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SEDATION IN PEDIATRIC EMERGENCY DEPARTMENT

A Thesis Submitted in Partial Fulfilment of the Requirements for the Degree Master of Medicine

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1. SUMMARY

Research title: Sedation in Pediatric Emergency Department

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Aim: To find out the best sedation methods for children in pediatric emergency department.

Objectives:

1. To review non-pharmacologic pain management in pediatric emergency department.
2. To analyse the most suitable route for drug administration during sedation and analgesia.
3. To analyse the most effective pharmacological agents for sedation and analgesia in pediatric emergency department.

Methodology: The study was a literature review. This literature review was carried out using principles from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) The selected articles were published in bibliographic data base of „PubMed" and "GoogleScholar". For search key words were used. During search the filters applied: English language, 5 years, free full text was applied. The key words were typed into the database of „PubMed" and "GoogleScholar". 19 publications were included into this literature review.

Results: 1012 publications were found during the search. 19 publications were included into this literature review. Publications included into this literature review were 7 systematic literature reviews, 3 online questionnaires, 3 randomized control trials, 1 narrative review, 1 meta-analysis, 1 single-blind randomized trial, 1 systematic review and meta-analysis, 2 observational studies.

Conclusion:

1. Non-pharmacologic methods are effective in reducing stress, discomfort prior to painful procedures. It should be used more frequently for better procedure performance.
2. Intranasal route of administration is most suitable for paediatric patients and agent of choice should be midazolam.
3. For laceration repair most suitable is topical anaesthetic. For light pain ketamine or midazolam shows good effect. For acute pain fentanyl is preferred or benzodiazepine – opiate combination. Dexmedetomidine is preferred as premedication before anaesthesia.

2. ACKNOWLEDGEMENTS

I express my gratitude to my family who supported me through every step of the way.

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3. CONFLICTS OF INTERESTS

The author reports no conflicts of interest.

4. ETHICS COMMITTEE APPROVAL

Approved by: LSMU bioethical center

Biomedical research name: Sedation in pediatric emergency department

Number: BEC-MF-07

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5. ABBREVIATION LIST

BAER – brainstem auditory evoked response

DEXA – Dexmedetomidine

ED – emergency department

EEG - electroencephalogram

IM – intramuscular

IN – intranasal

IV – intravascular

MAD – mucosal atomizer device

MDZ - Midazolam

mg/kg/h – milligram per kilogram per hour

PE – parenteral

SQ - subcutaneous

µg/kg – microgram per kilogram

6. TERMS

1. Analgetics - an agent producing diminished sensation to pain without loss of consciousness.
2. Reye's syndrome - a rare but serious condition that causes swelling in the liver and brain.
3. Sedation - the action of administering a sedative drug to produce a state of calm or sleep.
4. Sedoanalgesia - is the practice of combining sedation with local anesthesia, usually in the case of surgery.

7. INTRODUCTION

Acute pain is one of the most common symptoms in children admitted to the pediatric emergency department and its management can cause clinical problem for physicians and healthcare providers. Different painful procedures like laceration repairs, incisions, extremities fractures and drainage, but also simply the placement of an intravenous catheter, can be stressful and painful to young children but also stressful for their parents. Child's pain perception can be worsened by some emotional factors like elevated anxiety, distress, anger, and low mood. This can make subsequent medical procedures and pain management even more difficult [1].

If the pain is not treated it could affect the child's mental health long-term, that will result in detrimental psychological effects, negative long lasting memories and possibly bad response to future painful clinical episodes [2]. The importance of providing adequate procedural sedation for children include decreasing patient anxiety and emotional trauma, decreasing parental emotional discomfort, and completion of the procedure, reducing stress for operators and shortening the time of procedure duration [3].

Physiological parameters such as heart rate, blood pressure, respiratory rate, oxygen saturation, or salivary cortisol are indirect pain measurements [4]. Although these measurements cannot be used alone. These meassurements is highly variable in the age group from 0 to 3 years [5]. The method of pain measurement is setting oriented and highly depends on medical staff experience as well as the individual patient [6].

Purpose of this work is to find the most effective sedation route and analgesia methods in pediatric emergency department and discuss the importance of non-pharmacological pain management by performing a litterature review.

8. AIM AND OBJECTIVES

Aim: To find out the best sedation methods for children in pediatric emergency department.

Objectives:

1. To review non-pharmacologic pain management in pediatric emergency department.
2. To analyse the most suitable route for drug administration during sedation and analgesia.
3. To analyse the most effective pharmacological agent for sedation and analgesia in pediatric emergency department.

9. LITERATURE REVIEW

9.1 Pain measuring scales

Children express and understand pain differently depending on their age. Pain must be assessed depending on the age. For younger than 1 year the Neonatal Infant Pain Scale (NIPS) is used. In this scale facial expressions, crying, breathing, position of arms and legs, and alertness of a baby are evaluated by a medical professional. The maximum score is 7. If the patient scores above 3, a newborn or a baby is in pain. Another scale, called FLACC. In this scale face, legs, activity, cry, and consolability are evaluated. This scale is recommended to assess pain for children from 2 months to 7 years old. Evaluation is done in at least 5 min if a patient is sleeping and 1–5 min if a patient is active. A score from 1 to 3 indicates mild pain, 4–6 average pain, and 7 and higher shows severe pain, in this scale the maximum score is 10. The Revised Faces Pain Scale (FPS-R) is used for children from 4 to 16 years of age. A scale with faces reflecting the mood is shown to a patient and explained that each face shows intensity of pain. A child is asked to show the face that is showing child's pain the best. Every face indicates a certain score (0, 2, 4, 6, 8, 10). The Visual Analogue Scale (VAS) is used only for older children, from the age of 7 or 8. In this scale, a medical professional draws a line of 10 cm. There are two sides of the line, one side of a line means absence of pain, the opposite side means unbearable pain. The child must show the point on the scale representing his/her pain the best. The score of VAS is measured and assessed. If a child marks 0–4mm score, it means no pain, 5–44 mm score as mild pain, 45–74 mm score as moderate pain, and a 75–100 mm score as severe pain. The Color Analog Scale (CAS) used by explaining which color means the highest and lowest pain. The line is measured and scores are calculated [7,8].

9.2 Sedation levels and general anaesthesia

Minimal Sedation (Anxiolysis) is a drug-induced state, patients are able to respond normally to verbal commands. cognitive function and physical coordination can be affected. Airway, spontaneous ventilation, and cardiovascular function are unaffected.

Moderate sedation/Analgesia (Conscious Sedation) is a drug-induced depression of consciousness and patients respond purposefully to verbal commands. For airway no intervention is required, spontaneous ventilation is adequate, cardiovascular function is unaffected.

Deep sedation/Analgesia causes depression of consciousness. Responsiveness is decreased even if repeated or painful stimulus is used. For airway intervention might be required, spontaneous ventilation might be impaired, cardiovascular function is usually maintained.

