Online Review Article

Dexmedetomidine for Prolonged Sedation in the PICU: A Systematic Review and Meta-Analysis*

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Objectives: We aimed to systematically describe the use of dexmedetomidine as a treatment regimen for prolonged sedation in children and perform a meta-analysis of its safety profile.

Data Sources: PubMed, EMBASE, Cochrane Library, Scopus, Web of Science, ClinicalTrials.gov, and CINAHL were searched from inception to November 30, 2018.

Study Selection: We included studies involving hospitalized critically ill patients less than or equal to 18 years old receiving dexmedetomidine for prolonged infusion (≥ 24 hr).

Data Extraction: Data extraction included study characteristics, patient demographics, modality of dexmedetomidine use, associated analgesia and sedation details, comfort and withdrawal evaluation scales, withdrawal symptoms, and side effects.

Data Synthesis: Literature search identified 32 studies, including a total of 3,267 patients. Most of the studies were monocentric (91%) and retrospective (88%); one was a randomized trial. Minimum and maximum infusion dosages varied from 0.1–0.5 μg/kg/hr to 0.3–2.5 μg/kg/hr, respectively. The mean/median duration range was 25–540 hours. The use of a loading bolus was reported in eight studies (25%) (range, 0.5–1 μg/kg), the mode of weaning in 11 (34%), and the weaning time in six of 11 (55%; range, 9–96 hr). The pooled prevalence of bradycardia was 2.6% (n = 10 studies; 14/387 patients; 95% CI, 0.3–7.3; I^2 = 75%), the pooled prevalence incidence of bradycardia was 2.6% (n = 10 studies; 14/387 patients; 95% CI, 0.3–7.3; I^2 = 75%), the pooled incidence of hypotension was 6.1% (n = 8 studies; 19/304 patients; 95% CI, 0.8–15.9; I^2 = 84%). Three studies (9%) reported side effects' onset time which in all cases was within 12 hours of the infusion starting.

Conclusions: High-quality data on dexmedetomidine use for prolonged sedation and a consensus on correct dosing and weaning protocols in children are currently missing. Infusion of dexmedetomidine can be considered relatively safe in pediatrics even when longer than 24 hours. (*Pediatr Crit Care Med* 2020; 21:e467–e474)

Key Words: bradycardia; dexmedetomidine; hypotension; pediatric intensive care unit; prolonged sedation; side effects

Dexmedetomidine is a highly selective α2-receptor agonist, with a structure similar to clonidine but with a higher α2:α1 specificity of nearly 1,600:1. It also has a shorter half-life, which allows titration by continuous infusion (1). These unique characteristics allowed intensive care physicians to recently introduce dexmedetomidine in the pediatric critical care setting as an off-label alternative agent to induce sedation and provide analgesia.

Dexmedetomidine received U.S. Food and Drug Administration approval in 1999 for sedation of mechanically ventilated adult patients in the intensive care setting for up to 24 hours or for procedural sedation. Dexmedetomidine displayed the potential to be used in pediatric critical care for prolonged sedation with the aim to maintain adequate comfort reducing the side effects of other sedatives. However, dexmedetomidine has possible side effects mainly associated with the cardiovascular system, for example, bradycardia and hypotension, which should be taken into consideration (2, 3). Furthermore, most of the pediatric experience with dexmedetomidine use was carried out in United States, probably secondary to the availability of the drug more than 10 years before Europe where the marketing authorization was granted only in September 2011 (4, 5).

In light of these limits of dexmedetomidine use in the pediatric population, the modality and safety of dexmedetomidine use for prolonged sedation in children have not been rigorously evaluated. Previous reviews and meta-analysis included only adult populations, were limited to specific indication or criteria, or were focused on different outcomes (6–9). We performed a systematic review of all published studies on the use

*See also p. 704.

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DOI: 10.1097/PCC.0000000000002325

of prolonged infusion of dexmedetomidine in patients admitted to the PICU, with the aim to describe its current practice in the pediatric age group. In addition, we performed a prevalence meta-analysis on its cardiovascular side effects.

MATERIALS AND METHODS

Study Design

We performed a systematic review of studies reporting data on dexmedetomidine use for prolonged sedation in critically ill patients less than or equal to 18 years. We also performed a prevalence-rate meta-analysis of the most common cardiovascular side effects of dexmedetomidine. This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (10).

