Pediatr Drugs (2015) 17:385–399
DOI 10.1007/s40272-015-0140-6

REVIEW ARTICLE

# Options and Considerations for Procedural Sedation in Pediatric Imaging

**John W. Berkenbosch**[1]

Published online: 9 July 2015


**Abstract** As pediatric imaging capabilities have increased in scope, so have the complexities of providing procedural sedation in this environment. While efforts by many organizations have dramatically increased the safety of pediatric procedural sedation in general, radiology sedation creates several special challenges for the sedation provider. These challenges require implementation of additional safeguards to promote safety during sedation while maintaining effective and efficient care. Multiple agent options are available, and decisions regarding which agent(s) to use should be determined by both patient needs (i.e., developmental capacities, underlying health status, and previous experiences) and procedural needs (i.e., duration, need for immobility, and invasiveness). Increasingly, combinations of agents to either achieve the conditions required or mitigate/counterbalance adverse effects of single agents are being utilized with success. To continue to provide effective imaging sedation, it is incumbent on sedation providers to maintain familiarity with continuing evolutions within radiology environments, as well as comfort and competence with multiple sedation agents/regimens. This review discusses the challenges associated with radiology sedation and outlines various available agent options and combinations, with the intent of facilitating appropriate matching of agent(s) with patient and procedural needs.

**Key Points**

Sedation within the radiology environment creates several unique conditions, which mandate additional preparation on the part of the sedation provider.

Efficient and effective radiology sedation requires careful consideration of patient and procedural needs.

While multiple agent options exist with which to provide radiology sedation, optimal regimens should attempt to match the pharmacokinetic and pharmacodynamic properties of the regimen with procedural needs and characteristics.

## 1 Introduction

The capabilities of pediatric imaging technology continue to expand. Significant examples include three-dimensional tomography, functional magnetic resonance imaging (MRI), and interventional radiology applications [1–3]. Consequently, requests for radiology procedural sedation continue to increase, accounting for 60 % of sedations reported to the Pediatric Sedation Research Consortium [4]. As such, pediatric sedation providers must maintain familiarity with radiology advances so they can, if necessary, adapt practices to continue to safely and effectively facilitate procedure completion.

This review focuses on the unique needs of radiology imaging sedation and their implications for the sedation provider, particularly the pharmacologic considerations relevant to regimen choices, and the options available.

✉ John W. Berkenbosch
john.berkenbosch@louisville.edu

[1] Division of Pediatric Critical Care, Department of Pediatrics, University of Louisville, Kosair Children's Hospital, 571 S. Floyd, Ste 332, Louisville, KY 40202, USA

Despite wide variability in sedation team composition and agent availability, the principles discussed below should apply to all sedation providers, regardless of the specialty or agents utilized.

## 2 Unique Aspects of Radiology Sedation

Several aspects of radiology sedation make this a particularly unique environment. Procedure coordination is more complex than in many other scenarios in that more providers (sedationists, radiologists, technologists) and devices must be brought together simultaneously. Despite the logistic challenges associated with this, institutions continue to demand efficient patient throughput. Consequently, efficient radiology sedation requires sophisticated scheduling processes, including robust screening procedures to accurately identify which patients require sedation, general anesthesia, or neither. This process requires staff knowledgeable about both sedation and radiology needs.

Because of room logistics and the number of providers present, access to the patient may be more challenging in radiology settings. While emphasis on family-centered care continues to grow, these limitations may impact the ability of parents to remain present, which may increase both parent and child anxiety [5].

More than with other procedures, radiology sedations often require patients to travel to or from non-radiology locations, such as sedation units, recovery rooms, or post-anesthesia care units. For studies to be performed on equipment centralized within hospital systems, these transport distances may be substantial. This impacts decisions regarding where sedation is to be induced (in a sedation unit versus a procedure room) and when travel is to occur (after sedation induction or after procedure completion). This choice is not trivial, as these two periods are associated with the greatest adverse event risk [6] and therefore represent periods when caregivers must be especially vigilant despite increased distractions.

While many radiology procedures require absolute motionlessness, it should be noted that this is not universal (i.e., many ultrasound or fluoroscopy procedures). In such instances, lighter, and likely safer, sedation may be sufficient. As such, pre-procedure confirmation of motion tolerance should be a routine part of planning. On the other hand, certain procedures require special motion circumstances, such as breath holds (i.e., high-resolution thoracic computed tomography [CT]) and mandate use of general anesthesia to reliably and safely facilitate controlled apnea.

The need for intravenous (IV) contrast may additionally impact decisions regarding sedation, particularly the depth desired. While there are no known consensus guidelines, common practice is to avoid IV contrast administration for 24 h following previous administration. Consequently, if IV contrast is required, deeper sedation may be chosen to decrease the risk of procedure failure and resultant therapeutic delays.

Published guidelines from several societies, including the American Society of Anesthesiologists (ASA) [7] and American Academy of Pediatrics (AAP) [8], are clear regarding the recommended duration of nil per os (NPO) status prior to sedation (Table 1). However, these recommendations create conflict for the patient requiring oral contrast (i.e., an abdominal CT scan), as optimal visualization of the stomach and small bowel requires contrast administration 15 min to 1 h prior to scanning [9]. As a compromise, many institutions have implemented protocols in which contrast is initiated at 2 h and completed 1 h prior to sedation. While limited, reports to date suggest that images remain adequate and sedation is tolerated [10].