General Anaesthesia is drugs induced loss of consciousness. Patients are not arousable. Independent ventilatory function is impaired and patients usually need support to maintain the patent airway and positive pressure ventilation is usually needed due to depressed spontaneous ventilation. Cardiovascular function might also be impaired [9,10].

It is estimated that more than around 50% of children benefits from minimal to moderate sedation during perioperative or procedural periods to treat or prevent behavioral stress and anxiety caused by separation from their families, the presence of an unfamiliar environment, or fear of pain. It is much easier to make interventions with a child who is calm, in order to prevent psychological distress prior to or during the intervention, to avoid poor communication or cancelation, and any negative impact on postoperative recovery or other possible long-term psychological consequences [11].

9.3 Routes of sedation

Different routes can be used of drug administration to provide analgesia and anxiolysis to children. Drugs can be administered via oral, parenteral, rectal, intramuscular, or intranasal route. Oral administration has a slower onset of action, and the child can cooperate. The parenteral route requires intramuscular administration or placement of an intravenous catheter, which can be painful and cause anxiety for the child. Therefore, it might require a person who is able to place an IV catheter quickly and effectively. Although this is a safe route that can provide rapid and almost immediate analgesia. Administration via IN route is easy, non-invasive, and almost always well tolerated by children. Drugs administered intranasal have a rapid onset of action and high bioavailability [12,13].

Intranasal route of sedation is practical and non-invasive. Sedation is reached via IN administration due to the rich vascular plexus cavity which communicates with the subarachnoid space via the olfactory nerve. Absorption of intranasal administered drugs depends on anatomical properties and specific properties of the drug used. About 3–5% of surface area in the nasal cavity is covered by the olfactory epithelium that offers direct contact to the central nervous system (CNS). Volumes of 0.3 ml or less for nostril are easily tolerated. Larger volumes are contraindicated as the drug ends up in the nasopharynx [14]. Absorption depends on the time during which drug is in a direct contact with the

mucosa. The drug absorption occurs within 30 minutes from the IN administration, then the remaining drug may be eliminated by the mucociliary apparatus [15].

Two ways are available to administer IN medications: by dripping or atomization. By dripping only a syringe is required and a compliant child. In the second way atomized mucosal device (MAD) is used. Medication is broken down to smaller pieces which makes it more easily absorbed and leads to rapid administration [16]. Most used for intranasal sedation is fentanyl [17].

If parenteral route is used, Midazolam is most common used agent. Usually used for premedication or anxiolysis for children. It must be combined with other medications. It causes decreased memory of unpleasant procedures. Midazolam is not suitable for irritated patients and adequate breathing must be checked [18].

For inhalational route mostly used agent is nitrous oxide. Nitrous oxide is delivered with oxygen and has a rapid anxiolytic, analgetic or sedative effect. Sevoflurane or fluorinated methyl isopropyl has been used frequently for inhalation induction of anaesthesia. As it causes rapid induction and quick elimination, Sevoflurane may be useful for sedation only by professionals who are skilled in general anaesthesia [19].

Rectal route is disliked by children and adolescents but is well tolerated by young infants that are younger than 12 months. Drug absorption can be variable. This route is useful in the peri-operative setting and for infants and children especially who have severe nausea and vomiting. Always ask consent from parents/ carers before using this route [17].

Intramuscular injections are very painful and not recommended to use in children [17].

9.4 Sedative drugs

9.4.1 Non-pharmacological sedation

Distraction techniques such as music, videogames, virtual reality, or simple talk about movies, friends, or hobbies as well as cutaneous stimulation, vibration, cooling sprays, or devices are effective to relieve procedural pain and anxiety. A choice of distraction technique should be individualized, based on children who could benefit from non-pharmacological pain treatment methods or tools.

Non - pharmacological pain management may reduce dosage of pain medication or exclude pharmacological pain management. Most non-pharmacological treatment methods are cheap, easily

accessible, and safe to use on every child, so it should always be a first choice when planning a patient's care [7].

According to the age of a child and procedure performed various methods and techniques can be used. Calm, comfortable, and safe environment, parent and trained staff should be near the child. Different methods can be used such as distraction techniques and equipment such as deep breathing, guided imagery, music, iPad, hypnosis leading to progressive muscle relaxation, coetaneous stimulation methods such as counter irritation (cold, vibration, pressure), touch or sweet solutions [20]. Canbulat et al. [21] demonstrated that distraction cards and kaleidoscopes significantly reduced pain and anxiety caused by venipuncture in 7–11 year-old children.

Music has been shown to have a calming effect as a therapeutic method. There are different types of music therapy that includes active or live music, passive music, or music videos which could be used before or during the procedure. All these methods have showed benefits in decreasing procedural pain and anxiety [22]. In addition to this research Nguyen et al. [23] showed that music therapy reduced pain and anxiety in children undergoing lumbar puncture.

9.4.2 Midazolam

Midazolam is a short acting benzodiazepine and is the sedative of choice in most PICUs. Midazolam can be administered orally, rectally, intramuscularly, intranasally and intravascularly. Mainly used for procedural sedation. Side effects can be tolerance, dependence, and withdrawal. Could be a risk of paradoxical hyperactivity when given as a bolus dose [8]. Midazolam also causes amnesia, could cause mild depression of hypoxic ventilator drive [10]. Shapiro et al. [24] showed that midazolam spray causes relief to children that are anxious about minor medical procedures, for example insertion of a needle in a subcutaneously implanted intravenous venous blood sampling and venous cannulation. Besides sedation and anxiolysis, midazolam also provides anterograde amnesia, minimising children's recall of unpleasant experiences after a PICU admission [25].

Used for anxiolysis for non-invasive radiologic imaging. If painful procedures analgesic should be added [19]. Incombination, midazolam and fentanyl provide moderate sedation for painful procedures. However, the risk of respiratory depression and apnea are increasedin a dose-dependent manner. It is generally advisable to choose one drug for initial administration and titrate slowly to reach the effect with the second drug [25].

9.4.3 Ketamine

Ketamine is one of the medications, which is used commonly for moderate sedation in pediatric patients [25]. It was from the beginning developed as ananesthetic agent but now is used more commonly for anaesthesia but also as sedation and amnesia [25]. Ketamine causes least adverse effects when used alone [10]. Ketamine is a central sympathetic nervous system stimulant and may lead to mild hypertension and tachycardia. Unlike opioids, it does not produce respiratory depression or decrease airway tone [25]. Side effects include sialorrhea, psychotogenic reactions such as emergence delirium, disorientation, hallucinations and combativeness at higher serum concentrations [8]. Other side effects can be emesis, apnoea, hypersalivation, laryngospasm [25]. Brown et al. [27] showed in a retrospective study, that in children with autism spectrum disordersin ED, the most common sedatives used were IV ketamine and IN midazolam. Ketamine is contraindicated in psychosis, intraocular trauma or glaucoma, systemic hypertension and thyrotoxicosis [25].

