Intensive Care Med (2013) 39:1524–1534
DOI 10.1007/s00134-013-2971-3

SYSTEMATIC REVIEW

Nienke J. Vet
Erwin Ista
Saskia N. de Wildt
Monique van Dijk
Dick Tibboel
Matthijs de Hoog

Optimal sedation in pediatric intensive care patients: a systematic review

Received: 12 March 2013
Accepted: 18 May 2013
Published online: 19 June 2013
© Springer-Verlag Berlin Heidelberg and ESICM 2013

N. J. Vet (✉) · E. Ista · S. N. de Wildt · M. van Dijk · D. Tibboel · M. de Hoog
Intensive Care, Erasmus MC, Sophia Children's Hospital, Dr. Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands
e-mail: n.vet@erasmusmc.nl
Tel.: +31-10-7036922

N. J. Vet · E. Ista · M. de Hoog
Department of Pediatrics, Erasmus MC, Sophia Children's Hospital, Dr. Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands

S. N. de Wildt · M. van Dijk · D. Tibboel
Department of Pediatric Surgery, Erasmus MC, Sophia Children's Hospital, Dr. Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands

Abstract *Purpose:* Sedatives administered to critically ill children should be titrated to effect, because both under- and oversedation may have negative effects. We conducted a systematic review to examine reported incidences of under-, optimal, and oversedation in critically ill children receiving intensive care. *Methods:* A systematic literature search using predefined criteria was performed in PubMed and Embase to identify all articles evaluating level of sedation in PICU patients receiving continuous sedation. Two authors independently recorded: study objective, study design, sample size, age range, details of study intervention (if applicable), sedatives used, length of sedation, sedation scale used, and incidences of optimal, under-, and oversedation as defined in the studies. *Results:* Twenty-five studies were included. Two studies evaluated sedation level as primary study outcome; the other 23 as secondary outcomes. Together, these studies investigated 1,163 children; age range, 0–18 years. Across studies, children received many different sedative agents and sedation level was assessed with 12 different sedation scales. Optimal sedation was ascertained in 57.6 % of the observations, under sedation in 10.6 %, and oversedation in 31.8 %. *Conclusions:* This study suggests that sedation in the PICU is often suboptimal and seldom systematically evaluated. Oversedation is more common than undersedation. As oversedation may lead to longer hospitalization, tolerance, and withdrawal, preventing oversedation in pediatric intensive care deserves greater attention.

Keywords Pediatrics · Intensive care · Sedation · Clinical pharmacology

Introduction

The provision of adequate sedation and analgesia to critically ill children is an important aspect of care in the pediatric intensive care unit. Sedatives and analgesics reduce anxiety, pain, and agitation, enhance synchronization with mechanical ventilation, and enable invasive procedures to be performed. Adequate sedation is defined as the level of sedation at which patients are asleep but easily arousable [1]. Oversedation delays recovery, as greater sedatives consumption is associated with longer duration of ventilation as well as extubation failure [2]. Oversedation also induces tolerance and withdrawal syndrome [3, 4]. Undersedation, on the other hand, may lead to increased distress and adverse events such as unintentional extubation or displacement of catheters. All this may also lead to a longer ICU stay.

Children are usually sedated through a combination of hypnotics (e.g., midazolam) and analgesics (e.g., morphine or fentanyl) [5–7]. Regrettably, there is little evidence from randomized trials on the efficacy of these drugs for sedation in critically ill children [8]. Nevertheless, efforts are being made to improve sedation management, for example with the use of sedation algorithms and standardized sedation management [9, 10].

To achieve the optimal level of sedation in individual patients, doses of sedatives are individually titrated to effect. This process is guided by scores on a variety of observational sedation scales [5]. The COMFORT score or COMFORT behavior scale and the Hartwig sedation scale are widely used and validated for this setting [11, 12]. Other scales used are the Ramsay scale [13], Richmond Agitation Sedation Scale (RASS) [14], State Behavior Scale (SBS) [15], and the University of Michigan Sedation Scale (UMSS) [16]. In addition, methods derived from the electro-encephalogram (EEG), such as the Bispectral Index (BIS) and middle latency auditory-evoked potential index (AEP), are applied, although their use is not validated in young children [17].

The aim of this systematic literature review is to evaluate the reported incidences of under-, optimal, and oversedation in pediatric intensive care patients and to determine to what extent the goal of adequate sedation is met [18].

Methods

Search strategy

A systematic literature search was performed in the PubMed and Embase databases from inception to July 2012, using the terms sedation, child, intensive care unit, and sedation quality/sedation level. We used a comprehensive search strategy to identify all published articles evaluating the level of sedation, measured with an observational scale, in pediatric intensive care patients. For Embase, appropriate search terms were applied. Full details of the search strategy are presented in Appendix 1. Furthermore, reference lists of retrieved articles were searched to identify other relevant papers that complied with the inclusion criteria.

Selection criteria

We used the following inclusion criteria:

1. Study population of PICU patients (0–18 years) on mechanical ventilation and receiving continuous sedation.
2. Reporting level of sedation and/or the incidence of under-, over-, and optimal sedation, as defined in the study.

Studies published in any language with an English-language abstract were eligible for review.

Exclusion criteria were:

1. Procedural sedation
2. Preterm patients
3. Patients treated with muscle relaxants, which preclude the use of sedation scores
4. Studies using only the BIS monitor in children aged <1 year, since this method is not validated for this patient group [17].

Two authors (NV, EI) independently reviewed titles and abstracts of all retrieved citations to identify eligible studies. Of all included studies, the full-text articles were again reviewed to ensure that they met inclusion criteria. Disagreements between reviewers were resolved by consensus.

Data extraction

Two authors (NV, EI) each independently recorded the following data: country of origin, study objective, study design, study population, age of patients, sample size, details of study intervention (if applicable), sedatives used (drug, dose), length of sedation, sedation scale used, and the incidence of optimal sedation, and under- and over-sedation. We used the definitions for optimal sedation as used by the researchers in the individual studies (as percentage of number of observations, patients or time) to be able to pool the data, despite different sedation assessment methods (Table 1).