As alluded to above, physical access to the patient may be limited in radiology, especially for MRI and some nuclear medicine studies. This may increase the difficulty with which intra-procedure complications, particularly apnea or airway obstruction, may be identified, so the provider becomes especially dependent on the available monitoring devices. Several published guidelines exist regarding monitoring during sedation (Table 2) [7, 8, 11]. Electrocardiographic (ECG) monitoring in MRI may be challenging because of magnetic field distortion of the ECG waveform and, while lead packs designed for MRI exist, many programs opt to monitor the heart rate via pulse oximetry. In our experience, interference from the MRI magnet at times causes alterations in the oximeter waveform that result in display of an inaccurate heart rate. Consequently, if the oximeter is used to monitor the heart rate, intermittent verification of the displayed rate by manually counting the oximeter waveform should be performed. To fully assess adequacy of respiratory effort and airway patency, routine use of end-tidal $CO_2$ ($ETCO_2$) monitoring during all sedated MRI studies is also recommended. In light of the limitations noted above, it is disturbing that adherence to recommended monitoring guidelines appears to be limited. In a review of almost 115,000 sedations, only 52 % of encounters met the minimal ASA/AAP monitoring guidelines [12].

**Table 1** American Society of Anesthesiologists (ASA) recommendations for pre-sedation fasting times [7]

| Type of food | Minimum fasting time (h) |
|---|---|
| Clear liquids | 2 |
| Breast milk | 4 |
| Infant formula/non-human milk | 6 |
| Light meal (i.e., toast and clear liquids) | 6 |
| Full meal (especially fried/fatty foods) | 8 |

**Table 2** Guidelines for monitoring during procedural sedation

| Organization | $SpO_2$ | Respiratory rate | Heart rate | Blood pressure | $ETCO_2$ |
|---|---|---|---|---|---|
| AAP | Continuous | Intermittent | Continuous | Intermittent | Encouraged |
| ASA | Continuous | Continuous | Continuous | Intermittent | Consider |

*AAP* American Academy of Pediatrics, *ASA* American Society of Anesthesiology, *$ETCO_2$* end-tidal $CO_2$, *$SpO_2$* oxygen saturation

## 3 Components of Successful Sedation

The key components of safe and successful sedation have been defined by many professional organizations [7, 8, 11, 13]. A summary of these components follows; the reader should refer to the original guidelines for further detail. While some differences exist between guidelines, adherence to the themes they articulate has been shown to decrease sedation-related adverse events [14, 15].

### 3.1 Definitions

Sedation occurs along a continuum, which has been typically divided into four categories, primarily based on the degree of responsiveness and/or the potential risk for airway protective reflex loss [7]:

- Minimal sedation (anxiolysis): a state in which the patient remains awake but calm and is normally responsive to verbal stimulation. Cardiorespiratory function should not be altered.
- Moderate "conscious" sedation: a state in which patients are sleepy but purposefully respond to verbal commands and/or light tactile stimuli. Cardiorespiratory function and airway patency should be spontaneously retained.
- Deep sedation: a state of controlled unconsciousness. Patients cannot be easily aroused and only respond purposefully to repeated painful stimuli. Airway patency and ventilatory or cardiovascular function may be impaired. Artificial airway support may be required.
- General anesthesia: a state of controlled unconsciousness in which there is complete loss of purposeful response to physical or verbal stimuli. Adequate respiratory drive, airway patency, and protective reflexes are often lost, requiring artificial support. Cardiovascular function may be impaired.

### 3.2 Qualifications

Sedation provision involves a variety of practitioners, including registered nurses, advance practice providers, non-anesthesiologist physicians, and anesthesiologists. Scope of practice and agent access are determined by local licensing boards and individual institutions.

Regardless of restrictions, all sedation providers should possess certain skills. Providers must be adept at identifying the depth of sedation achieved and be prepared to rescue from one level deeper than intended. Providers must be able to rapidly identify loss of airway patency/ventilatory function and be skilled at providing artificial respiratory support. Providers should be intimately familiar with the pharmacology of the sedative/analgesic agents they administer, including doses, routes of administration, expected adverse events, and potential drug interactions. They must maintain knowledge of and have access to available antagonists, and they must maintain competency to intervene should any adverse event occur [7, 8].

### 3.3 Pre-sedation Assessment

All patients require a pre-sedation assessment, the primary purpose of which is to determine his/her fitness for sedation. Key components include a focused review of the child's current health status, chronic illnesses, and medication history to determine potential drug interactions. As the majority of sedation-related adverse events are respiratory [4], particular attention is paid to airway and respiratory status. Physical examination should include a complete upper airway assessment to evaluate for risks of airway obstruction and potential intubation difficulty, which may be predicted by documenting a modified Mallampati score in patients old enough and/or developmentally capable of spontaneously opening their mouth to allow pharyngeal structure assessment [16]. A score of 3 or 4 has been correlated with intubation difficulty. In such patients, the lightest depth of sedation possible should be aimed for to minimize intra-procedure airway obstruction or loss of patency. Alternatively, as discussed below, while absolute criteria do not exist, referral to anesthesiology may also be considered. The patient's NPO status should be confirmed. Previous sedation/anesthesia encounters should be discussed to identify previous complications, adverse reactions to particular agents, or sources of anxiety that need to be further addressed.

This assessment should also help guide the development of an individualized sedation plan which includes the agent(s) to be used, consideration of additional personnel or equipment requirements, transport requirements, and the need for pre-medication. Agent choice is further discussed below.

### 3.4 Monitoring and Equipment

Recommendations for monitoring have been alluded to above [7, 8, 11, 13] and are outlined in Table 2. The heart rate, respiratory rate, and oxygen saturation ($SpO_2$) should all be monitored continuously. While heart rate monitoring via ECG is preferred, monitoring via pulse oximetry may be appropriate, assuming a reliable waveform. The respiratory rate may be monitored via impedence plethysmography via the ECG leads although capnography provides additional information and is increasingly encouraged. These vital signs, as well as the blood pressure, should be documented intermittently during the procedure, with the AAP recommending a frequency of at least every 5 min during deep sedation [8]. Documentation should also continue until abnormal vital signs have resolved.

