Clinical efficacy of dexmedetomidine versus propofol in children undergoing magnetic resonance imaging: a meta-analysis

Hongwei Fang1,2*, Liu Yang3*, Xiangrui Wang2, Hao Zhu2

1Department of Anesthesiology, Bengbu Medical College, Anhui, Bengbu 233004, P.R. China; 2Department of Anesthesiology, RenJi Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China; 3Department of Anesthesiology, School of Medicine, Wannan Medical College, Wuhu, Anhui, China. *Equal contributors.

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Abstract: Dexmedetomidine, as a sole or combinable sedative, has served in pediatric sedation undergoing MRI. However, clinical effects of dexmedetomidine are still controversial. This meta-analysis was to assess the effects between dexmedetomidine and propofol in children undergoing MRI, especially outcomes and adverse events of patients. Multiple Electronic Database searched including MEDLINE, Embase and the Cochrane library, and updated to April 2015. All statistical analysis utilized review manager to perform, the Cochrane collaboration’s software preparation and maintenance of Cochrane systematic reviews. Five trials with a total of 337 patients were included. Compared with propofol group, dexmedetomidine significantly increased the recovery time (WMD: 10.70 min; 95% CI: 4.26-17.13; P = 0.001). The duration of sedation did not appear to decrease for the patients who received dexmedetomidine than for those who received propofol (WMD: 19.96 min; 95% CI: -4.12-44.04; P = 0.1). There were statistically significant increased in the pediatric anesthesia emergence Delirium scores of 5-min after awakening (WMD: 2.40; 95% CI: 1.00 to 3.81; P = 0.0008) and 10-min after awakening (WMD: 3.06; 95% CI: 1.81 to 4.31; P < 0.00001) in patients who were treated with dexmedetomidine than propofol. Improved the prognosis of patients, nonetheless, dexmedetomidine must have an indispensable role to undergoing pediatric MRI scanning. Compared with propofol, however, dexmedetomidine did not induce the duration of sedation and might lead to a longer recovery time.

Keywords: Dexmedetomidine, propofol, general anesthetics, children, MRI, randomized controlled trials, meta-analysis

Introduction

In recent years, a growing number of pediatrics with complex medical conditions, such as the brain, spine, abdomen, and/or limbs, have proposed the multicomponent magnetic resonance imaging (MRI), much lengthy MRI scanning time for multi-body-part scan with frequent scanner coil changes and children body reposition are required [1]. Therefore, in the children MRI, deep sedation or anesthesia technology is demanded for eliminating movement. According to the current guidelines, the patient’s interests and security must be guaranteed [2].

Anesthesiologists can effectively use propofol for patients’ sedation and/or anesthesia [3, 4]. Undergoing MRI scanning, unlike other sedative drugs (such as pentobarbital, midazolam and fentanyl), propofol has a shorter emergence, faster induction and recovery, shorter duration in postanesthesia care unit (PACU) and less movement interference of patients [5-7]. However, an infusion of propofol, arterial desaturation and hypotension have been reported occasionally [8]. Aun CS et al. [9] concluded that, in the case of improper application of drug dose, propofol could cause bradycardia, respiratory depression and lose the protection of airway reflexes.

Dexmedetomidine, a highly selective α-2 adrenergic agonist, occasionally combined with midazolam, used to provide a better sedation, and it can become a wonderful alternative drug of propofol undergoing pediatric MRI scanning.
Dex vs Pro in children undergoing MRI

[10, 11]. Dexmedetomidine and propofol respectively reduced the incidence and severity of emergence delirium in children [12, 13]. Bong CL et al. [13] found that the incidence of emergence delirium was 10% in ambulatory surgery patients, but there were as much as 40% of the children in MRI and used sevoflurane as general anesthetic drug (unpublished data). However, Heard CM et al. [14] summarized that, in the process of MRI scans, if deep sedation anesthesia was required, whether dexmedetomidine could achieve adequate dose and the duration of recovery time were unforeseen. In addition, it was also pointed out, dexmedetomidine could lead to lower arterial pressure and increase the induction time and recovery time along with the occasional bradycardia, though rarely need for drug intervention [15, 16].