Quality assessment

Study quality was determined with the “Quality Assessment Tool for Quantitative Studies” by the McMaster University, School of Nursing [19] as strong, moderate, or weak.

Statistical analysis

We analyzed studies separately on study design, sedation scale used, and proportion of under-, over-, and optimal sedation. Proportion was expressed as percentage of number of observations, patients or time (h). If similar outcome measures were used, the results of individual studies were quantitatively pooled to calculate a weighted mean, using descriptive statistics. The large heterogeneity

Table 1 Summary of included studies reporting the incidence of optimal, under-, and oversedation

Authors	Country	Study design	Study population	*n*	Sedatives used	Sedation scale	Definition optimal sedation	Incidence of optimal sedation	Incidence of under-sedation	Incidence of over-sedation	Comments
Parkinson et al. [34]	UK	RCT of sedative drugs	Critically ill children 1 day–15 years	44	Midazolam vs. chloral hydrate and promethazine	Clinical sedation scale	2–4, depending on patients condition	96 and 90 % (413/432 and 332/367 obs)	4 and 9 % (19/432 and 32/367 obs)	0 and 1 % (0/432 and 3/367 obs)	
Amigoni et al. [22]	Italy	Observational study of sedation scales	Critically ill children 1 month–18 years	46	Not reported	Comfort behavior scale nurse (and BIS)	COMFORT-B 11–22 (BIS 40–80)	34.8 % (16/46 pts) 73.9 % (34/46 pts)	0 % (0/46 pts) 4.3 % (2/46 pts)	65.2 % (30/46 pts) 21.7 % (10/46 pts)	
Ista et al. [9]	The Netherlands	Observational study, before-after introduction of sedation protocol	Critically ill children 0–3 years	131	Midazolam, morphine	COMFORT behavior scale and NISS	COMFORT-B 11–22 with a NISS of 2	64 % (2273/3573 obs)	12.9 % (461/3573 obs)	19.7 % (704/3573 obs)	
Ista et al. [11]	The Netherlands	Observational study of sedation scale	Critically ill children 0–18 years	78	Midazolam, morphine, ketamine, fentanyl	COMFORT behavior scale and NISS	COMFORT-B 11–22 with a NISS of 2	48.8 % (411/843 obs)	11.2 % (94/843 obs)	40.1 % (338/843 obs)	
Froom et al. [23]	UK	Observational study of sedation scales	Critically ill children 0–16 years	19	Midazolam, morphine, chloral hydrate	COMFORT score	17–26	14.8 % (4/27 obs)	3.7 % (1/27 obs)	81.5 % (22/27 obs)	
Triltsch et al. [24]	Germany	Observational study of sedation scales	Critically ill children <18 years	40	Benzodiazepines, opioids, propofol, ketamine	COMFORT score	17–26	27.5 % (11/40 pts)	0 %	72.5 % (29/40 pts)	
de Wildt et al. [40]	The Netherlands	Observational PKPD study	Critically ill children 2 days–17 years	21	Midazolam	COMFORT score	17–26	46.1 % (244/497 obs)	6 % (30/497 obs)	44.9 % (223/497 obs)	
Arenas-Lopez et al. [35]	UK	Observational study of sedative drug	Critically ill children <5 years	14	Morphine and clonidine	COMFORT score	13–23	81.9 % (837/1022 h)	10.8 % (110/1022 h)	7.3 % (75/1022 h)	
Marx et al. [20]	USA	Observational study of sedation scale	Critically ill children 1–102 months	85	Opiates, benzodiazepines, barbiturates	COMFORT score	17–26	57.1 % (32/56 obs)	12.5 % (7/56 obs)	30.4 % (17/56 obs)	
Brunow de Carvalho et al. [12]	Brazil	Observational study of sedation scales	Critically ill children 16 days–5 years	18	Opiates, benzodiazepines, barbiturates	COMFORT score Hartwig sedation scale	COMFORT 17–26 Hartwig 15–18	CF 60 % (18/30 obs) Hartwig 56.7 % (17/30 obs)	CF 6.7 % (2/30 obs) Hartwig 16.7 % (5/30 obs)	CF 33.3 % (10/30 obs) Hartwig 26.7 % (8/30 obs)	
Aneja et al. [25]	USA	Observational study of sedation scales	Critically ill children 3 months–18 years	24	Opioids, benzodiazepines, propofol	Ramsay	2–3	33.8 % (155/458 obs)	9.2 % (42/458 obs)	Deeply 38.8 % (179/458 obs) Oversedated 18.2 % (82/458 obs)	
Berkenbosch et al. [26]	USA	Observational study of sedation scales	Critically ill children 1 month–20 years	24	Midazolam, fentanyl, propofol	Ramsay	2–4	50.9 % (217/426 obs)	8.7 % (37/426 obs)	40.4 % (172/426 obs)	
Curley et al. [15]	USA	Observational study of sedation scales	Critically ill children 6 weeks–6 years	91	Opioids, benzodiazepines	State Behavioral Scale	0 and −1	42.9 % (85/198 obs)	4 % (8/198 obs)	53 % (105/198 obs)	
Johansson et al. [27]	Sweden	Observational study of sedation scales	Postoperative patients 0–10 years	40	Midazolam, morphine	NISS	NISS of 2	70 %	17 %	13 %	
Ambrose et al. [36]	UK	Observational study of sedative drug	Critically ill children <10 years	20	Midazolam and clonidine	Clinical sedation score	2–7	89 %	–	–	
Playfor et al. [21]	UK	Observational study of sedation scale	Critically ill children 1 month–16 years	28	Midazolam, morphine, chloral hydrate, antihistamines	Clinical sedation score (response to tracheal suction)	1, 2, or 4	79 % ideal 11 % acceptable (64/81 obs and 9/81 obs)	10 % (8/81 obs)	–	
Hartwig et al. [37]	Germany	Observational PKPD study	Critically ill children 26 days–5 years	24	Midazolam, fentanyl	Clinical sedation score	15–18	60 % (9/15 points)	6.7 % (1/15 points)	33.3 % (5/15 points)	