Adapted from the ASA guidelines [7], Table 3 lists the minimum equipment that should be present and immediately available from induction through recovery. For a condensed list, the acronym SOAPME (suction, oxygen, airway, pharmacy, monitors, equipment) may be used [8]. Since some equipment and/or medications are not routinely present in radiology departments, arrangements such as having an anesthesia/sedation cart or a portable equipment bag housed in radiology that can be brought to specific sedation locations may be necessary.

### 3.5 Sedation Candidates

Because of developmental, technical, and patient health–related issues, determining which child needs sedation may not be immediately intuitive. In general, most otherwise healthy children over 6–8 years of age can cooperate for non-invasive studies (i.e., ultrasound, CT scans, shorter MRI scans) without sedation. This age may decrease further for very brief studies. Most infants under 3–4 months of age can also successfully complete non-invasive scans if allowed to feed and fall asleep just prior to the study. Infant immobilizers [17] or distraction techniques, including child life therapists, audiovisual projections, and music therapy [18, 19], can further decrease the need for sedation in patients otherwise considered borderline for cooperation. Identifying these patients is important, as avoiding sedation removes sedation-related risk.

Despite non-pharmacologic adjuncts, certain populations require sedation for almost all radiology procedures. Significant underlying pain may prevent a child from remaining still. While in the older child, appropriate analgesia ± distraction may suffice, in younger, developmentally delayed/behavior-disordered children, or particularly anxious patients, additional sedation (often deep) will be required.

Lastly, certain children are poor sedation candidates and should be either referred for general anesthesia or have their procedures deferred, if non-emergent, until acute health issues resolve. While no specific guidelines exist, examples of high-risk populations in which anesthesia referral should be considered include those with a history of baseline airway obstruction or central apnea disorder (as most sedatives further impair pharyngeal muscle tone [20, 21] or respiratory drive), active upper respiratory infection, an ASA classification score of 3 or higher, obesity, and cyanotic/unrepaired congenital heart disease [4, 22–24].

**Table 3** Recommended emergency equipment/medications

| Airway | Medications |
|---|---|
| Suction apparatus and catheters | Oxygen |
| Oral/nasal airways | Albuterol |
| Oxygen delivery devices (nasal cannula, facemask) | Atropine/glycopyrrolate |
| Bag–valve–mask system (self-inflating or anesthesia type) | Calcium chloride/gluconate |
| Laryngoscope handles/blades | Dextrose 10 %/50 % |
| Endotracheal tubes and stylets | Diphenhydramine |
| IV access supplies, including catheters, tourniquets, tape, arm boards | Epinephrine |
| | Flumazenil |
| Intraosseous needle | Methylprednisolone |
| IV fluid tubing, T-connectors, 3-way stopcocks | Naloxone |
| | Racemic epinephrine |
| | Sodium bicarbonate |
| | Neuromuscular blocker (succinylcholine/rocuronium) |

Use of appropriate pediatric sizes of all equipment is implied in the above

*IV* intravenous

## 4 Pharmacologic Options

### 4.1 Considerations in Regimen Determination

Once the need and appropriateness for sedation have been established, an appropriate regimen must be chosen. The ideal regimen would possess the following desirable characteristics: (1) rapid onset of action, (2) predictable duration, (3) easy titratability, (4) rapid cessation of effects, (5) multiple delivery options, (6) wide therapeutic window, (7) minimal cardiorespiratory effects/interactions, (8) minimal drug interactions, and (9) minimally affected by renal or hepatic disease. As such an agent/regimen does not exist, decisions regarding agent(s) to be used will be influenced by these primary factors:

1. Degree of cooperation/immobility required: whereas moderate sedation will often suffice if movement tolerance exists, studies requiring complete immobility (i.e., PET scanning, MRI) usually require deep sedation.
2. Procedure duration: ideally, the pharmacokinetic properties of the agent(s) used would match the expected procedure duration. For longer procedures, either bolus-only use of longer-acting agents or bolus + infusion use of short-acting agents is appropriate. For brief procedures, bolus use of short-acting agents is optimal. However, if agent restrictions exist, longer-acting agents than desired may be necessary, which may have implications for efficiency of patient flow [25].
3. Invasiveness of the procedure: this will determine if analgesia is required in addition to sedation.
4. Previous sedation experiences: this will help determine if previous reactions, such as allergy or an adverse/paradoxical reaction, preclude use of any agents.

As many radiology procedures do not otherwise require IV access, the route of administration is another consideration. Non-parenteral routes (intranasal [IN], intramuscular [IM], oral, rectal, or buccal) may be appropriate, since obtaining IV access may be viewed as being more distressful than the procedure itself. However, this choice must be balanced against the risk of adverse events, which may require IV access for resuscitative interventions, and the increased variability of onset and recovery times associated with non-parenteral administration, which may impact sedation success and efficiency. As improved topical anesthetics to facilitate IV starts have made this procedure less distressing, our practice is to routinely require IV access in all patients undergoing sedation.

A summary of the available sedative, analgesic, anesthetic, and reversal agents; doses; and applications can be found in Table 4.

### 4.2 Sedative Agents

#### *4.2.1 Barbiturates*

Barbiturates have a long history of use for radiology sedation. They provide potent sedation but no analgesia. Sedation is achieved via $GABA_A$ receptor agonism–induced inhibition of post-synaptic neuronal chloride conduction in the reticular activating system. Sodium pentobarbital and methohexital are currently the most commonly administered barbiturates for procedural sedation.

Sodium pentobarbital (Nembutal®) is a medium-duration barbiturate still widely used for radiology sedation. It is attractive because non-parenteral administration routes, primarily oral, exist in addition to IV. Following IV administration, the onset of action begins as quickly as 2–3 min, with peak effects seen in 10–15 min. Despite an elimination half-life of 20 h, the clinical duration of sedation is 45–60 min owing to rapid redistribution [26]. This makes pentobarbital most viable for MRI and nuclear medicine studies [27, 28]. While its use for CT sedation has been reported [28, 29], the discrepancy between its action and procedure durations make this application less appealing.