Before, several studies have made the contrast of dexmedetomidine and propofol in the clinical effects of pediatrics undergoing MRI. However, individual research results were not accurate enough. Therefore, we propose that systematically gathered all the available clinical research together, then increase understanding of the process as much as possible. Here, we proceeded to a meta-analysis to evaluate the efficacy of dexmedetomidine sedation for children undergoing MRI scanning, including all associated studies.

Methods

Electronic literature search strategy

Related articles in any language identification and selection through multiple electronic database searched including MEDLINE, Embase, The Cochrane library and Cochrane Central Register of Controlled Trials (CENTRAL), and updated to April 2015, and all bibliographies were identified in the reference lists to identify eligible studies. Key words included: “dexmedetomidine” and “propofol” and “MRI” or “magnetic resonance imaging” or “nuclear magnetic resonance”. The major international conference was hand-searched journal. Reference lists of articles also reviewed any additional research. The electronic search was conducted by two investigators (Hong-Wei Fang and Liu Yang) working independently. The abstracts of all articles identified as potential related retrieval and were examined in the study selection process.

Study selection

Inclusion criteria: The primary objective of this meta-analysis was to estimate the influence of dexmedetomidine and propofol for children undergoing magnetic resonance imaging, with respect to patient outcomes and adverse events. Only RCTs that met all of the following criteria were included: (1) the setting was patients’ age ≤ 18 years, and scheduled to undergo magnetic resonance imaging under general anesthesia; (2) the study compared dexmedetomidine with propofol for sedative therapy; and (3) the primary or secondary outcomes included recovery time, sedation time, The Pediatric Anesthesia Emergence Delirium (PAED) scores, hypotension, bradycardia, hypertension and/or other effects.

Exclusion criteria: We excluded studies if they (1) used dexmedetomidine or propofol for anesthesia plus other agents simultaneously in the same group, (2) included patients with developmental delay, cognitive impairment, behavioral or psychological disorders, severe central nervous system diseases including brain tumors or uncontrolled seizures, children who had received more than three general anesthetics previously, and children who required sedative premedication, and (3) did not report the specific results comparing dexmedetomidine with propofol. Divisions caused by the selection process were resolved that after consensus-based discussion.

Data extraction and risk of bias assessment

This part was done by the same two investigators, worked independently, and assessed, with any divisions being solved by consensus-based discussion involving a third investigator (Xiang-Rui Wang).

Extracted information included recovery time, the duration of sedation, overall side effects (i.e., PAED scores, hypotension, bradycardia, Post Operative Nausea and Vomiting (PONV), urine retention, respiratory depression, pruritus, and neurological complications). In inclusion/exclusion criteria research, those who provided data for at least one of the above consequences parameters were included in this analysis.

Carried out quality assessment of the studies contained in the present meta-analysis, we
used the Review Manager (REVMAN) software (version 5.2; The Nordic Cochrane Centre, Copenhagen, Denmark) constructed the ‘risk of bias’ table. The table included six parameters of bias, sequence generation (representing selection bias), allocation concealment (representing selection bias), blinding (representing performance bias or detection bias), incomplete data (representing attrition bias), and selective reporting (representing reporting bias). Classifying its risk of bias, each parameter would be split into “low”, “high” or “unclear” one of the three different levels.

Meta-analysis and statistical methods

Recovery time and duration of sedation data were recorded as mean (± standard deviation [SD]) in minutes. PAED scores of 5-min and 10-min data were recorded as mean (±SD) in scores. The minimum MAP was recorded as mean (±SD) in mmHg. The minimum HR and the minimum RR were recorded as mean (±SD) in rates. For continuous outcomes (Recovery time, Duration of sedation, PAED scores of 5-min and 10-min, the minimum MAP, the minimum HR and the minimum RR), the weighted mean difference (WMD) with 95% confidence interval (CI) was calculated. Besides, the WMD was considered statistically significant if the 95% confidence interval (CI) was not equal to 0 for the WMD.

