

Pediatric sedation for emergency, imaging and endoscopic procedures: a worldwide review from the last five years

Abstract

Introduction: Anatomical, physiological, pharmacokinetic, pharmacodynamic and behavioral particularities relevant to the pediatric population make its sedation challenging for quick and low-complexity procedures. Robust evidence on this subject is still scarce, and the variety of drugs available, with their multiple routes of administration and dosage schemes, makes it difficult for providers to make a decision.

Methods: Through research in four databases, we found 170 articles that addressed pediatric sedation and, after applying the exclusion criteria, we selected 32 articles for analysis.

Results: In sedation for invasive or painful procedures, Esketamine in monotherapy was effective, despite the significant incidence of adverse effects.

Satisfactory responses were also obtained with associations between Esketamine and Propofol and Fentanyl with Propofol or Midazolam. To perform imaging tests, continuous infusions of Propofol or Dexmedetomidine were sufficient, with associations with Esketamine or opioids associated with a higher incidence of adverse effects.

Endoscopic procedures have been successfully performed after administration of continuous infusion of Propofol or Dexmedetomidine, associated with Remifentanyl infusion or Fentanyl bolus. Esketamine in monotherapy was also effective.

Discussion: The drugs studied have an adverse effect profile compatible with safe pediatric sedation, whether administered by a specialist or not. However, alternative administration routes and dosages still need further studies before being routinely applied.

Conclusion: Sedation in pediatrics is still an open field for research in our country.

Keywords: deep sedation, dexmedetomidine, ketamine, pediatric anesthesia, propofol

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Ana Clara Monteiro Laranjeira,¹ Fernanda Cardoso Andrade,² Léa Jenifer Souza Cordeiro,² Leticia Barros Cardoso,² Beatriz Metedeiro Nunes Câmara,² Júlia Carvalho de Miranda,² Patrícia Fabiane Monteiro Laranjeira³

¹Anesthesiologist, Professor of Anesthesiology, State University of Health Sciences of Alagoas, Brazil

²Medical student at the State University of Health Sciences of Alagoas, Brazil

³Neonatologist, Professor and preceptor of the Pediatrics discipline at the State University of Health Sciences of Alagoas, Brazil

Correspondence: Ana Clara Monteiro Laranjeira, Anesthesiologist, graduated in Medicine from the State University of Health Sciences of Alagoas, Coordinator of the Anesthesiology service at Hospital da Criança de Alagoas, Professor of Anesthesiology at the State University of Health Sciences of Alagoas, Brazil, Tel 55 82 99999-8925, Email Clarinha_ana_@hotmail.com

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Introduction

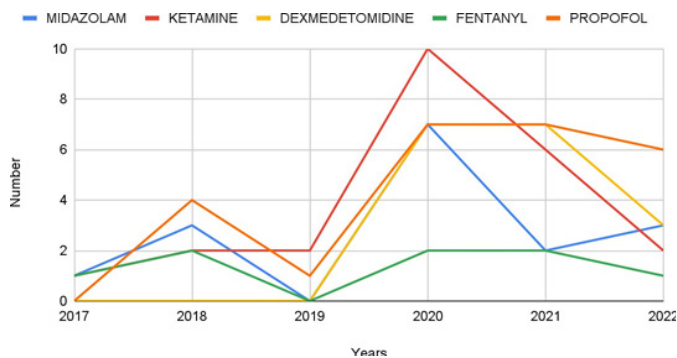
Sedation is about pharmacologically inducing anxiolysis or drowsiness – from mild to deep – with or without analgesia, in patients undergoing quick and low-complexity procedures. Sedation has particularly relevant role in pediatric interventions. This population is often not able to cooperate and has low pain tolerance, which can result in a longer procedure with more risks and complications associated. Furthermore, a high incidence of post-traumatic stress disorder was observed in children undergoing procedures without sedation or with insufficient sedation and under physical restraint, which contributes to equally traumatic future experiences in a hospital environment.^{1,2}