Search Strategy

Two authors (M.D., Z.L.) independently performed an extensive search of the literature through MEDLINE, EMBASE, Scopus, CINAHL, Web of Science, Cochrane Library, and ClinicalTrials.gov. Our strategy used terms covering the drug dexmedetomidine and pediatric age. Details of the search strategy are reported in **Table S1** (Supplemental Digital Content 1, http://links.lww.com/PCC/B298). Bibliographic records are updated to November 30, 2018.

Inclusion Criteria

Studies were eligible for full-text review if they involved hospitalized critically ill patients less than or equal to 18 years old receiving dexmedetomidine for prolonged infusion for a mean/median or minimum length of infusion greater than or equal to 24 hours. Eligible study designs included quantitative studies, such as randomized controlled trials, controlled or uncontrolled before-and-after studies and time series, and cohort studies.

Exclusion Criteria

We excluded review articles, case series (< 4 cases), letters, editorials, notes, conference abstracts, studies conducted on animal models, opinion articles, and articles with unavailable full text. We also excluded studies addressing dexmedetomidine use in adults or both in adults and children where pediatric data could not be extracted. Studies were also excluded if they involved only neonates, as they form a distinct group with different pharmacokinetic, pharmacodynamic, and sedative requirements. Finally, we excluded studies in which data on infusion time were unclear or not available.

Study Selection

The study selection was conducted independently by two investigators (M.D., Z.L.) both at "title and abstract" and "full text" level. Three rounds of article assessment were conducted before selecting the final list for data extraction. After the third round, relevant papers cited in the reference list of the included articles were evaluated and included in the selection if they fulfilled the eligibility criteria. Any differences in opinion regarding inclusion criteria were resolved by discussion.

Data Collection

Data extraction included study characteristics, patient demographics, modality of dexmedetomidine use, associated analgesia and sedation details, comfort and withdrawal evaluation scales, withdrawal symptoms, and side effects. When the required data on the outcome measures were not present or unclear, we contacted the study corresponding author for clarity. If no response to correspondence was obtained, only the clear available data were included.

Quality Assessment

Each included study was analyzed for quality using the 14-item National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies checklist (**Table S2**, Supplemental Digital Content 2, http://links.lww.com/PCC/B299) (11). We omitted item 10, as it was not applicable to the included observational studies. Two investigators (M.D., Z.L.) independently rated each study quality as poor, fair, or good. We then calculated the percentage of agreement to measure the overall agreement between the reviewers reporting the CI using the binomial method. We then calculated percentage agreement and a weighted k to measure overall agreement between the two independent reviewers' assessments of study quality with level of agreement interpreted as follows: 0.81–1.00 almost perfect, 0.61–0.80 substantial, 0.41–0.60 moderate, 0.21–0.40 fair, and 0–0.20 slight (12). Any disagreement between investigators about overall quality assessment was resolved via consensus with a third investigator (A.A.).

Quantitative Analysis: Prevalence Meta-Analysis

We performed a quantitative analysis of the frequency of the most common dexmedetomidine side effects which were identified as the presence of clinically significant bradycardia and hypotension. Significance was defined as when bradycardia or hypotension needed to be rectified with any intervention. In order to reduce the heterogeneity of the results, the meta-analysis included only studies of patients receiving dexmedetomidine for a minimum length of greater than or equal to 24 hours.

Statistical Analysis

To describe the overall characteristics of the studies, we performed a descriptive analysis of data reporting frequencies and percentages for qualitative data, as well as ranges for quantitative variables.

To calculate the pooled-prevalence data, we quantified the heterogeneity across studies using the I^2 statistic. I^2 levels were defined as follows: potentially unimportant (0–19%), moderate (20–49%), substantial (50–79%), and considerable heterogeneity (> 80%). We assessed the publication bias using both the visual inspection of the funnel plot and the Egger test. We therefore calculated a random-effects pooled-prevalence for both bradycardia and hypotension as a proportion with 95% CI (13).

Data were entered into an Excel database (Microsoft Office 365; Microsoft Corporation, Redmond, WA) and all the

analyses were conducted using the SAS 9.4 statistical software (SAS Institute, Cary, NC).