Initial induction doses are 1–2 mg/kg, with repeat 0.5–1 mg/kg doses administered every 3–5 min until sleep is achieved. The average dose required to achieve deep sedation is 3.5–5 mg/kg [27–30]. Reported sedation success rates are high (91–99 %) [28].

Oral pentobarbital has high bioavailability (>95 %). It is most commonly administered using the IV formulation alone or in a syrup to improve palatability. This route has been predominantly described in the infant/toddler population for radiologic procedures [27, 32]. To decrease the onset time, oral dosing is higher than IV dosing, starting at 4–5 mg/kg, with successive 2–2.5 mg/kg doses administered every 30 min as needed [27, 32]. The onset of sedation is 20–30 min and lasts 60–90 min. Reported success rates are 95–99 % [32, 33], with toddlers being more likely than infants to require repeat doses [33]. The overall sedation duration (time from administration to discharge) is longer than with IV pentobarbital, but adverse events are uncommon, <1 % for both respiratory and behavioral issues [26, 27, 32].

The most common side effects with IV use are respiratory and behavioral. Apnea is rare, the highest risk being with infant use and rapid IV administration. Mild hypoxemia or upper airway obstruction occur in roughly 5 % of patients [26, 27]. As early studies did not report capnography use, the incidence of hypopnea is unknown. Paradoxical and/or recovery-related agitation occurs in up to

**Table 4** Summary of procedural sedation, analgesia, anesthetic, and reversal agents; doses; and properties

| Agent | Route | Dose | Onset (min) | Duration (min) | Applications/comments |
|---|---|---|---|---|---|
| Sedative agents | | | | | |
| Barbiturates | | | | | |
| Pentobarbital | IV | 1–2 mg/kg initial | 3–5 | 45–60 | Medium to longer non-invasive |
| | | 0.5–1 mg/kg subsequent | | | |
| | PO | 4–5 mg/kg initial | 20–30 | 60–90 | Medium to longer non-invasive |
| | | 2–2.5 mg/kg subsequent | | | |
| Methohexital | IV | 1 mg/kg initial | 2–5 | 10–20 | Short non-invasive |
| | | 0.5–1 mg/kg subsequent | | | |
| | PR | 20–30 mg/kg initial | 10 | 30–40 | Short to medium non-invasive |
| | | 15–20 mg/kg subsequent | | | |
| Benzodiazepines | | | | | |
| Midazolam | IV | 0.05–0.1 mg/kg (maximum 4 mg per dose) | 2–5 | 30–45 | Anxiolysis for non-invasive |
| | | | | | Add analgesic for painful/invasive |
| | PO | 0.5–0.7 mg/kg | 15–20 | Up to 60 | Adjunct/pre-medication for deeper regimens |
| | IN | 0.2–0.4 mg/kg | 5–10 | 30–45 | Adjunct/pre-medication for deeper regimens |
| Chloral hydrate | PO/PR | 50–70 mg/kg initial | 20–40 | 60–120+ | Longer non-invasive |
| | | Repeat 50 % of initial (maximum 105 mg/kg or 2 g) | | | Reliability decreased in autism, age >48 months |
| Dexmedetomidine | IV | Induction 1–3 μg/kg | 10–15 | 30–45 | Sole agent for medium to longer non-invasive |
| | | Infusion 1–2 μg/kg/hour | | | Combine with ketamine for painful/invasive |
| | Buccal | 3–4 μg/kg | 45–60 | 60–90 | Medium to longer non-invasive |
| | | | | | Pre-medication for deeper sedation |
| | IM | 2.5–3 μg/kg | 15–20 | 45–60 | Medium to longer non-invasive |
| | IN | 2–4 μg/kg | 30–45 | 45–60 | Medium to longer non-invasive |
| | | | | | Pre-medication for deeper sedation |
| Etomidate | IV | 0.2 mg/kg initial | 5 | 20–25 | Short non-invasive |
| | | 0.1 mg/kg subsequent | | | Add analgesic for painful procedure |
| Nitrous oxide | Inhaled | 50–70 % | 3–5 | 5–10 | Short non-invasive or minimally invasive |
| Analgesic agents | | | | | |
| Opioids | | | | | |
| Fentanyl | IV | 0.5–1 μg/kg initial | 2–3 | 30–45 | Alone or with sedative for painful/invasive |
| | | 0.5 μg/kg subsequent | | | Slow administration to avoid chest wall rigidity |
| Remifentanil | IV | Induction 0.5–1 μg/kg | 2–3 | 8–10 | Alone or with sedative for painful/invasive |
| | | Infusion 0.05–0.1 μg/kg/minute | | | |
| Anesthetic agents | | | | | |
| Ketamine | IV | 1 mg/kg initial | 1–2 | 10–15 | Brief painful/invasive |
| | | 0.5 mg/kg subsequent | | | Other sedative adjunct to limit cardiorespiratory effects |
| | IM | 4–6 mg/kg initial | 10–15 | 30–40 | Short- to medium-duration invasive if uncooperative patient or no IV access |
| | | 2–4 mg/kg subsequent | | | |
| Propofol | IV | 1–2 mg/kg every 2–3 min | 2–3 | 10–15 | Short (bolus) to long (infusion) non-invasive |
| | | Infusion 120–300 μg/kg/hour | | | Add analgesic for painful procedure |
| Reversal agents | | | | | |
| Benzodiazepines | | | | | |
| Flumazenil | IV | 0.01–0.01 mg/kg | 1–2 | 30–45 | Reverses primarily sedation |
| Opioids | | | | | |
| Naloxone | IV | 0.01–0.02 mg/kg | 1–2 | 30–45 | Reverses both sedation and respiratory depression |
| Nalmefene | IV | 0.25 μg/kg (maximum 1 μg/kg) | 2–3 | 120–180 | Reverses both sedation and respiratory depression |

*IN* intranasal, *IM* intramuscular, *IV* intravenous, *PO* oral, *PR* per rectum

10 % of patients, mostly after IV use. Midazolam pretreatment does not appear to reduce this [34], although caffeine may be helpful [35]. In large part because of agitation, many practitioners are using other agents, such as dexmedetomidine, with which recovery-related agitation is almost non-existent [36].