Sedation – although apparently not very complex – can be considered one of the most challenging anesthetic techniques, since equivalent doses of the same drug present considerable variability of responses in a similar population, a fact that demands provider's parsimony and patience. The technique also implies in unprotected airway, through maintenance of spontaneous ventilation and non-invasive oxygen support. For the pediatric population, with all its anatomical and physiological particularities that favor rapid arterial oxygen desaturation and low tolerance to hypoxia, this is yet another aspect that limits large-scale practice by a greater variety of physicians.³ Other particularities of the child involve differentiated pharmacodynamics and pharmacokinetics, with an impact on the results and adverse effects profile of the drugs chosen by the providers, which generates insecurity and limitations for the practice

of sedation by non-anesthesiologists, mainly in circumstances of precarious infrastructure and unavailability of adequate monitoring and equipment. However, in certain circumstances, small procedures under sedation performed outside the operating room may be the fastest and even more cost-effective option,^{4,5,6} which emphasizes the importance of expanding pharmacological knowledge and highlighting the best evidence-based indications for the practice of safe and effective pediatric sedation.

Methods

The present article consists on a narrative review of the literature, with the aim of synthesizing results of studies referring to sedation techniques for low-complexity procedures, with varied pain stimuli, performed in patients from zero to eighteen yearsold, in the emergency sectors, ward, intensive care unit and diagnostic center, for anesthesiologists, pediatric assistants or pediatric intensivists, using the drugs Ketamine, Midazolam, Fentanyl, Remifentanyl, Dexmedetomidine and Propofol. The article has publications produced on all continents, with the exception of Oceania, see Graph 1, gathered through research carried out from November 2022 to February 2023, in journals indexed in the following databases: PubMed/ Medical Literature Analysis and Retrieval System Online (MEDLINE), Latin American and Caribbean Health Sciences Literature (Lilacs), Cochrane and Biblioteca Virtual de Saúde (BVS). Methodological steps used were:



Graph 1 Pharmacological choice temporal evolution for sedation in pediatrics in the last 5 years.

- 1) Definition of inclusion and exclusion criteria;
- 2) Definition of information to be extracted from selected studies;
- 3) Data analysis and interpretation;
- 4) Evaluation of the results included in the narrative review;
- 5) Presentation of knowledge review/synthesis.

The search format in the databases was: “pediatric” or “children” and “sedation” or “propofol” or “dexmedetomidine” or “ketamine” or “midazolam”. The filter restricted the results to publications from the last 5 years, and these were selected according to the inclusion criteria:

- 1) Presence of descriptors chosen in the title of the work or inserted in the abstract;
- 2) Full text articles;
- 3) Productions in Portuguese, English or Spanish;
- 4) Publication between January 2017 and December 2022.

The established exclusion criteria were: failure to fill in the information in the title or abstract, systematic reviews and articles unrelated to the topic; unavailability of full text; studies whose population included patients with congenital heart disease or any other critical condition, which represented an imminent threat to life; duplicate articles present in more than one database. In some selected studies, data regarding sedation with Etomidate, Thiopental, Chloral Hydrate and volatile anesthetics were disregarded. A total of 170 articles were found in the consulted databases, 39 in MEDLINE, 27 in Lilacs, 99 in Cochrane and 5 in BVS. Among the 170, only 32 met the established inclusion criteria and were added to the sample, as shown in Figure 1.

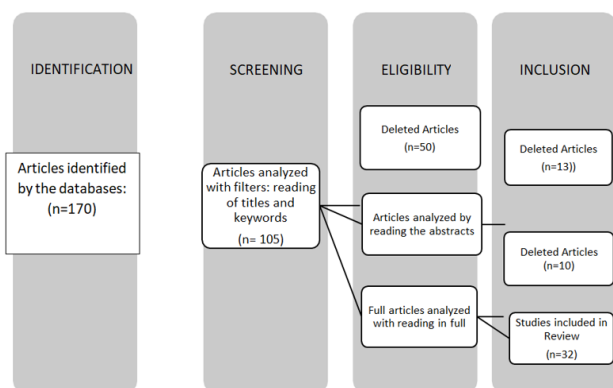


Figure 1 Selection process description of found studies.