RESULTS

Study Selection and Characteristics

A total of 8,865 potential records were identified by searching the reference databases. Finally, 32 studies met the inclusion criteria and 18 studies reported the use of dexmedetomidine for a minimum time greater than or equal to 24 hours (**Fig. 1**) (14–45).

The majority of studies were monocentric (91%) and retrospective (88%); one was a randomized controlled trial. The vast majority of the studies (25/32, 78%) were performed in the United States. Two studies (6%) were registry-based. Characteristics of the studies are reported in **Table S3** (Supplemental Digital Content 3, http://links.lww.com/PCC/B300).

Quality Assessment

On the three-level quality scale, we judged the majority of the included studies (29/32, 91%) to be fair or good (Table S3, Supplemental Digital Content 3, http://links.lww.com/PCC/B300). Reviewers' classifications of quality were concordant in 27 of 32 studies (percentage agreement, 84.4%; 95% CI, 67.2–94.7%] for a substantial overall agreement (weighted k statistic 0.72) (Table S2, Supplemental Digital Content 2, http://links.lww.com/PCC/B299).

Dexmedetomidine Use

Overall, a total of 3,267 patients were included in the analysis with a median age from 4 months to 6.2 years. Among patients with available demographic and clinical data, the majority were males (1,613/2,992, 54%) and noncardiac medical patients (1,474/2,840, 52%).

Dexmedetomidine was used as monotherapy in three studies (11%). When used in polytherapy, details of associated analgesics and sedatives were reported in 26 of 29 studies (90%). The main drugs associated were opioids (23/26, 88%) and benzodiazepines (15/26, 58%).

Indications for dexmedetomidine use were reported in 28 studies (88%) and the most frequent indications were: adjuvant for drugs sparing (11/28, 39%), first-line drug for sedation (10/28, 36%), failure of first-line drugs for sedation (8/28, 29%), facilitation to extubation (6/28, 21%), adjuvant for analgesic and sedation weaning (5/28, 18%), and adjuvant for treatment of withdrawal (2/28, 7%). The use of a scale for monitoring the level of sedation was reported in 16 of 32 studies (50%), which were validated scales in 11 of 16 studies (State Behavioral Scale [four studies], Comfort Behavioral Scale [two studies], Richmond Agitation-Sedation Scale [two studies], Ramsay Sedation Scale [two studies], Riker Sedation-Agitation Scale [one study]) and local/internal scales for five studies. The use of a validated withdrawal scale (Withdrawal Assessment Tool-1) was reported in three of 32 studies (9%).