Table 1 continued

Authors	Country	Study design	Study population	n	Sedatives used	Sedation scale	Definition optimal sedation	Incidence of optimal sedation	Incidence of under-sedation	Incidence of over-sedation	Comments
Lamas et al. [28]	Spain	Observational study of sedation scales	Postoperative cardiac and non-cardiac surgery patients <14 years	50	Midazolam, fentanyl (vecuronium)	BIS monitor MLAEPs Ramsay score COMFORT score	BIS $\geq$ 60 MLAEPs $\geq$ 30 Ramsay $\leq$ 5 COMFORT $\geq$ 18	8 % (4/50 pts)	–	BIS 56 % MLAEPs 73.3 % Ramsay 83.9 % COMFORT 92.9 %	40 % of the obs in paralyzed patients
Lamas et al. [29]	Spain	Observational study of sedation scales	Critically ill children 6 months–19 years	50	Opioids, benzodiazepines	BIS MLAEPs	BIS $\geq$ 60 MLAEPs $\geq$ 30	44 % (62/141 obs)	–	56 % (79/141 obs)	39 % of the obs in paralyzed patients
Lamas et al. [30]	Spain	Observational study of sedation scales	Critically ill children <19 years	77	Midazolam, fentanyl (vecuronium)	BIS monitor AEPs Ramsay score COMFORT score	BIS $\geq$ 60 AEPs $\geq$ 30 Ramsay 1–5 COMFORT 18–40	BIS 35 % AEPs 32.5 % Ramsay 27 % COMFORT 18 %	–	BIS 65 % AEPs 67.5 % Ramsay 73 % COMFORT 82 %	40 % of the obs in paralyzed patients
Twite et al. [31]	USA	Observational study of sedation scales	Critically ill children 1 month–13 years	75	Fentanyl, midazolam	BIS	BIS 61–80	26.5 % (230/869 obs)	9.5 % (83/869 obs)	64 % (556/869 obs)	
Courtman et al. [32]	UK	Observational study of sedation scales	Critically ill children 1 month–16 years	40	Midazolam, morphine	BIS	BIS 60–80	63 %	–	24 %	
Crain et al. [33]	USA	Observational study of sedation scales	Critically ill children	31	Opioids, benzodiazepines, propofol	BIS	BIS 61–80	27.4 % (17/62 obs)	22.6 % (14/62 obs)	50 % (31/62 obs)	
Chrysostomou et al. [38]	USA	Retrospective study of sedative drug	Postoperative cardiothoracic surgery patients	38	Dexmedetomidine	Sedation scale	0–2	93 %	–	–	33 patients not on MV
Rosen et al. [39]	USA	Retrospective study of sedative drug	Critically ill children	55	Midazolam	Five-point activity scale for sedation	3	±90 %	<10 %	–	

Studies are categorized by study design and sedation scale used
Obs observations, *pts* patients, *h* hours

in study aims and study designs precluded further statistical analysis.

Results

Study selection

After filtering out duplicate studies, our search yielded 392 potentially relevant articles. Of these studies, 348 were excluded on the grounds of information in title and abstract (Fig. 1). Of the remaining 44 articles, the full-text was retrieved and assessed for eligibility. Nineteen studies were excluded for lack of quantitative data on sedation level or incidence of optimal-, under-, or oversedation, or for absence of a definition of optimal sedation. Details of the remaining 25 studies are presented in Table 1.

Study characteristics

One study was a randomized controlled trial (comparing two sedative regimens); 22 studies were prospective observational studies; and two were retrospective studies on a sedative drug. Of all 25 studies, only two determined the level of sedation as primary study outcome [20, 21]. Fifteen studies investigated one or more sedation scales or sedation monitoring systems (such as the BIS) [11, 12, 15, 22–33]; six studies investigated a sedative drug [34–39]; one was a pharmacokinetic-pharmacodynamic study [40]; and one study described the effect of implementation of a sedation protocol on amount of sedatives administered [9]. Although assessment of level of sedation was not the primary objective in the latter 23 studies, they reported incidences of under-, optimal-, and oversedation.

Since sedation practices may differ between countries, we also looked at the country of origin. Of the 25 studies, eight were conducted in the United States, 16 in six European countries, and one in Brazil.

All studies together investigated a total of 1,163 critically ill children. The most frequently used drugs were benzodiazepines (midazolam, in 22 studies) and opioids (morphine, in 14 studies). Other drugs used were fentanyl, ketamine, clonidine, propofol, barbiturates, chloral hydrate, first-generation antihistamines, and dexmedetomidine in different combinations.

Quality assessment

Only two studies had level of sedation as their primary outcome, all other studies varied by aim and study design. Therefore, assessment of study quality with the "Quality Assessment Tool for Quantitative Studies" was not possible, and this makes direct comparison between the studies difficult.

Sedation scales

Across all studies, 12 different observational sedation scores were used, of which four were validated for the PICU setting, i.e., the COMFORT-score, the COMFORT-B scale, the Hartwig sedation scale, and the State Behavior Scale. Most frequently (11/25) used were the COMFORT-score and COMFORT-behavior scale (COMFORT-B), followed by the Ramsay score, the State Behavioral Scale, and the Hartwig sedation scale. Six studies (23 %) used the BIS monitor. In 13 studies two or more sedation scales or monitors were used.

All studies defined optimal sedation in terms of cut-off values (Table 1). The definition of optimal sedation differed between studies, even when the same sedation scale was used. For example, a COMFORT score between 17 and 26 is thought to indicate adequate sedation [20]. However, one study applied the 13–23 range to define adequate sedation [35]. This range was chosen a priori to target a level of sedation that would produce a patient who was under analgesics, calm, with minimal risk of self-extubation, but able to maintain an appropriate cough reflex and spontaneous respiratory effort to achieve ventilator synchrony. Furthermore, different cut-off values for the Ramsay score were used: i.e., 2–3 [25]; 2–4 [26]; and 1–5 [28, 30]. Assessment frequency also varied considerably between studies; from once daily to hourly.