Methohexital (Brevital®) is a short-acting oxybarbiturate. Its initial use was primarily rectal [35, 36], although IV use is increasing, likely because of its short duration of action, making it more attractive than pentobarbital for short procedures [31, 39, 40]. Like pentobarbital, the parent drug has a relatively long half-life (2–5 h) but rapid tissue redistribution.

IV induction dosing is 1 mg/kg, followed by 0.5–1 mg/kg supplements every 2–3 min titrated to effect. Significantly more variability in dosing (range 1–9 mg/kg) is seen in comparison with pentobarbital [39, 40]. The clinical onset of action is rapid (2–5 min). The average sedation duration is 10–20 min, with recovery usually being complete by 40–50 min. Sedation failure rates are <1 % [31, 39, 40]. Consequently, methohexital is a particularly attractive agent for short radiologic procedures.

Because of limited bioavailability (17 %), rectal methohexital dosing is significantly higher than IV dosing at 20–30 mg/kg, and repeat doses of 10–15 mg/kg may be given as soon as 10–15 min [41]. Absorption is rapid, with sleep onset in about 10 min. The mean duration of sedation is 30–40 min, and recovery is complete 90–120 min after initial dosing. These kinetics make rectal administration appropriate for several procedures, including CT, ultrasound, and shorter MRI studies.

The adverse effect profile of IV methohexital differs from that of pentobarbital in that respiratory depression is more common (12–16 %) but recovery-related agitation is rare [40]. Rectal use is also associated with more frequent hypoxemia (up to 10 %) and sedation failures (5–13 %) in comparison with oral pentobarbital [37, 38]. Seizures may be precipitated in patients with convulsive disorders [42].

#### *4.2.2 Benzodiazepines*

Benzodiazepines are sedative–hypnotic agents that produce amnesia and sedation but no analgesia. Sedation is induced via $GABA_A$ receptor–mediated potentiation of neuroinhibitory chloride currents. They are seldom used alone as, at more deeply sedating doses, significant respiratory depression is frequent. Because of its pharmacokinetic profile, midazolam tends to be the preferred benzodiazepine for procedure-related applications.

A significant advantage of midazolam (Versed®) is that it can be effectively administered via multiple routes, although, if vascular access is present, IV administration is preferred. IV dosing starts at 0.1 mg/kg (maximum 4 mg) with repeat 0.05 mg/kg doses titrated every 5 min to effect. The onset of the clinical effect typically occurs within 3–5 min and it lasts 30–45 min.

IV midazolam is most commonly used as an adjunct sedative with either opioids or ketamine for painful procedures [42–45], making it appropriate for interventional radiology applications. When it is combined with opioids, the purpose is to add sedation and amnesia to opioid-induced analgesia. When it is combined with ketamine, the primary intent is to mitigate unpleasant adverse reactions—particularly emergence phenomena—although the literature regarding this benefit is inconclusive [46, 47].

If IV access is neither available nor desired, non-parenteral routes may be utilized. Oral midazolam is administered in doses of 0.5 mg/kg [48]. The sedation produced is typically mild to moderate, develops in 15–20 min, and lasts an average of 60 min. Deeper sedation is uncommon, as is significant respiratory depression [48]. A significant disadvantage is that the IV formulation, which is most commonly administered, tastes unpleasant.

IN administration is becoming more popular and is replacing oral use for many procedural applications. Midazolam is rapidly and reliably absorbed across nasal mucosal surfaces, with sedation occurring in as little as 5–10 min. Higher bioavailability allows lower doses than oral administration (0.2–0.4 mg/kg) [49, 50]. The more concentrated 5 mg/mL IV preparation should be used to minimize the administered volume, and use of a mucosal atomizer will further optimize drug dispersion and absorption [51]. Nasal irritation and discomfort during administration due to the benzoyl peroxide preservative can be significant but may be decreased by pre-medication with lidocaine spray [52]. Sedation achieved with IN midazolam is typically mild to moderate and may be sufficient for short radiologic procedures, such as CT or those with moderate motion tolerance.

When midazolam is used as a sole agent to produce mild to moderate sedation, adverse cardiorespiratory events (hypoxemia, airway obstruction, hypotension) are uncommon and typically minor [49–52]. More significant synergistic cardiorespiratory depression may occur when midazolam is coadministered with other agents, especially opioids. Paradoxical excitement or delirium have been reported, usually following IV use, and may be managed with low-dose flumazenil [53].

Flumazenil (Romazicon®) is the only benzodiazepine antagonist currently available for clinical use. It competitively binds to central benzodiazepine receptors, displacing the primary agent and preventing ongoing GABA activation [54]. Flumazenil primarily reverses sedation with less effect on respiratory depression, so airway management must be continued. As it is highly lipophilic, its onset of action is rapid (1–2 min), but its duration is relatively short

(30–45 min), so monitoring for re-sedation is necessary [55]. The recommended dose is 0.01–0.02 mg/kg every 1–2 min to a maximum of 1 mg. Adverse effects are frequent but may be related as much to sedative reversal as to direct reactions to flumazenil. The most common reactions are behavioral (agitation, crying, aggression; 10–20 %), while less frequent effects include headache, nausea/vomiting, and dizziness (2–5 % each) [55]. Use in chronic benzodiazepine users may precipitate an acute withdrawal reaction. Flumazenil has been used as a reversal agent following procedural sedation but, while it was effective, no discharge time benefits were observed and interest appears to have waned [55, 56]. It should also be stressed that the availability of a reversal agent does not alter the immediate bedside need for prompt detection of respiratory depression and appropriate intervention with respiratory assistance.