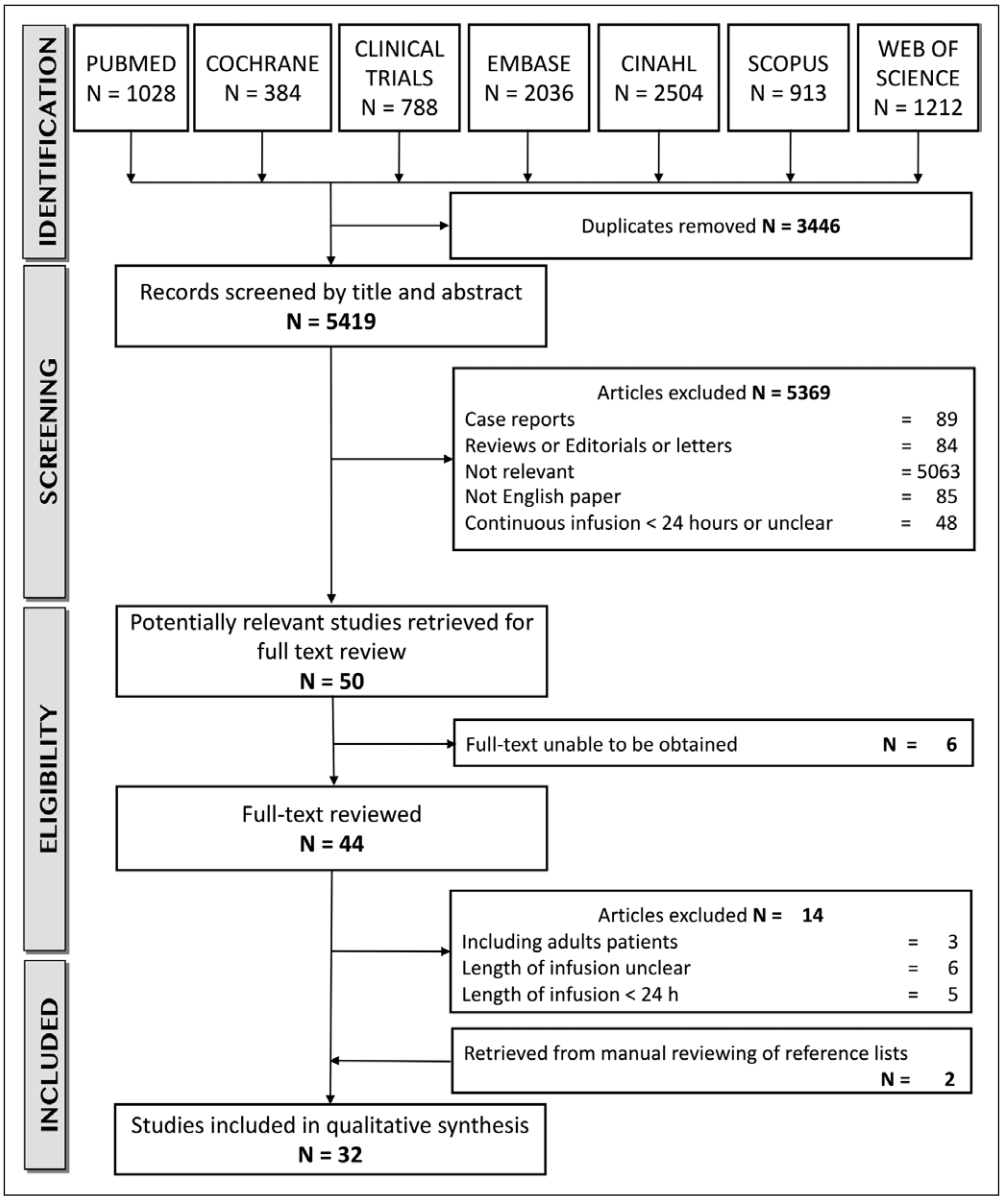

Figure 1. Flowchart of study selection process.

Minimum and maximum infusion dosages ranges were 0.1–0.5 µg/kg/hr and 0.3–2.5 µg/kg/hr respectively, while mean/median duration range was 25–540 hours. The use of a loading bolus was reported in eight studies (ranged 0.5–1 µg/kg).

The modality of dexmedetomidine weaning was reported in 11 of 32 studies (34%) for a total of 1,245 patients. The weaning was reported as mixed, both abrupt and gradual, in six of 11 (55%) of the studies, only abrupt in one of 11 (9%), and only gradual in four of 11 (36%). The weaning time was reported in six of 11 studies (55%) with a range of time between 9 and 96 hours.

Less than half of the studies reported sedation-withdrawal symptoms (14/32, 44%), which were present in 0–27% of patients. Dexmedetomidine rebound effects were reported in 11 of 32 studies (34%) and were present in 0–24% of patients.

Dexmedetomidine Safety Profile

The most frequent side effects were bradycardia and hypotension (**Table 1**). The main interventions for significant bradycardia were dexmedetomidine dose reduction (36/58, 62.1%) and dexmedetomidine discontinuation (15/58, 25.9%). The main interventions for significant hypotension were the administration of a fluid bolus (51/78, 65.4%) and dexmedetomidine reduction dose (36/78, 46.2%). The onset time of bradycardia and hypotension was registered in three of 32

TABLE 1. Type of Patients, Side Effects, Interventions, and Time of Onset in Patients Receiving Dexmedetomidine for Prolonged Sedation