Over 2000 sedations are delivered in the hospitals every year and ketamine is the most frequently used. Green et al. [28] report that ketamine at doses of 4 to 5 mg/kg intramuscularly produced adequate sedation in 98% of children. Airway complications occurred in 1.4% of patients that included laryngospasm, apnoea, and respiratory depression, all were quickly identified and treated without intubation [28].

9.4.4 Fentanyl

Fentanyl is used for analgesia. It is a synthetic morphine derivative that is highly lipophilic and fat soluble, it is more than 100 times potent than morphine and causes very quick onset in less than 1 to 2 minutes and acts around 1 hour with intermittent doses [8]. Morphine and fentanyl together are the most used peroral analgesics. Intranasal fentanyl at dose 1–2 mcg/kg, is an alternative to achieve rapid analgesia in the hospitalized child who does not have intravascular access [29].

Fentanyl depresses the heart rate response, and if a child is heart rate dependent fentanyl can cause increased heart rate. Fentanyl has also advantages, especially for reducing heart rate response to intubation and laryngoscopy [8]. Other adverse effects can occur such as nausea and vomiting, pruritus, bradycardia, chest wall rigidity usually with doses >5 μg/kg but can occur at all doses and treatment with naloxone or neuromuscular blockade is given. Rarely causes cardiovascular instability (relatively safer in hypovolemia, congenital heart disease, or head trauma). Respiratory depression effect is longer than

analgesic effect around 4 hours. Levels of unbound drug are higher in newborns. Fentanyl is most commonly used opioid for short, painful procedures [10].

9.4.5 Propofol

Propofol is an intravenous sedative-hypnotic agent that is used for induction and maintenance of deep sedation and general anaesthesia. Propofol is a diisopropylphenyl anaesthetic and has a significant importance in critical situations because it has a rapid onset 1–2 minutes, high potency that constantly produces the wanted sedative effect and antiemetic and euphoric properties that lead to more positive patient experience [8]. Used for anxiolysis for non-invasive radiologic imaging. If painful procedures are performed analgetic should be added [19]. Side effects include hypotension and/or bradycardia, respiratory depression, apnoea, hypertriglyceridemia, and pancreatitis. If used prolonged infusion rates of >4 to 5 mg/kg/h and use of long time propofol infusion in paediatric patients it can lead to propofol infusion syndrome (PRIS) characterized by lactic acidaemia, rhabdomyolysis, dysrhythmias, cardiac arrest, and a high mortality rate [8]. Other side effect includes pain at the injection site. It Is contraindicated in allergy to soybean oil, egg lecithin (yolk), glycerol and EDTA [25].

9.4.6 Morphine

Is an hydrophilic opioid, standard bolus dose reaches its action in 10-20 minutes and acts 2-4 hours. Dosing of morphine must be done paying attention to the age, physiology, and medical condition of the child. Morphine is still the most used sedative in the PICU. Side effects include vasodilation, hypotension, bronchospasm, and pruritus, however they are not usually clinically significant [8].

Common dose of morphine IV 0,1 mg/kg/dose, onset of action in 5-10 min and acts 3-4 h, IM/SQ 0,1-0,2 mg/kg/dose onset of action is 10-30 min and duration 4-5 h, given PO doses 0,3-0,4 mg/kg/dose, onset of action is 30-60 min and acts for 4-5 h. Can cause histamine release, seizures in neonates. Morphine is mainly used for chronic pain [10].

9.4.7 Dexmedetomidine

Dexmedetomidine is a highly selective α 2-adrenoreceptor agonist and has sedative, analgesic, and anxiolytic properties. It has been widely used in clinical practice. In systematic review and meta-analysis that compared the efficacy and safety of intranasal dexmedetomidine with oral chloral hydrate in infants and toddlers. The results showed that patients who were sedated with intranasal Dexmedetomidine had considerably higher success rate of sedation when compared with those patients

sedated with oral chloral hydrate [30]. The primary indication for dexmedetomidine use is sedation but analgesia occurs a side effect. Dexmedetomidine does not depress respiration or airway reflexes. Adverse events if bolus is administered are transient bradycardia or mild hypertension [31,32]. Used for non-invasive radiologic imaging, BAER or EEG. During painful procedures can be combined with ketamine [19].

9.4.8 Nitrous Oxide

Nitrous oxide is an anaesthetic gas. It can be delivered in different concentrations with oxygen. It causes modest analgesia and sedation with minimal respiratory and cardiovascular depression. Nitrous oxide can be delivered painlessly through inhalation. It has quick onset of action 3-5 min and quick recovery which makes it ideal for use in the ED. Usually known as Entonox (50% nitrous oxide/50% oxygen). Nitrous oxide is useful for procedures such as suturing, insertion of an intravenous cannula and burns dressings. Nitrous oxide has no effect for procedures such as incision and drainage of complex or deep abscesses. Side effects include vomiting, nausea, dizziness, light headedness and more severe side effects aspiration, airway obstruction and diffusion hypoxia. Nitrous oxide is contraindicated in infants under 12 months, acuter upper respiratory tract infection or exacerbation of asthma, chest injury or abdominal distension or bowel obstruction, head injury, pulmonary hypertension and folate or b12 deficiency [25]. As well as airway obstruction or impaired consciousness. Child needs to be fasted for 2 hours to prevent vomiting. And is usually safe because it has low risk of upper airway reflexes loss [17]. Nitrous oxide can be combined with intranasal fentanyl, oral opioids, and midazolam [25].

9.4.9 Paracetamol

Paracetamol is effective for mild to moderate pain. It has good effect in post-operative or chronic pain like musculoskeletal or migraine. For severe pain it can be combined with NSAIDs to reduce opioid requirements. In the peri-operative pain patients, paracetamol should be administered up to two hours before expected painful procedures because there are delays between dosing and peak analgesic effect. Paracetamol is effective and can be used for elective and urgent surgery if given as a part of any pre-medication for anaesthesia. Peri-operative analgesia can be combined with local or regional analgesia, opioids, and nonsteroidal anti-inflammatory drugs. Rectal administration should be avoided unless oral route is not available [33].

9.4.10 Ibuprofen

Ibuprofen is not recommended for use in pediatric acute pain management due to the risk of Reye's syndrome although it is regularly used in pediatric rheumatology and cardiology. It is very effective in post-operative pain, headache and musculoskeletal pain. Indicated in surgical patients who require IV analgesia particularly those undergoing orthopaedic surgery, general surgery such as appendectomy and dental surgery. Patients requiring IV analgesia not suitable to receive opioid analgesia or where opioid-sparing is important in for example patients that are at risk of respiratory depression. Patients unable to tolerate oral medication immediately following surgery [17].