#### 4.2.3 Chloral Hydrate

Chloral hydrate is an alcohol-based sedative–hypnotic agent with no analgesic properties. Despite a long history of use, its availability in the USA is progressively becoming limited because the suspension is no longer being manufactured. While reported doses range from 30 to 100 mg/kg (maximum 2 g), sedation failure is high with doses of <60–70 mg/kg [57]. Administration may be oral or rectal, although the onset and duration of action are more predictable with oral use.

Chloral hydrate is rapidly absorbed from the gastrointestinal tract and metabolized to the active compound, trichloroethanol, which undergoes hepatic metabolism to inactive compounds. The time to sleep onset averages 20–40 min but is highly variable [28, 57, 58]. Similarly, the mean duration of sleep is 60–120 min but may be significantly longer. While chloral hydrate has historically been considered a moderate sedation agent, deep sedation is not uncommon [59]. Thus, it is most appropriate for longer radiology studies, although its use for CT sedation has been reported [60, 61].

Chloral hydrate has a relatively lengthy side-effect profile. Gastrointestinal upset with emesis (6–7 %), ataxia (17 %), and paradoxical agitation (2–18 %) are common. Significant respiratory depression has been reported [62, 63], as have deaths due to airway obstruction and/or respiratory depression following discharge [64, 65], highlighting the importance of adherence to established discharge criteria [7, 8]. Sedation failure is high (5–15 %), particularly in older children [59–61].

#### 4.2.4 Dexmedetomidine

Dexmedetomidine (Precedex®) represents the most recent arrival in the sedation practitioner's toolkit. It is a centrally acting $\alpha_2$-adrenergic receptor agonist which, compared with its oral precursor clonidine, is sevenfold more $\alpha_2$- than $\alpha_1$-receptor specific, resulting in fewer cardiovascular effects at equally sedating doses [66]. Dexmedetomidine is primarily a sedative with effects mediated via inhibition of the locus ceruleus. It also produces mild analgesia via inhibition of substance P release within the spinal cord [66], although the analgesia is insufficient to allow sole use for noxious or painful procedures [67]. It has rapidly become a popular agent for radiology sedation [68–73].

With use of the IV formulation, multiple administration routes are available, including buccal, IM, and IN. Buccal bioavailability is significantly greater than gastric bioavailability (82 versus 16 %) [74]. Consequently, careful administration to minimize swallowing is required and may be accomplished by slow dripping of the undiluted IV solution (100 μg/mL) along the buccal mucosa or gum line. Palatability does not appear to be problematic. The onset of sedation is relatively slow (45–60 min). While lower doses have been used, a reliable effect generally requires doses >3 μg/kg [75–77], which may provide adequate sedation for short radiologic procedures [70, 75]. Significant adverse cardiorespiratory events have not been reported with this route.

IM dexmedetomidine, also using the undiluted IV preparation, is effectively and more rapidly absorbed than buccal dexmedetomidine. This route has been successfully reported for CT and MRI sedation using doses of 2.5–3 μg/kg. The mean time to clinical sedation is roughly 15 min. Mild hypotension is not uncommon (14 %), but significant bradycardia or respiratory events have not been observed [68].

Interest in IN administration has grown more recently. Bioavailability in adults is roughly 65 % [78], but no data in children exist. Administration should be of the undiluted IV formulation via a mucosal atomizer device. Burning and pain on administration have not been reported. The onset of sedation typically takes 30–45 min. While reports to date have described use at doses of 1–2 μg/kg for anesthetic pre-medication [76, 79], in our experience, doses of 3–4 μg/kg fairly reliably produce moderate to deep sedation lasting 45–60 min, making this a viable option for ultrasound, nuclear medicine, and some MRI studies. The recovery time is typically 45–60 min.

Despite these options, IV use remains the most popular route. The concentrated formulation is diluted in 0.9 % saline to a final concentration of 4 μg/mL. Pre-mixed vials of this concentration are now commercially available. While initial reports used relatively low doses [69, 70], current reports suggest improved success rates (98–99 %) with higher induction doses (2–3 μg/kg) and maintenance infusion rates (1–2 μg/kg/hour) [71, 72]. To avoid significant bradycardia or sinus pause, induction should be slow,

over 5–10 min. Sedation develops over roughly 10 min, and recovery typically occurs 45–60 min following infusion cessation [69–72]. For studies of <30–40 min, we have recently begun using dexmedetomidine without a maintenance infusion, with excellent success (99.6 %) and more rapid recovery times [73].

Clinically significant respiratory depression requiring intervention appears to be uncommon with dexmedetomidine [69–73]. However, Ahmed et al. [80] recently reported a mean decrease of approximately 25 % in the respiratory rate from baseline with high-dose (2 μg/kg) dexmedetomidine use for MRI sedation, although no interventions were required. Its impact on upper airway morphology also appears to be less than that seen with other sedative agents, suggesting a decreased likelihood of airway obstruction development [21]. The major adverse effects reported with IV use are bradycardia and hypotension (15–20 % each) [71–73]. Self-limited hypertension during induction is also common [81]. Bradycardia may be more frequent or profound in patients taking heart rate–modulating medications and/or in patients with conduction disturbances [82, 83]. Possibly because the sleep induced by dexmedetomidine closely resembles natural sleep [84, 85], recovery-related agitation is almost non-existent, even in patients with underlying behavioral disorders [72].