References	Total No. of Patients	Type of Patients Receiving Dexmedetomidine[a] (*n*)	Bradycardia, *n* (%)	Intervention for Bradycardia (*n*)
Andreolio et al (14)	77	a (19), b (53), d (5)	1 (1)	Stop infusion (1)
Banasch et al (15)	219	NA	47 (22)	NA
Bejian et al (16)	54	c (54)	0 (0)	Not app
Buck and Willson (17)	17	a (1), b (2), c (13), d (1)	0 (0)	Not app
Burbano et al (18)	62	c (56), d (6)	5 (8)	Pacing for atrioventricular block (3); NA (2)
Chrysostomou et al (19)	80	c (80)	1 (1)	Stop infusion (1)
Estkowski et al (20)	99	a (15), b (84)	55 (56)	Stop infusion (3)
Fagin et al (21)	21	b (21)	1 (5)	Stop infusion (1)
Gupta et al (24)	52	c (40), d (12)	0 (0)	Not app
Horvath et al (26)	107	c (107)	3 (3)	Stop infusion (3)
Jiang et al (27)	77	c (77)	3 (4)	Stop infusion (3)
Kalyanaraman et al (28)	5	c (5)	1 (20)	Stop infusion (1)
Lam et al (29, 30)	21	d (21)	1 (5)	Stop infusion (1)
Lee et al (32)	5	b (5)	1 (20)	Dose reduction (1)
Lin et al (33)	17	b (11)	1 (6)	NA
Piotrowski et al (35)	33	a (12), b (19), d (2)	2 (6)	Dose reduction (1), stop infusion (1)
Sperotto et al (40)	47	a (6), b (39), c (2)	21 (45)	Dose reduction (7)
Tokuhira et al (42)	9	c (9)	4 (44)	Pacing (4) (already in place for cardiac surgery)
Venkatraman et al (43)	202	b (202)	26 (13)	Dose reduction (26)
Walker et al (44)	65	b (65)	0 (0)	Not app
Whalen et al (45)	98	a (NA), b (NA), c (NA), d (NA)	0 (0)	Not app

NA = not available, not app = not applicable.

[a]a = noncardiac surgical patients, b = noncardiac nonsurgical patients, c = cardiac surgical patients, and d = cardiac nonsurgical patients.

studies (9%). In all cases, their occurrence was reported within 12 hours after the start of the infusion. Details of side effects are reported in Table 1.

Among studies including patients with a minimum length of infusion greater than or equal to 24 hours, 10 studies (56%) reported on the occurrence of significant bradycardia during dexmedetomidine infusion.

Overall, 14 of 387 patients (proportion range, 0–15%) developed significant bradycardia. The pooled estimate prevalence of bradycardia was 2.6% (95% CI, 0.3–7.3; I^2 = 75%) (**Fig. S1*a***, Supplemental Digital Content 4, http://links.lww.com/PCC/B301; **legend**, Supplemental Digital Content 6, http://links.lww.com/PCC/B303).

Eight studies (44%) reported on the occurrence of significant hypotension during dexmedetomidine infusion. Overall, 19 of 304 patients (proportion range, 0–80%) developed significant hypotension. The pooled estimate prevalence of hypotension was 6.1% (95% CI, 0.8–15.9%; I^2 = 84%) (**Fig. S2*a***, Supplemental Digital Content 5, http://links.lww.com/PCC/B302; legend, Supplemental Digital Content 6, http://links.lww.com/PCC/B303).

A subgroup analysis of studies including only cardiac patients (both medical and surgical diseases) showed the following results: 1) four studies (22%) reported on the occurrence of significant bradycardia with a pooled estimate prevalence of 3.0% (95% CI, 0.03–10.5%; I^2 = 64%) (**Fig. S1*b***, Supplemental Digital Content 4, http://links.lww.com/PCC/B301;

Hypotension, *n* (%)	Intervention for Hypotension (*n*)	Other Side Effects (*n*)	Intervention (*n*)	Time of Onset
4 (5)	Stop infusion (4)	Somnolence (1)	Stop infusion (1)	NA
59 (27)	NA	No	Not app	NA
0 (0)	Not app	No	Not app	Not app
0 (0)	Not app	No	Not app	Not app
9 (15)	NA	No	Not app	NA
1 (1)	Stop infusion (1)	No	Not app	At 8 and 11 hr
30 (30)	Fluid bolus (12)	No	Not app	NA
NA	Not app	No	Not app	NA
0 (0)	Not app	Accelerated junctional rhythm (1)	Stop infusion (1)	NA
1 (1)	Stop infusion (1)	Hypertension (1); hypopnea (1)	Stop infusion (1)	NA
NA	Not app	No	Not app	NA
1 (20)	Stop infusion (1)	No	Not app	NA
2 (10)	Dose reduction + inotropes (2)	No	Not app	Within 3 hr
4 (80)	Dose reduction (4)	No	Not app	NA
NA	NA	No	Not app	NA
0 (0)	Not app	No	Not app	NA
7 (15)	Dose reduction (5)	No	Not app	NA
0 (0)	Not app	No	Not app	NA
41 (20)	Dose reduction (25), fluid bolus (32)	Hypopnea (136); cardiac arrest (1)	Titration administration (1); cardiopulmonary resuscitation (1)	NA
0 (0)	Not app	No	Not app	Not app
7 (7)	Fluid bolus (7)	No	Not app	Within 4 hr

