

EFFICACY OF DEXMEDETOMIDINE AND VERSED IN PEDIATRIC ANESTHESIA

**The Efficacy of Using Dexmedetomidine Compared to Midazolam in Pediatric
Anesthesia: An Integrative Review**

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Abstract

Aims and objectives: The aim of this integrative review is to provide a practice recommendation for the administration of dexmedetomidine versus midazolam in the pediatric population prior to undergoing anesthesia.

Methods: Articles published from 2011-2018 were critically evaluated for their validity, reliability, and rigor of study. Articles were selected based on study designs and methods that assisted in answering the guided research questions.

Results: The efficacy of preoperative dexmedetomidine and midazolam were compared in pediatrics. The initial search using keywords yielded 163 articles. Articles were chosen based on their relevance. Common variables within studies were chosen to examine and data was recorded. Data was considered statistically significant if p-value was less than 0.05.

Implications for practice: Practice implications encourage the use of both dexmedetomidine and midazolam as premedication in pediatrics. Premedication should only be administered in the pediatric population when adequate monitoring is available and there are no contraindications noted. Dexmedetomidine was found to have a statistically significant decrease in blood pressure and/or heart rate.^{1,2,5,12} However, there was never a need to treat vital signs and patients were considered stable hemodynamically.^{1,3-9}

Conclusion: A conclusion cannot be made from this integrative review whether dexmedetomidine or midazolam is superior. Current literature comparing dexmedetomidine and midazolam has shown statistically significant results. Dexmedetomidine was shown in more than half of the studies to have a deeper sedation, better mask acceptance, and better separation from parents.

Keywords: dexmedetomidine, precedex, midazolam, versed, pediatric, premedication, anesthesia

Introduction

Surgery brings on fear, stress, and anxiety in surgical patients of all ages. Children, are more susceptible because of their limited cognitive capabilities and dependency.³ Medications are frequently given pre-operatively to decrease anxiety and relieve the fear of surgery; while making the separation from parents easier, and smoothing induction and emergence.⁴ To prevent the psychological distress and pain, providers typically avoid intravenous cannulation prior to the induction of anesthesia. Another option to decrease psychological distress is with premedication; However, there are only a select few premedication's that can be given intranasal and oral routes. Children's compliance with premedication intranasally is better than orally.⁵ The nasal route of premedication administration is proven to have the potential for high absorption rate making the onset faster because of the rich nasal vascular network.^{5,6} Orally, medications take time to absorb and a percentage of the medication is lost to first pass metabolism.

For years, midazolam has been used to pre-medicate children prior to induction, although dexmedetomidine is a newer medication also available. Each of these medications have different mechanisms of action to aid in anxiolysis and sedation.

Dexmedetomidine is an alpha 2 adrenoreceptor agonist. This medication stimulates the inhibitory neurons in the locus coeruleus providing analgesia and sedation with milder respiratory depression.¹ Dexmedetomidine is a newer and more selective alpha 2 receptor agonist with a higher bioavailability, a high quality hypnotic action, and a shorter half-life.⁵ However, it has poor oral bioavailability and absorption is better through the mucosal routes.⁷ The effects of dexmedetomidine are unique for a number of reasons making it popular. Not only does dexmedetomidine not cause respiratory depression, but it can be used as an alternative or an

adjunct to opioids to treat pain. Further, the intranasal route does not have the nasal irritation effect that midazolam has.⁷

Midazolam is a water-soluble benzodiazepine and the most commonly used premedication in children.⁸ This medication stimulates gamma-aminobutyric acid (GABA) receptors in the cerebral cortex of the brain to uptake chloride ions causing a hyperpolarization which inhibit the inhibitory neurons resulting in sedation and possibly respiratory depression.¹ Benzodiazepines such as midazolam, produce a number of effects: anxiolysis, sedation, anterograde amnesia, alcohol potentiation, and anticonvulsant/skeletal muscle relaxant effects. Midazolam is also said to lower the chances of post-operative nausea/vomiting, increasing its use.

The purpose of this integrative review is to evaluate current literature and compare the effects of dexmedetomidine and midazolam when given preoperatively to pediatric patients receiving general and monitored anesthesia care anesthetics. To begin, guided questions were used to focus the research.

