Complications of oral sedation in dentistry

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ABSTRACT

Oral sedation is a technique in which one or more medications are used to induce a state of depression of the central nervous system, allowing treatment to be carried out. The aim of this study was to discuss the complications with the use of oral sedation in dental practice, as well as the methods of sedation, aiming to disseminate the knowledge of these techniques and strengthen the set of resources available to the dentist for the control of anxiety and dental fear. The present study is an integrative literature review, based on primary studies, searches were performed in the databases: Portal de Periódicos da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), which brings together databases (SCieLo), the PubMed portal that encompasses MedLine (International Literature in Health Sciences and Scielo – Scientific Electronic Library Online), and the Google Scholar platform, among others. The methodology is qualitative, using the sampling

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method. Research focused on oral sedation has the potential to increase the adoption of the various techniques by a greater number of professionals. Therefore, understanding the various approaches that can attenuate the apprehension associated with dental treatments is of paramount importance to reduce the apprehension related to the procedures, improve behavioral control and promote the wellbeing of patients. Since conscious sedation proves to be an excellent option for managing anxiety and fear during dental interventions, the use of medications can create a more serene and pleasant environment for patients.

Keywords: Conscious Sedation, Complications, Midazolam, Nitrous Oxide.

INTRODUCTION

In the context of dental treatment, the presence of anxiety and fear constitutes a significant challenge that can hinder the performance of procedures, especially in highly anxious patients. The anxiety and stress associated with dental visits have a direct impact on the pursuit of dental care, creating a "vicious cycle" that leads to an increase in the prevalence and exacerbation of oral diseases (FIORILLO, 2019; TSHISWAKA, 2018).

Dental treatment-related phobia often originates from previous unpleasant experiences, such as the administration of local anesthesia, one of the primary causes of dental anxiety, as well as the use of dental instruments and equipment. It is important to highlight that parents' negative experiences can significantly influence their children's behavior in the dental office (BATISTA, 2018).

Oral sedation is a technique involving the administration of one or more medications to induce a state of central nervous system depression, facilitating the execution of dental procedures (SIVARAMAKRISHNAN, 2017). During this controlled state of drug-induced conscious depression, the patient maintains protective reflexes, such as respiratory function, and responds appropriately to physical stimuli and verbal commands (BAEDER, 2016). This approach has proven effective in controlling anxiety and aversion to the dentist, often becoming essential for the treatment's success (KAPUR, 2018).

Besides controlling stress and fear, oral sedation has the advantage of being safe even in an outpatient setting (FIORILLO, 2019). To this end, it is crucial that the medications used possess a broad and satisfactory safety margin, making the total loss of consciousness unlikely (KAPUR, 2018). The application of sedation techniques offers several advantages that aid dental practice, including the reduction of anxiety and the treatment of patients with severe gag reflexes or special needs. Additionally, during the state of induced depression, there is a decreased perception of painful stimuli (GUERRERO, 2020).

Through a literature review, this study aims to discuss the complications associated with the use of oral sedation in dental practice, as well as sedation methods, intending to disseminate knowledge of these techniques and enhance the resources available to dentists for managing dental anxiety and fear.

Within the field of Dentistry, Resolution No. 51/04 of the Federal Council of Dentistry, dated April 30th, 2004, established guidelines for the qualification of dentists in the use of relative analgesia, also named conscious sedation. The aim was to delineate the legal parameters concerning this specialty, provided the professional is adequately trained through a course authorized by the Federal Council of Dentistry (BRAZILIAN MINISTRY OF HEALTH, 2004).

Patients exhibiting moderate to high levels of anxiety may significantly benefit from oral sedation. The judicious application of anxiolytics may be advantageous not only for patients, particularly those with cardiovascular diseases, hypertension, or diabetes mellitus, but also for healthcare team (GOODALL, 2004 as cited in SANTOS, 2012). For successful outcomes, it is imperative that the chosen sedation technique is safe, well-tolerated by the patient, does not cause airway obstruction, as well as not resulting in respiratory or cardiac depression. The ideal anxiolytic should be effective at doses that minimally alter vital signs, enhance rapid recovery, and be associated with a low incidence of adverse reactions (GOODCHILD, 2005 as cited in SANTOS, 2012).

