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REVIEW ARTICLE

Efficacy of ketamine in pediatric sedoanalgesia for orotracheal intubation: a systematic review

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Abstract

Objective: To compare the efficacy and effects of ketamine administration with other drugs for sedoanalgesia during orotracheal intubation in hospitalized pediatric patients. Method: A systematic review in English and Portuguese was conducted using the PUBMED/MEDLINE and LILACS databases. The descriptors “Ketamine” AND “Fentanyl” AND “Propofol” AND “Midazolam” AND “Children” were used. After applying the inclusion and exclusion criteria, 114 articles were initially selected for analysis, resulting in the inclusion of 11 articles for data extraction. Results: The study included 7,868 individuals aged 0 to 18 years. Intranasal ketamine administration was found to be an excellent alternative in cases where opioid use is contraindicated. When compared with sevoflurane for agitation prevention, sevoflurane was found to be unsafe, whereas the combination of intranasal ketamine with midazolam showed better effects on anesthetic induction and recovery. Additionally, one study revealed that the combination of ketamine with fentanyl increased blood pressure and relative risk up to 30 minutes after laryngeal mask insertion, although it provided more stable hemodynamic parameters and advantageous effects on patient recovery. Conclusion: The efficacy of ketamine may vary depending on the route of administration and dosage used, with the nebulized form at doses between 1.5 mg/kg and 2 mg/kg demonstrating the greatest efficacy. Thus, ketamine is an effective, safe, and versatile option for orotracheal intubation in pediatric patients, representing a viable non-opioid alternative with a favorable safety profile.

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INTRODUCTION

The maintenance and integrity of the airway are priorities in the care of patients in emergency settings[1]. Orotracheal intubation (OTI) consists of inserting a tube into the trachea via the oral route, with the purpose of relieving compromised airways and enabling adequate ventilation[2]. It is a common procedure in medical emergencies and is considered definitive, although invasive and complex, as it ensures appropriate ventilatory support by maintaining airway patency, ventilation, and adequate oxygenation[1,3].

Invasive ventilatory support is indicated when, despite oxygen supplementation, the patient is unable to achieve adequate gas exchange[2]. In such cases, invasive ventilation via OTI is preferred, while nasotracheal intubation and cricothyrotomy are reserved for specific situations[4]. Rapid sequence intubation (RSI) is the preferred technique in the emergency department, as it combines manual skills with pharmacological knowledge of hypnotic, sedative, and neuromuscular blocking agents[5].

In the pediatric population, the need for OTI arises in situations such as shock or respiratory failure, frequently associated with upper airway obstruction, pulmonary diseases, or central nervous system dysfunction[6]. Anatomical particularities of the pediatric airway, such as the smaller tracheal diameter (averaging approximately 6 cm in infants and up to 12 cm in adolescents), make the procedure more challenging and require specific expertise and technical skills[7]. In addition, pediatric emergencies often involve additional barriers, including the absence of detailed clinical information, difficulties in patient positioning, inadequate equipment, the need for rapid decision-making, and limited data regarding the safe administration of medications in this age group[8].

RSI includes premedication with 2% lidocaine without vasoconstrictor (1.5 mg/kg) and fentanyl (2–3 mcg/kg), administered approximately three minutes before induction[6]. These agents help reduce sympathetic activity associated with the procedure, minimizing laryngeal reflexes and airway reactivity[5,8]. Ketamine, at doses of 1.5 to 2 mg/kg, stands out as a potent sedative and has been widely used during the COVID-19 pandemic due to its bronchodilatory properties and hemodynamic stability. However, its contraindication in patients with arterial hypertension may require the use of alternatives, such as etomidate (0.3 mg/kg)[5].

