Dexmedetomidine compared with propofol for pediatric sedation during cerebral angiography

Ke Peng, Jian Li, Fu-hai Ji, Zhi Li[1]

Departments of Anesthesiology, and [1]Radiology, First Affiliated Hospital of Soochow University, Suzhou 215006, Jiangsu Province, China

Background: Sedation of pediatric patients undergoing cerebral angiography is challenging. Although dexmedetomidine is used for sedation in various procedures, it has not been reported for pediatric patients undergoing cerebral angiography. This study compared the safety and efficacy of dexmedetomidine with that of propofol for cerebral angiography in pediatric patients. **Materials and Methods:** Sixty-two patients (6-15 years) scheduled for elective cerebral angiography were apportioned randomly and equally to receive either propofol or dexmedetomidine sedation. Patients in the propofol group received an initial bolus of intravenous propofol (1 mg/kg) and a maintenance infusion of 100 μg/kg/min. Patients in the dexmedetomidine group received an initial bolus of intravenous dexmedetomidine (1 μg/kg over 10 min) and a maintenance infusion of 1 μg/kg/h. An additional bolus of propofol 0.5 mg/kg or dexmedetomidine 0.25 μg/kg was repeated if needed. Procedure time, time to recovery and adverse events associated with sedation were recorded. **Results:** All cerebral angiographies were completed successfully under sedation with dexmedetomidine or propofol. Mean cerebral angiography time was 36 ± 10 min in the propofol group and 31 ± 7 min in the dexmedetomidine group ($P = 0.047$). The percentage of airway events and total adverse events were significantly higher in the propofol group ($P < 0.05$). Heart rate decreased in the dexmedetomidine group and mean arterial pressure decreased in the propofol group ($P < 0.05$, each). **Conclusion:** Although cerebral angiography can be performed successfully under sedation with either propofol or dexmedetomidine, dexmedetomidine may be a better alternative because of fewer respiratory adverse events.

Key words: Cerebral angiography, dexmedetomidine, pediatric sedation, propofol

INTRODUCTION

Pediatric cerebrovascular diseases include arteriovenous malformation, cavernous hemangioma, moyamoya disease, venous aneurysm, and capillary telangiectasia. Central to the diagnosis, planning of treatment and management of cerebrovascular diseases is the cerebral angiography,[1] a procedure to image blood vessels in the brain. Children are rarely able to complete the exam under local anesthesia because of anxiety, agitation, pain and discomfort from the femoral artery puncture and injection of contrast agent, and brain dysfunction caused by hemorrhage or ischemia. Deep sedation or general anesthesia is therefore warranted, but general endotracheal anesthesia may prolong postoperative recovery. Provision of motionless sedation with rapid recovery and acceptably low risk of adverse events may be challenging.

Propofol is widely used for anesthesia and sedation in pediatric patients, but adverse side effects include hypotension, respiratory depression and hypertriglyceridemia.[2] An alternative option is dexmedetomidine, a highly selective α-2 adrenoceptor agonist that provides sedation, analgesia, and anxiolytic effects. It has been used in pediatric patients for premedication,[3] intraoperative administration,[4-7] computed tomography (CT) scanning,[8,9] magnetic resonance imaging (MRI),[10,11] mechanical ventilation,[12,13] and other procedures.[14-16] Unlike other sedatives, dexmedetomidine has been shown to induce sedation similar to natural sleep, without significant respiratory depression.[17,18] However, dexmedetomidine has not been reported for pediatric patients undergoing cerebral angiography.

Therefore, the present study compared the safety and efficacy of dexmedetomidine relative to that of propofol for sedation during cerebral angiography in pediatric patients. In particular, we evaluated the number of respiratory events and hemodynamic complications during the procedure.

PATIENTS AND METHODS

Patients

The study was entered into the Chinese Clinical Trial Registry (www.chictr.org, ChiCTR-TRC-12002713) and approved by our institutional review board for human

subjects. A parent or legal guardian of each patient provided written informed consent to participate in the study. Children between the ages of 6 and 15 years with American Society of Anesthesiologists (ASA) classification of I or II were eligible for inclusion in the study [Figure 1]. Exclusion criteria were: Known allergy to the medications used, obesity (body weight >20% of the ideal), ASA classification III or more (severe systemic disease or worse), cardiac abnormalities, craniofacial anomaly, respiratory problems (pneumonia, asthma, bronchitis, or severe obstructive sleep apnea), Glasgow coma scale <15, intracranial hypertension and uncontrolled epilepsy.