Level of sedation

Reported incidences of optimal, under-, and oversedation are presented in Table 1.

Studies varied in the way incidence was reported (as a proportion of observations, patients or hours). Fifteen studies reported the incidence as a proportion of observations, as summarized in Fig. 2. Optimal sedation was ascertained in 15–93 % of observations, undersedation in 0–22 %, and oversedation in 0–82 % of observations. In these 15 studies, patients were optimally sedated in 57.6 % of the observations, undersedated in 10.6 % of the observations, and oversedated in 31.8 % of the observations.

Two studies reported proportions of patients; in these two studies together, 68.6 % of patients were oversedated at any time during admission (Fig. 3).

The two studies that used both an observational score and the BIS score reported considerably different results [28, 30]. The incidence of oversedation measured with the BIS was lower than that measured with a validated observational scale (56 vs. 92.9 % and 65 vs. 82 %).

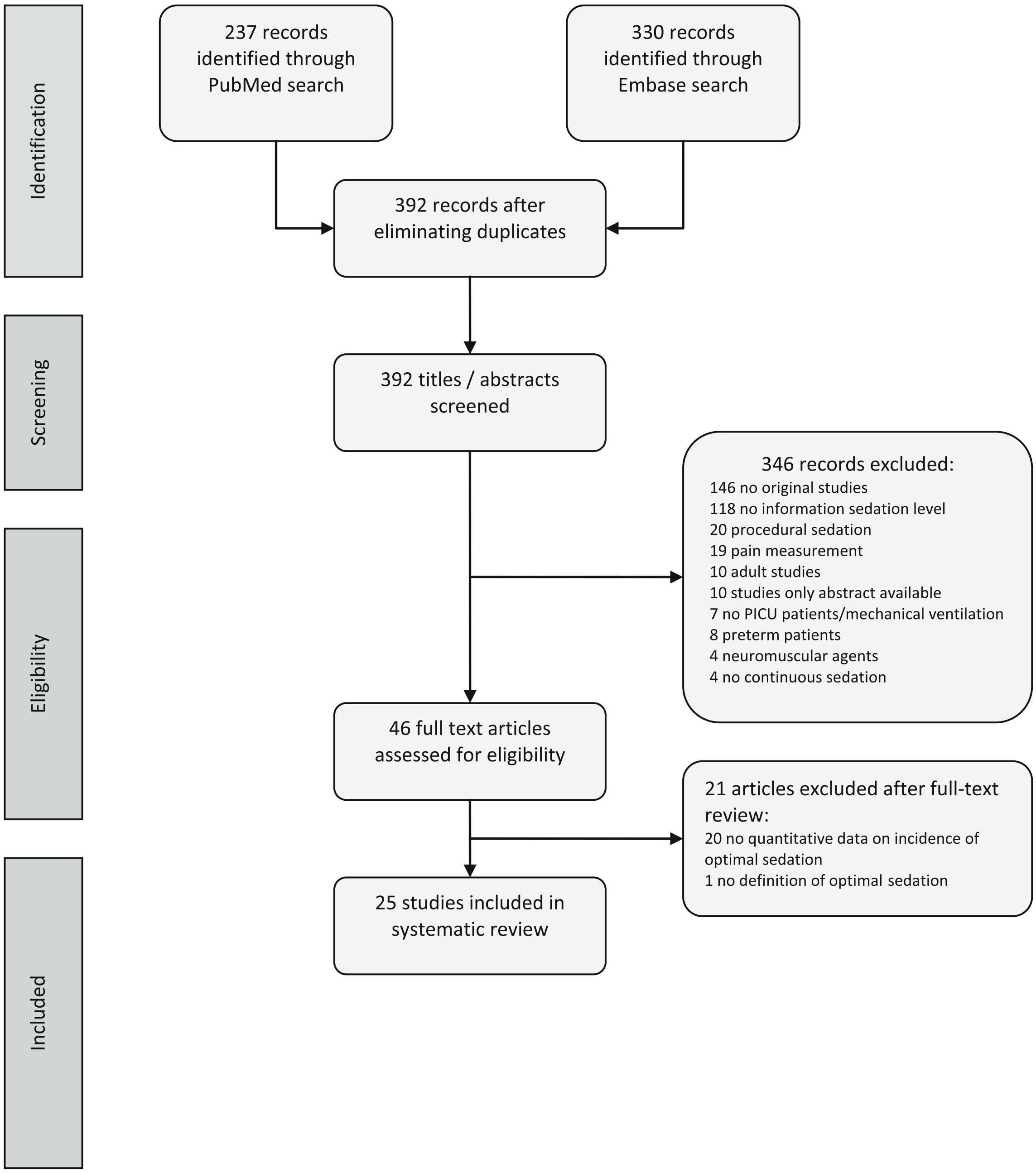

Fig. 1 Flowchart search results

Discussion

This review shows that the level of sedation in critically ill children is often suboptimal during their ICU stay, at least in ICUs that apply sedation assessment in daily practice. Patients are optimally sedated in only 60 % of assessments. Under- and oversedation occur in 10 and 30 % of the assessments, respectively. However, across all studies, there is a large variation in incidence of oversedation, i.e., from 0 to 82 % of assessments. Most studies, however, report incidence in the range of 40 to 65 %, which corresponds to that reported in adult ICU patients [41–43].

Our results indicate that in critically ill children oversedation is more common than undersedation. We suggest several reasons for the relatively high incidence of oversedation. First, there may be a tendency to avoid undersedation at all cost, as this may lead to discomfort and potential adverse effects as self-extubation and removal of lines and catheters. Since children, especially preverbal infants, cannot clearly communicate their well-being and are often bewildered by the ICU setting, nurses and doctors may also tend to avoid undersedation. Second, nurses believe that mechanical ventilation is uncomfortable and stressful, and this perception might lead to higher sedation level than necessary [42, 44]. Third, sedation protocols are not fully adhered to, so that sedatives are not tapered off when possible [45]. These tendencies are unwanted, as oversedation may be even more detrimental to patients.