legend, Supplemental Digital Content 6, http://links.lww.com/PCC/B303) and 2) three studies (17%) reported on the occurrence of significant hypotension with a pooled estimate prevalence of 4.5% (95% CI, 0.00–22.4; I^2 = 76%) (**Fig. S2*b***, Supplemental Digital Content 5, http://links.lww.com/PCC/B302; legend, Supplemental Digital Content 6, http://links.lww.com/PCC/B303).

Bias Assessment

For bradycardia, two studies laid outside of the funnel plot (Fig. S1a, Supplemental Digital Content 4, http://links.lww.com/PCC/B301; legend, Supplemental Digital Content 6, http://links.lww.com/PCC/B303). The *p* value for Egger test was 0.187. For hypotension, three studies laid outside of the funnel plot (Fig. S1b, Supplemental Digital Content 4, http://links.lww.com/PCC/B301; legend, Supplemental Digital Content 6, http://links.lww.com/PCC/B303). The *p* value for Egger test was 0.325.

DISCUSSION

In the absence of definite guidelines and clear safety data on the use of dexmedetomidine for prolonged sedation in children, we conducted a systematic review and meta-analysis of side effects to clarify its most frequent modalities of use and safety profile.

A previous narrative review focusing on dexmedetomidine used for prolonged sedation included five studies on the pediatric population and showed a lack of knowledge in this field (7). Our systematic review seeks to address this gap and reflects an increased interest in this new agent over recent years. However, the vast majority of data resulted from retrospective and monocentric studies which have intrinsic biases. We identified only one randomized controlled trial and a retrospective analysis of a prospective multicenter study (23, 39). The randomized trial included 108 patients treated with dexmedetomidine or placebo before cardiac surgery and evaluated the effect of dexmedetomidine on the occurrence rate of paradoxical hypertension after surgical repair of isolated aortic coarctation. A reduction in anti-hypertensive drug use after surgical repair was demonstrated in patients receiving dexmedetomidine, with a slight increase in the risk of bradycardia and hypotension. However, this small and specific population may not be generalizable and precludes any definite conclusions about the dexmedetomidine safety profile (39). The wider study included in our report was a retrospective analysis of prospectively collected multicenter data comparing the usual sedation care to a nurse-implemented goal-directed sedation algorithm in children with acute respiratory failure. This study demonstrated the possible role of dexmedetomidine used as a primary sedative to reach a targeted sedation in "low critically" patients (i.e., patients with a lower value of Pediatric Risk of Mortality III-12 scores compared with the population of patients receiving dexmedetomidine as a secondary sedative or as a periextubation agent) at a rapid rate, as well as reduced length of ventilation in children intolerant to an awake-intubated state. However, this study is limited by the fact that the results are a secondary analysis of previously collected data and does not provide detailed data on dexmedetomidine adverse events, weaning modality, or presence of rebound symptoms (23).

Most of the studies included in our analysis were implemented in United States, most likely due to the earlier availability of dexmedetomidine compared with Europe, where the marketing authorization was granted only in September 2011 (4, 5). Populations included were cohorts of patients of all postnatal ages and with different medical or surgical diagnosis, again demonstrating the increased interest in this agent in different medical contexts.

Overall, data on the indication for starting dexmedetomidine in pediatric age appear accurately reported, highlighting a wide number of different possible indications that mirror its potentiality as analgo-sedative drug. This again emphasizes that dexmedetomidine can be widely implemented in all phases of sedation management.

Dexmedetomidine was used as monotherapy in three retrospective studies for various indications such as noninvasive ventilation, burns patients and in cardiac patients after Fontan procedure (21, 38, 42). These studies presented interesting opportunities for dexmedetomidine use, even though its efficacy in monotherapy remains unclear. In fact, a recent randomized trial involving adult patients did not demonstrate a greater efficacy of dexmedetomidine used as monotherapy or first sedative compared with the usual care of sedation (46). Further prospective studies involving pediatric populations are needed in order to understand its potential as monotherapy in children.