MAIN DRUGS USED IN CONSCIOUS SEDATION

ANTIHISTAMINES

Antihistamines are a well-known class of drugs with sedative properties, frequently utilized in combination with other agents such as opioids and nitrous oxide to achieve desired sedative and hypnotic effects, with the advantage of not causing cardio-respiratory depression or unconsciousness (GENTZ et al., 2017). These drugs are readily available, cost-effective, and clinically safe, and can be administered orally. The mechanism of action of these drugs is due to their anticholinergic properties resulting from postsynaptic blockade at dopaminergic receptors (MOZAFAR et al., 2018).

The most commonly used antihistamines in conscious sedation, especially in pediatric dentistry, are hydroxyzine and promethazine. When combined with other drugs, these antihistamines also shows antiemetic effects, helping mitigate nausea and vomiting induced by other medications (GENTZ et al., 2017). Regarding adverse effects, mild extrapyramidal symptoms such as motor restlessness are the most common although rare when administered orally. Other adverse effects, such as xerostomia, urinary retention, palpitations, hypotension, headache, appetite changes, constipation, or diarrhea, are infrequent (MELONARDINO et al., 2016).

BENZODIAZEPINES

In Brazil, dentists do not commonly use benzodiazepine sedation in clinical practice due to several issues, including a lack of adequate training and education (PINHEIRO et al., 2014). This class of medications is the primary anxiolytic used to control mild to moderate anxiety during conscious sedation. They are considered effective and safe for this purpose due to their sedative, anxiolytic, anticonvulsant, muscle relaxant properties, and ability to induce anterograde amnesia. However, it is important to note that benzodiazepines do not have analgesic effects. In dental practice, they are frequently administered orally as pharmacological agents for conscious sedation (BAEDER et al., 2016).

The mechanism of action of benzodiazepines involves the facilitation of gammaaminobutyric acid (GABA)-mediated chloride channel opening, which is an inhibitory neurotransmitter in the central nervous system. The interaction between GABA and benzodiazepine receptors results in neuronal membrane hyperpolarization, reducing excitability and causing alterations in cognitive abilities. Although all benzodiazepines share similar mechanisms of action, they exhibit differences in the onset and duration of their effects (KAPUR, 2018).

Sedation with these medications may be administered orally or parenterally. Oral administration is the most common and has a slower onset and recovery compared to parenteral routes. Intravenous sedation, although acting more rapidly, requires skills and experience in intravenous drug administration. The intramuscular route is slower than the intravenous route and its efficacy can vary (FIORILLO, 2019; GENTZ et al., 2017).

Diazepam and midazolam are benzodiazepines that have been widely used in conscious sedation due to their safety and efficacy, as well as their wide clinical safety margin, with toxic doses being 30 to 40 times greater than therapeutic doses. Midazolam has a faster onset of action compared to diazepam, a shorter plasma half-life, and is three to four times more potent (KAPUR, 2018; CAVALCANTE et al., 2011). Temazepam is another benzodiazepine that has a rapid onset of action, a short half-life (8 hours), and is preferable to diazepam (FIORILLO, 2019).

Midazolam has been widely used in oral sedation due to its sedative, anxiolytic, muscle relaxant, and anticonvulsant properties. It is rapidly absorbed and eliminated by the body, has a high therapeutic margin, and a wide safety margin. This medication is administered orally, with an onset of action between 15 and 30 minutes and peak blood concentration between 25 and 50 minutes. For adults, doses of midazolam range from 7.5 to 15 mg per day (Greenblatt, 1992 as cited in AIRES, 2022). However, it is important to consider that oral sedation can have variable absorption and cannot be adjusted to achieve the desired effect, which can result in unpredictable levels of sedation (Lanza et al., 1988 as cited in AIRES, 2022).