Continuous sedation as such is an independent predictor of prolonged mechanical ventilation in adults, and consequently leads to longer ICU and hospital stay [46]. Oversedation, in addition, is also associated with tolerance, withdrawal, and delirium. Especially longer duration of use and high drug doses are risk factors for development of withdrawal symptoms in children [4]. Moreover, longer use of sedatives has been associated with symptoms of depression and post-traumatic stress symptoms in adults [47]. In a study in children, almost one-third of children reported delusional memories, and these were the children with the longest duration of administration of opiates/benzodiazepines and the highest risk of posttraumatic stress [48]. The administration of sedatives to children may also be associated with adverse neurodevelopmental outcomes at later age, probably by inducing neuroapoptosis [49–51].

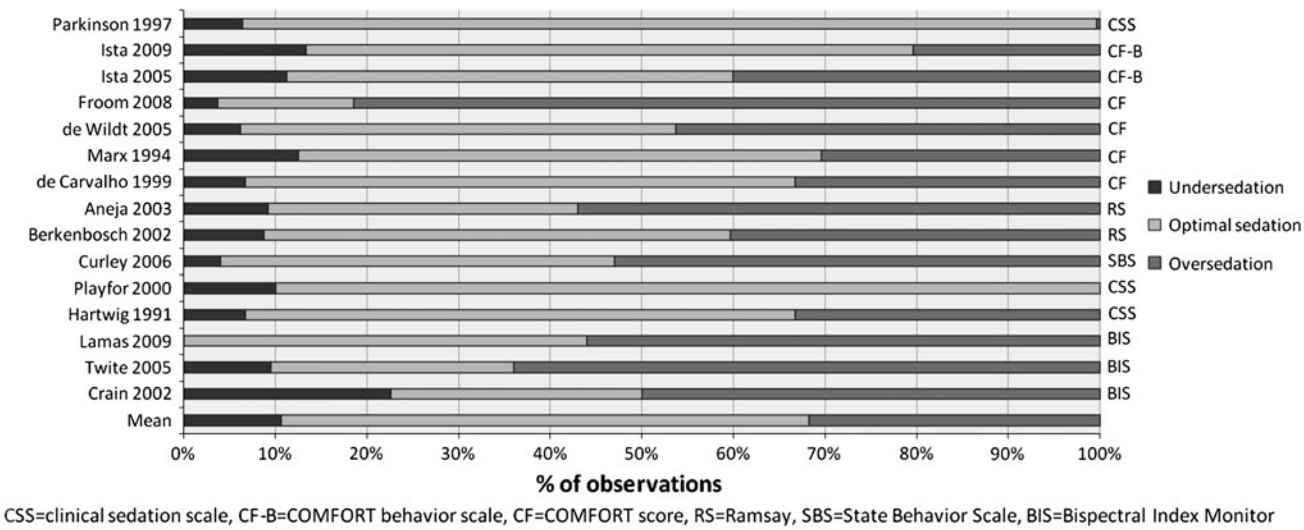

Fig. 2 Incidence of under-, optimal, and oversedation (% of observations)

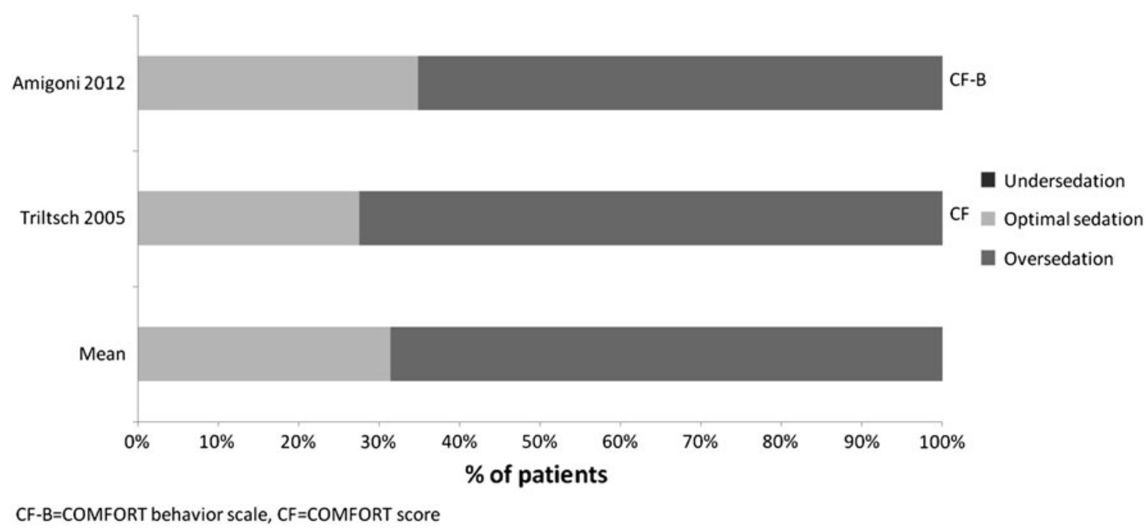

Fig. 3 Incidence of under-, optimal, and oversedation (% of patients)

The implementation of sedation algorithms aimed at less sedation has led to shorter duration of mechanical ventilation, ICU stay, and hospital stay in adults [52]. Also, daily sedation interruption significantly improved short- and long-term outcomes in adults [53]. A more recent "no-sedation" protocol is even more promising in this respect [54]. All evidence indicates that the use of sedative drugs should be reduced. In children, daily sedation interruption seems feasible and safe, but effectiveness needs to be demonstrated in large trials [55].

