Midazolam in Pediatric Dentistry

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Foreword

In the world of Pediatric Dentistry, ensuring the well-being and comfort of young patients is of paramount importance. This generation of children and their parents walk into our practices with different expectations from Pediatric Dentistry, thus throwing new challenges. As practitioners in this field, we are continually searching for ways to alleviate anxiety, reduce pain, and create positive dental experiences for children. It is with great pleasure that I introduce this comprehensive and insightful book on *Midazolam in Pediatric Dentistry*.

Midazolam, a well-known sedative with good margin of safety, has emerged as a valuable tool in our efforts to make dental visits more pleasant for children. This book, authored by Dr. Ashwin Rao and Dr. Shweta Tiwari, experts in the field, explores the various aspects of minimal and moderate sedation using midazolam in Pediatric Dentistry, from its pharmacological properties to practical clinical applications.

The authors have gone to great lengths to share their expertise, providing a detailed account of the drug's mechanism of action, appropriate dosages, and administration techniques. They also discuss the critical importance of patient selection and evaluation, ensuring that midazolam is used safely and effectively.

As you delve into the pages of this book, a first of its kind and very focused on the topic, you will find not only a wealth of information but also practical insights into case selection where midazolam can make a significant difference in the lives of young dental patients. The book will underscore the genuine impact that this drug can have in Pediatric Dentistry, transforming what might otherwise be a daunting experience into one that is manageable and even pleasant.

In today's world, Pediatric Dentists and their teams strive to provide holistic care that prioritizes the physical and emotional needs of children. Midazolam is a crucial tool in achieving this goal, and this book serves as a valuable guide for those looking to enhance their practices and improve the lives of young patients.

I commend the authors Dr. Ashwin Rao and Dr. Shweta Tiwari for their dedication and expertise in compiling this important resource. It is my hope that this book will not only educate and inform but also inspire those in the field of Pediatric Dentistry to continue pushing the boundaries of what is possible in delivering compassionate and effective care.

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Preface

"***Sedation***" caught our imagination very early in our career in Pediatric Dentistry. We realized that we were duty bound to provide anxious children, with high-quality pain-free treatment even when their age and cognition did not allow them to cooperate for demanding dental procedures. Inhalation sedation with nitrous oxide and oxygen helped us fulfill this objective more often than not. But yet, we learnt in the steep learning curve of procedural sedation that a small group of children cannot comprehend the nasal hood and require other modes to help them through. We worked with various drugs like chloral hydrate, hydroxyzine, midazolam, dexmedetomidine, etc., only to find inconsistent success. Experience gradually taught us that understanding the limitations of these drugs was as important as understanding their indications and advantages. We also learnt that success with sedation should not come at the cost of unintentional deep sedation or the associated risks. As we worked more with midazolam with an understanding of its limitations, this drug started revealing its magic in terms of producing reliable, consistent, and safe anxiolysis, sedation, and amnesia along with a host of other advantages. Proper case selection in conjunction with a good local anesthetic technique proved to be the game changers in this journey.

But, as we shared our successful experiences with this drug at various professional forums, we observed that many of our Pediatric Dentist colleagues were only finding their feet with the use of midazolam. They in their effort to provide the highest quality of dental care to children had various queries on its practical application in practice including case selections, safety, routes of administration, timing of its use, role of behavior guidance, and local anesthesia. We felt a need to bridge this lacunae between theoretical knowledge and the actual effective use of midazolam in clinical Pediatric Dentistry. Therein conceptualized the idea of penning a structured work on the subject eventually leading to the genesis of this textbook. We have nine thoughtfully written chapters and numerous hand drawn figures (Credits: Dr. Shweta Tiwari) in the book. Each chapter has been written with a specific objective to help the reader enhance her/his understanding of "Sedation with Midazolam" and gain confidence in its use.