Protocol

A random number table was used to equally allocate patients to either a propofol or dexmedetomidine treatment group (*n* = 31, each). The anesthesiologists and data collectors in the radiology procedure room were not blinded to the treatment. The subjects, their parents or legal guardians, and observers in the recovery room and follow-up were blinded to the study group.

The preoperative fasting period was 2 h for clear fluids and 6 h for solid food. No premedication was given. All patients received an intravenous infusion of 5 mL/kg/h lactated Ringer's solution. Monitoring by pulse oximetry (blood oxygen saturation [SpO$_2$]) and electrocardiography was conducted throughout the procedure. Arterial blood pressure was monitored noninvasively at 3-min intervals.

Patients in the propofol group received an initial bolus of intravenous propofol, 1 mg/kg (Diprivan; AstraZeneca Pharma, Cheshire, UK) over 30 s and then a maintenance infusion of 100 µg/kg/min. Patients in the dexmedetomidine group received an initial bolus of intravenous dexmedetomidine 1 µg/kg (Dexmedetomidine Hydrochloride Injection; Jiangsu HengRui Medicine, Lianyungang, Jiangsu, China) over 10 min, and then a maintenance infusion of 1 µg/kg/h (dexmedetomidine was diluted in normal saline to a dose of 4 µg/mL). Local anesthesia was performed with 1% lidocaine before the femoral artery puncture. Additional boluses of propofol (0.5 mg/kg) or dexmedetomidine (0.25 µg/kg) were administered if needed to maintain sedation.

Oxygen was administered at 3 L/min via nasal cannula throughout the procedure. Ephedrine boluses of 3–5 mg administered intravenously were allowed in addition to fluid infusion to treat hypotension (systolic arterial pressure <90 mmHg or mean arterial pressure <65 mmHg). Atropine boluses of 0.3-0.5 mg were administered intravenously to treat bradycardia (heart rate <60 bpm).

Clinical signs of airway obstruction or desaturation (SpO$_2$ <90%) were managed with airway manipulations (jaw thrust, chin lift, or shoulder roll) to relieve obstruction. If this was

not effective, an artificial airway (oral or nasal airway, or face mask) was used. Endotracheal intubation was used as the last resort. All the above respiratory events were recorded.

All the angiography procedures were performed by the same radiologist. Once the imaging was complete, the propofol or dexmedetomidine infusion was discontinued. All patients were transferred to a recovery room and observed continuously by observers blinded to the study group. Oxygen administration was continued until discharge from the recovery room. A total modified Aldrete score of ≥18 indicated the patient's readiness for discharge [Table 1].[19] Adverse events in the recovery room and the time required to meet the discharge criterion were recorded. Patients were followed for complications related to sedation (desaturation, agitation, nausea, and vomiting) by observers blinded to the study group for 24 h after the procedure.

Statistical analysis

The number of subjects required in each group was determined before the study by a power calculation based on data from a previous study[20] and the results of our institution database. Twenty-eight patients in each group were required to detect a 20% difference in the incidence of airway events with an α level of error of 0.05 (two-sided) and power of 0.8 (PASS 11.0.7 Statistical Software, NCSS, Kaysville, Utah). Thirty-one cases were allocated to each group to compensate for possible dropped cases.