This review also shows a great variety of assessment instruments used in clinical practice. No more than four of the 12 observational sedation scores have been validated for PICU patients, i.e., the COMFORT-score, the COMFORT-B scale, the Hartwig sedation scale, and the State Behavior Scale. This is remarkable, as there is consensus that the level of sedation should be assessed and documented using a validated sedation assessment scale [5]. The reliability of the other scales is questionable. Furthermore, six studies used the BIS monitor. There is insufficient evidence, however, to support the use of the BIS monitor, or any other neurophysiological sedation scoring technique, such as auditory evoked potentials, in children below the age of 6 months [56]. The suitability of the adult-derived EEG algorithm to assess children's BIS values is doubted. Furthermore, pre-awakening BIS values in children aged <1 year are lower than in older children [57]. This could explain why in some pediatric studies BIS monitoring resulted in a lower incidence of oversedation than did application of the COMFORT score [28, 30].

In all studies the authors defined optimal level of sedation. Remarkably, different studies applied different cut-off values of the COMFORT score and Ramsay score [25, 26, 28, 30]. This variation may be explained by the uncertainty in what constitutes optimal sedation, but may also be the result of patient-specific factors. For example, a deeper level of sedation is often aimed for in patients with pulmonary hypertension, traumatic brain injury or difficult airway. Playfor et al. [21] used a clinical sedation score based on the response to tracheal suction, categorizing the response on a five-point scale. A score of 1 (no response to tracheal suction) was considered as the desired level of sedation for children with severe head injury; a score of 2 for children receiving a high level of intensive care with frequent invasive procedures, and a score of 4 for children prior to extubation.

In addition, the relatively high incidence of suboptimal sedation shown in this review reflects the fact that titrating the correct amount of sedation for each child can be complex. There may be several reasons for this. First, PICU populations are quite heterogeneous with respect to disease type and severity, age, and neurodevelopmental stage, so optimal sedation management may differ widely. Second, pharmacokinetics and pharmacodynamics, largely insufficiently studied, may be unpredictable, particularly in patients with multiorgan failure [58]. Dosing regimens are often based on healthy adult volunteers and do not take into account factors such as altered protein binding, distribution, and clearance in critically ill children. Also, sedation requirements may change over the course of illness [59].

With the risks of oversedation and the difficulties of reaching adequate sedation in mind, a critical appraisal of sedation strategies in critically ill children is needed. Optimal sedation could perhaps be achieved with the use of validated sedation scales and standard sedation protocols and by studying promising interventions such as daily sedation interruption. These studies are needed in pediatric intensive care.

Conclusions

This review shows that optimal sedation for critically ill children remains challenging for health professionals. These children are often oversedated and consequently run the risk of adverse outcomes. It is high time to find conclusive evidence on optimal sedation strategies in the PICU setting.

Acknowledgments The authors declare that they have no conflicts of interest. This research was supported by ZonMw Priority Medicines Kinderen (project number 113202002), ZonMw AGIKO Stipendium (project number 92003549), and Erasmus MC Doelmatigheidsonderzoek.

Appendix 1. Search strategy

PubMed

(child*[tw] OR infan*[tw] OR pediatr*[tw] OR paediatr*[tw])

AND

(intensive car*[tw] OR critical car*[tw] OR critically ill*[tw] OR ICU[tw] OR PICU[tw])

AND

(sedat*[tw] OR midazolam[tw] OR lorazepam[tw] OR diazepam[tw] OR benzodiazepin*[tw] OR fentanyl[tw] OR remifentanyl[tw] OR morphine[tw] OR ketamine[tw] OR clonidine[tw] OR pentobarbital[tw] OR opioid*[tw] OR propofol[tw])

AND

(sedation qualit*[tw] OR quality of sedation[tw] OR sedation level*[tw] OR level of sedation[tw] OR sedation score*[tw] OR sedation scale*[tw] OR sedation assess*[tw] OR assessing of sedation[tw] OR sedation protocol*[tw] OR sedation guideline*[tw] OR sedation algorithm*[tw] OR assessment tool*[tw] OR conscious sedation/standards[mesh] OR conscious sedation/methods[mesh] OR nursing assessment[mesh] OR nursing assess*[tw] OR nursing diagn*[tw] OR COMFORT score*[tw] OR COMFORT scale*[tw] OR COMFORT behavio*[tw] OR bispectral inde*[tw] OR state Behavior Scale*[tw] OR state behaviour scale*[tw] OR pharmacodynamic*[tiab])

Embase

(child*:ti,ab,de OR infan*:ti,ab,de OR pediatr*:ti,ab,de OR paediatr*:ti,ab,de) AND (((intensive OR critical*) NEAR/2 (car* OR ill*)):ti,ab,de OR ICU:ti,ab,de OR PICU:-ti,ab,de) AND (sedat*:ti,ab,de OR midazolam: ti,ab,de OR lorazepam:ti,ab,de OR diazepam:ti,ab,de OR benzodiazepin*:ti,ab,de OR fentanyl:ti,ab,de OR remifentanyl:ti,ab,de OR morphine:ti,ab,de OR ketamine:ti,ab,de OR clonidine:ti,ab,de OR pentobarbital:ti,ab,de OR opioid*:ti,ab,de OR propofol:ti,ab,de) AND ((sedation NEAR/2 (qualit* OR level* OR score* OR scale* OR assess* OR protocol* OR guideline* OR algorithm*)):ti,ab,de OR (assess* NEAR/2 tool*):ti,ab,de OR 'conscious sedation':de OR 'nursing assessment'/exp OR (nurs* NEAR/2 (assess* OR diagn*)):ti,ab,de OR (COMFORT NEAR/1 (score* OR scale* OR behavio*)):ti,ab,de OR (bispectral NEAR/1 inde*):ti,ab,de OR (('state Behavior' OR 'state behaviour') NEAR/1 scale*):ti,ab,de OR pharmacodynamic*:ti,ab)