In this meta, all statistical analysis used Review Manager to perform, the Cochrane Collaboration’s software preparation and maintenance of Cochrane systematic reviews. Being dependent on the absence or presence of significant heterogeneity, meta-analysis was selected fixed effect or random effect model. P-values < 0.10 were considered to be proof of heterogeneity, higher χ² and I² values prompted higher levels of inconsistencies, than the random effects model was utilized to compute. The summary estimates and 95% CIs were also calculated to assess clinical heterogeneity.

Results

Firstly, through keyword search of the electronic libraries, we determined 129 potentially relevant studies (Figure 1). Then, after retrieval and review of the articles’ abstracts, 113 studies were excluded depending on the title or abstract. Moreover, 6 articles were excluded in study design (i.e., not comparing dexmedetomidine with propofol alone), and a further 5 studies were excluded in that they did not examine children or patients with a history of obstructive sleep apnea (OSA). Therefore, 5 studies [15-19], with a total of 337 patients were enrolled in the meta-analysis. Evaluated trials included data published between July 2006 and August 2014. The characteristics of the identified studies were presented in Table 1. Risk assessment was set out in Table 2.

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Figure 1. Flowchart of the literature search.
### Table 1. Characteristics of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Included studies</th>
<th>Country</th>
<th>Patients</th>
<th>Procedure</th>
<th>Intervention (No.)</th>
<th>Outcomes used in this meta-analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmet Koroglu 2006</td>
<td>Turkey</td>
<td>1-7 y II</td>
<td>MRI</td>
<td>1 μg/kg initial dose followed by continuous infusion of 0.5 μg/kg/h (No. 30)</td>
<td>Recovery time, the minimum MAP, the minimum HR and the minimum RR after sedation</td>
</tr>
<tr>
<td>Byron Bernal 2012</td>
<td>USA</td>
<td>8 m-14 y unclear</td>
<td>MRI</td>
<td>Continuous infusion, mean dose 1.8 μg/kg/h (No. 24)</td>
<td>Recovery time, duration of sedation</td>
</tr>
<tr>
<td>C.L.Bong 2014</td>
<td>Singapore</td>
<td>2-7 y II</td>
<td>MRI</td>
<td>A single intravenous dose of Dex 0.3 μg/kg (No. 40)</td>
<td>Recovery time, duration of sedation, PAED scores of 5-min and 10 min after awakening</td>
</tr>
<tr>
<td>Jaydev Dave 2011</td>
<td>India</td>
<td>1-7 y II</td>
<td>MRI</td>
<td>1 μg/kg initial dose followed by continuous infusion of 0.5 μg/kg/h (No. 30)</td>
<td>Recovery time, the minimum MAP, the minimum HR and the minimum RR after sedation</td>
</tr>
<tr>
<td>Junzheng Wu 2014</td>
<td>USA</td>
<td>1-7 y II</td>
<td>MRI</td>
<td>2 μg/kg initial dose followed by continuous infusion of 2 μg/kg/h (No. 46)</td>
<td>Recovery time, duration of sedation, PAED scores of 5-min and 10 min after awakening</td>
</tr>
</tbody>
</table>

ASA, American Society of Anesthesiology; MRI, Magnetic Resonance Imaging; PAED, the Pediatric Anesthesia Emergence Delirium.
Primary outcome

Recovery time: Recovery time was evaluated in five studies. All of them showed a longer mean recovery time in the dexmedetomidine group, the pooled mean difference between dexmedetomidine and propofol groups was 10.70 min (95% CI: 4.26 to 17.13; P = 0.001), which suggested a statistically significant difference between the two groups. However, the χ² and I² were 18.26 (P = 0.001) and 78%, which indicated heterogeneity among the studies (Figure 2A).