9.4.11 EMLA

Eutectic mixture of local anaesthetic (EMLA) cream is a topical anaesthetic mixture combined of Lidocaine (2.5%) and Prilocaine (2.5%) in a cream base. EMLA cream is commonly used for pain after paediatric procedures such as venipuncture. It is applied over the needle injection site, where it is absorbed into the skin. Many previous studies have shown that the EMLA cream is effective in reducing injection-related pain [34].

Local application of EMLA at least 30 minutes before the procedure over both groins and any other access site can significantly reduce the amount of sedation required for insertion of catheters and the remainder of the usually painless procedure [35].

10. RESEARCH METHODOLOGY AND METHODS

10.1 Research Type

Literature review.

10.2 Literature search methods

This literature review was carried out using principles from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist 2020 [35] and Final Master Thesis (FMT) requirements proposed by Lithuanian University of Health Sciences (LUHS). The search was performed using PUBMED/ NCBI and GoogleScholar. The search and analysis was performed between 2021.07.10 – 2022.04.07. For search these words and word combinations were used: „midazolam", „ketamine", „propofol", „fentanyl", „morphine", „nitrous oxide", „dexmedetomidine", „pediatric sedation", „emergency".

10.3 Publication inclusion and exclusion criteria

Publications were analysed according to the aim and questions applied for this work. The research question was performed using PEOS (population, exposure, outcome, and study design) in accordance with Final Master Thesis (FMT) requirements proposed by Lithuanian University of Health sciences (LUHS).

Population: Paediatric patients in paediatric emergency department.

Exposure: Sedation and analgesia during procedures in emergency department.

Outcome: Effectiveness of sedation and analgesia.

Study design: Observational studies including systematic reviews and meta-analysis, randomized control trials articles, retrospective/ prospective analysis, narrative reviews, and cohort studies.

Inclusion criteria

Primary scientific studies that evaluated various aspects sedation and analgesia in paediatric emergency department in accordance with the aim and objective of this literature review were eligible.

Main inclusion criteria were english language, free full text, 5 years, articles containing paediatric sedation, analgesia, anaesthesia.

Exclusion criteria

Exclusion criteria were publications older than 5 years, articles not in English language, not free articles, articles containing other than paediatric patients, adults, procedures outside emergency department or other procedures performed outside of the hospital.

10.4 Information sources

A comprehensive literature search was conducted to find and collect articles relative to the topic sedation and analgesia in pediatric emergency department. The included data were provided from: PUBMED/ NCBI and GoogleScholar.

10.5 Study selection

Initial screening

The key words were typed into the database of PubMed and Google scholar including all types of studies like for example cohort studies, meta-analyses etc. After the initial search, 1012 publications were found. Duplicates were automatically removed by the reference manager programme “Mendeley” leaving 500 publications. Filters were applied; publications that were in English language, not older than 5 years, free of charge and available in full text, 182 publications were left. The titles and abstracts were read, and 136 publications were selected for the second screening.

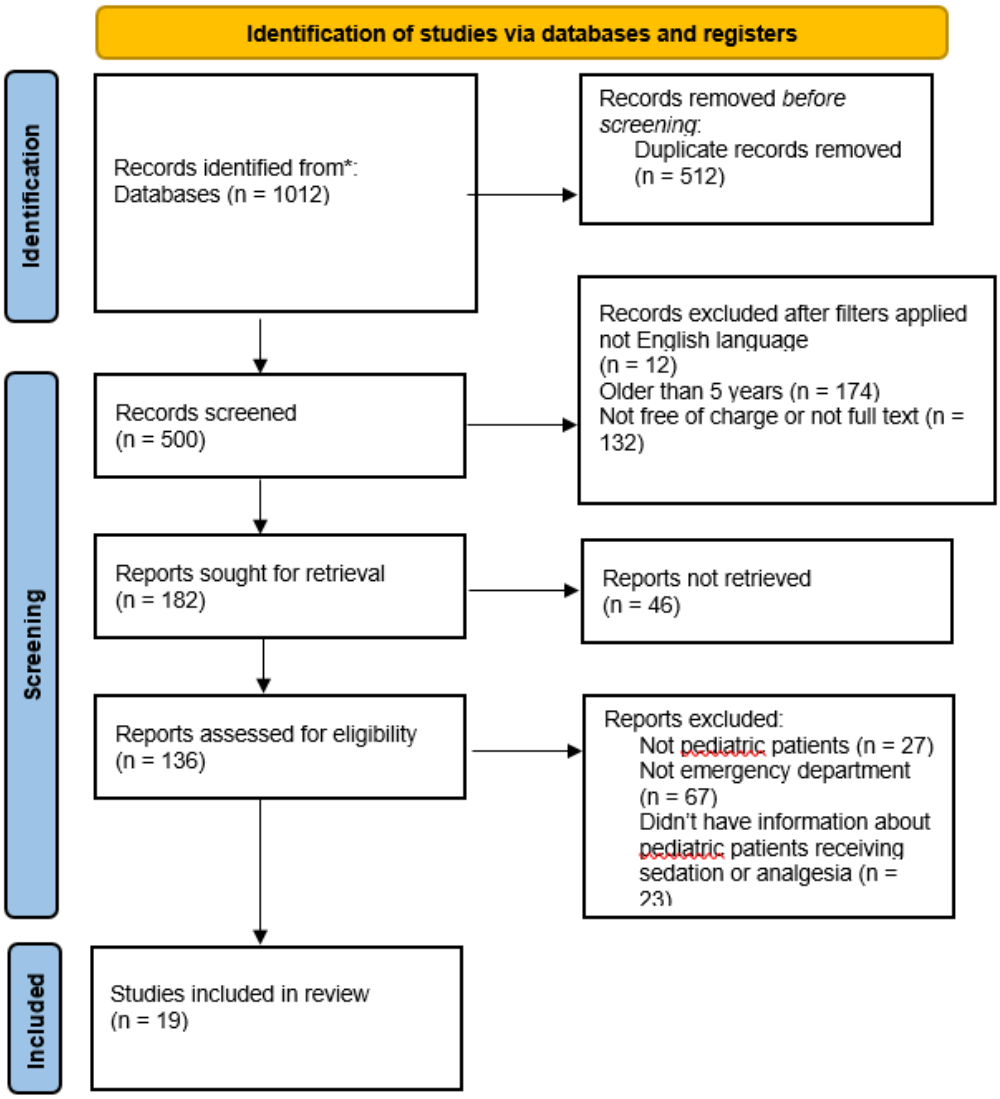
Second screening

In the second screening process the full text of the remaining articles were analysed according to inclusion and exclusion criteria for this systematic review. Once all 19 publications were included into this literature review. 7 systematic literature reviews, 3 online questionnaires, 3 randomized control trial, 1 narrative review, 1 meta-analysis, 1 single-blind randomized trial, 1 systematic review and meta-analysis, 2 observational studies.