References

1. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, Chalfin DB, Masica MF, Bjerke HS, Coplin WM, Crippen DW, Fuchs BD, Kelleher RM, Marik PE, Nasraway SA Jr, Murray MJ, Peruzzi WT, Lumb PD (2002) Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 30:119–141
2. Randolph AG, Wypij D, Venkataraman ST, Hanson JH, Gedeit RG, Meert KL, Luckett PM, Forbes P, Lilley M, Thompson J, Cheifetz IM, Hibberd P, Wetzel R, Cox PN, Arnold JH (2002) Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: a randomized controlled trial. JAMA 288:2561–2568
3. Fonsmark L, Rasmussen YH, Carl P (1999) Occurrence of withdrawal in critically ill sedated children. Crit Care Med 27:196–199
4. Ista E, van Dijk M, Gamel C, Tibboel D, de Hoog M (2008) Withdrawal symptoms in critically ill children after long-term administration of sedatives and/or analgesics: a first evaluation. Crit Care Med 36:2427–2432
5. Playfor S, Jenkins I, Boyles C, Choonara I, Davies G, Haywood T, Hinson G, Mayer A, Morton N, Ralph T, Wolf A (2006) Consensus guidelines on sedation and analgesia in critically ill children. Intensive Care Med 32:1125–1136
6. Benini F, Farina M, Capretta A, Messeri A, Cogo P (2010) Sedoanalgesia in paediatric intensive care: a survey of 19 Italian units. Acta Paediatr 99:758–762
7. Jenkins IA, Playfor SD, Bevan C, Davies G, Wolf AR (2007) Current United Kingdom sedation practice in pediatric intensive care. Paediatr Anaesth 17:675–683
8. Hartman ME, McCrory DC, Schulman SR (2009) Efficacy of sedation regimens to facilitate mechanical ventilation in the pediatric intensive care unit: a systematic review. Pediatr Crit Care Med 10:246–255
9. Ista E, de Hoog M, Tibboel D, van Dijk M (2009) Implementation of standard sedation management in paediatric intensive care: effective and feasible? J Clin Nurs 18(17):2511–2520
10. Deeter KH, King MA, Ridling D, Irby GL, Lynn AM, Zimmerman JJ (2011) Successful implementation of a pediatric sedation protocol for mechanically ventilated patients. Crit Care Med 39:683–688
11. Ista E, van Dijk M, Tibboel D, de Hoog M (2005) Assessment of sedation levels in pediatric intensive care patients can be improved by using the COMFORT "behavior" scale. Pediatr Crit Care Med 6:58–63
12. Brunow de Carvalho W, Lucas da Silva PS, Paulo CS, Fonseca MM, Belli LA (1999) Comparison between the Comfort and Hartwig sedation scales in pediatric patients undergoing mechanical lung ventilation. Sao Paulo Med J 117:192–196
13. Ramsay MA, Savege TM, Simpson BR, Goodwin R (1974) Controlled sedation with alphaxalone-alphadolone. Br Med J 2:656–659
14. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP, Elswick RK (2002) The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med 166:1338–1344
15. Curley MA, Harris SK, Fraser KA, Johnson RA, Arnold JH (2006) State Behavioral Scale: a sedation assessment instrument for infants and young children supported on mechanical ventilation. Pediatr Crit Care Med 7:107–114
16. Malviya S, Voepel-Lewis T, Tait AR, Merkel S, Tremper K, Naughton N (2002) Depth of sedation in children undergoing computed tomography: validity and reliability of the University of Michigan Sedation Scale (UMSS). Br J Anaesth 88:241–245
17. Sadhasivam S, Ganesh A, Robison A, Kaye R, Watcha MF (2006) Validation of the bispectral index monitor for measuring the depth of sedation in children. Anesth Analg 102:383–388
18. Vet NJ, Ista E, de Wildt SN, van Dijk M, Tibboel D, de Hoog M (2013) The struggle for optimal sedation in pediatric intensive care patients: a systematic review. Clin Pharmacol Ther 93:S121
19. National Collaborating Centre for Methods and Tool (2008) Quality Assessment for Quantitative Studies. McMaster University, Hamilton. http://www.nccmt.ca/registry/view/eng/14.html
20. Marx CM, Smith PG, Lowrie LH, Hamlett KW, Ambuel B, Yamashita TS, Blumer JL (1994) Optimal sedation of mechanically ventilated pediatric critical care patients. Crit Care Med 22:163–170
21. Playfor SD, Thomas DA, Choonara I, Jarvis A (2000) Quality of sedation during mechanical ventilation. Paediatr Anaesth 10:195–199
22. Amigoni A, Mozzo E, Brugnaro L, Gentilomo C, Stritoni V, Michelin E, Pettenazzo A (2012) Assessing sedation in a pediatric intensive care unit using Comfort Behavioural Scale and Bispectral Index: these tools are different. Minerva Anestesiol 78:322–329
23. Froom SR, Malan CA, Mecklenburgh JS, Price M, Chawathe MS, Hall JE, Goodwin N (2008) Bispectral Index asymmetry and COMFORT score in paediatric intensive care patients. Br J Anaesth 100:690–696