Duration of sedation: Three trials evaluated the effect of dexmedetomidine on the duration of sedation compared with that of propofol [17-19], of which three reported mean (±SD) duration time. The combined data suggested that the use of dexmedetomidine for sedation of
patients undergoing MRI did not appear to increase the GA time compared with that of propofol (WMD: 19.96 min; 95% CI: -4.12-44.04; \( P = 0.1 \)), but manifested heterogeneity of statistical evidence among the studies (\( \chi^2: 14.53; I^2: 86\% \)) (Figure 2B).

Secondary outcomes

PAED scores by follow-up time since awakening: Complications of PAED scores by follow-up time since awakening were recorded in two studies. [17, 18]. Both studies included PAED scores of 5-min after awakening and 10-min after awakening. There were statistically significant increase in PAED scores of 5-min after awakening (WMD: 2.40; 95% CI: 1.00 to 3.81; \( P = 0.0008 \)) (Figure 3A) and PAED scores of 10-min after awakening (WMD: 3.06; 95% CI: 1.81 to 4.31; \( P < 0.00001 \)) (Figure 3B) in dexmedetomidine group compared with propofol group.

Hemodynamic changes: Two studies with a total of 120 children reported the mean arterial blood pressure (MAP), heart rate (HR) and respiratory rate (RR) after sedation [15, 16]. Due to a different norm for hypotension, bradycardia and respiratory depression, only the minimum MAP, the minimum HR and the minimum RR after sedation were eligible for inclusion in the present meta-analysis.

Between dexmedetomidine and propofol group, there was no statistically significant difference about the minimum HR (WMD: -0.05; 95% CI: -2.53 to 2.44; \( P = 0.97 \)) (Figure 4B). However, there were statistically significant increase in the minimum MAP (WMD: 3.92; 95% CI: 2.44 to 5.40; \( P < 0.00001 \)) (Figure 4A) and the minimum RR (WMD: 2.98; 95% CI: 2.02 to 3.94; \( P < 0.00001 \)) (Figure 4C) in the dexmedetomidine group compared with the propofol group.

Duration of MRI scanning and discharge time were assessed respectively in three [15-17] or two studies [15, 16]. Between dexmedetomidine and propofol group, there was no statistically significant difference about the duration of MRI scanning (WMD: 1.09; 95% CI: -3.44 to 5.62; \( P = 0.64 \)) (Supplementary Figure 1A). On the contrary, there were statistically significant prolong in the discharge time (WMD: 12.74; 95% CI: 8.10 to 17.37; \( P < 0.00001 \)) (Supplementary Figure 1B) in the dexmedetomidine group compared with the propofol group.

Discussion

Our meta-analysis included five studies, and the purpose of this study was tantamount to investigate the difference of the recovery time, the duration of sedation and possible complications of intravenous infusion of dexmedetomidine as sedative drug for pediatric used when compared with propofol.
This meta-analysis conclusively revealed that dexmedetomidine significantly increased the recovery time and PAED scores by follow-up time since awakening (i.e., PAED scores of 5-min or 10-min after awakening) compared with propofol, whereas there was no difference in the duration of sedation between the two agents. In addition, compared with propofol, after transfusing dexmedetomidine, the pooled analysis proposed that the induction degree of hemodynamics changed (i.e., the minimum MAP and the minimum RR).

Unlike with GABA receptor agonists, dexmedetomidine, a highly selective α-2 adrenergic agonist, through a unique binding with α-2 receptor produces its pharmacological effects, and Gerresheim G [20] detected this may explain how it improved clinical outcomes. Dexmedetomidine could also reduce the demand of opiate drugs, thereby reducing the risk of over sedation associated with it [21]. However, children with obstructive sleep apnea syndrome (OSAS), compared with dexmedetomidine and propofol for MRI sleep induction, showed that effective calm without the need for extra airway device was 88.5 versus 70% [22]. Koroglu A et al. [15] and Dave J et al. [16] had concluded that dexmedetomidine could increase recovery time in 60 pediatrics between 1 and 7 years old in successful MRI scanning. Our sensitivity analysis showed that the recovery time was extended for patients, dexmedetomidine in decreasing recovery time there was no advantage.