10.6 Data extraction and synthesis

Data extracted were paediatric patients receiving some sedation or analgesia in emergency department.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



11. RESULTS

11.1 Publication characteristics included into the systematic literature review

43 articles after filters English language, free full text, not older than 5 years from which 19 were suitable answering the question which pharmacologic agent is most suitable for sedation in analgesia in podiatric emergency department.

For the final analysis all inclusion criteria fitted 19 publications. In this literature review publications that were included had relationship between sedation and analgesia in paediatric emergency department. Most of the publications were systematic reviews, one narrative review, one meta-analysis, one prospective observational study and one randomised control trial.

Table 1. Main publication characteristics

Nr.	Research author	Research year	Parameters investigated	Research type	Results
1.	E. D. Trottier, et al. [36]	2019	Managing pain and distress in children during diagnostic and therapeutic procedures.	Systematic literature review	Non-pharmacological pain management reduce pain and distress during procedures.
2.	V. Susam et al. [37]	2018	Efficacy of the Buzzy System for pain relief during venipuncture in children.	Randomised control trial	The Buzzy System combined to distraction cards showed a greater reduction of perceived pain than.
3.	C. E Chumpitazi et al. [38]	2022	Managing acute pain in children presenting to the emergency department without opioids.	Systematic literature Review	Traumatic patients vital signs should be evaluated and opioids used appropriate.
4.	S. J Friedrichsdorf [39]	2019	Pediatric pain treatment and prevention.	Systematic literature review	Different non-pharmacological techniques can improve acute pain.
5.	C. Fentacci et al. [40]	2018	Intranasal administration of drugs in pediatric	Systematic literature review	IN sedation is safe in pediatric ED. IN sedation via MAD is

			emergency department.		effective and safe and should be one of the first choices for procedural sedation in children.
6.	V. Pansini et al. [41]	2021	Intranasal agent administration to pediatric ED patients.	A narrative review	IN analgosedation is a simple, rapid and painless option to prevent and treat the pain and anxiety in the Pediatric Emergency Department.
7.	J. L. Miller et al. [42]	2018	Extravasclular drug administration.	Systematic literature review	Midazolam and N_2O were the most common agents, with oral (PO) midazolam being the most common agent.
8.	M. Mayel et al.[43]	2020	Intranasal Midazolam sedation.	Single-blind randomized trial	Is effective for sedation in pediatric ED.
9.	T. M Frey et al. [44]	2019	Effect of Intranasal Ketamine vs Fentanyl on Pain Reduction for Extremity Injuries in Children.	Randomized clinical trial	Intranasal Ketamine is more effective than Fentanyl in pediatric ED patients.
10.	L. Oliveira et al. [45]	2020	Intranasal Ketamine for acute pain management.	Systematic review and meta-analysis	Intranasal analgesic-dose ketamine may be considered as an alternative to opioids for acute pain management in children.
11.	S. L Reynolds et al.[46]	2017	Comparison of intranasal Ketamine to Fentanyl for analgesia in	Randomised control trial	Intranasal ketamine was associated with causing less side effects.

			children with suspected fracture.		
12.	C. E. Ramalho et al. [47]	2017	Sedation and analgesia for procedures in pediatric ED.	Systematic literature review	Indications of appropriate drugs were described in pediatric ED.
13.	C. Sahyoun et al. [48]	2021	Sedation and analgesia in Europe in pediatric ED	Online questionnaire	19 countries answered and participated in this study and agents used were analysed
14.	D. Marco et al. [49]	2022	Pain and sedation monitoring in pediatric ED across Europe	Online questionnaire	Most used drug combinations across 21 countries were opioid with a benzodiazepine mainly fentanyl and midazolam
15.	F. Ekinci et al. [50]	2021	Sedation and analgesia in pediatric ED in 27 centers.	Online questionnaire	27 centers out of 33 to participate and most common used drugs were analysed.
16.	N. Gupta et al. [51]	2022	Nitrous oxide use in pediatric ED patients.	Systematic literature review	Using of nitrous oxide combined with local anaesthetics has shown to be significant to use in pediatric patients.
17.	W. S. Kim et al. [52]	2017	Ketamine use in sedation for children in ED.	Observation study	Ketamine administration via IV route should be considered using in children.
18.	M. Bhatt et al. [53]	2017	Risk factors for adverse events during sedation in pediatric ED.	Observational study	Ketamine used alone than in combination showed better outcomes.
19.	J. F Feng et al. [54]	2017	Comparison of dexmedetomidine versus Midazolam for premedication in pediatric patients.	Meta-analysis	Dexmedetomidine is better alternative.

11.2 Non-pharmacologic importance prior to painful procedure.

As E. D. Trottier, et al. [36] reviewed ssual medical procedures to assess and treat patients can cause significant pain and distress. Clinicians should have a basic method for minimizing pain and distress in children, mostly for frequently used diagnostic and therapeutic procedures. As shown in practice upright sitting position is more comfortable for children as it improves children's sense of control. For infants breastfeeding or sucrose solution has positive effect in reducing stress in venipunctures, intramuscular injection etc. Communication with children as a parent or a clinician is important from 4 years by explaining the procedure, showing tools to be used might help to reduce stress and make the procedure easier. Distraction strategies like blowing bubbles, reading a story, showing an animated video, an interactive game is effective in reducing the pain and distress related to a variety of needle procedures. Music therapy seems to reduce distress and pain in some children undergoing acute painful procedures. Additionally V. Susam et al. [37] demonstrated that Buzzy system to decrease pain in pediatric patients also had positive effects. The experimental group showed significantly lower levels of pain (p =.039; 95% CI: -2,11; -0,06) in terms of the mean = 3.65 ± 2.011; median = 3, compared to the control group (mean: 4.67±2.14, median = 4). Caregivers were satisfied with the Buzzy System.

Although as presented in review by C. E Chumpitazi et al. [38] in emergency department patients should be evaluated as trauma present and vital signs. Appropriate pain management is chosen as sometimes non - pharmacological strategies are not enough but it can decrease anxiety and stress.

According to S. J Friedrichsdorf [39] for elective procedures like needle sticking, venipunture or vaccination there are 4 ways to decrease pain and reduce anxiety for pediatric patients admitted to ED. Those include topical anaesthesia such as lidocaine, comfort positioning, sucrose or breastfeeding for infants and techniques appropriate for age nitrous oxide.