Coadministration with ketamine, because of its sympathomimetic and analgesic properties, is increasing in popularity to try to mitigate cardiovascular effects and/or to facilitate use during painful procedures. With ketamine doses of 1–2 mg/kg, this addition appears to provide good analgesia with minimal cardiorespiratory changes during cardiac catheterization [86, 87]. For MRI studies, low-dose ketamine (0.5–1 mg/kg) is also associated with less bradycardia and no emergence reactions [88].

#### *4.2.5 Etomidate*

Etomidate (Amidate®) is an imidazole, non-barbiturate, GABA-mediated sedative–hypnotic agent. Properties include potent sedation and amnesia but no analgesia. For procedural sedation, induction is initiated with 0.2 mg/kg IV followed by 0.1 mg/kg doses every 2–3 min as needed. Sedation onset is rapid, occurring within 5 min, and most patients return to baseline in 20–25 min. As etomidate is a short-acting agent, its use in radiology has been limited to CT sedation, for which the median effective dose is 0.3 mg/kg [89, 90].

Adverse effects are relatively common but mostly minor. Pain on injection (40 %), myoclonus (22–25 %), and post-sedation nausea and vomiting (8–10 %) are the most frequently reported ones [91, 92]. While myoclonus would seem to limit utility for imaging sedation, success rates of >99 % have been reported [91]. When etomidate is used alone, clinically significant respiratory depression is uncommon (0.2 %) but increases significantly with opioid coadministration (15–20 %) [91, 92].

#### *4.2.6 Nitrous Oxide*

Nitrous oxide ($N_2O$) has many characteristics of a desirable sedation agent and is increasing in popularity. Clinical effects include sedation, amnesia, and mild analgesia. For procedural sedation, free-flow (versus demand-flow) systems are most appropriate. Portable systems equipped with appropriate scavenging systems are also available, allowing use in multiple locations.

For short radiology procedures, gas flow is initiated at 50 % $N_2O$ and titrated to effect [93–96], although even at maximum concentrations (70 %), most patients remain minimally sedated [93, 94]. The onset of the effect occurs within minutes and the mean recovery time is 30–40 min [95, 96]. This rapid offset makes $N_2O$ particularly appealing for procedures requiring a degree of intra-procedure cooperation, such as a voiding cystourethrogram (VCUG) [94–96].

Adverse effects are relatively uncommon (5–8 %), the most frequent being nausea/vomiting (3.5–5.7 %), followed by agitation (1 %). Clinically significant respiratory depression is rare (0.1 %). Administration of 100 % oxygen for several minutes after discontinuation can mitigate diffusion hypoxemia, which may occur because of the drug's high blood solubility.

### 4.3 Analgesic Agents

#### *4.3.1 Opioids*

Opioids remain the mainstay of analgesia for procedural sedation, especially fentanyl and remifentanil. Analgesia occurs via stimulation of $\mu_2$ and κ opioid receptors. κ receptors also mediate sedation effects, while $\mu_2$ stimulation mediates respiratory depression [97].

Fentanyl (Sublimaze®) is a synthetic opioid producing potent analgesia but minimal sedation. It is highly lipid soluble, enabling rapid blood–brain barrier penetration and onset of action. The analgesic effects last 20–30 min, making fentanyl an attractive option for short invasive procedures (i.e., vascular access, biopsies, aspirations) or non-invasive procedures during which underlying pain must be controlled.

Fentanyl is most frequently used in combination with a sedative. Dosing starts at 0.5–1.0 μg/kg, with repeat doses of 0.5 μg/kg administered every 2–3 min and titrated to effect. As rapid administration, especially of larger doses, may result in chest wall muscle rigidity requiring rapid neuromuscular blockade and assisted ventilation, doses

should be administered over at least 2–3 min. Other significant adverse effects include respiratory depression and hypotension, which are uncommon when fentanyl is used alone but increase with other sedative coadministration.

Remifentanil (Ultiva®) is an ultra-short-acting synthetic opioid also producing potent analgesia with minimal sedation. It has a half-life of 8–10 min, making it increasingly popular for brief painful procedures when combined with another sedative [98, 99]. Alone, remifentanil is administered as an infusion of 0.05–0.1 μg/kg/minute ± an induction bolus of 0.5–1 μg/kg. Coadministered propofol may be infused separately or mixed with remifentanil in a single syringe, using a final remifentanil concentration of 15–20 μg/mL. Administration is based on standard propofol infusion rates (see below). This mixture provides good sedation and analgesia with rapid recovery [99]. In comparison with fentanyl, however, respiratory depression is significantly more common (20–25 %). Other uncommon adverse effects include nausea and pruritus. While a remifentanil–propofol mixture has been reported for MRI sedation [100], many practitioners will find fentanyl a more comfortable option. It seems unlikely that remifentanil-based regimens will develop a significant niche in radiology sedation other than for very brief procedures.

Two opioid receptor antagonists are available, naloxone (Narcan®) being the most familiar. It competitively binds μ and κ receptors, reversing analgesia, sedation, and respiratory depression [101]. It may be administered via IV, IM, or endotracheal routes, although IV is preferred. While the full resuscitation dose is 0.1 mg/kg, management of procedural sedation–related respiratory depression may be accomplished with much smaller doses (0.01–0.02 mg/kg) [101], which are also less likely to completely reverse analgesia or precipitate an opioid withdrawal reaction. The mean duration of reversal following IV administration is dose dependent, ranging from 30 to 45 min. However, respiratory depression may redevelop, so monitoring should continue until the effects of the original agent have dissipated. Nalmefene has the same receptor binding profile as naloxone, but its duration of action is 2–3 h [102]. IV dosing is 0.25 μg/kg every 2 min, up to 1 μg/kg. Experience in pediatric patients is limited but suggests that it may be effective [103].