Results

Sedation for invasive and/or painful procedures

We gathered 15 studies^{1,2,3,6-18} that described sedation techniques for procedures with some degree of invasion or pain, such as suturing lacerations, fracture reduction, chest drainage and central venous access. In these, Ketamine has shown to be a increasing popularity drug in recent years (Graph 1); and, although the bioavailability and efficacy of the drug by other routes besides the intravenous route is acceptable, this continues to be the most used route (Table 1), in doses from 1 to 4 mg/kg.^{2,7} For procedures lasting up to 30 minutes, 1.5 mg/kg bolus, in a monotherapy regime, was effective and dispensed additional boluses.⁷ Intranasally, doses from 3 to 4 mg/kg were effective and, via rectally, 0.75 to 3 mg/kg, associated or not with Midazolam by the same route.^{2,7} With regard to adverse events after the exclusive use of Ketamine, nausea, vomiting and agitation upon awakening, especially in patients younger than 12 months, were the most reported.³ Population aged 1 to 2 years seems to have a lower incidence of these events.³ When in association with Propofol, these adverse events were notably less frequent, and the incidence of respiratory complications and recovery time resulting from sedation with Propofol tend to be reduced.⁸ Association with Midazolam was also used, showing improvement in agitation of the awakening and nausea.⁹

Table 1 Administration routes of choice for the drugs analyzed in the selected articles

Drugs	Administration route choice
Ketamine	
EV	19 (70, 37%)
IN	7 (25, 92%)
IR	1 (3, 70%)
Midazolam	
EV	8 (44, 44%)
IN	7 (38, 88%)
IR	1 (5, 55%)
VO	1 (5, 55%)
Fentanyl	
EV	9 (69, 23%)
IN	4 (30, 76%)
Dexmedetomidine	
EV	8 (47, 05%)
IN	9 (52, 94%)

Midazolam in isolated use, either intravenously (0.05 to 1 mg/kg), intra nasally or rectally, has ceased to be the first choice drug for sedation in pediatrics.^{2,6,10,11} Its adverse effects profile, which may include diplopia, dizziness, hiccups, paradoxical agitation and nasal burning, has led professionals to opt for other drugs.^{2,12,13}

However, Midazolam and Fentanyl association still proves to be a very popular option (29%) for procedural sedation in pediatric emergencies, surpassing the use of intravenous Ketamine (9%).^{1,9} The most used Fentanyl rout in studies was intranasal, with a good safety profile, bioavailability and rapid onset of action.¹² However, considering the low or absent ability of the study population to cooperate, it is almost always necessary to associate an hypnotic agent with Fentanyl. Association with Propofol (0.5 to 1 mcg/kg + 0.5 to 1 mcg/kg of Fentanyl, intravenously) seems more attractive than Ketamine + Midazolam association (0.25 to 1 mg/kg + 30-50 mcg/kg), due to the shorter recovery time of the first.¹¹ Fentanyl and Midazolam

association was related with a longer induction time (1:23 min vs. 0:58 min), shorter sedation (5:50 min vs. 9:02 min) with consequent faster awakening (0:56 min vs. 4:26 min), in addition to a higher incidence of pain and vomiting upon awakening.¹³ Fentanyl alone was associated with longer recovery time (20 minutes) when compared to sedation with Propofol (10 minutes) and Ketamine (15 minutes), in addition to a higher incidence of vomiting and complaints of nasal burning.^{10,12}

Propofol as a single sedation drug for invasive or emergency procedures was effective at induction doses ranging from 0.5 to 1.5 mg/kg, associated with a mean maintenance dose of 100-250 mcg/kg/min or 6-15 mg/kg/h in continuous infusion.^{9-11,15,16} Main associated side effects include respiratory depression, hypoxemia, hypotension, laryngospasm and rare complaints of nausea and vomiting.^{14,17,18}

Dexmedetomidine proved to be favorable for pediatric sedation in a monotherapy regimen, considering its balanced hypnosis, similar to physiological sleep, and also its analgesic potential. So far, safe use of this drug in the studied population is restricted to the intravenous route, as a continuous infusion, with doses ranging from 0.2 to 0.7 mcg/

kg/h.¹⁰ Bolus doses and alternative routes still require more evidence to prove their safety on a large scale, especially for children.

Sedation for imaging exams

Sedation for imaging tests mainly requires immobility, which ends up being achieved through moderate hypnosis, without the need for analgesia if there are no invasive procedures associated, such as guided biopsies. Long duration exams and difficult access to the patient, such as in magnetic resonance imaging, require sedation techniques that differ considerably from those described in the previous section.