Here we would like to express our heartfelt gratitude to Dr. Srinivas Namineni, Pediatric Dentist, Rainbow Children's Hospital Hyderabad, a pioneer of dental sedation in India who flagged us off on this journey of sedation in Pediatric Dentistry. He was kind enough to consent writing the foreword for this work. We also remain

grateful to the entire Indian Pediatric Dental community for always encouraging us through this exciting undertaking.

We dedicate this book to our entire family whose unconditional love and support gave us the time to focus, deliberate, write and rewrite every chapter leading to the treatise that you are now reading.

Mangaluru, India Ashwin Rao

December 2023 Shweta Tiwari

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The Practical Role of Midazolam in Pediatric Dentistry

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1.1 Overview

Midazolam has a definite role in the behavior guidance armamentarium of the Pediatric Dentist. But to make its use predictable and consistent requires not only an in-depth understanding of the drug but also an understanding of its limitations. This introductory chapter deals with the need for pharmacological management in children, the roles of midazolam and inhalation sedation, and the unique properties that make midazolam an almost ideal sedative agent in Pediatric Dentistry. This chapter also helps the reader appreciate that midazolam in prescribed doses will lead to minimal/moderate sedation only. Minimal/moderate sedation won't be able to overcome the extreme fear of a combative child. Hence, midazolam on its own will *not* be effective in combative children. It will work best for anxious children in conjunction with non-pharmacological behavior guidance and good local anesthetic techniques, which are ultimately the cornerstones of child management in Pediatric Dentistry.

1.2 Background and Objective

Midazolam is currently the dental sedative of choice in children [1]. But numerous questions accompany its use among clinicians learning the ropes of sedation (Fig. 1.1).

The objective of this introductory chapter will be to address these questions in a nutshell and elaborate upon them in the subsequent chapters.

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Fig. 1.1 Questions accompanying the use of midazolam in Pediatric Dentistry

1.3 Need for Pharmacological Management in Children

Non-pharmacological behavior guidance with good local anesthetic techniques is still the cornerstone of child management in Pediatric Dentistry. But it cannot be denied that dental treatment even for the most cooperative child can be anxiety provoking and intimidating. This is where pharmacological management steps in, helping anxious children cope up positively with the treatment.

1.4 The Role of Inhalation Sedation and Other Sedative Drugs

Inhalation sedation with nitrous oxide and oxygen along with non-pharmacological behavior guidance and local anesthesia completes the powerful troika of behavior guidance tools capable of managing most apprehensive children. But inhalation sedation requires the child to sportingly wear the nasal hood. Most children do that with good communicative behavior guidance. But age, extreme anxiety, and an inability to comprehend instructions impede many children from doing so. This is where the need for other drugs come into play. Drugs, which will sedate the child predictably for short procedures or facilitate the acceptance of the nasal hood for long procedures. A long list of prospective drug classes become relevant in this space. Benzodiazepines, barbiturates, opioids, antihistamines, and other drugs like

ketamine are the frontrunners. Among these, the benzodiazepine class of drugs have currently established themselves as the most effective oral anxiolytic drugs [2].

1.5 The Benzodiazepines

The discovery of chlordiazepoxide, the first drug in the benzodiazepine class, in 1957 by L. H. Sternbach and L. O. Randall represents a milestone in the journey of psychoactive drugs. It leads the way for the synthesis of more than 2000 benzodiazepines ever since [2].

The popularity of benzodiazepines is because of their high therapeutic index. The therapeutic index signifies the relative safety of the drug. It is a comparison of the dosage of the drug that will bring about the desired effect as opposed to the dosage triggering severe side effects [3]. In other words, benzodiazepines have a wide margin of safety. The availability of an antagonist flumazenil also adds to the safety profile of benzodiazepines [4].

1.5.1 Classification of Benzodiazepines and their Clinical Applications

This big family of benzodiazepine drugs are broadly classified as benzodiazepine antianxiety agents and benzodiazepine sedative hypnotic agents [2].

