. Most at risk were children with a history of hypoxic ischemic encephalopathy. They have smaller than normal airway diameters whenever breathing spontaneously, which decreases further during sedation [31]. Hypoxic events can occur after the examination, especially in children with obstructive sleep apnoea (OSA). Trost *et al.* [32] investigated whether it is necessary to hospitalise children ($n = 96$) with OSA in presence of a comorbidity after MRI under sedation. Ten patients developed overnight obstructive respiratory events that were solved by adjusting noninvasive ventilation. The authors suggest that targeting high-risk patients may avoid unnecessary hospitalizations.

CONCLUSION

The anesthetic management of ambulatory patients in the MRI environment carries specific challenges and safety issues. However, the implementation of the 2016 pediatric safety guidelines for monitoring and management of pediatric patients during sedation diagnostic procedures, new pharmacological agents as dexmedetomidine, the development of alternative nonpharmacological sedation strategies, end-tidal carbon dioxide monitoring and technological MRI improvements, offer interesting perspectives to tackle these challenges.

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Conflicts of interest

There are no conflicts of interest.

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