11.3 Route of administration in pediatric emergency department

According to C. Fentacci et al. [40] in a systematic literature review intranasal drug including midazolam, fentanyl, ketamine, sufentanyl, dexmedetomidine and nitrous oxide were reviewed. administration in paediatric emergency department were analysed. Analysis on type of administration also was made, better to administer by mucosal atomizer device or by drop instillation. Intranasal route doesn't require venous access such as IV catheter placement as it is quickly absorbed through nasal mucosa into the circulation. Procedural sedation is now being used in a variety of conditions, both for diagnostic purposes, such as urine sampling and lumbar punctures, and therapeutic purposes, such as

intravenous insertion, wound care, and orthopaedic trauma. As stated in the article best way to administer IN agents is MAD. Most studied agent is IN midazolam. Atomized IN midazolam and Ketamine are useful also. Midazolam at dose route of 0.4-0.5 mg/kg causes amnesia and anxiety. Nitrous oxide and sufentanil doesn't control pain otherwise has similar action as midazolam. Opposite, ketamine and fentanyl are used for their pain controlling action at the administration dose of respectively 5-9 mg/kg and 1.5-2.0 μg/kg. They state that IN drugs are safe and effective. Use of IN dexmedetomidine is also being more frequently used. In addition V. Pansini et al. [41] described in the narrative review described Intranasal drugs for analgesia and sedation in children admitted to pediatric emergency department described that in recent years intranasal route of administration has become more used as this route is reducing children's pain and suffering, and parent's worries. If MAD is available, it should be used since drops are primarily deposited on the ciliary surface with excess runoff down the throat. In this publication authors state that IN midazolam is most used and studied sedative drug in paediatric patients. It causes sedation, anxiolysis and amnesia. Doesn't cause respiratory and circulatory depression. IN fentanyl and ketamine according to authors are good for moderate to severe pain. Ketamine compared to opioids doesn't cause nasal itching and congestion. Dexmedetomidine has some properties that make it a tempting option. IN dexmedetomidine is odourless and tasteless, has minimal respiratory depression and acceptable cardiovascular effects. It is sedative, anxiolytic, and analgesic and some studies showed her neuroprotective effect, reducing apoptosis both in animals and humans.

J. L. Miller et al. [42] concluded that priority should be given for intranasal midazolam and nitrous oxide but also peroral midazolam administration. In addition M. Mayel et al. [43] selected two groups receiving 0.5 mg/kg midazolam administration via oral route and 0.2 mg/kg midazolam via intranasal route administration. Results showed that children in the intranasal sedation group had a faster onset of sedation compared to the oral group (17.94 ± 8.99 vs. 34.50 ± 11.45; $P \leq 0.001$). The frequency of midazolam side effects had no difference between the groups (29.7% vs. 15.8%; $P = 0.15$). They state that midazolam administered via IN route causes faster onset and better availability and requires a lower dose.

According to T. M Frey et al. [44] in a randomised control trial including 90 patients, 45 in ketamine and 45 in fentanyl group. Incidence of side effects was higher in the ketamine group (relative risk, 2.5; 95% CI, 1.5-4.0), but all events were minor and transient. Rescue analgesia was similar between groups (relative risk, 0.89; 95% CI, 0.5-1.6). Additionally in a systematic review and meta-analysis by L. Oliveira et al. [45] analysed intranasal ketamine for acute pain management in children. 546 studies and 4 trials were evaluated. In these 4 trials intranasal analgesic-dose ketamine was found to be as effective as IN fentanyl for management of moderate to severe acute pain for children in the emergency department. Children who received IN ketamine had more non serious adverse events

compared to those who received IN fentanyl. Intranasal ketamine and fentanyl resulted in similar reductions in pain. The weighted mean difference was −1.42 (CI−9.95 to 7.10, I^2 = 60%) at 10–15 minutes after intervention. For pain reduction from baseline to 30 minutes, the weighted mean difference was 0.40 (CI −6.29 to 7.10, I^2 = 24%). And at 60 minutes, the weighted mean difference was −0.64 (CI −6.76 to 5.47, I^2 = 0%). Results showed that the risk of having an side effects was higher among children receiving IN ketamine compared to those receiving IN fentanyl (pooled RR 2.00, CI 1.43 to 2.79, I^2 = 49%). Using IN fentanyl instead of ketamine or opioids is considered to be more effective. S. L Reynolds [46] showed that in suspected extremity fractures intranasal ketamine was associated with less side effects than intranasal fentanyl.

11.4 Pharmacological agents used in paediatric emergency department for sedation and analgesia

As C. E. Ramalho et al. [47] describes in the systematic literature review, sedative selection should be based on its characteristics, peak time, effectiveness, and risks. It is important to administer sedatives and analgesics in small, incremental doses while keeping a close eye on the patient's reaction to avoid adverse events until the planned sedation level is reached. described sedoanalgesiafor emergency procedures as summarised in the Table 2.

Table 2. Sedoanalgesia for emergency procedures. Author C. E. Ramalho et al.

Type of procedure	**Indications**	**Desired effect**	**Suggestion**
Non-invasive procedures	Computed tomography **Echocardiogram** **Electroencephalogram** **Ultrasonography**	Motor control	Comfort measures Midazolam[a] Dexmedetomidine
Procedures associated with light pain and high degree of anxiety	Tracheostomy exchange **Gastrostomy exchange** **Dental procedures** **Nasofibroscopy** **Peripheral venous puncture** **Suture** **Lumbar puncture**	Analgesia Sedation Motor control Reduction of anxiety	Comfort measures Midazolam[b] Ketamine Topical or local analgesia
Procedures associated with	Abscess drainage **Arthrocentesis**	Sedation	Fentanyl Midazolam + Fentanyl

Type of procedure	Indications	Desired effect	Suggestion
high level of pain, high level of anxiety, or both	**Bone marrow aspiration** **Pericardial puncture** **Cardioversion** **Central venous puncture** **Burn debridement** **Reduction of fractures** **Hernia reduction** **Paraphimosis reduction** **Thoracentesis** **Thoracic drainage** **Paracentesis** **Physical examination of victims of sexual violence**	Analgesia Motor control Reduction of anxiety Amnesia	Ketamine Ketamine + Propofol Propofol + Fentanyl Morphine

Table 3. Pharmacological characteristics of drugs used in sedation and analgesia. Author C. E. Ramalho et al.