The antianxiety agents are commonly used for pretreatment anxiolysis in adults. They are intended to produce the "minimal" level of sedation usually without impairing the mental alertness, psychomotor performance, and ventilator or cardiovascular performance. Oxazepam and diazepam are popular drugs in this category. Diazepam introduced in 1963 is considered the poster boy of this benzodiazepine subcategory and still continues to be a very popular drug in this category.

The benzodiazepine sedative hypnotic agents manifest sedation, clinically producing a calming effect along with drowsiness and ataxia. Higher doses of this group of drugs produce hypnosis or sleep. Midazolam and triazolam are the popular drugs in this category. Triazolam is commonly prescribed as a sedative/hypnotic in adults, whereas midazolam is currently the dental sedative of choice in children [1].

1.6 Midazolam

Midazolam was first synthesized by Walser and Fryer at Hoffmann-La Roche, Inc., in the United States in the year 1976 [5]. It inherits all the desired pharmacological actions of benzodiazepines including anxiolysis, sedation, hypnosis, anticonvulsant properties, muscle relaxant properties, and the ability to produce anterograde amnesia [6]. In addition, it brings to the table several unique properties of its own. These unique properties have propelled it to be the most extensively used drug for pediatric procedural sedation [7]. More specifically, in Pediatric Dentistry, it is the

most commonly used sedative agent with the exception of nitrous oxide and oxygen [8].

1.6.1 Desirable Characteristics of Midazolam

The high water solubility facilitates its intravenous/intramuscular injection without any local irritation [9]. Its water solubility also makes it nonirritant to the mucosa enabling the administration of the injectable solution orally, rectally, or nasally. The injectable solution can be flavored to be administered orally in case commercial oral formulations are not available [10]. This interesting water solubility aspect in the chemistry of midazolam along with its pharmacokinetics and pharmacodynamics has been discussed in detail in Chap. 2.

The rapid absorption, onset of action, and rapid metabolism without the "rebound" effect seen with diazepam makes it an ideal short-acting agent for dental procedures in children. It can be used as a primary anxiolytic and sedative for short procedures or can be safely combined as a premedication prior to inhalation sedation with nitrous oxide and oxygen for long procedures [11]. The short period of clinical action also facilitates a faster discharge, thereby also saving clinical time in a busy practice.

Its availability in various forms as injectable solutions, syrups, tablets, and sprays makes it a versatile drug compatible with multiple routes of drug administration (See Chap. 5). The Pediatric Dentist can choose the most appropriate route depending on the child's behavior.

The other desirable properties of midazolam making it an attractive proposition for Pediatric Dentistry are:

Anxiolysis and Sedation: Most alternatives to midazolam for moderate sedation like meperidine, hydroxyzine, ketamine, or dexmedetomidine have primary clinical indications, which are *not* anxiolysis and sedation. Meperidine, for example, is primarily an analgesic. Sedation is its secondary clinical effect activated at higher doses. The same holds good for hydroxyzine, which is essentially an antihistamine. Ketamine is a general anesthetic drug, and dexmedetomidine is intended as a premedication to facilitate general anesthesia or intravenous cannulation. Midazolam on the other hand is manufactured to be used as an anxiolytic and sedative.

Antianxiety Properties: It is very important to differentiate concepts of anxiolysis, sedation, and hypnosis. Anxiolysis is the anxiety relief or "calming effect" obtained after administration of an anxiolytic medication. Sedation literally translates to drowsiness, whereas hypnosis is natural sleep. Midazolam possesses all the three properties depending on the dosage administered. But it is the anxiolytic property with the minimal/moderate sedation that it causes, which makes it a useful pharmacological agent in Pediatric Dentistry. It calms the anxious child and causes mild drowsiness creating a conducive environment to implement basic behavior guidance techniques.

