

Propofol-based sedation regimen for infants and children undergoing ambulatory magnetic resonance imaging

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Background. Propofol is widely used for infants and children requiring sedation for magnetic resonance imaging. However, increased doses of propofol may quickly lead to an unintended deep sedation and respiratory depression. Thus, an appropriate low dosage, which nevertheless ensures sufficient sleep for successful magnetic resonance imaging (MRI) completion, would probably minimize respiratory adverse events. We investigated the safety and efficacy of a low-dose propofol-based sedation regimen in a broad age range of children.

Methods. We investigated 500 infants and children, prospectively. Premedication consisted of i.v. midazolam 0.1 mg kg⁻¹. Sedation was induced with i.v. nalbuphine 0.1 mg kg⁻¹ and propofol 1 mg kg⁻¹, and maintained with propofol 5 mg kg⁻¹ h⁻¹. Outcome measures were induction time, sedation time, recovery time, need for additional sedation, respiratory events, cardiovascular events, paradoxical reactions, and sedation failure.

Results. Data were obtained from 53 infants and 447 children. Median (IQR) age was 5.3 (4.5, 6.1) yr and body weight was 19.3 (16.5, 24.7) kg. The induction time was 2 (1, 2) min, sedation time 55 (45, 65) min, and recovery time 8 (8, 9) min. Additional sedation was necessary in 11 patients (2.2%), mild respiratory events occurred in five patients (1%). All MRI examinations could be completed without paradoxical reaction or sedation failure.

Conclusion. This sedation regimen provides the shortest induction time so far described, a rare demand for additional sedation, a low incidence of respiratory events, and a rapid recovery.

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Magnetic resonance imaging (MRI) requires the patient to stay still up to an hour or more in a noisy and claustrophobic environment. Especially infants and children may not lie still for long enough without special care or drug-induced sleep. As a consequence, a variety of concepts are used by nurses, paediatricians, and anaesthesiologists. Each concept has advantages and disadvantages.^{1–8}

Propofol is discussed to be the best of all i.v. drugs for paediatric sedation.⁹ However, its narrow therapeutic window and the vulnerability of children to the sedative effects may lead quickly to unintended deep anaesthesia with loss of protective reflexes even after small dosage increases.⁷ Thus, an appropriate low dosage of propofol, which nevertheless ensures sufficient sleep for successful MRI completion, would probably minimize these adverse events.

The aim of this study was to investigate the safety and efficacy of a low-dose propofol-based sedation regimen in infants and children requiring sedation for ambulatory cranial and spinal MRI examinations.

Methods

After IRB approval, 500 consecutive ASA I–II infants and children, aged up to 19 yr, who required sedation for elective cranial, spinal MRI examination, or both during a 15 month period, were enrolled in this prospective study. Informed consent was obtained from the parents of all infants and children. Exclusion criteria were ASA status \geq III, severe pulmonary or cardiovascular disease, anatomic airway abnormalities or extreme tonsillar hypertrophy,

a history of propofol intolerance, known fat metabolism disorder, and diagnostic imaging for acute trauma. Children with cognitive impairment or developmental delay were not excluded.

In a pre-procedure interview, all parents were instructed about the patient fasting as recommended by the 'American Society of Anesthesiologists Preprocedure Fasting Guidelines': clear liquids were withheld for at least 2 h, breast milk for 4 h, and infant formula and solid food for 6 h. The fasting periods were applied to all ages.^{10 11}

On the day of the procedure, all patients were admitted with their parents at the paediatric day care ward. An i.v. cannula was inserted and then the patient was transferred to the MRI suite accompanied by his/her parents. The care team at the MRI suite included at least one consultant in paediatric anaesthesia, an anaesthesia nurse, a paediatric neuroradiologist, and a PhD imaging researcher.

Before the procedure, the consultant in paediatric anaesthesia evaluated each child carefully: fasting was verified, an exact medical history was taken, the use of medications was noted, and also the existence of allergies, details of previous sedations, and adverse reactions to anaesthesia. The physical examination included an evaluation of the airway and auscultation of both lungs. If the patient did not meet the strict fasting criteria or presented with symptoms or history consistent with upper respiratory tract infection (i.e. history of coughing at night, 'runny nose', or congested breath sounds at auscultation), the procedure was rescheduled.