- 1. What affects do dexmedetomidine and midazolam have on parental separation and anxiety in pediatrics?
- 2. What are the sedating effects of dexmedetomidine and midazolam when given preoperatively in pediatrics?
- 3. What affects do dexmedetomidine and midazolam have on mask acceptance in children prior to induction?
- 4. Are there hemodynamic changes when dexmedetomidine and midazolam are utilized for preoperative sedation in pediatric patients?

Methods

The integrative review will compare research on the efficacy and safety of dexmedetomidine and midazolam as a premedication in the pediatric patient (0-18 years old). A literature review was conducted using the following databases: MEDLINE/PubMed, CINAHL, Academic Search Premier, and EBSCO. Keywords searched: dexmedetomidine, precedex, midazolam, versed, premedication, pediatric and anesthesia. A minimum of 10 research articles were needed that fit the topic of review. The search gathered articles within the last 8 years of primary, secondary, and tertiary type literature.

Articles were critically evaluated for their validity, reliability, and rigor. The strengths and weaknesses were also taken into consideration. Articles were picked based on study designs and methods that gave conclusions to answer the guided research questions created. Articles were excluded if they did not answer the guided questions.

After selection of studies, data was analyzed. Information was entered into a matrix form to organize and refer to in an easy manor. Items identified were: purpose, variables, setting, sample, study design, instruments, results, limitations, and the level of evidence. Data was analyzed one more time to ensure the article should be included. After analyzing the findings, results were summarized in a narrative form.

Results

The initial search using keywords: dexmedetomidine, precedex, midazolam, versed, premedication, and pediatric found 1,696 relevant articles. The search term anesthesia was added and articles were limited to the last 5 years which then yielded 163 articles. Articles were then evaluated for validity, reliability, and rigor. Research questions were reviewed, revised, and altered to guide what types of articles were needed for review. Articles were chosen based on their relevance as related to the aim and purpose of this integrative review. Common variables

within studies were chosen to study and data was recorded. Data was considered statistically significant if p-value was less than 0.05. Variables were then compared to form results and a conclusion.

Discussion

Anxiety and Parental Separation

Premedication in the pediatric population may be helpful to separate a pediatric patient from their parent and reduce the child's stress and anxiety.⁶ Some risk factors may be associated with higher anxiety in this population such as: ages 2-9 years old, a shy or inhibited nature personality, prior negative encounters with healthcare, a child that doesn't adapt well in social situations, and parental anxiety.⁴ Often, children are anxious about the intravenous cannulation even after thoroughly explaining the process and planning to complete this under general anesthesia.⁶ To avoid long-term psychological problems in the child and fear of healthcare professionals, various routes of premedication may be used.⁶ Dexmedetomidine was found to have better efficacy at the time of parental separation compared to midazolam in 6 out of the 11 studies.^{1,2,4,8,9} One of these studies was a meta-analysis by Sun et al., which found that in 8 out of 11 randomized controlled trials there were statistically significant results for dexmedetomidine having better efficacy for parental separation.⁸ A study by Messeha and El-Morsy reported dexmedetomidine to have significantly lower anxiety scores than midazolam after twenty minutes of administration.¹ In another study by Chatrath et al., it was reported both Fentanyl and dexmedetomidine to be superior in comparison to midazolam at time of parental separation.³

Mask acceptance

Sedative medications may be given pre-operatively to ease the process of inhalation induction so the child remains calm and cooperative without distress. It has been reported more than 40% of children ages 2-10 years old display distress during induction, and more than 30% resist anesthetics during this time.¹⁰ Inadequate premedication can result in the child experiencing a turbulent induction and adverse behavioral sequelae.⁷ With adequate premedication, anesthesia providers hope to provide anxiolysis and smooth the induction of inhalation agents. Examining the literature for mask acceptance revealed in 4 of 9 studies dexmedetomidine was superior to midazolam for satisfactory sedation with statistically significant results.^{3,4,8,9} One of these studies was a meta-analysis by Sun et al., this analysis reported dexmedetomidine to be superior in 7 out of 11 studies.⁸ In a study by Chatrath et al., Fentanyl and dexmedetomidine were both a better premedication as compared to midazolam for mask acceptance.³