Anterograde Amnesia: Though anxiolysis and mild sedation continue to be the primary reasons for choosing midazolam, its ability to cause anterograde amnesia is

especially useful in children during stressful procedures like local anesthesia. The child may still cry during the local anesthetic administration due to the lack of analgesic properties in midazolam. But, post procedure, the child may not remember how the soft tissues got numb. This property of lack of recall after administration of midazolam is called anterograde amnesia.

Wide Therapeutic Margin: Midazolam has a high safety index. This is because of the wide margin in the dose of midazolam that causes the desired clinical effect to the dose that can cause a complication.

Muscle Relaxant and Anticonvulsant Properties: The muscle relaxant property facilitates a more comfortable mouth opening and insertion of a mouth-restraining device like a molt prop. The anticonvulsant property is an additional bonus in epileptic children or during a seizure episode secondary to a local anesthetic over dosage.

1.6.2 Midazolam: A Minimal and Moderate Sedation Drug

We should be absolutely clear at this point that midazolam, regardless of the route of administration, is a drug safely intended at recommended doses, only for minimal/moderate sedation. The concept of "minimal to moderate" sedation underlines that the drug will only help an anxious child cope up with the stress of dental treatment. Minimal/moderate sedation drugs will not be able to override the extreme fear of a combative child. They will work best in conjunction with good local anesthetic techniques, which in turn will require the clinician to use the entire gambit of non-pharmacological behavior guidance techniques. The concept of "minimal to moderate" sedation is therefore essentially a triangle where these three components are interrelated (Fig. 1.2).

The above concept is explained in detail in Chap. 6.

A combative child with a true objective fear towards dentistry may try and fight the anxiolytic (calming) effect of midazolam. This may lead to a paradoxical reaction with the child becoming more aggressive and fearful instead of calming down [12]. Hence, minimal/moderate sedation drugs like midazolam should *not* be expected to be effective in combative children or those displaying disruptive behavior. These children are best treated under deep sedation or general anesthesia. The only exception to this rule could be pre-cooperative children (3 years or less) requiring short procedures like extractions.

1.6.3 Deep Sedation with Midazolam

Deep sedation is also possible with midazolam by increasing its dosage or by combining it with other sedatives. But the clinician should be aware that deep sedation or essentially an ultra-light plane of general anesthesia [13] may also bring with it life-threatening complications like desaturations, respiratory depression, or loss of protective reflexes [14]. If the clinician desires deep sedation to treat a combative/disruptive child with objective fears, then there are other suitable drugs like

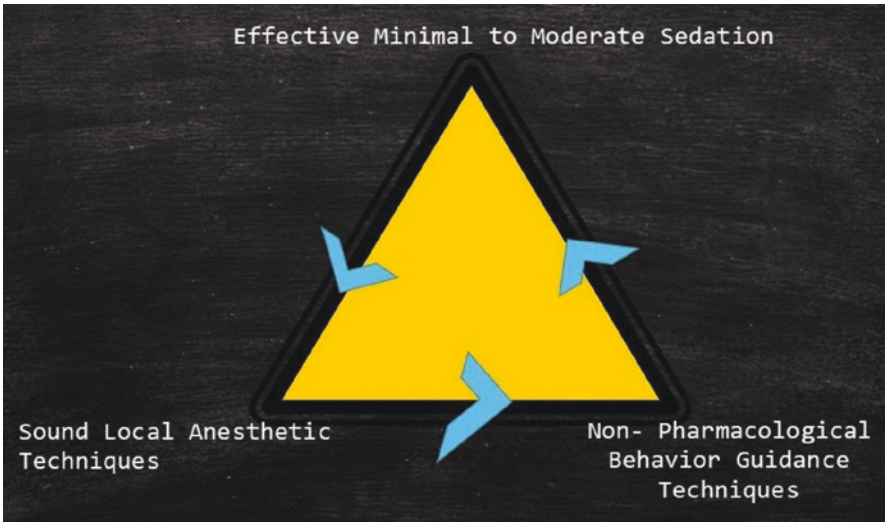

Fig. 1.2 Triangle depicting the importance of sound local anesthetic and non-pharmacological behavior guidance techniques for effective minimal/moderate sedation

propofol and ketamine which will do the job. These drugs in the experienced hands of an anesthetist will provide deep sedation safely at smaller dosages.