Dosages and length of dexmedetomidine infusion were systematically reported, showing a wide range of dosages and demonstrating a lack of consensus. The low number of studies reporting a bolus dose demonstrated a lack of agreement. Weaning modality and time of weaning were underreported and protocols were mostly unclear.

Our review has shown that in less than half of the studies, there was a reported use of validated scales to evaluate the level of sedation and the presence of withdrawal syndrome from any of the sedatives received during the sedation management. The absence of a validated scale to evaluate dexmedetomidine's withdrawal syndrome could have led to a reduction in the number of reports with available data on this topic; on the other hand, the lack of a systematic use of sedation and withdrawal scales is an emerging issue pointed out by various studies also for other "conventional" sedatives (47, 48). We strongly encourage an effort in education in using appropriate validated tools and we believe that data on sedation level and withdrawal symptoms are imperative to improve dexmedetomidine use and patients' care.

Few studies reported a clear definition of the safety profile for dexmedetomidine, especially for hypotension and bradycardia, which made comparisons between studies difficult and resulting in an elevated heterogeneity of the meta-analysis data. Some other studies lacked a systematic recording system for side effects and most of the studies were retrospective and not designed to evaluate these outcomes. We therefore decided

to include only studies presenting side effects related with the need of any intervention in our meta-analysis to provide more appropriate insight for clinical practice and decision-making for the physician working in the intensive care setting.

The pooled prevalence of significant bradycardia and hypotension demonstrated a relatively low frequency of these events. Furthermore, these events were easily reversible in the majority of cases with dose reduction, interruption of the infusion or administration of a fluid bolus in case of hypotension. Therefore, the low frequency of such events should reassure clinicians of the risks of dexmedetomidine for prolonged sedation in the pediatric population, while maintaining strict monitoring during the first hours of the infusion.

The presence of hemodynamic rebound signs after drug suspension, that is, tachycardia and hypertension, was rarely reported. Further research is needed to define this aspect for different dosages of dexmedetomidine or in different categories of patients. Other possible signs of dexmedetomidine withdrawal were not clearly reported. In fact, in the majority of studies, patients received a sedation with various drugs in association with dexmedetomidine. Since onset of withdrawal symptoms was not clearly reported, it is unclear to which drug these symptoms should be attributable. On the other hand, another recent study suggested a possible role of dexmedetomidine in reducing the occurrence of opioids or sedatives withdrawal symptoms in pediatric patients (49), suggesting that the relation between dexmedetomidine and withdrawal symptoms could be more complex than expected. The implementation of a prospective randomized controlled trial in this area seems to be an urgent need.

Our results must be interpreted in the context of some limitations. Despite a broad search strategy and manually reviewed references in an endeavor to capture all the available data, there is a possibility that we may have missed associated studies. There is also a limitation by the lack of quality published studies and data in this area. Some articles reported missing information, and we were not able to recover them even with attempts at contacting the authors. The majority of studies in this review were also monocentric and retrospective which may affect the data. Furthermore, we found considerable heterogeneity between the included studies which may have impacted our ability to combine them; therefore, we put in place some strategies in order to reduce the I^2 score (i.e., subgroup analysis). With respect to publication bias of the included studies in the meta-analyses, inspection of the Figure 1, *A* and *B*, shows visual symmetry of the funnels, suggesting that publication bias was unlikely to significantly affect the results of our meta-analysis. It should be noted that the accuracy of this approach for detecting publication bias is not optimal when less than 10 studies are included (50). We therefore reported the *p* values of Egger test that indicate absence of statistical significance for funnel's asymmetry. Finally, bradycardia and hypotension criteria varied widely between studies, as well as the withdrawal symptoms evaluation. However, we believe that our work accurately represents the currently available data we have on the use of continuous infusions of dexmedetomidine in children.

CONCLUSIONS

High-quality data on dexmedetomidine use for prolonged sedation in children are currently missing. Indications reported were variable, suggesting a high potentiality of this drug as prolonged infusion agent. There was a lack of consistency on dosages and weaning protocols. Bradycardia and hypotension were relatively rare, even in younger ages, and seemed to be easily reversible with simple interventions. Overall, infusions of dexmedetomidine can be considered relatively safe in pediatric age even when longer than 24 hours.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/pccmjournal).

The authors have disclosed that they do not have any potential conflicts of interest.

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