From the analysis of 10 studies,^{2,19-27} we observed that Propofol, in monotherapy, has been effective for this purpose with bolus from 1 to 2 mg/kg, with an average maintenance of 100 mcg/kg/min.^{19,20} Most commonly described adverse effects were desaturation, laryngospasm and hypotension.^{21,22} Combinations with Ketamine, Fentanyl and Dexmedetomidine were associated, respectively, with increased emesis with 1% incidence, optimized analgesia and bradycardia (Table 3).^{19,20,23}

Table 2 Summary of drugs, routes, doses and combinations most used for pediatric sedation in invasive and/or painful procedures

First author, publication year	Drug	Dose	Comments
Lam, 2018 ²	Midazolam	EV Bolus: 0,05 – 1 mg/kg (Monotherapy) 30-50 mcg/kg (In association)	Monotherapy is not advantageous. Association with Fentanyl is interesting for procedures with an average duration of 5 minutes. Association with Ketamine reduces nausea and awakening agitation, but prolongs it.
Azarfar, 2022 ¹¹ Monsereenusorn, 2022 ¹³			
Nemeth, 2017 ¹²			
Miller, 2014 ^{9,14}			
Sahyoun, 2021 ⁶ Homma, 2020 ¹⁰			
Homma, 2020 ¹⁰	Dexmedetomidine	Infusion: 0,2- 0,7 mcg/kg/h	There is still not enough evidence to recommend IM and IN bolus use.
Miller, 2018 ^{9,14}	Propofol	Induction: 0,5 – 1,5 mg/kg Continuous	Association with Ketamine improves side effect profile of both drugs.
Azarfar, 2022 ¹¹			
Yabrodi, 2022 ¹⁷			
Zhang, 2022 ¹⁵			
Guo, 2021 ¹⁶			
Homma, 2020 ¹⁰	Ketamine	infusion: 100-250 mcg/kg/min or 6-15 mg/kg/h	Combined use with Fentanyl increases the risk of significant respiratory depression.
Librov, 2020 ¹⁸			
Lam, 2018 ²			
Miller, 2018 ^{9,14}			
Azarfar, 2022 ¹¹			
Monsereenusorn, 2022 ¹³	Ketamine	EV Bolus: 0,25-4 mg/kg	Monotherapy is effective and safe. Better pharmacoeconomic profile. Associations with Midazolam and Propofol are recommended to reduce adverse effects, especially in children younger than 12 months.
Yabrodi, 2022 ¹⁷			
Zhang, 2022 ¹⁵			
Nemeth, 2017 ¹²			
Guthrie, 2019 ⁸			
Kumar, 2021 ¹			
Kwon, 2020			
Forrester, 2018 ⁷			
Homma, 2020 ¹⁰			
Librov, 2020 ¹⁸			
Schlegelmilch, 2021 ³	Fentanyl	Rectal Bolus: 0,75-3 mg/kg	Intranasal route was considered the best option for analgesia in emergencies.
Azarfar, 2022 ¹¹			
Monsereenusorn, 2022 ¹³			
Nemeth, 2017 ¹²			
Miller, 2014 ^{9,14}			
Homma, 2020 ¹⁰	Fentanyl	mcg/kg	Associations with Propofol or Midazolam are related to a shorter awakening time compared to Ketamine. Nausea, vomiting and nasal burning are frequent adverse events.
Kumar, 2021 ¹			

Table 3 Summary of drugs, routes, doses and combinations most used for pediatric sedation in imaging tests

First author, publication year	Drug	Dose	Comments
Lam, 2018 ² Malia, 2018 ²⁴ Cossovel, 2022 ²⁶ Mayel, 2020 ²⁵ Sayed, 2022 ²⁰	Midazolam	IN ou VO: 0,2 – 1 mg/kg	Consider for premedication. When in association, it was related to higher latency and longer time until awakening.
Chauhan, 2020 ¹⁹ Cossovel, 2022 ²⁶ Pfizer, 2021 ²⁷ Xu, 2022 ²³ Sayed, 2022 ²⁰	Dexmedetomidine	Bolus: 1-2 mcg/kg in 10 minutes Maintenance: 0,3 - 1 mcg/kg/h	Infusion in monotherapy more favorable than Propofol for longer procedures. By IN route, and in association with IN Ketamine, it seems to have a good safety profile and better results than association with Midazolam.
Chauhan, 2020 ¹⁹ McAndrew, 2021 ²¹ Gurcan, 2021 ²² Xu, 2022 ²³ Sayed, 2022 ²⁰	Propofol	Bolus: 1-2 mg/kg Maintenance: 100 mcg/kg/min	Infusion in monotherapy is associated with a higher desaturation incidence. Best choice when the goal is early awakening with a lower incidence of nausea.
Lam, 2018 ² Cossovel, 2022 ²⁶ Gurcan, 2021 ²² Xu, 2022 ²³	Ketamine	EV Bolus: 0,5-1 mg/kg	Consider for exams with an average duration of 15 minutes, to the detriment of Midazolam, and opt for the association with Propofol, with the intention of reducing the occurrence of vomiting.