In the MRI induction room, patients were seated in their parent's lap chest-to-chest and premedicated with i.v. midazolam 0.1 mg kg⁻¹. Then, patients were moved into the MRI suite.

Sedation was induced by i.v. nalbuphine 0.1 mg kg⁻¹ and followed by a loading dose of propofol 1 mg kg⁻¹, administered over 30 s. Lidocaine 0.25 mg ml⁻¹ was mixed in the same syringe to reduce pain induced by the injection of propofol. Supplemental doses of propofol 0.5 mg kg⁻¹ were administered until adequate sedation was achieved. Sedation was considered adequate, when the patient slept, arousable only with significant physical stimulation [University of Michigan Sedation Scale (UMSS) 3].¹² The maintenance of spontaneous respiration was verified. Then soft supports were placed under the patient's neck and shoulders to position the patient with the head forward and the neck slightly extended to maximize airway patency. Supplemental oxygen was delivered by paediatric face mask with a gas flow rate of 2 litre min⁻¹. Sedation was maintained with propofol 5 mg kg⁻¹ h⁻¹ using syringe pumps suitable for MRI.

Special monitors, not interfering with the MRI procedure, were placed in the examination room and in the observation room to monitor vital signs. Heart rate, peripheral oxygen saturation (Sp_{O₂}), and end-tidal carbon dioxide (E'_{CO₂}) were monitored continuously during the procedure and recorded at 5 min intervals by the anaesthesiologist.

Non-invasive arterial pressure was determined immediately before induction of sedation and at the end of the examination, but not during the MRI procedure, as stimulation from the blood pressure cuff would arouse an appropriately sedated patient.¹⁰ Hypotension after sedation was defined as a decrease in arterial pressure of >20% from baseline values.

Intervention was considered necessary when a decrease in Sp_{O₂} to <94%, an increase in E'_{CO₂} >6.7 kPa, apnoea (cessation of spontaneous respiration for 20 s), or bradycardia (>20% decrease in heart rate from baseline), and also occurrence of arrhythmia.

For safety reasons, a camera was placed in the MRI suite to monitor patients, and the anaesthesiologist closely observed the patients and provided interventions as needed. In case of inadequate sedation, such as spontaneous movements and agitation during the imaging process, an additional bolus of propofol 0.5 mg kg⁻¹ was administered, and the propofol infusion rate was increased by 1 mg kg⁻¹ h⁻¹ up to a total of 8 mg kg⁻¹ h⁻¹. In case of coughing or suspected airway obstruction, the MRI examination was interrupted, the patient was taken out of the MRI unit, and the airway patency was assessed. When partial airway occlusion was diagnosed, the neck was again extended slightly and the chin was supported with a tape. When total airway occlusion was noted, bag-valve-mask ventilation was initiated and a laryngeal mask airway was inserted, if necessary. Tracheal intubation was performed, when these manoeuvres did not relieve obstruction.

After the MRI examination was completed, the propofol infusion was terminated and the patients were transferred from the MRI suite to the induction room, where they rejoined their parents. An anaesthesia nurse monitored heart rate and Sp_{O₂}, and observed the patients until discharge criteria were fulfilled. Discharge readiness was achieved, when a modified Aldrete score of ≥8 (each parameter from scale of 0–2 for activity, respiration, circulation, consciousness, and colour) and a comfort scale of ≥3 (crying, agitation, and pain complaints; scale 0–2) were reached.^{13–15} A specialized paediatric team (paediatrician and paediatric nurse) transferred the patients back to the paediatric day care ward, where they were discharged home.

The following definitions were applied, according to the definitions used by Dalal and colleagues¹⁵ and Pershad and colleagues:¹⁶

1. Induction time: time in minutes from the administration of the premedication drug to the start of the MRI examination.
2. Sedation time: time in minutes from the start until the termination of the MRI examination.
3. Recovery time: time in minutes from the end of the examination up to the time that the patient recovered and fulfilled discharge criteria.

4. Additional sedation: administration of further propofol bolus and infusion rate increase to achieve deeper sedation (see: sedation protocol).
5. Respiratory event: evidence of partial or total airway obstruction with need for manoeuvres to improve patency of the airway, such as additional shoulder roll, bag-valve-mask ventilation, laryngeal mask airway insertion, or tracheal intubation.
6. Cardiovascular event: documented arrhythmias.
7. Paradoxical reaction: documented irritability or combativeness after administration of the sedative drug.
8. Sedation failure: sedation remains inadequate even after the administration of the maximum dose of propofol, resulting in an inability to perform the MRI examination. These patients would receive general anaesthesia at the discretion of the attending anaesthesiologist.