Data were analyzed using SPSS software (IBM SPSS Statistics, version 19, Chicago, Illinois). Data are presented as mean ± standard deviation, number of samples (*n*), and
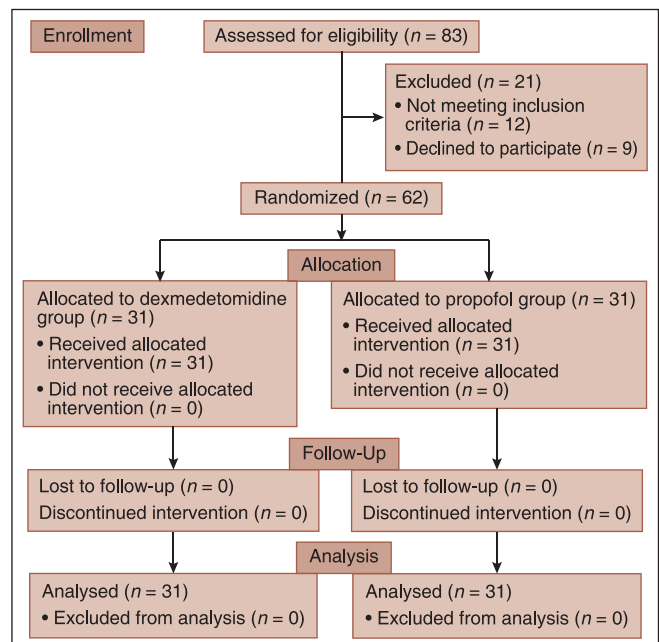

Figure 1: CONSORT flow diagram

percentage (%) as appropriate. Age, weight, procedure time, and time to meet discharge criteria were compared using Student's *t*-test. Heart rate and mean arterial pressure over time were compared using the two-way repeated-measures analysis of variance. Gender and ASA classification were compared with Pearson's Chi-squared test. The percentages of patients in each group with a radiologic diagnosis or adverse events were compared using Fisher's exact test. A two-tailed $P < 0.05$ was considered to be statistically significant.

RESULTS

Demographics and radiologic diagnosis
This analysis consists of 62 patients, ages 6-15 years, who completed the study during the period March 2011 and May 2012 [Figure 1]. There were no statistically significant differences between the groups with regard to age, and gender, weight, ASA physical status, or radiologic diagnoses [Table 2].

Procedure duration and time to recovery
The procedure time for the propofol group (35.8 ± 10.7 min) was significantly longer than that of the dexmedetomidine group (31.2 ± 7.0 min, $P = 0.047$). There was no difference in time to meet discharge criteria between the two groups.

Adverse events
The differences in the adverse events between propofol and dexmedetomidine sedation groups are shown in Table 3.

Table 1: Modified aldrete classification

Variables	Criteria	Score
Activity	Able to move 4 extremities voluntarily on command	2
	Able to move 2 extremities voluntarily on command	1
	Able to move no extremities voluntarily on command	0
Respiration	Able to breathe deeply and cough freely	2
	Dyspnea or limited breathing	1
	Apneic	0
Circulation	Blood pressure + 20 of preanesthetic level	2
	Blood pressure + 22–49 of preanesthetic level	1
	Blood pressure + 50 of preanesthetic level	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Not responding	0
Oxygen saturation	Able to maintain O_2 saturation >92% on room air	2
	Needs oxygen inhalation to maintain O_2 saturation >90%	1
	O_2 saturation <90% even on oxygen supplement	0
Dressing	Dry	2
	Wet, but stationary	1
	Wet, but growing	0
Pain	Pain free	2
	Mild pain	1
	Pain requiring parenteral meds	0
Ambulation	Able to stand up and walk straight	2
	Vertigo when erect	1
	Dizziness when supine	0
Fasting-feeding	Able to drink fluids	2
	Nauseated	1
	Nausea and vomiting	0
Urine output	Has voided	2
	Unable to void, but comfortable	1
	Unable to void, but uncomfortable	0

Table 2: Demographics and clinicopathology of the propofol and dexmedetomidine treatment groups[a]

Variables	Propofol	Dexmedetomidine	P value
Age (years)	11.2±3.1	10.4±2.8	0.302
Gender (male/female)	19/12	15/16	0.307
Weight (kg)	33.7±6.0	31.5±5.3	0.147
ASA classification (I/II)	13/18	10/21	0.43
Procedure time (min)	35.8±10.7	31.2±7.0	0.047[b]
Time to meet discharge criteria (min)[c]	22.3±8.6	24.5±11.2	0.383
Radiologic diagnosis			
Arteriovenous malformation	14 (45.2)	19 (61.3)	0.238
Cavernous hemangioma	8 (25.8)	4 (12.9)	
Moyamoya disease	5 (16.1)	7 (22.6)	
Others[d]	4 (12.9)	1 (3.2)	