After sedation, with loss of the eyelash reflex and responsiveness (45 seconds to 1 minute), a neuromuscular blocking agent—such as succinylcholine (1.0 mg/kg) or rocuronium (1.2 mg/kg)—is administered to facilitate intubation and prevent reflexes such as coughing[2,6]. Following OTI, immediate sedation and analgesia may be maintained with fentanyl and midazolam. Nevertheless, the risk of bradycardia and hypotension underscores the need for vasopressors (such as phenylephrine, ephedrine, and norepinephrine) and crystalloids to be readily available[5].

Team organization is essential to ensure procedural safety, including preparation of resuscitation equipment and vasopressors, particularly in contexts such as the COVID-19 pandemic, in which the risk of contamination is increased[5,6]. In this context, the present study aims to compare the efficacy and effects of ketamine administration with those of other drugs used for sedoanalgesia during orotracheal intubation in hospitalized pediatric patients.

METHOD

This systematic review was conducted using articles retrieved from the electronic databases PUBMED, Medical Literature Analysis and Retrieval System Online (MEDLINE), and Latin American and Caribbean Health Sciences Literature (LILACS), covering publications from 2009 to 2023. The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and included studies involving pediatric patients, defined as children and adolescents under 19 years of age.

The descriptors were selected based on consultation of DeCS (Health Sciences Descriptors – BIREME) and MeSH (Medical Subject Headings), using the terms “Ketamine,” “Fentanyl,” “Propofol,” “Midazolam,” and “Children,” combined with the Boolean operator “AND” to optimize the search strategy.

The guiding research question was developed according to the PICO strategy (Patient, Intervention, Comparison, Outcome), serving as the basis for formulating the scientific question and selecting relevant studies. Accordingly, the following research question was defined: *“Does ketamine demonstrate superiority in terms of efficacy and severity of adverse effects during orotracheal intubation in children when compared with other drugs used?”*, as detailed in Table 1.

Table 1. PICO strategy for the review.

P: Patients	Pediatric patients undergoing orotracheal intubation
I: Intervention	Use of ketamine at any dose or available formulation
C: Comparison	Comparable sedoanalgesia treatments
O: Outcome	Efficacy and severity of adverse effects associated with the use of ketamine

Source: Authors (2025)

The titles of all retrieved articles were independently evaluated by two reviewers in order to identify and remove duplicate publications or those with limited accessibility. Potentially eligible studies were subjected to abstract screening and subsequently to full-text analysis, with exclusion of those that did not address the central research question of this review. Final selection was established during a consensus meeting with the participation of a third author.

The extracted data included the article title, first author's name, study design, country of the population analyzed, journal of publication, year of publication, main findings, strengths, limitations, and other relevant observations. The number of studies analyzed at each stage of the process was presented in the PRISMA diagram (Figure 1).

Database searching and data extraction were conducted between June and August 2024. The initial search yielded 573 articles. After applying platform filters, only freely accessible full-text articles published in English or Portuguese were selected, restricted to clinical studies, observational studies, controlled clinical trials, and randomized trials. Following this screening, the number of publications eligible for initial analysis was reduced to 114.

After analysis of titles and abstracts, considering the inclusion and exclusion criteria—such as removal of duplicates, exclusion of review articles, and relevance to the research question—11 studies were selected for data extraction. It should be noted that, as this is a review based exclusively on previously published studies, the research was exempt from evaluation by a Research Ethics Committee (REC), in accordance with Resolution No. 510/2016 of the Brazilian National Health Council (CNS).

RESULTS

After the selection of the 11 articles published between 2009 and 2023, the final sample comprised 7,868 children and adolescents aged 0 to 18 years. These studies evaluated the efficacy and effects of ketamine compared with other drugs used for sedoanalgesia during orotracheal intubation in hospitalized pediatric patients, as shown in Table 2.

Regarding study design, seven randomized controlled trials, two prospective cohort studies, one non-randomized cohort study, and one randomized cohort study were identified. The geographical distribution of the studies was as follows: one conducted in Nigeria, one in Australia, two in the United States, one in China, one in Spain, two in South Korea, two in Turkey, and one in Canada, demonstrating considerable heterogeneity in both the study populations and the interventions evaluated. The collected data included comparisons between the study drug and other medications commonly used for intubation, such as fentanyl for analgesia and propofol for sedation, with monitoring of hemodynamic parameters including blood pressure, heart rate, and oxygen saturation, which varied according to the route of administration and dosage used.