Table 4 Summary of drugs, routes, doses and combinations most used for pediatric sedation for endoscopic procedures

First author, publication year	Drug	Dose	Comments
Mason, 2019 ²⁹ Amer, 2020 ²⁸	Dexmedetomidine	EV Bolus: 0,5 mcg/kg Maintenance: 0,15 ug/kg/min	Association with a Ketamine single bolus was effective until the end of the exam. Monotherapy infusion showed better results than Propofol infusion.
Amer, 2020 ²⁸ Mason, 2020 ²⁹ Bilgin, 2019 ³⁰ Gunathilaka, 2019 ³¹	Propofol	Induction: 1 mg/kg Maintenance: 0,4 ug/kg/min	Combined use is more favorable than isolated use.
Amer, 2020 ²⁸ Bilgin, 2019 ³⁰	Ketamine	EV Bolus: 0,5-1 mg/kg	Good results in association with Propofol.
Tschiedel, 2020 ³² Gunathilaka, 2019 ³¹ Bilgin, 2019 ³⁰	Fentanyl	EV Bolus: 2 ug/kg	There are no studies comparing this dosage with lower ones (eg 1 mcg/kg).
Tschiedel, 2020 ³²	Remifentanyl	0,06 mcg/kg/min	No episodes of chest tightness or apnea have been reported during its use.

Intranasal Midazolam has gained more adherence, due to better acceptance by the patient, need for lower doses and faster sedation onset, compared to oral route, despite sedation effectiveness and side effects incidence being similar between the two routes.^{24,25,26} Doses from 0.2 to 1 mg/kg showed good results in sedation for quick exams – such as computed tomography – or as pre-medication to facilitate cooperation and separation from parents.^{2,20,25,26} Most reported side effects were: agitation on awakening, diplopia, dizziness and hiccups.²

For imaging exams, only one study²⁶ discussed Dexmedetomidine intranasal sedation, while others reported the traditional intravenous use. As a single sedative, the dose used was 2 mcg/kg during 10 minutes (or until reaching RASS -5), followed by infusion of 0.3 mcg/kg/h.¹⁹ This scheme favored a lower desaturation incidence (6.8%) and a longer sedation mean time (25-28 minutes) when compared to Propofol infusion.¹⁹

Association with Midazolam (0.2 mg/kg IN), with a Dexmedetomidine bolus of 1 mcg/kg during 10 minutes before maintaining rate of 1 mcg/kg/h, was related to a longer latency (12-15 minutes) and a higher bradycardia incidence (22.9%).²⁰

Intranasally (4 mcg/kg), and associated with Ketamine, Dexmedetomidine had a shorter time (13.5 minutes) until the onset of

action.²⁶ Higher Dexmedetomidine maintenance doses (1.5 mcg/kg/h) save Propofol during combined sedation, which does not occur when using lower doses.²⁷

Analysis of intravenous Ketamine (1 mg/kg) and Propofol (1.2 mg/kg), in comparison with Fentanyl (1 mcg/kg) and Dexmedetomidine (0.3 mcg/kg), showed higher vomiting incidence, despite shorter waking up and recovery, with a 10.1 minutes difference between them, when the first combination was chosen. This one also required lower doses of both drugs.²² When associated with Dexmedetomidine, sedation with Ketamine was linked to a higher incidence (11%) of bradycardia and airway obstruction.²³ Intranasally, Ketamine as a pre-medication was compared to oral Midazolam, with a 0.5 mg/kg dose, with both medications associated with intranasal Dexmedetomidine with a 4 mcg/kg dose. Ketamine group presented a shorter sedation (13.5 minutes average), while Midazolam group guaranteed longer sedation, about 35 minutes.²⁶

Rectal route Ketamine was considered an alternative to oral route due to its faster reaction onset (15-30min). Its use with Midazolam was studied, obtaining satisfactory results using a 0.75 to 3 mg/kg dose. However, its isolated administration was not successful.²