[a]Data are expressed as mean±SD or *n* (%); [b]*P* < 0.05 indicates a significant difference; [c]Discharge criteria: modified Aldrete score ≥18; [d]Others: Rare cerebrovascular disease in children (aneurysm, venous aneurysm, capillary telangiectasia). SD = Standard deviation; ASA = American Society of Anesthesiologists

Table 3: Adverse events associated with sedation in the propofol and dexmedetomidine groups[a]

Variables	Propofol	Dexmedetomidine	P value
During sedation, airway events	7 (22.6)	0 (0)	0.011[b]
Additional airway manipulations[c]	5 (16.1)	0 (0)	0.053
Need for artificial airway[d]	2 (6.5)	0 (0)	0.492
Endotracheal intubation	0 (0)	0 (0)	1
Hypotension	1 (3.2)	0 (0)	1
Bradycardia	0 (0)	1 (3.2)	1
Vomiting	0 (0)	0 (0)	1
Agitation	0 (0)	0 (0)	1
Allergic reaction	0 (0)	0 (0)	1
Failed sedation	0 (0)	0 (0)	1
Total	8 (25.8)	1 (3.2)	0.026[b]
During recovery			
Desaturation	0 (0)	0 (0)	1
Hypotension	0 (0)	0 (0)	1
Bradycardia	0 (0)	1 (3.2)	1
Nausea and vomiting	1 (3.2)	0 (0)	1
Agitation	1 (3.2)	0 (0)	1
Total	2 (6.5)	1 (3.2)	1
24 h after sedation			
Sedation-related complications[e]	0 (0)	0 (0)	1

[a]Data are expressed as *n* (%); [b]*P* < 0.05 indicates a significant difference; [c]Jaw thrust, chin lift, shoulder roll; [d]Oral or nasal airway, mask ventilation; [e]Desaturation, agitation, nausea, and vomiting

Ephedrine was administered to one patient (3.2%) in the propofol group to treat hypotension and atropine was administered to one patient (3.2%) in the dexmedetomidine group for bradycardia. Vomiting, agitation, and allergic reactions did not occur in either group.

Seven patients (22.6%) in the propofol group had airway events, whereas none of the patients in the dexmedetomidine group had an airway event ($P = 0.011$). Airway manipulations (jaw thrust, chin lift, shoulder roll) were required for the seven patients in the propofol group to relieve airway obstruction; for two, artificial airways (oral or nasal airway, mask ventilation) were needed. None of the patients in either group required intubation.

The percentage of total adverse events during sedation was also significantly higher in the propofol group (25.8%) than in the dexmedetomidine group (3.2%; $P = 0.026$). There were no differences in the percentages of other adverse events between the two groups.

Hemodynamic effects

At baseline, the mean heart rate and mean arterial pressure were similar between the groups. After induction, the mean heart rate of the dexmedetomidine group was significantly lower than in the propofol group. The baseline heart rate did not change significantly after induction with propofol. However, patients receiving dexmedetomidine experienced a significant reduction in heart rate, especially 5 min after induction [Figure 2].

After induction, the mean arterial pressure of the propofol group was significantly lower than that the dexmedetomidine group. In the dexmedetomidine group, the mean arterial pressure did not change significantly relative to the baseline. However, patients receiving propofol experienced a significant reduction in mean arterial pressure, especially at the end of induction [Figure 3].

DISCUSSION

The main finding of this study was that dexmedetomidine sedation for cerebral angiography in pediatric patients was associated with fewer respiratory events than propofol sedation.

Since 2011, our institution began to use dexmedetomidine as the sedative for CT, MRI, digital subtraction angiography, and other procedures in adult and pediatric patients. Many pediatric patients with cerebrovascular diseases suffer from brain dysfunction caused by hemorrhage or ischemia. Intracranial hypertension and epilepsy are the most common symptoms. Provision of anesthesia or sedation for these patients can often be challenging. For critically ill patients, general anesthesia by endotracheal intubation is the only choice. Nevertheless, most cases are relatively mild, and it is possible to complete the procedure under sedation.