DISCUSSION

Three randomized controlled trials compared the efficacy and effects of ketamine and fentanyl, both administered intranasally. The pioneering study by Graudins et al. (2013)[10] was the first to compare these drugs in a prospective trial that assessed vital signs and pain intensity at 30 minutes post-administration, as well as monitored adverse events at 15, 30, and 60 minutes. This study demonstrated that intranasal ketamine is an effective non-opioid analgesic alternative for children when compared with fentanyl. Subsequent studies by Frey et al. (2018)[9] and Reynolds et al. (2017)[11] corroborated these findings, showing significant and comparable reductions in pain in both groups. However, adverse effects—predominantly dizziness and drowsiness—were more frequent in the ketamine group, especially at 15 minutes, although they were transient and mild. These results indicate that ketamine is an effective option in situations where opioid use is contraindicated, given that its adverse effects are manageable. In addition, it is noteworthy that, in the context of orotracheal intubation in pediatric patients, physicians—particularly pediatricians—tend to underuse medications due to concerns about potential side effects[2].

Two randomized controlled trials evaluated the administration of alfentanil and ketamine in preanesthesia. Begec et al. (2009)[12] investigated hemodynamic changes and conditions for insertion of the ProSeal Laryngeal Mask Airway (PLMA) when ketamine and alfentanil were administered prior to induction with propofol. Although insertion conditions were comparable, the ketamine group consistently exhibited higher heart rates. Conversely, Bilgen et al. (2014)[13] compared these agents after midazolam administration to prevent agitation in children anesthetized with sevoflurane, observing that the ketamine group had lower postoperative agitation scores without serious adverse events, reinforcing the efficacy of the