Sedation for endoscopic procedures

We gathered 5 articles²⁸⁻³² with quality evidence regarding sedation for endoscopic procedures in pediatrics. None of them reported the use of Midazolam. Propofol was administered as a bolus (1 mg/kg) at the beginning of the procedures, followed by a maintenance rate of 0.23 mcg/kg/min, being effective for performing the tests.^{28,29} Among observed adverse effects, application pain, nausea and desaturation stand out. Associations with Ketamine, Dexmedetomidine and Fentanyl resulted in an improvement in recovery time and adverse effects profile.²⁸⁻³¹

Intravenous Dexmedetomidine (0.5 mcg/kg) was associated with Ketamine (1 mg/kg) in a single bolus to perform the tests, with the advantage of not requiring additional doses.²⁸ However, recovery time and adverse effects incidence was greater than when Ketamine was associated with Propofol.²⁸ For this, 0.23 mg/kg/min rate was used after a 0.5 mcg/kg Dexmedetomidine bolus, with a subsequent maintenance rate of 0.15 mcg/kg/h of Dexmedetomidine.²⁹ This association was more advantageous than isolated Propofol, reducing adverse effects incidence.²⁹

Ketamine use was reported only intravenously, showing good results with bolus doses between 0.5 and 1 mg/kg.^{28,30}

Despite endoscopic procedures painless character, opioids use was analyzed by Gunathilaka, in association with hypnotics. 2 mcg/kg of Fentanyl was administered in slow bolus for one minute after Propofol, and only 2 children out of 27 had a brief apnea episode.³¹ Remifentanyl (40 mcg/ml) proved to be an effective and safe alternative, with doses of 0.1 ml/kg/h or 0.06 mcg/kg/min, with a lower incidence of coughing, shorter recovery time and reduced Propofol consumption.³²

Discussion

Sedation can be subdivided into mild, moderate and deep sedation. Each subdivision has different purposes for performing procedures that are also different in terms of need for anxiolysis, analgesia and relative immobility. While in adult population, mild or moderate sedation are well indicated and sufficient for most procedures eligible for this anesthetic modality, in children, there may be a need to use deep sedation for procedures that could be performed with mild or moderate sedation in adult patients.

Fear and little or no cooperation, characteristic of this age group, mean that light sedation – which essentially consists of anxiolysis – cannot be used in the vast majority of cases. Then, alternatives fall into moderate sedation - more pronounced hypnosis plus an analgesic component - or deep, in which the chance of airway control loss and/or hemodynamic instability, in addition to an increased side effects incidence related to higher drugs doses, brings more insecurity to medical providers.

However, many of sedation related fears in pediatrics have their origin in past practices, mainly those involving the administration of older drugs, with a profile that today can be considered unacceptable in terms of adverse effects. Drugs such as Thiopental and Chloral Hydrate gave way to emerging drugs in sedation, such as Esketamine, Dexmedetomidine and Remifentanyl. And drugs that were already being used successfully gained new evidence, presenting new associations, optimized doses and more convenient and effective administration routes.

Association between Midazolam and Fentanyl was, for many years, the main choice among professionals for sedating children of all ages when performing invasive or painful procedures. However,

adverse reactions profile and its short duration sedation after a single dose of both drugs make this combination not the most recommended in the current context, taking into account the availability of effective and safe drugs such as Esketamine. Dissociative sedo-analgesia, which is this drug exclusivity, is attractive because it combines hypnosis and analgesia in the same drug, and because of the absence of respiratory depression, even at the highest doses recommended by the package leaflet. This advantage puts Esketamine as the first choice, as monotherapy, for many of the physicians involved in the administration of pediatric sedation. Despite this practice being very successful, both with intravenous (0.25-2 mg/kg) and intranasal (3-4 mg/kg) administrations, and being a good choice for procedures with significant short and medium term pain potential and also for those of longer duration (20-30 minutes), it should be taken into account that incidence of nausea, vomiting and hypersalivation is considerable. This fact demands selection of patients; perhaps those with a previous history of post-anesthesia emesis or those with more than one risk factor for such an event are not the best candidates. Hypersalivation with little swallowing control – a typical situation of infants – may be a factor that discourages this drug use in higher doses in this age group. For cases in which Esketamine monotherapy does not seem to be the best option, its association with Propofol (1 mg/kg for both) proved to be the most favorable in reducing nausea and vomiting incidence, as well as respiratory and cardiovascular depression, which may result from administration of higher doses (3-4 mg/kg) of Propofol. For shorter painful procedures, such as fracture reduction or biopsies, with a 10 minutes average duration, associations of Fentanyl (0.5-1 mcg/kg) with Propofol (0.5-1 mg/kg), and Fentanyl (0.5-1 mcg/kg) with Midazolam (30-50 mcg/kg), for procedures lasting about 5 minutes, can be considered.