### 4.4 Anesthetic Agents

#### *4.4.1 Ketamine*

Ketamine is a dissociative anesthetic chemically related to phencyclidine, producing potent sedation, amnesia, and analgesia. It undergoes hepatic metabolism to norketamine, an active metabolite with one third of the analgesic potency of ketamine [104]. It is attractive for procedural sedation because of its relatively short duration of action, multiple routes of administration, and sympathomimetic properties, resulting in a favorable cardiovascular profile.

Because ketamine has combined sedation and analgesic properties, its primary attraction in radiology sedation will be for interventional and invasive procedures. While it may be used as a sole agent for these applications, most practitioners combine ketamine with other sedatives. Some also recommend pre-medication with atropine or glycopyrrolate to reduce hypersalivation and the risk of laryngospasm [105].

IV use is preferred if IV access is available. The onset of action is rapid (1–2 min), the duration is brief (10–15 min), and the recovery time is short (30–60 min) [104]. The initial dose is 1 mg/kg, and additional 0.5 mg/kg doses may be administered every 2–3 min and titrated to effect.

IM use is typically limited to situations where IV access cannot be obtained or where severe aggressive behavior prevents cooperation in obtaining IV access. The initial dosing is 4–6 mg/kg, with subsequent 2–4 mg/kg doses administered after 10 min as needed. The onset of action is 10–15 min, and clinically effective sedation lasts 30–40 min [104, 106, 107]. The more concentrated 100 mg/mL preparation should be used to minimize the injected volume. Atropine (10 μg/kg) may be mixed in the ketamine syringe to enable a single injection.

The primary disadvantage of ketamine is its lengthy adverse effect profile. Hypersalivation is common. This is especially pertinent in radiology, as patients are frequently supine during their studies. This may promote pooling of secretions in the posterior pharynx and can trigger laryngospasm or uncontrolled coughing fits, which may prevent successful procedure completion. Nausea and vomiting occur in 7–8 % of sedated children [47, 108], and premedication with an antiemetic may be considered. While hypopneic hypoventilation, based on capnography, has been reported to occur in up to 50 % of patients receiving ketamine alone or with coadministration [109], no patient required more than simple intervention. Clinically significant respiratory depression appears to be uncommon [106–108] outside younger infants, in whom apnea has been reported, prompting some to prohibit ketamine use in children <3 months of age [106]. Emergence delirium and/or frank hallucinations occur in 7.6 and 1.4 % of sedations, respectively [108], and may be particularly distressing to both the patient and the parent.

Historically, coadministration has been with midazolam to reduce emergence delirium, although this benefit is increasingly questioned [46, 47]. More recently, coadministration with propofol has gained popularity. As both agents are short acting, recovery is rapid, and the sympathomimetic effects of ketamine appear to counterbalance the cardiorespiratory depressing effects of propofol [110,

111], making the combination appropriate for both invasive and non-invasive procedures.

#### 4.4.2 *Propofol*

Propofol is an IV anesthetic agent with potent sedative but no analgesic properties. As with many other sedatives, the effects of propofol are mediated via $GABA_A$ potentiation and sodium-channel blockade [112]. Propofol is rarely used to produce less than deep sedation or general anesthesia [113]. Because of its rapid onset and short recovery times, it has become the most popular primary sedative for many invasive and non-invasive pediatric procedures [114–117]. Unlike with other agents, propofol use is limited to the IV route.

Poorly soluble in water, propofol is marketed in a 1 % lipid emulsion containing soybean oil, glycerol, and egg lecithin. While safe use has been reported in patients with non-anaphylactic allergies to these components [118, 119], caution or avoidance in soy- or egg-allergic patients is advised.

Deep sedation typically occurs following doses of 1–3 mg/kg. Additional 0.5–1 mg/kg boluses may be administered every 1–2 min and titrated to effect. For brief procedures (<10–15 min), intermittent bolus use is effective, while for longer procedures or those during which patient access is limited, a maintenance infusion of 2–5 mg/kg/h (120–300 μg/kg/min) is recommended [116, 120].

For painful procedures, addition of an analgesic agent, most commonly shorter-acting opioids, is appropriate [121, 122]. As alluded to above, ketamine–propofol combinations are also becoming popular to minimize cardiorespiratory depression. Ketamine (0.5–1 mg/kg) may be administered prior to induction using standard or possibly decreased propofol doses [109, 110, 123]. Alternatively, equal volumes of the 10 mg/mL formulations of each agent may be mixed in a single syringe and administered on the basis of standard propofol doses [124, 125].

Propofol commonly causes transient hypotension (rarely requiring intervention [126]) and modest respiratory depression, although airway obstruction and apnea requiring assisted ventilation are not infrequent [114–116]. These effects may be exaggerated with concomitant opioid use. Pain during peripheral vein injection can be distressing to the parent and the child but may be limited with low-dose lidocaine (0.2–0.5 mg/kg), fentanyl (0.5–1 μg/kg), or ketamine (0.25–0.5 mg/kg) pre-treatment [127, 128].

## 5 Conclusion

Radiology sedation continues to increase in scope and complexity, and sedation practitioners must continue to adapt their practices to facilitate safe and efficient procedure completion. As efficient patient flow through busy radiology departments remains a priority, practitioners should embrace the development of new agents or agent combinations that allow better matching of procedural needs with regimen pharmacology. However, "favorite" regimens may not be appropriate or effective for all patients, so comfort with a variety of agents remains important. Regardless of the regimen chosen, a high degree of preparedness and vigilance for adverse event development must be present during every sedation encounter.

**Acknowledgments** John W. Berkenbosch's institution, the University of Louisville/the Kosair Charities Pediatric Clinical Research Unit, has received research funding from Hospira to support the conduct of clinical trials evaluating dexmedetomidine in critically ill children.

**Compliance with Ethical Standards**

***Conflict of interest*** Dr. Berkenbosch has no other relevant conflicts of interest to report.

***Funding*** No sources of funding were used to assist with the preparation of this manuscript.

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