Drug	Effects	Side effects	Indications	Dose	Onset of action	Duration of action
Sedative-hypnotic						
Midazolam	Sedation, motor control, anxiety reduction, no analgesic effect	Hypotension, respiratory depression, paradoxical effect	Procedures that require sedation, Reduced anxiety or amnesia	IV (age 6 months–5 years): initial 0.05–0.1 mg/kg, maximum of 0.6 mg/kg IV (6–12 years): initial 0.025–0.05 mg/kg, maximum of 0.4 mg/kg IM: 0.1–0.15 mg/kg PO: 0.5–0.75 mg/kg IN: 0.2–0.5 mg/kg RR: 0.25–0.5 mg/kg	2–3 min 2–3 min 10–20 min 15–30 min 10–15 min 10–30 min	45–60 min 45–60 min 60–120 min 60–90 min 60 min 60–90 min
Diazepam	Sedation, motor control, anxiety reduction, no analgesic effect	Hypotension, respiratory depression, paradoxical effect	Seldom used due to long half-life	IV: initial 0.05–0.1 mg/kg, Max 0.25 mg/kg	2–3 min	45–60 min

Drug	Effects	Side effects	Indications	Dose	Onset of action	Duration of action
Propofol	Fast and short sedation	May cause pain at infusion, hypotension, apnea and bradycardia	Short-term procedures, associated or unassociated with analgesics	IV: 1–2 mg/kg, may repeat 0.5 mg/kg every 3–5 min	1 min	5–15 min
Etomidate	Fast and short sedation	May cause local pain, myoclonus, transient adrenal suppression	Short-term procedures, associated or unassociated with analgesics	IV: 0.2–0.3 mg/kg	30–60 s	5–15 min
Dexmedetomidine	Sedation with respiratory drive maintenance Does not change EEG tracing Off-label use in pediatrics	May cause arrhythmia, hypotension, and hypertension	Imaging procedures (CT and MRI), endoscopy, EEG	IV: 2 mcg/kg IN/oral mucosa: 1–3 mcg/kg IM: 1–4.5 mcg/kg Oral: 5 mcg/kg	5–10 min	60–120 min
Analgesics						
Fentanyl	Analgesia	Bradycardia, chest stiffness, respiratory depression	Procedures with moderate to severe pain	IV: 1.0 μg/kg/dose, may be repeated every 3 min IN: 1.5 μg/kg/dose	2–3 min 2–5 min	30–60 min 30–60 min
Morphine	Analgesia	Release of histamine, hypotension, nausea, reduction of gastrointestinal motility	Procedures with moderate to severe pain	IV: initial 0.05–0.15 mg/kg, may be repeated every 5 min	5–10 min	30–60 min
Ketamine	Dissociative agent with analgesic and sedative properties	Laryngospasm, hypersalivation, emergency reactions, vomiting	Short-term painful procedures or when amnesia is desired	IV: 1–2 mg/kg, may repeat 0.5–1 mg/kg every 5–10 min IM: 2–5 mg/kg, may repeat 2–4 mg/kg after 10 min IN: 1–9 mg/kg	IV: 1 min IM: 3–5 min	IV: 15 min (dissociation), 60 min (recovery) IM: 15–30 min (dissociation), 90–150 min (recovery)
Antidotes						
Flumazenil	Benzodiazepine antagonist	Increased intracranial pressure, reduction of	Reversal of unwanted effects	IV: 0.02 mg/kg/dose, may be repeated at each min up to	1–2 min	30–60 min

Drug	Effects	Side effects	Indications	Dose	Onset of action	Duration of action
		convulsive threshold		a maximum of 1 mg		
Naloxone	Opioid antagonist	Nausea, anxiety, sympathetic stimulation, hypertension, tachycardia, pulmonary edema, return of pain	Reversal of unwanted effects	IV or IM: 0.1 mg/kg/dose, maximum 2 mg/dose; can be repeated every 2 min if necessary[a]	IV: 2 min IM: 10–15 min	IV: 20–40 min IM: 60–90 min

C. Sahyoun et al. [48] in the survey questionnaire analysed pediatric sedation and analgesia in emergency department in Europe. An online analysis, multi-national, and cross-sectional survey of paediatric PSA (prompt analgesia, anxiolysis, and sedation) was performed. The study was performed by the research in the European paediatric emergency medicine (REPEM) network. 10 emergency departments were chosen from countries with more than 20 million inhabitants like Italy, France, Germany, and Spain. For countries with less than 20 million inhabitants, 5 emergency departments were chosen. From other countries number of emergency departments, 1 in Latvia, 2 in Malta. Different routes and proportion of children are shown in table 4.

Table 4. Availability of selected medications and routes in European emergency departments. Author C. Sahyoun et al.

	As a proportion of sites surveyed	**As a proportion of children represented**
Systemic medications		
Ketamine		
- IV	152 (89%)	4,391,813 (88%)
- IN	65 (38%)	1,358,347 (27%)
- At least one route	154 (90%)	4,509,795 (91%)
Midazolam		
- IV	161 (94%)	4,718,081 (95%)
- IN	130 (76%)	3,468,247 (70%)
- PO	110 (64%)	2,731,395 (55%)
- At least one route	170 (99%)	4,975,081 (100%)

	As a proportion of sites surveyed	As a proportion of children represented
Nitrous oxide	93 (54%)	2,770,386 (56%)
- Excluding Turkey	93/157 (59%)	2,770,386/3,740,599 (74%)
Propofol IV	123 (72%)	3,319,582 (67%)
Fentanyl		
- IV	133 (78%)	3,788,481 (76%)
- IN	100 (58%)	2,355,686 (47%)
Etomidate IV	60 (35%)	1,554,819 (31%)
Dexmedetomidine IN	18 (10%)	476,089 (10%)
Chloral hydrate		
- PO	54 (32%)	1,472,314 (30%)
- PR	46 (27%)	1,311,395 (26%)
- At least one route	74 (43%)	2,086,532 (42%)
Topical anesthetics and tissue adhesive		
Topical anesthetics		
- For laceration carea	109 (68%)	3,313,787 (71%)
- For intravenous catheterization	110 (64%)	2,756,071 (55%)
Tissue adhesive[b]	147 (91%)	4,209,719 (91%)

D. Marco et al. [49] in an online survey across 21 countries in Europe resulted in most used drug combination was an opioid with a benzodiazepine, fentanyl (51%) and midazolam (71%). Additionally F. Ekinci et al. [50] made similar research across hospitals in several countries. In Turkey results showed that most of the units preferred paracetamol and opiates mostly fentanyl for postoperative pain management and ketamine for short-term procedures. For prolonged sedation in mechanically ventilated children, the combination of benzodiazepines and opiates were the most preferred first-line agents. Second line agents were ketamine and dexmedetomidine 62.9% and 18.5% separately. Propofol was never preferred for sedoanalgesia in this study as it has been reported to have potentially fatal adverse effects and is not advised for use as a sedation drug in paediatric intensive care units. In the same publication some other countries were analysed. In New Zeeland most of the centres preferred benzodiazepine and opiate use as their first-line regimen. In United Kingdom Propofol was also not preferred. Most used were morphine (78%) and midazolam (55%), respectively. A study of 19 PICUs from Italy showed the highest rate of sedation protocol presence (73.6%) and that a benzodiazepine–

opioid combination was the first-line treatment of choice. Physicians in the United States preferred fentanyl over morphine.

N. Gupta et al. [51] reviewed nitrous oxide use in pediatric ED. If used in appropriate doses it doesn't cause hamatologic or neurobehavioral side effects. It is commonly used as anesthetic gas or a mixture for light to moderate pain during procedures.