Another drug that has been gaining prominence and applicability in recent years is Dexmedetomidine. Its low incidence of respiratory depression, when administered in continuous infusion with usual doses of 0.2-0.7 mcg/kg/h, and its analgesic potential, in addition to its hypnotic pattern that resembles “physiological sleep” - very different from the dissociative state of Esketamine, which can be accompanied by hallucinations and nightmares - has aroused much interest from researchers and providers. Despite its undeniable advantages, Dexmedetomidine has a slow onset of action, in addition to promoting longer-lasting sedation without the possibility of immediate reversal, factors that still make its widespread use as monotherapy in pediatric procedural sedation unfeasible. Intranasal route was used almost equally in the reference articles for the present study, although the bolus use of Dexmedetomidine in the pediatric population, by any route, is indisputably associated with a considerable incidence of bradycardia, which is particularly worrying in this age group, due to the physiologically increased vagal tone. Its intramuscular administration, although it became popular in Brazil after publicizing the practice on social networks, never had minimal scientific evidence to support such a technique, so the authors of this article do not recommend such conduct.

Dexmedetomidine has been successfully used during longer sedation (from 15 to 35 minutes) to perform magnetic resonance imaging and colonoscopies, mainly, as well as Propofol (100 mcg/kg/min). In fact, we observed that there was no benefit in the association between drugs for pediatric sedation in imaging exams. All associations increased the incidence of adverse effects, in addition to making sedation unnecessarily long. For shorter imaging tests, such as computed tomography, the use of Propofol alone, preferably in continuous infusion and at lower doses, proved to be the best option. Premedication with Midazolam (0.2-1 mg/kg IN) or Esketamine (0.5-

1 mg/kg) can be considered with a view to facilitating the separation of parents at the time of the examination, with Midazolam being reserved for cases in which a sedation of about 30 minutes it's necessary. The isolated use of Midazolam as a sedative is not effective, but its value as oral premedication (0.25-0.5 mg/kg) is still relevant. Although the intranasal route of administration has been used almost as often as the intravenous route, significant nasal discomfort resulting from this technique must be taken into account. Therefore, although the oral latency time (10-20 minutes) is not so attractive, the acceptability and satisfaction of the patient and his/her caregiver are higher.

Propofol can also be considered a drug of choice for performing upper digestive endoscopies, preferably associated with an opioid such as Fentanyl or Remifentanyl. The use of Remifentanyl for this purpose and for the pediatric population is recent, but successful, ensuring comfort, analgesia and autonomic stability at low doses (up to mcg/kg/min), with no reports of adverse events. An incidence of apnea of 7% was found after administration of 2 mcg/kg Fentanyl slow bolus during sedation for endoscopic procedures, contrasting with the absence of this event when Fentanyl was administered at a dose of 1 mcg/kg in other studies. Fentanyl doses greater than 1 mcg/kg in pediatric sedation also do not seem to bring greater benefits, which invalidates the risk, in the authors' opinion. Considering the apparent success of Remifentanyl in sedating endoscopic procedures, its use for the same purpose in invasive and/or painful procedures deserves further investigation and construction of robust evidence, with a view to a possible reduction in the incidence of adverse events resulting from the use of other opioids and increasing the safety and effectiveness of sedation in pediatrics.

Conclusion

Pediatric sedation still an open field for research, especially in our country. The multiplicity of age groups, procedures and potential routes of administration still leaves questions about the best approaches. However, we can immediately infer that emerging drugs such as Dexmedetomidine do not meet all demands nor are they the best choice in all circumstances. On the other hand, more traditional drugs such as Midazolam and Propofol still have well established roles, and should not be neglected.

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Author's contribution

Ana Clara Monteiro Laranjeira was involved in Ideation, structuring, planning, search and selection of articles, translation, revision, approval of the submitted version.

Fernanda Cardoso Andrade, Léa Jenifer Souza Cordeiro, Letícia Barros Cardoso, Beatriz Metedeiro Nunes Câmara, Júlia Carvalho de Miranda were involved in searching for articles, tabulating data, creating tables, approval of the submitted version.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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