Data are presented as median (IQR) dependent on distribution. Normal distribution was assessed with q-q plot and Shapiro-Wilk test. Serial measurements were documented at 5 min intervals; data were averaged over time during the whole investigation period within each patient, and then averaged among the patients. The values of times were compared between five different age ranges with Kruskal-Wallis test. Categorical outcomes were compared using χ^2 test.

A *P*-value of 0.05 was considered significant. Analysis was conducted with SPSS software (SPSS Inc., Chicago, IL, USA, Version 12.0.1).

Results

Data were obtained from 500 consecutive patients who received sedation for elective, ambulatory MRI examinations during a 15 month period (September 2006–January 2008). Of these, 53 were infants and 447 were children. Median (IQR) age was 5.3 (4.5, 6.1) yr; body weight was 19.3 (16.5, 24.7) kg. Fifty-two per cent of patients were classified as ASA I and 48% as ASA II. Pertinent data are shown in Table 1.

One hundred and eighty-one patients were undergoing MRI because of epilepsy, 281 patients for cerebral tumour staging, 18 because of retardation, and 20 because of autism.

Median (IQR) induction time was 2 (1, 2) min, sedation time 55 (45, 65) min, and recovery time 8 (8, 9) min in our patients. The median induction, sedation, and recovery time (in min), and also the need for addition sedation, the respiratory and the cardiovascular events, and the paradoxical reactions or agitations to sedation, divided into five age groups, are as shown in Table 2.

The induction time was longest in infants and shortest in children in the age groups 3 to <5 and 5 to <10 yr. Similarly, recovery was longest in infants and shortest in the age groups 3 to <5 and 5 to <10 yr.

Children in the age group of 10 to <19 yr required sedation for MRI examination because of developmental delay caused by their underlying disease. Induction time and recovery was slightly prolonged in this age group.

The median duration of the procedure was nearly identical in all five age groups. Eleven patients (2.2%), two infants and nine children, moved during MRI examination and required additional sedation. One rescue propofol bolus and one step-up of continuous propofol infusion to $6 \text{ mg kg}^{-1} \text{ h}^{-1}$ were sufficient to complete the procedure in these patients.

Median SpO_2 was 98 (97, 99)% and median \dot{V}_{CO_2} was 5.3 (5.1, 5.6) kPa in our patients.

Systolic arterial pressure decreased by 10 (SD 3)%, but none of the patients met the criteria for hypotension.

Respiratory events occurred in five patients (1%). All of them suffered from oxygen desaturation <92%. Three children (16, 18, and 42 months old) experienced partial airway obstruction, which was treated immediately with slight neck extension and chin support. The two other children (3 and 89 months old) required short-time assistance of spontaneous respiration via bag-valve-mask ventilation and afterwards further reposition of neck and shoulders. Sufficient spontaneous respiration reoccurred in all of these patients, so that MRI scanning could be completed without further airway support.

None of our patients suffered from cardiovascular events such as bradycardia or arrhythmia during and after sedation. Paradoxical reaction to sedation or agitation was not seen in our patients.

All scheduled MRI examinations could be completed without any sedation failure.

Discussion

To our knowledge, this prospective, observational study documents the largest series of propofol-based sedation for ambulatory MRI examinations in spontaneously breathing infants and children. This regimen provides the shortest induction time in the recent literature, even in the group of infants. Only 2.2% of patients required additional sedation, and all examinations were completed without sedation failure or any paradoxical reaction to sedation. Recovery was rapid without nausea and vomiting. Respiratory adverse events occurred in only 1% of the patients and required simple support measures to re-establish airway patency. We applied this sedation regimen safely to a large number of patients in a broad range of age and did not find any age-group predominance of side-effects.