In a prospective observational study by W. S. Kim et al. [52] examined paediatric patients that needed suturing of the lacerations. 116 patients were analysed 87 in the IV group and 29 in the IM group. Differences such as induction time for IV 54s and for IM 4,6min. Only minor temporary respiratory distress occurred on prolonged sedation. It states that IV ketamine is effective to use in procedures such as laceration repairs. Additionaly F. Ekinci et al. [50] showed that using ketamine alone and not in combination with propofol or fentanyl had least side effects. Use of ketamine alone resulted in the lowest incidence of side effects (17 [0.4%]). The incidence of side effects using propofol alone (3.7%; odds ratio [OR], 5.6; 95% CI, 2.3-13.1) and the combinations of ketamine and fentanyl citrate (3.2%; OR, 6.5; 95% CI, 2.5-15.2) and ketamine and propofol (2.1%; OR, 4.4; 95% CI, 2.3-8.7) had the highest incidence of side effects.

In a meta-analysis by J. F Feng et al. [54] conducted a study to analyse effects of dexmedetomidine versus midazolam for premedication in a pediatric anaesthesia with sevoflurane454 patients were included in the DEXA group and 480 patients in the MDZ group. Clinical assortment was mostly chosen from the type of surgery and the dose, route, and timing of drug administration. Two routes of DEXA administration were used: intranasal in five trials and oral in seven trials DEXA was administered at different doses that were ≤2 μg/kg in nine trials, 2.5 μg/kg in one trial, and 4μg/kg in two studies. The route and dose of MDZ administration also differed from 0.5- and 1.0 - μg/kg. Study concluded that premedication with DEXA significantly promotes the recovery quality during sevoflurane-inhaled anaesthesia in pediatric patients, reducing unsatisfaction with sedation and separation from the parents and the need for rescue analgesia compared with MDZ. Results showed the incidence of unsatisfactory patients in DEXA group was lower than in the MDZ group (RR [95%Cl] = 0,71 [0,57-0,89].

Limitations for this study were to small sample number, only 20 articles. Many of the articles compared only one drug or two drug combination and repeated in many studies. Many of the studies were done earlier than 5 years ago and were excluded from the review.

12. DISCUSSION

As results show prior to procedures to minimise anxiety and distress for children and to make the performance of further procedures has a significant importance. Simply using distraction techniques such as upright position, communications, breastfeeding or sucrose or sweet solutions can be helpful. All articles analysed states that non-pharmacological interventions for pain management are helpful and should be used [36,37,39]. Although patients admitted to ED should be evaluated as injuries, traumas and vital signs. As pain can be strong sometimes it's not enough only with non-pharmacological managing techniques [38].

IN route of drug administration has been discussed mostly for pediatric patients as it is not invasive, doesn't require venous access such as IV catheter placement, it is rapidly absorbed through nasal mucosa into the circulation. As it is non-invasive it causes less stress and anxiety for pediatric patients. Every procedure for a child is stressful and painful therefore most appropriate route for sedation should be intranasal. As also compared to another publications that also concluded that IN route is the best option in pediatric patients. Mucosal atomizer device is discussed as the best way of IN agent administration. In midazolam is discussed as the best agent for IN route administration [40]. Also, in another study midazolam is described as the best agent delivered via IN route using MAD. But also IN Dexmedetomidine is an optionas it is odourless and tasteless, has minimal respiratory depression and acceptable cardiovascular effects; it is sedative, anxiolytic, and analgesic and some studies showed her neuroprotective effect, reducing apoptosis both in animals and humans [41]. Another studies states that midazolam is the most effective [42],43]. Intranasal ketamine can also be used to manage moderate to severe pain prior to fentanyl and ketamine to be used for acute pain management [44,45,46].

C. E. Ramalho et al. [47] conducted a study that showed that most used agents for non-invasive procedures are Midazolam and Dexmedetomidine, for light pain causing procedures Midazolam, Ketamine and topical or local analgesia such as EMLA, for severe pain Fentanyl, Midazolam + Fentanyl, Ketamine, Ketamine + Propofol, Propofol + Fentanyl, Morphine. Similar results are described in another research as well. In another study also described that Ketamine + Propofol combinations is used. In addition, in Europe IV ketamine and midazolam are used most. Least used nitrous oxide and dexmedetomidine. For laceration repairs, IV catheter insertions and tissue adhesives topical anaesthetics were most used [48].

Inanother online survey across 21 countries in Europe resulted in most used drug combination was an opioid with a benzodiazepine, fentanyl (51%) and midazolam (71%) [49]. Additionally in a study made in Turkey showed that most of the units preferred paracetamol and opiates mostly fentanyl for

postoperative pain management and ketamine for short-term procedures. For prolonged sedation in mechanically ventilated children, the combination of benzodiazepines and opiates were the most preferred first-line agents. Second line agents were ketamine and dexmedetomidine 62.9% and 18.5% separately. Propofol was never preferred for sedoanalgesia due to side effects. In New Zeeland most of the centres preferred benzodiazepine and opiate use as their first-line regimen. In United Kingdom Propofol was also not preferred. Most used were morphine (78%) and midazolam (55%), respectively. A study of 19 PICUs from Italy showed the highest rate of sedation protocol presence (73.6%) and that a benzodiazepine–opioid combination was the first-line treatment of choice. Physicians in the United States preferred fentanyl over morphine [50]. Nitrous oxide is used in laceration repairs or procedures causing light to moderate pain [51]. Also in another study it states that IV ketamine is effective in laceration repairs [52]. Although other articles states that only topical anesthesia is enough as it is invasive and causes stress for children [48]. If ketamine is used it should be given alone and not in combination with other agents [50].

DEXA is also good for non-invasive procedures as it mimics the natural sleep, doesn't cause any respiratory depression, have quite fast onset of action and quite long durations of action. It can be given via IN route which is mostly preffered for pediatric patients. Usually preferably used prior to midazolam as premedication before procedures [54].

Recommendations from this literature review include that prior to procedures non-pharmacological techniques should be used to calm down the patient. Always, when possible, drugs should be administered via intranasal route in pediatric patients as it is least invasive and shows good effect. Propofol should be avoided in pediatric patients as it causes many side effects. Priority should be given to drugs such as ketamine, midazolam, fentanyl, and benzodiazepine-opiate combination for more severe pain. DEXA in recent years show low grade of adverse effects, good effect and is considered to use as premedication before anaesthesia or in radiological procedures.

13. CONCLUSSIONS

1. Non-pharmacologic methods are effective in reducing stress, discomfort prior to painful procedures. It should be used more frequently for better procedure performance.

2. Intranasal route of administration is most suitable for pediatric patients and agent of choice should be midazolam.

3. For laceration repair most suitable is topical anaesthetic. For light pain ketamine or midazolam shows good effect. For acute pain Fentanyl is preferred or benzodiazepine–opiate combination. Dexmedetomidine is preferred as premedication before anaesthesia.

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