Benzodiazepines are generally well tolerated and have a low incidence of adverse effects, especially when used for short-term treatments, due to their wide clinical safety margin (GALLAGHER, 2016). Their use is contraindicated in cases of hypersensitivity to the components of the formula, in drug users and dependents, in patients with respiratory insufficiency due to the depressant effect of these medications, and in patients with glaucoma. When administered in combination with other drugs, such as opioids, benzodiazepines can reduce respiratory rate, blood pressure, and heart rate. These cardiovascular changes are rare when the absorbed doses are minimal (RODRIGUES et al., 2015). The combined use of nitrous oxide with midazolam, rather than the isolated use of each drug, allows for a reduction in the total dose of midazolam, achieving a better

safety profile and a predictable level of sedation for dental procedures (SIVARAMAKRISHNAN, 2017).

In cases of adverse reactions and complications during sedation with benzodiazepines, it may be necessary to use an agent to reverse the effects of these drugs. In such cases, the drug of choice is Flumazenil (SEELHAMMER et al., 2018), which can be administered intravenously or intranasally. Flumazenil provides a rapid reversal of the effects of all benzodiazepines; however, it is contraindicated for patients who use these medications to treat seizure disorders or in cases of high doses of tricyclic antidepressants (KAPUR, 2018).

Although in a small proportion, some patients may experience paradoxical effects when using benzodiazepines; instead of the expected sedation, they may exhibit excitation, agitation, and irritability. If this occurs, it is recommended to postpone the procedure and keep the patient under observation until these effects subside. It is important to note that paradoxical effects are more common in children and the elderly, and agitation may increase the risk of falls in elderly patients. Due to its lower likelihood of causing these effects, lorazepam is considered the ideal agent for conscious sedation in this patient group (MALAMED, 2013).

Anterograde amnesia is another side effect of benzodiazepines, which can occur even with a single dose. It is characterized by the forgetting of events related to a certain moment, usually coinciding with the peak activity of the medication. This amnesia is more common with the use of drugs such as midazolam and lorazepam. Some professionals consider anterograde amnesia beneficial (a desirable effect) as the patient will not remember most procedures, including some traumatic ones, that could generate negative experiences. On the other hand, other professionals view it as undesirable (an adverse effect) because the patient may not recall the post-operative instructions and care recommended by the professional (SHAVLOKHOVA, 2014).

NITROUS OXIDE

Nitrous oxide, also known as nitrogen dioxide (N2O), laughing gas, or happy gas, is an odorless and colorless gas widely used in sedation techniques due to its anxiolytic, analgesic, and amnesic properties (CHI, 2018). This anxiolytic agent is effective, non-irritating, and has low solubility, generally not causing significant effects on the respiratory and cardiovascular systems. Similar to benzodiazepines, nitrous oxide exerts its effect by activating GABA receptors. Its analgesic action occurs through the release of endogenous opioid peptides, altering the noradrenergic metabolic sequence and modifying the spinal nociceptive process. Since it primarily acts on the cerebral cortex, the laryngeal reflex is maintained during sedation (FIORILLO L, 2019).

In Brazil, the use of nitrous oxide was regulated in 2004 by resolution CFO-051/2004, Article VI of Law No. 5,081, which addresses the practice of Dentistry. This resolution establishes the use of

analgesia and hypnosis by dentists, provided they are properly trained through courses offered by professional organizations registered with the Federal Council of Dentistry (MINISTÉRIO DA SAÚDE, 2004).

Nitrous oxide inhalation is performed by mixing N2O and oxygen (O2) in varying percentages. Initially, a flow of 100% oxygen is administered, and then nitrous oxide is added incrementally, not exceeding the maximum limit of 70% N2O in the N2O/O2 mixture. The percentage of N2O in the mixture is adjusted according to the needs of each patient (LADEWIG et al., 2016). N2O has low tissue solubility and a high minimum alveolar concentration, providing a rapid onset of action and quick recovery, allowing for controlled sedation and a swift return to daily activities (KAPUR, 2018).