24. Triltsch AE, Nestmann G, Orawa H, Moshirzadeh M, Sander M, Grosse J, Genahr A, Konertz W, Spies CD (2005) Bispectral index versus COMFORT score to determine the level of sedation in paediatric intensive care unit patients: a prospective study. Crit Care 9:R9–R17
25. Aneja R, Heard AM, Fletcher JE, Heard CM (2003) Sedation monitoring of children by the Bispectral Index in the pediatric intensive care unit. Pediatr Crit Care Med 4:60–64
26. Berkenbosch JW, Fichter CR, Tobias JD (2002) The correlation of the bispectral index monitor with clinical sedation scores during mechanical ventilation in the pediatric intensive care unit. Anesth Analg 94:506–511
27. Johansson M, Kokinsky E (2009) The COMFORT behavioural scale and the modified FLACC scale in paediatric intensive care. Nurs Crit Care 14:122–130
28. Lamas A, Lopez-Herce J, Sancho L, Mencia S, Carrillo A, Santiago MJ, Martinez V (2009) Assessment of the level of sedation in children after cardiac surgery. Ann Thorac Surg 88:144–150
29. Lamas A, Lopez-Herce J, Sancho L, Mencia S, Carrillo A, Santiago MJ, Martinez V (2009) Analysis of bispectral index and middle latency auditory-evoked potentials parameters in critically ill children. J Clin Neurophysiol 26:150–154
30. Lamas A, Lopez-Herce J, Sancho L, Mencia S, Carrillo A, Santiago MJ, Martinez V (2008) Assessing sedation in critically ill children by bispectral index, auditory-evoked potentials and clinical scales. Intensive Care Med 34:2092–2099
31. Twite MD, Zuk J, Gralla J, Friesen RH (2005) Correlation of the bispectral index monitor with the COMFORT scale in the pediatric intensive care unit. Pediatr Crit Care Med 6:648–653
32. Courtman SP, Wardurgh A, Petros AJ (2003) Comparison of the bispectral index monitor with the Comfort score in assessing level of sedation of critically ill children. Intensive Care Med 29:2239–2246
33. Crain N, Slonim A, Pollack MM (2002) Assessing sedation in the pediatric intensive care unit by using BIS and the COMFORT scale. Pediatr Crit Care Med 3:11–14
34. Parkinson L, Hughes J, Gill A, Billingham I, Ratcliffe J, Choonara I (1997) A randomized controlled trial of sedation in the critically ill. Paediatr Anaesth 7:405–410
35. Arenas-Lopez S, Riphagen S, Tibby SM, Durward A, Tomlin S, Davies G, Murdoch IA (2004) Use of oral clonidine for sedation in ventilated paediatric intensive care patients. Intensive Care Med 30:1625–1629
36. Ambrose C, Sale S, Howells R, Bevan C, Jenkins I, Weir P, Murphy P, Wolf A (2000) Intravenous clonidine infusion in critically ill children: dose-dependent sedative effects and cardiovascular stability. Br J Anaesth 84:794–796
37. Hartwig S, Roth B, Theisohn M (1991) Clinical experience with continuous intravenous sedation using midazolam and fentanyl in the paediatric intensive care unit. Eur J Pediatr 150:784–788
38. Chrysostomou C, Di Filippo S, Manrique AM, Schmitt CG, Orr RA, Casta A, Suchoza E, Janosky J, Davis PJ, Munoz R (2006) Use of dexmedetomidine in children after cardiac and thoracic surgery. Pediatr Crit Care Med 7:126–131
39. Rosen DA, Rosen KR (1991) Midazolam for sedation in the paediatric intensive care unit. Intensive Care Med 17(Suppl 1):S15–S19
40. de Wildt SN, de Hoog M, Vinks AA, Joosten KF, van Dijk M, van den Anker JN (2005) Pharmacodynamics of midazolam in pediatric intensive care patients. Ther Drug Monit 27:98–102
41. Payen JF, Chanques G, Mantz J, Hercule C, Auriant I, Leguillou JL, Binhas M, Genty C, Rolland C, Bosson JL (2007) Current practices in sedation and analgesia for mechanically ventilated critically ill patients: a prospective multicenter patient-based study. Anesthesiology 106:687–695
42. Weinert CR, Calvin AD (2007) Epidemiology of sedation and sedation adequacy for mechanically ventilated patients in a medical and surgical intensive care unit. Crit Care Med 35:393–401
43. Jackson DL, Proudfoot CW, Cann KF, Walsh TS (2009) The incidence of sub-optimal sedation in the ICU: a systematic review. Crit Care 13:R204
44. Guttormson JL, Chlan L, Weinert C, Savik K (2010) Factors influencing nurse sedation practices with mechanically ventilated patients: a U.S. national survey. Intensive Crit Care Nurs 26:44–50
45. Burns SM (2012) Adherence to sedation withdrawal protocols and guidelines in ventilated patients. Clin Nurse Spec 26:22–28
46. Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G (1998) The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest 114:541–548
47. Hughes CG, Pandharipande PP (2011) Review articles: the effects of perioperative and intensive care unit sedation on brain organ dysfunction. Anesth Analg 112:1212–1217
48. Colville G, Kerry S, Pierce C (2008) Children's factual and delusional memories of intensive care. Am J Respir Crit Care Med 177:976–982
49. Olney JW, Young C, Wozniak DF, Jevtovic-Todorovic V, Ikonomidou C (2004) Do pediatric drugs cause developing neurons to commit suicide? Trends Pharmacol Sci 25:135–139
50. Wilder RT, Flick RP, Sprung J, Katusic SK, Barbaresi WJ, Mickelson C, Gleich SJ, Schroeder DR, Weaver AL, Warner DO (2009) Early exposure to anesthesia and learning disabilities in a population-based birth cohort. Anesthesiology 110:796–804
51. DiMaggio C, Sun LS, Kakavouli A, Byrne MW, Li G (2009) A retrospective cohort study of the association of anesthesia and hernia repair surgery with behavioral and developmental disorders in young children. J Neurosurg Anesthesiol 21:286–291
52. Patel SB, Kress JP (2012) Sedation and analgesia in the mechanically ventilated patient. Am J Respir Crit Care Med 185:486–497
53. Kress JP, Pohlman AS, O'Connor MF, Hall JB (2000) Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 342:1471–1477
54. Strom T, Martinussen T, Toft P (2010) A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. Lancet 375:475–480
55. Wildschut ED, Hanekamp MN, Vet NJ, Houmes RJ, Ahsman MJ, Mathot RA, de Wildt SN, Tibboel D (2010) Feasibility of sedation and analgesia interruption following cannulation in neonates on extracorporeal membrane oxygenation. Intensive Care Med 36:1587–1591
56. Playfor SD (2005) The use of bispectral index monitors in paediatric intensive care. Crit Care 9:25–26

57. Davidson AJ, McCann ME, Devavaram P, Auble SA, Sullivan LJ, Gillis JM, Laussen PC (2001) The differences in the bispectral index between infants and children during emergence from anesthesia after circumcision surgery. Anesth Analg 93:326–330
58. Zuppa AF, Barrett JS (2008) Pharmacokinetics and pharmacodynamics in the critically ill child. Pediatr Clin North Am 55:735–755
59. Vet NJ, de Hoog M, Tibboel D, de Wildt SN (2011) The effect of inflammation on drug metabolism: a focus on pediatrics. Drug Discov Today 16:435–442