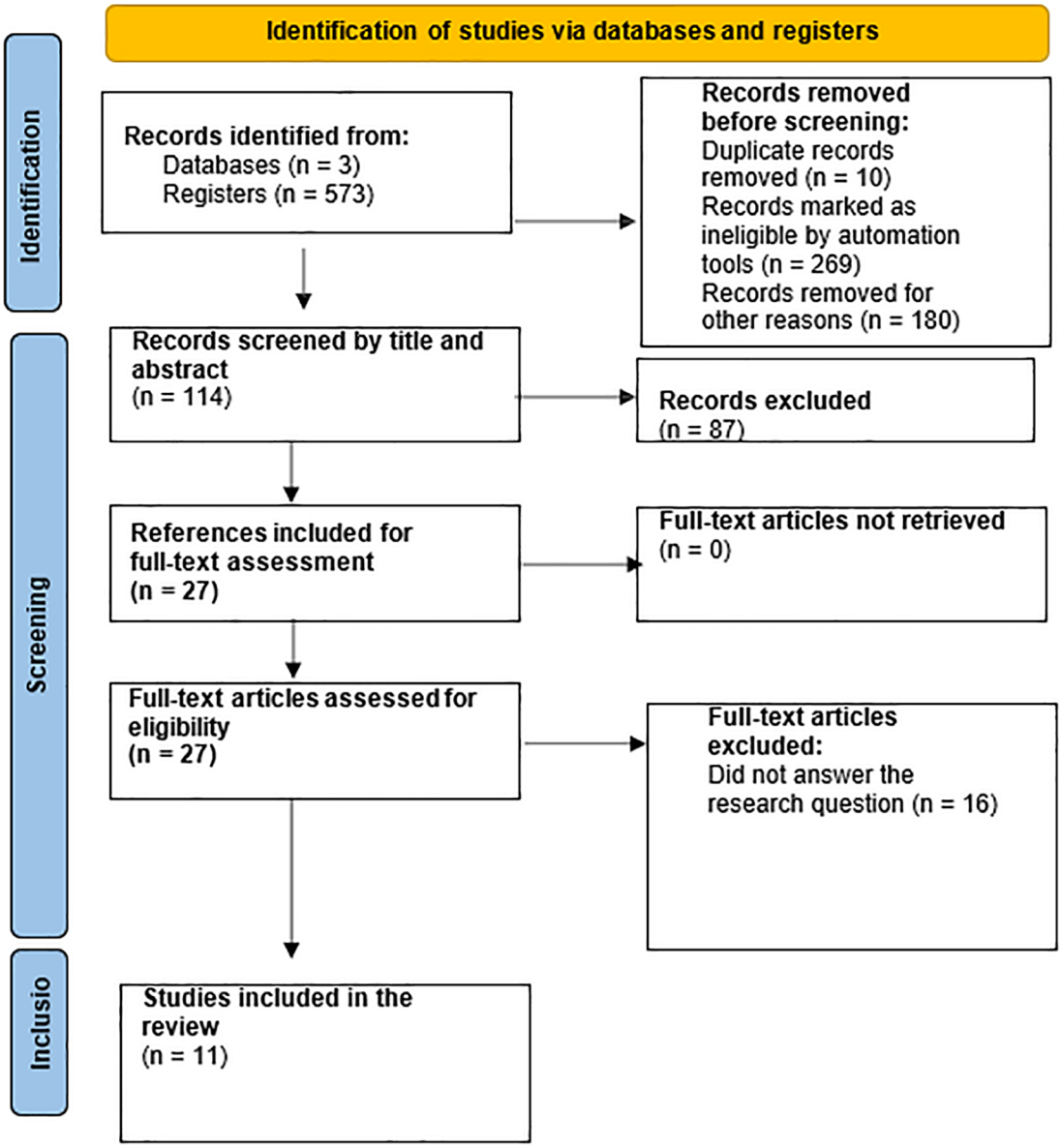

Figure 1. Study selection flowchart using the PRISMA strategy. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only. Source: Authors (2025).

ketamine–midazolam combination in improving anesthetic induction without compromising recovery.

One randomized controlled trial and one retrospective study investigated different doses and routes of ketamine administration. Chen et al. (2021)[14] compared the efficacy and safety of nebulized versus oral ketamine for postoperative pain control, demonstrating that the nebulized route provided greater sedation and analgesia, with a lower incidence of adverse effects, in addition to reducing the need for additional doses of fentanyl and paracetamol until hospital discharge. It should be noted, however, that many patients do not receive adequate post-intubation sedation, contrary to studies demonstrating the sedative and analgesic efficacy of ketamine[2]. In the study by Hwang et al. (2019)[15], doses of 1 mg/kg, 1.5 mg/kg, and 2 mg/kg were evaluated for pediatric intubation, with findings indicating that doses of 1.5 mg/kg and 2 mg/kg provided superior intubation conditions, without significant differences in hemodynamic parameters or recovery time.

In a prospective study, Soblechero et al. (2023)[16] analyzed the continuous intravenous infusion of ketamine and propofol within a sedation protocol and found no significant improvements in analgesia or sedation scores, although the combination was considered effective. Okeyemi et al. (2022)[17] compared the intraoperative effects of ketamine–fentanyl

Table 2. Methodological characteristics and sample profiles of the studies included in this systematic review.