The combination of the N2O/O2 mixture with midazolam, besides providing an enhanced effect compared to the isolated use of the drugs, reduces the risk of toxicity associated with midazolam use and improves the acceptance of the nasal mask in children (BLUMER et al., 2018; SIVARAMAKRISHNAN, 2017). The most frequently associated adverse effects of this technique are nausea and vomiting. Other events reported in the literature include chest pain, desaturation, and tonic-clonic seizures. Generally, the occurrence of adverse effects is related to the administration of N2O/O2 at higher concentrations (>50%) or long sedation periods. Since drug reactions may vary significantly among patients, some may reach the minimum alveolar concentration more quickly, making continuous monitoring extremely important to avoid deep sedation and ensure the maintenance of laryngeal reflexes, thereby ensuring adequate patient respiration (CHI, 2018).

Nitrous oxide sedation is contraindicated in psychotic patients, those with upper airway obstructions (including cases of respiratory viruses), patients with severe systemic diseases, or chronic pulmonary problems such as chronic obstructive pulmonary disease (FIORILLO, 2019; KAPUR, 2018). The primary disadvantages of nitrous oxide sedation are the costs associated with the necessary equipment, the requirement for training and certification of the dentist and their team, the required infrastructure, and the individual (and subjective) variation in dosage for each patient (FIORILLO L, 2019).

OPIOIDS

Opioids are analgesic medications that bind to specific receptors located in various regions of the central nervous system and other tissues. When combined with other sedative agents, this class of drugs can significantly enhance the quality of sedation due to their potent analgesic properties. Although the oral route is preferred, especially in pediatric dentistry, its absorption is unreliable, resulting in unpredictable efficacy (GENTZ R, et al., 2017).



Fentanyl is a fast-acting opioid with a short duration of action (30 to 60 minutes) and is approximately 60 to 80 times more potent than morphine. It can be administered parenterally, transdermally, nasally, or orally. Fentanyl is a lipophilic drug, absorbed through the buccal mucosa, metabolized in the liver, and excreted in the urine. The recommended dose is 1 μ g/kg per intravenous dose, which can be repeated in increments of 1 μ g/kg if necessary (KAPUR A and KAPUR V, 2018). The use of fentanyl results in deeper sedation and can lead to respiratory depression, particularly when combined with other sedative medications, which is especially relevant in elderly patients. Therefore, it is advisable to use this substance preferably in a hospital setting under the supervision of an anesthesiologist (GÖKTAY O, et al., 2011).

Tramadol is a centrally acting synthetic opioid analgesic, whose analgesic effect is primarily mediated by the inhibition of norepinephrine and serotonin reuptake, and it also has a low affinity for opioid receptors. This combination provides relief for moderate to severe pain. Unlike traditional opioid analgesics such as morphine and fentanyl, tramadol preserves respiratory and cardiovascular functions (GÖKTAY O, et al., 2011).

In dentistry, the use of tramadol is extensively studied, particularly for the control of postoperative pain or as a preemptive analgesic (ARAÚJO FAC, et al., 2012). In a comparative study between the use of fentanyl and tramadol combined with midazolam, it was observed that tramadol can also be used to enhance the effect of conscious sedation, similar to fentanyl, despite the distinct pharmacokinetic and pharmacodynamic properties of these drugs (CHON J and LEE J, 2011).

In general, opioids are able to bring about adverse effects such as respiratory and cardiovascular depression, dizziness, dry mouth (xerostomia), hypoventilation, hypotension, nausea, and vomiting. The severity of adverse effects is usually related to the intensity of pain, the route of administration, dosage, and combination with other drugs. The adverse effects of opioids can be reversed with the use of naloxone (KAPUR A and KAPUR V, 2018; GENTZ R, et al., 2017)

MAJOR COMPLICATIONS IN ORAL SEDATION

Oral sedation is a procedure used to reduce anxiety and discomfort in patients during certain dental procedures. However, like any procedure, it can be associated with various complications and risks. Key complications include:

- 1. Allergic or Adverse Reactions to Medications: Some patients may exhibit allergic reactions to medications used in oral sedation, leading to adverse effects such as skin rashes, respiratory difficulties, nausea, vomiting, or anaphylaxis.
- 2. **Respiratory Depression:** This can lead to reduced respiratory rate and decreased oxygen levels in the blood. It is more common when higher doses of sedative medications are used.