An ideal sedative should cause rapid onset, adequate maintenance of the sedative state to allow completion of the procedure, and rapid recovery. It should also be safe with few adverse events. Respiratory depression is the most important risk and predictor of sedation-related morbidity and mortality.[21]

Propofol is one of the most widely used anesthetics in anesthesia and sedation for adult and pediatric patients. It has been used to induce deep sedation for CT and MRI in pediatric patients,[20,22] mainly because it has a rapid onset and recovery time, an absence of nausea or vomiting, and less respiratory depression. However, in the present study, we demonstrated that the incidence of airway events and the
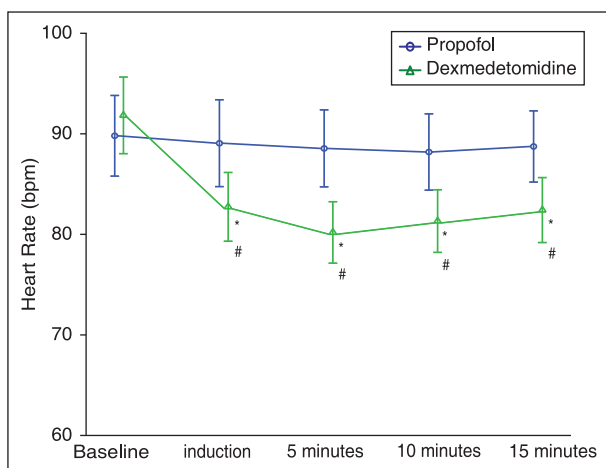
Figure 2: Heart rates at baseline, at the end of induction, and 5, 10, and 15 min afterward in the propofol and dexmedetomidine groups. Data are mean ± 95% confidence interval. *$P < 0.05$ between the two groups; #$P < 0.05$ in comparison to baseline values
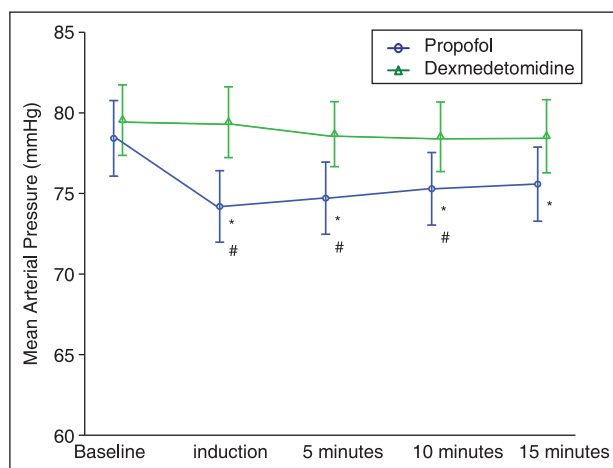
Figure 3: Mean arterial pressures at baseline, at the end of induction, and 5, 10, and 15 min afterward in the propofol and dexmedetomidine groups. Data are mean ± 95% confidence interval. *$P < 0.05$ between the two groups; #$P < 0.05$ in comparison to baseline values

subsequent need for airway intervention to relieve airway obstruction were significantly greater in the propofol group than in the dexmedetomidine group. Similar to our findings, Zgleszewski *et al.*[20] showed that propofol is associated with a significantly greater incidence of adverse respiratory events compared with pentobarbital.

The changes in the configuration that cause obstruction in the upper airway during anesthesia with propofol in pediatrics have been studied. Litman *et al.*[23] showed that the dimensions of the upper airways of children change significantly on awakening from propofol anesthesia, and in most children the narrowest point in the pharynx was at the level of the soft palate. In their study Evans *et al.*[24] they found that increasing the depth of propofol anesthesia in children was associated with upper airway narrowing throughout the upper airway, and was most pronounced in the hypopharynx at the level of the epiglottis. Our results are consistent with the imaging findings of these studies.

Pharmacologically, propofol induces anesthesia through the inhibitory neurotransmitter γ-aminobutyric acid, while dexmedetomidine acts by stimulation of α-2 adrenergic receptors in the locus coeruleus. Propofol may cause more intense rapid-eye-movement sleep, which is associated with central inhibition of ventilation,[25,26] whereas dexmedetomidine has been shown to induce sedation similar to natural sleep.[17,18]

Another important finding of the present study was that the cerebral angiography took significantly longer for the propofol group than for patients who received dexmedetomidine. This can be explained by the significantly greater number of airway events in the propofol group, which required the radiologist to hold the procedure to allow for correction of the problem.