The concepts discussed in the paragraph above are explained elaborately in Chaps. 4 and 8.

We will strive to explain in further chapters the predictable ways to achieve minimal/moderate sedation through midazolam in children. Proper systemic history (Chap. 3), the correct intraoperative protocol (Chap. 7), and meticulous documentation (Chap. 9) are the roadmaps through which midazolam can become a valuable asset in the child management armamentarium of the Pediatric Dentist.

Clinically Relevant Points

1. Midazolam is the most commonly used sedative agent in Pediatric Dentistry with the exception of nitrous oxide and oxygen.
2. The rapid absorption, onset of action, and rapid metabolism without the "rebound" effect seen with diazepam makes midazolam an ideal short-acting agent for dental procedures in children.
3. Midazolam will sedate an anxious child predictably for short procedures or will facilitate the acceptance of the nasal hood for long procedures.
4. Midazolam has a high therapeutic index and hence a wide margin of safety.

5. The water solubility of midazolam makes it nonirritant to the mucosa enabling the administration of the injectable solution orally, rectally, or nasally.
6. Midazolam regardless of the route of administration is a drug safely intended at recommended doses, only for minimal/moderate sedation.
7. Moderate sedation drugs like midazolam should *not* be expected to be effective in combative children or those displaying disruptive behavior.
8. Midazolam has to be used in conjunction with non-pharmacological methods of behavior guidance along with sound local anesthetic techniques.
9. Anxiolysis is the anxiety relief or "calming effect" obtained after administration of an anxiolytic medication. Sedation literally translates to drowsiness, whereas hypnosis is natural sleep. Midazolam possesses all the three properties depending on the dosage administered.
10. Though anxiolysis and mild sedation continue to be the primary reasons for choosing midazolam, its ability to cause anterograde amnesia is especially useful in children during stressful procedures like local anesthesia.
11. A combative child with a true objective fear towards dentistry may try and fight the anxiolytic (calming) effect of midazolam. This may lead to a paradoxical reaction with the child becoming more aggressive and fearful instead of calming down.
12. Deep sedation is also possible with midazolam by increasing its dosage or by combining it with other sedatives. But the clinician should be aware that deep sedation or essentially an ultra-light plane of general anesthesia may also bring with it life-threatening complications like desaturations, respiratory depression, or loss of protective reflexes.

References

1. Wilson S. Minimal and moderate sedation agents. In: Wright GZ, Kupietzky A, editors. Behavior management in dentistry for children. 2nd ed. Wiley Blackwell; 2014. p. 159–75.
2. Malamed SF. Oral sedation. In: Sedation: a guide to patient management. 6th ed. St. Louis, Missouri: Elsevier; 2018. p. 95–119.
3. Trevor A, Katzung B, Masters S, Knuidering-Hall M. Pharmacodynamics. In: Pharmacology examination & board review. 10th ed. New York: McGraw-Hill Medical; 2013. p. 17.
4. Glass PS, Jhaveri RM, Ginsberg B, Ossey K. Evaluation of flumazenil for reversing the effects of midazolam-induced conscious sedation or general anesthesia. South Med J. 1993;86(11):1238–47. https://doi.org/10.1097/00007611-199311000-00011.
5. Kupietzky A, Houpt MI. Midazolam: a review of its use for conscious sedation of children. Pediatr Dent. 1993;15(4):237–41.
6. Gao F, Wu Y. Procedural sedation in pediatric dentistry: a narrative review. Front Med (Lausanne). 2023;10:1,186,823. https://doi.org/10.3389/fmed.2023.1186823.