Author /Year	Location	Journal of publication	Study design	Sample and study criteria
Graudins et al. (2013)[10]	Australia	Trials	Rehearsal double-blind, randomized clinical trial	73 children aged 3 to 13 years, weighing up to 50kg, with isolated limb injury. and EVE > 6/10 in screening.
Frey et al. (2018)[9]	USA	JAMA Pediatrics	Rehearsal double-blind, randomized clinical trial	90 children aged 8 to 17 were admitted. node department Emergency treatment following traumatic injuries to the limbs.
Reynolds et al. (2017)[11]	USA	Academic Emergency Medicine a Global Journal of Emergency Care	Rehearsal clinical, randomized, controlled	629 children aged 4 to 17 with pain acute put suspect of Isolated fractures of extremities.
Begec et al. (2009)[12]	Türkiye	Journal of the Association of Anaesthetists of Great Britain and Ireland	Study clinical double blind, randomized	80 children aged 3 to 132 months, states physical WING I, undergoing minor surgeries.
Bilgen et al. (2014)[13]	Türkiye	Journal of International Medical Research	Study clinical double blind, randomized	78 children of 1 the 8 years, Physical statuses ASA I and II, undergoing general anesthesia for procedures. surgical Urological.
Chen et al. (2021)[14]	China	Medicine	Study of cohort, non-randomized	383 children of 3 the 10 years, physical states ASA I and II.
Hwang et al. (2019)[15]	Korea South	European Review for Medical and Pharmacological Sciences	Study of cohort, randomized	60 children aged 2 to 12 years, scheduled for inguinal herniorrhaphy under general anesthesia.
Soblechero et al. (2023)[16]	Spain	Anales de pediatría	Study of prospective cohort	32 crianças de 1 mês a 16 anos foram admitidas na unidade de terapia intensiva pediátrica.
Okeyemi et al. (2022)[17]	Nigeria	Nigerian Postgraduate Medical Journal	Study clinical double blind, randomized	32 children of 1 month the 16 years have passed admitted in unit pediatric intensive care.
Kim et al. (2016)[18]	Korea South	Sage Journals	Rehearsal double-blind, randomized clinical trial	68 children aged 2 to 6 years underwent the surgery ophthalmic.
Bhatt et al. (2017)[19]	Canada	JAMA Pediatrics	Study of prospective, multicenter cohort study	6295 children between 0 and 18 years, physical states ASA I and II, which have passed put departments emergency.

Source: Authors (2025).

versus propofol–fentanyl, finding that the ketamine–fentanyl group exhibited significant increases in blood pressure (SBP, DBP, MAP) and a higher relative risk between 10 and 35 minutes after laryngeal mask insertion; nevertheless, hemodynamic stability favored recovery in this group.

Kim et al. (2016)[18] conducted a randomized controlled trial focusing on pediatric patients with emergence delirium, comparing midazolam and ketamine. Although the incidence of delirium was similar between groups, ketamine demonstrated superior outcomes by reducing the need for additional medication to control delirium.

Finally, a prospective observational study by Bhatt et al. (2017)[19] evaluated the efficacy and safety of sedation in 6,295 pediatric patients, identifying oxygen desaturation and vomiting as the main adverse risks. The use of ketamine alone was associated with the lowest incidence of serious adverse events, whereas propofol and the ketamine–fentanyl and ketamine–propofol combinations were linked to higher rates of serious adverse events (SAEs). These findings suggest that ketamine monotherapy is the safest option and is associated with fewer complications.

CONCLUSION

The analysis of the results concluded that ketamine, when compared with other anesthetic agents, demonstrates proven efficacy and hemodynamic stability, making it a viable option for orotracheal intubation in pediatric patients. Although transient adverse effects, such as dizziness and drowsiness, are more common within the first hour after administration, they are manageable and of low severity, without compromising patient safety. The route of administration and dosage influence the effectiveness and acceptability of ketamine, with nebulized administration and doses between 1.5 mg/kg and 2 mg/kg being the most recommended.

The isolated use of ketamine was associated with lower rates of serious adverse events and reduced need for additional interventions when compared with combinations involving

propofol or fentanyl, further reinforcing its safety in emergency settings. Thus, ketamine stands out as an effective, safe, and versatile non-opioid alternative, with a favorable profile for sedation and analgesia in a variety of pediatric clinical contexts, providing better control due to its hemodynamic stability and more reliable management of sedation and analgesia parameters with a lower risk of complications.

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