In this study, other adverse events were infrequent and incidence did not differ between the groups. Both propofol and dexmedetomidine sedation allowed completion of the cerebral angiography for all subjects. Dexmedetomidine caused significant reductions in heart rate, and propofol caused significant reductions in mean arterial blood pressure. These hemodynamic reductions were statistically, but not clinically, significant. Although there was one patient who required pharmacologic intervention in each group, the changes in hemodynamics were relatively mild and transient.

It is known that the most significant adverse reactions associated with dexmedetomidine are hypotension and bradycardia, resulting from its sympatholytic activity; both have been reported in several pediatric studies,[8,10,27] although rarely do either require clinical intervention. We found that dexmedetomidine caused significant reductions in heart rate, but did not change the mean arterial pressure significantly in this pediatric population. However, despite the high affinity of dexmedetomidine for the α-2 rather than the α-1 adrenergic receptor (1620:1),[28] it should be used cautiously in patients at risk of bradycardia or hemodynamic instability.

Our study has some limitations. First is the absence of blinding for the anesthesiologist administering sedation. However, this was not possible in view of the nature of drugs and the need to manage complications efficiently if they arose. Second, although our results showed a significant difference in the incidence of airway events it did not show differences in other adverse events. However, our study was not statistically designed to analyze differences in other adverse events. A larger sample size may be required to find the true incidence of adverse events in this population.

CONCLUSION

Dexmedetomidine was associated with fewer respiratory adverse events, and therefore may be better alternative as a sedative for cerebral angiography in pediatric patients.

ACKNOWLEDGMENTS

AUTHOR'S CONTRIBUTIONS

Peng K and Li J helped performing the research and data analysis and writing the manuscript. Ji FH contributed to the recruitment of patients. Li Z helped performing the study. Corresponding author (Peng K) conceived and designed the study. All authors have approved the final manuscript.

REFERENCES

1. Kaufmann TJ, Huston J 3rd, Mandrekar JN, Schleck CD, Thielen KR, Kallmes DF. Complications of diagnostic cerebral angiography: Evaluation of 19,826 consecutive patients. Radiology 2007;243:812-9.
2. Peck TE, Hill S. Pharmacology for Anesthesia and Intensive Care, 3rd edition. Cambridge, United Kingdom, Cambridge University Press 2008;378.
3. Cimen ZS, Hanci A, Sivrikaya GU, Kilinc LT, Erol MK. Comparison of buccal and nasal dexmedetomidine premedication for pediatric patients. Paediatr Anaesth 2013;23:134-8.
4. Olutoye OA, Glover CD, Diefenderfer JW, McGilberry M, Wyatt MM, Larrier DR, *et al*. The effect of intraoperative dexmedetomidine on postoperative analgesia and sedation in pediatric patients undergoing tonsillectomy and adenoidectomy. Anesth Analg 2010;111:490-5.

5. Patel A, Davidson M, Tran MC, Quraishi H, Schoenberg C, Sant M, *et al.* Dexmedetomidine infusion for analgesia and prevention of emergence agitation in children with obstructive sleep apnea syndrome undergoing tonsillectomy and adenoidectomy. Anesth Analg 2010;111:1004-10.

6. Meng QT, Xia ZY, Luo T, Wu Y, Tang LH, Zhao B, *et al.* Dexmedetomidine reduces emergence agitation after tonsillectomy in children by sevoflurane anesthesia: A case-control study. Int J Pediatr Otorhinolaryngol 2012;76:1036-41.

7. Schnabel A, Reichl SU, Poepping DM, Kranke P, Pogatzki-Zahn EM, Zahn PK. Efficacy and safety of intraoperative dexmedetomidine for acute postoperative pain in children: A meta-analysis of randomized controlled trials. Paediatr Anaesth 2013;23:170-9.

8. Mason KP, Zgleszewski SE, Prescilla R, Fontaine PJ, Zurakowski D. Hemodynamic effects of dexmedetomidine sedation for CT imaging studies. Paediatr Anaesth 2008;18:393-402.