Depth of Sedation

Literature compared the cooperation of children when separating from their parents and mask acceptance, but also measured and compared the depth of sedation achieved. In the studies examined 8 out of 10 reported dexmedetomidine was a better medication at sedating children when compared to midazolam^{1,2,4,6-9,11} A meta-analysis by Sun et al. discovered in 8 of 11 studies in which dexmedetomidine had a greater depth of sedation.⁸ In the study by Mahdavi et al., Ketamine was used as a supplement to provide a deeper sedation in addition to either dexmedetomidine or midazolam. It was discovered the dexmedetomidine group required less Ketamine as compared to the midazolam group, and decreased the need for rescue analgesia post operatively.⁵ The study reported this difference in dosage suggests the higher sedative effect of dexmedetomidine.⁵

Hemodynamics

When giving sedation, it's vital to be knowledgeable of potential effects medications can have including hemodynamic stability and respiratory status. When giving anesthetic medications the standard of care is to monitor vital signs every 5 minutes. Dexmedetomidine is known to decrease sympathetic outflow and circulating catecholamine levels.² This in turn can depress vital signs. When vital signs were monitored within the literature, it was found in 8 studies dexmedetomidine significantly altered vital signs when compared to midazolam. Dexmedetomidine when compared to midazolam lowered the heart rate and systolic blood pressure in 7 of 13 studies; two of which were meta-analysis^{1,2,6-8,12}. In the first meta-analysis, a study by Jun et al., 6 out of 15 RCT's showed a significant decrease in the systolic blood pressure being 6.7mmHg on average lower from baseline.⁶ This same study reported a significant decrease in heart rate with an average of 6.8 beats per minute lower in 8 RCT's of the 15 evaluated.⁶ In the second meta-analysis by Sun et al., 6 of 11 studies had a reduction in heart rate, and 3 of 11 studies showed a drop in systolic blood pressure.⁸ Chatrath et al. found a significant change in respiration rate in midazolam as compared to dexmedetomidine.³ Overall, these vital sign changes never required interventions and were reported stable, however significantly lower than baseline.

Current literature comparing dexmedetomidine and midazolam has shown statistically significant results. There are limitations with this review. The paucity of studies in the pediatric population as compared to other populations was a limiting factor in this review. Another limitation was the variance in these studies regarding dosing, sedation scales, types of surgery, age of patient, and documentation of onset time.

Implications for Practice

Pediatrics appear to have different degrees of fear and anxiety and therefore taking advantage of various levels of sedation.⁵ The superior premedication is still unclear. Midazolam provides sedation, anxiolysis, and amnesia with valuable properties such as anticonvulsant activity, rapid onset, and a short duration.⁵ The anterograde amnesia is greater with midazolam over other benzodiazepines.⁵ A few adverse effects that may limit midazolam's use include restlessness, paradoxical reactions, cognitive impairment, postoperative behavioral changes, respiratory depression, and nasal irritation.^{5,6} Dexmedetomidine provides sedation, anxiolysis, and analgesic effects without respiratory depression especially in pediatrics.^{5,6} Side effects of dexmedetomidine can include hypotension and bradycardia.¹³

The practice implications include continuing the use of both dexmedetomidine and midazolam for premedication in pediatrics. Premedication should only be administered in the pediatric population when adequate monitoring is available and there are no contraindications noted. Dexmedetomidine was found to have a statistically significant decrease in blood pressure and/or heart rate.^{1,2-5,12} However, there was never a need to treat vital signs and patients were considered stable hemodynamically.^{1,3-9,12} These premedication's may be given intravenously, intramuscularly, orally or intranasally. The most common route of premedication in children being orally and second most common, intranasal.⁶ The nasal route of premedication administration is proven to have the potential of high absorption rate making the onset faster because of the rich nasal vascular network.^{5,6} Intranasal midazolam can cause nasal irritation and burning making it an unpopular route.⁶ When administering dexmedetomidine and midazolam it is important consider the route and time of onset.

Dexmedetomidine was statistically significant in more than half of the studies in this literature review for the following effects: deeper sedation, better mask acceptance, and better separation from parents as compared to midazolam. Overall, dexmedetomidine may be used for these indications, however both medications were efficient with similar efficacies.

Conclusion

The purpose of premedication in the pediatric population prior to anesthesia is to decrease anxiety, smooth induction, and ease the separation from parents to the operating room. A conclusion cannot be made from this integrative review whether dexmedetomidine or midazolam is superior prior to undergoing anesthesia as a preoperative medication. Dexmedetomidine was statistically significant in more than half of the studies in this literature review for the following effects: deeper sedation, better mask acceptance, and better separation from parents as compared to midazolam. There is need for more research with larger sample sizes studying the same variables, route, and a standard weight-based dose to show a more reliable comparison.

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