The goals of paediatric sedation are not only to ensure adequate sedation, but also to control anxiety, minimize psychological trauma, maximize the potential for amnesia, control unintentional movements, and provide short recovery. These goals can be best achieved by selecting appropriate drugs in the lowest possible, but just adequate dose

Table 1 Patients characteristic data. Values are median (IQR)

	Age (yr)					Total
	<1	1 to <3	3 to <5	5 to <10	10 to <19	
Number of patients	53	138	120	143	46	500
Age (month)	5 (4, 7)	26 (18, 31)	46 (40, 53)	82 (68, 93)	157 (139, 182)	63 (54, 73)
Weight (kg)	6.6 (5.7, 8.7)	12 (11, 13.9)	17 (15, 19.9)	22 (19, 27)	38.8 (32, 54)	19.3 (16.5, 24.7)
Gender (m/f)	25/28	68/70	52/68	87/56	34/12	266/234

Table 2 Outcome measures in the five age groups. Asterisks indicate shortest induction times and shortest recovery times Data are presented as medians (IQR) or as counts for categorical outcomes. *P*-values are for Kruskal–Wallis tests except for ‘Additional sedation’ and ‘Respiratory event’ (χ^2 test). NS, non-significant

	Age (yr)					<i>P</i> -value
	<1	1 to <3	3 to <5	5 to <10	10 to <19	
Induction time (min)	3 (3, 3)	2 (2, 2)	1 (1, 2)*	1 (1, 2)*	2 (1, 2)	<0.001
Sedation time (min)	55 (40, 62.6)	55 (45, 65)	55 (45, 60)	55 (45, 60)	55 (45, 56)	NS
Recovery time (min)	10 (10, 11)	8 (8, 9)	8 (7, 8.8)*	8 (7, 8)*	9 (8, 10)	<0.001
Additional sedation (<i>n</i>)	2	4	1	2	2	NS
Respiratory event (<i>n</i>)	1	2	1	1	–	NS
Cardiovascular event (<i>n</i>)	–	–	–	–	–	–
Paradoxical reaction (<i>n</i>)	–	–	–	–	–	–

for the procedure.^{11–17} However, the potential for adverse events may be increased when three or more sedating medications are administered.^{11–18} Nevertheless, we have used the described regimen successfully in our department since several years. To control anxiety and to ensure amnesia, midazolam is administered as pre-medication drug and not as an integral part of the sedation regimen.^{1–19} Unintentional movements are controlled by the addition of the partial agonist–antagonist opioid nalbuphine, administered only at sedation induction. One may argue that adding nalbuphine is not necessary for a painless MRI examination. According to recent guidelines, sedatives or hypnotics alone have to be preferred for non-painful procedures.¹¹ However, nalbuphine was included in our regimen, since nalbuphine 0.1 mg kg^{−1}, administered before anaesthesia induction, is described to decrease the frequency of spontaneous movements induced by propofol.²⁰ Furthermore, Dalens and colleagues²¹ documented that nalbuphine 0.1 mg kg^{−1}, administered at the end of MRI examinations, prevents emergence agitation without prolonging discharge times from the post-anaesthesia care unit. In addition, propofol alone seems not always to suppress unintentional movements during sedation.^{9–22}

Even if propofol is discussed to be the ideal agent for i.v. paediatric sedation, its use in infants and children is still controversial. Propofol, administered in high doses for long-term sedation, seems to increase the risk of ‘propofol infusion syndrome’ in both children and adults.²³ In the daily clinical routine, propofol is administered safely for short-term procedural sedation, and no

case report of propofol infusion syndrome is documented until now, even if most institutions administered higher propofol doses than we did.^{15–24–28} We recommend keeping the propofol dose as low as effective, and restricting its use to the shortest possible duration. We provide sufficient paediatric sedation with one of the lowest continuous infusion rates documented in the recent literature.²⁹

With regard to the increasing demand of paediatric sedation for diagnostic procedures, variability in onset of sedative action, inadequate sedation, and sedation failure are significant clinical problems. Prolonged induction time, repeated MRI sequences, or rescheduled investigations are costly with respect to increased personnel time, downtime of the MRI scanner, and inconvenience to children and parents.¹ Sedation failure rates up to 20%³⁰ and inadequate sedation up to 22.5%¹⁵ are reported depending on the sedation regimen used. This is in contrast to our results, which show not a single sedation failure highlighting the efficacy of our sedation regimen.

This study describes as the largest case series the safety and efficacy of a propofol-based sedation regimen for infants and children undergoing ambulatory MRI examinations. This regimen provides the shortest induction time, a rare need for additional sedation, a low incidence of mild respiratory events, and a rapid recovery in a broad age range of patients. All examinations were completed without sedation failure. Therefore, this timesaving regimen is an effective way to meet the increasing demand for paediatric MRI examinations.

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