9. Mason KP, Prescilla R, Fontaine PJ, Zurakowski D. Pediatric CT sedation: Comparison of dexmedetomidine and pentobarbital. AJR Am J Roentgenol 2011;196:W194-8.

10. Mahmoud M, Gunter J, Donnelly LF, Wang Y, Nick TG, Sadhasivam S. A comparison of dexmedetomidine with propofol for magnetic resonance imaging sleep studies in children. Anesth Analg 2009;109:745-53.

11. Mason KP, Fontaine PJ, Robinson F, Zgleszewski S. Pediatric sedation in a community hospital-based outpatient MRI center. AJR Am J Roentgenol 2012;198:448-52.

12. Tobias JD, Berkenbosch JW. Sedation during mechanical ventilation in infants and children: Dexmedetomidine versus midazolam. South Med J 2004;97:451-5.

13. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, *et al.* Dexmedetomidine vs midazolam for sedation of critically ill patients: A randomized trial. JAMA 2009;301:489-99.

14. Lubisch N, Roskos R, Berkenbosch JW. Dexmedetomidine for procedural sedation in children with autism and other behavior disorders. Pediatr Neurol 2009;41:88-94.

15. Mason KP, Lubisch N, Robinson F, Roskos R, Epstein MA. Intramuscular dexmedetomidine: An effective route of sedation preserves background activity for pediatric electroencephalograms. J Pediatr 2012;161:927-32.

16. Watt KM, Walgos J, Cheifetz IM, Turner DA. Dexmedetomidine for transport of a spontaneously breathing combative child. Pediatrics 2012;130:e690-4.

17. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003;98:428-36.

18. Hsu YW, Cortinez LI, Robertson KM, Keifer JC, Sum-Ping ST, Moretti EW, *et al.* Dexmedetomidine pharmacodynamics: Part I: Crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology 2004;101:1066-76.

19. Aldrete JA. Modifications to the postanesthesia score for use in ambulatory surgery. J Perianesth Nurs 1998;13:148-55.

20. Zgleszewski SE, Zurakowski D, Fontaine PJ, D'Angelo M, Mason KP. Is propofol a safe alternative to pentobarbital for sedation during pediatric diagnostic CT? Radiology 2008;247:528-34.

21. Coté CJ, Notterman DA, Karl HW, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: A critical incident analysis of contributing factors. Pediatrics 2000;105:805-14.

22. Usher AG, Kearney RA, Tsui BC. Propofol total intravenous anesthesia for MRI in children. Paediatr Anaesth 2005;15:23-8.

23. Litman RS, Weissend EE, Shrier DA, Ward DS. Morphologic changes in the upper airway of children during awakening from propofol administration. Anesthesiology 2002;96:607-11.

24. Evans RG, Crawford MW, Noseworthy MD, Yoo SJ. Effect of increasing depth of propofol anesthesia on upper airway configuration in children. Anesthesiology 2003;99:596-602.

25. Millman RP, Knight H, Kline LR, Shore ET, Chung DC, Pack AI. Changes in compartmental ventilation in association with eye movements during REM sleep. J Appl Physiol (1985) 1988;65:1196-202.

26. Smith CA, Henderson KS, Xi L, Chow C, Eastwood PR, Dempsey JA. Neural-mechanical coupling of breathing in REM sleep. J Appl Physiol (1985) 1997;83:1923-32.

27. Hammer GB, Drover DR, Cao H, Jackson E, Williams GD, Ramamoorthy C, *et al.* The effects of dexmedetomidine on cardiac electrophysiology in children. Anesth Analg 2008;106:79-83.

28. Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anaesthesia 1999;54:146-65.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/topic	Item no.	Checklist item	Reported on page no.
Title and abstract	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, and factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	5-6
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5-7
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	9-11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	7-8
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomization			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomization; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5-7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	7
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	9
	13b	For each group, losses and exclusions after randomization, together with reasons	9
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	9,22
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	9
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	9-10
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	9-10
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	NA
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	9-10
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	14-15
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	15
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	12-15
Other information			
Registration	23	Registration number and name of trial registry	2, 5
Protocol	24	Where the full trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	5

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 explanation and elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomized trials, noninferiority and equivalence trials, nonpharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: For those and for up to date references relevant to this checklist, available from: http://www.consort-statement.org