To assess an emergence delirium, the PAED scale was developed for producing a reliable and effective measurement tool, by observing restlessness, eye contact, inconsolability, the purposeful actions and consciousness of the environment [23, 24]. Separate studies showed that both propofol and dexmedetomidine could reduce the occurrence of delirium [25, 26]. In C. L. Bong’s study, measuring appear delirium with PEAD scale, dexmedetomidine group in the incidence of delirium was not different from the propofol group [18]. Patel A et al. [27] summarized that dexmedetomidine infusion could effectively provide analgesia and prevent emergence delirium, in their children with OSAS undergoing tonsillectomy and adenoidectomy. In this meta-analysis, only two articles recorded the PAED scores by follow-up time since awakening. Contrasted with propofol, dexmedetomidine did not significantly reduce PAED scores by follow-up time since awakening.

Numerous studies had demonstrated that infusion of dexmedetomidine and propofol commonly used for procedural sedation in pediatric MRI scanning. Hemodynamic changes were frequent adverse effects of dexmedetomidine and propofol. Moreover, in the clinical application, dexmedetomidine, the most serious disadvantage is the adverse effects of hemodynamic, but these effects also have conflicting reports [28, 29]. Mason KP et al. [30] had concluded that using high-dose dexmedetomidine (a 10-min loading dose of 2-3 μg/kg/h) was associated with reduce in heart rate and blood pressure outside the set up ‘awake’ norms, the standard deviation was in commonly 20%, no adverse sequelae. Propofol was upheld, it could cause bradycardia, respiratory depression, loss of airway protection reflection, and other related side effects in the case of improper dosage [9, 31]. However, our meta-analysis of dexmedetomidine sedation versus propofol in pediatric MRI scanning recorded hemodynamic changes in only two studies unfortunately. Estimation based on the two trials, involving 120 patients, the minimum MAP and the minimum RR had significantly increased in the dexmedetomidine group compared to the propofol group.

We acknowledge that several limitations are worthy of discussion in this meta-analysis. Firstly, only four relevant individual RCTs are integrated with the results; our conclusions are still based on a relatively small amount of studies. Secondly, in all included studies, dexmedetomidine and propofol sedation management were not the equivalent method (Table 1). In C. L. Bong study, [18] 120 patients were randomly allocated to receive a single intravenous infusion, respective dose of dexmedetomidine 0.3 g/kg or propofol 1 mg/kg. This may be considered as a source of heterogeneity. Thirdly, different definition of calm goals and protocols were used for all experimental research. Moreover, caused by inadequate sedation, the different additional supplementary methods may lead to an uncertain result, especially for the duration of recovery time. In addition, the impact of publication bias cannot be neglected. Finally, between these two kinds of sedatives,
some drugs related other important parameters were not included in this meta-analysis, caused by a lack of data, may make this research underpowered to test and did not reveal a statistically significant difference.

In summary, for improved the prognosis of patients, nonetheless, dexmedetomidine must have an indispensable role in pediatric MRI scanning. However, compared with propofol, dexmedetomidine did not induce the duration of sedation, and application of dexmedetomidine might result in a longer recovery time. Due to transient hemodynamic changes (i.e., hypotension, bradycardia and respiratory depression), PAED, PONV, pruritus, and neurological complications, which can be avoided by appropriately controlling infusion rates of dexmedetomidine. Larger samples, higher quality RCTs of dexmedetomidine are needed, with a focus on the recovery time, failure rates or quality of MRI scanning and PAED scores analysis.

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Disclosure of conflict of interest

None.

Address correspondence to: Drs. Xiang-Rui Wang and Hao Zhu, Department of Anesthesiology, Renji Hospital, School of Medicine, Shanghai Jiaotong University, 1630 Dongfang Road, Shanghai 200127, China. Tel: + 86 21 68383198; Fax: +86 21 509-03239; E-mail: xiangruiwang@gmail.com (XRW); zhuhaossmu@163.com (HZ)

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Supplementary Figure 1. Effect of dexmedetomidine versus propofol on (A) duration of MRI scanning and (B) discharge time.