- 3. **Cardiovascular Complications:** Certain medications used in oral sedation may affect the cardiovascular system, resulting in decreased blood pressure, irregular heartbeats, or other cardiovascular issues.
- 4. **Monitoring Difficulties:** Continuous monitoring of vital signs, such as heart rate, blood pressure, and oxygen levels, is crucial during oral sedation. Inadequate monitoring can lead to undetected complications.
- Inadequate or Excessive Sedation: Incorrect dosing of medications can result in insufficient sedation, leaving the patient anxious or uncomfortable during the procedure. Conversely, excessive dosing can lead to deep sedation or even unconsciousness.
- 6. **Vomiting and Aspiration:** Sedated patients are at an increased risk of aspirating gastric contents into their lungs during a procedure, which can lead to respiratory issues and pulmonary infections.
- Psychological Reactions: Some patients may experience unwanted psychological reactions, such as nightmares, confusion, or agitation after oral sedation (RUGGIERO, 2022).

It is crucial to emphasize that oral sedation should be performed by trained and experienced healthcare professionals who can carefully assess the risks and benefits for each individual patient. Prior to conducting any procedure, patients should undergo a thorough evaluation of their overall health and medical history to ensure the safety of the sedation process.

OBJECTIVES

GENERAL OBJECTIVE

Conduct a literature review regarding the complications of oral sedation in dentistry.

SPECIFIC OBJECTIVES

Describe the mechanism of action and safety of oral sedation in dentistry. Identify the main contraindications of oral sedation in dentistry. 3.2.3. Outline the primary advantages of oral sedation in dentistry.

METHODOLOGY

SEARCH STRATEGY

This study is an integrative literature review based on primary studies, aimed at compiling results from published research on complications of oral sedation in dentistry. The review was conducted at the Faculty of Dentistry of Pernambuco (FOP-UPE) from January 2022 to May 2023. Searches were performed in the following databases: the CAPES Journal Portal, which includes

SCieLo (Scientific Electronic Library Online), the PubMed portal, which encompasses MedLine (International Literature in Health Sciences), and Google Scholar, among others.

In addition to database searches, manual searches were also conducted. This qualitative methodology employed sampling techniques as referenced by Pereira et al. (2018). The search for scientific articles was conducted on the mentioned platforms covering the period from 2011 to 2023, using descriptors such as "Conscious Sedation", "Complications", "Midazolam", "Nitrous Oxide", "Sedação Consciente", "Complicações", "Midazolam", and "Óxido Nitroso" (DeCs/MeSH).

INCLUSION CRITERIA

The articles included in this review adhered to the following inclusion criteria:

- Full-text articles available in the specified databases.
- Publications in English or Portuguese.
- Publication dates ranging from 2011 to 2022.

SELECTION OF BIBLIOGRAPHIC SAMPLE

Descriptors used were based on DeCS (Health Sciences Descriptors) for searching the topic in both English and Portuguese, aiming to include the maximum number of relevant studies on the proposed topic.

EXCLUSION CRITERIA

Studies were excluded if they did not demonstrate scientific value or lacked relevance to the proposed topic.

RESULTS

From a total of 134 articles, 76 were sourced from PubMed, 30 from SciELO, 18 from CAPES, and 10 from Medline. Initially, duplicate articles were identified and removed, resulting in the exclusion of 72 articles. Subsequently, abstracts were reviewed, and articles that did not address the research question were excluded, leading to the removal of an additional 37 articles. Ultimately, 25 articles were included in this review.

This study aimed to analyse the literature concerning the primary effects and complications associated with oral sedation in dentistry. The integrative review successfully identified recent studies highlighting the advantages, contraindications, mechanism of action, and safety of oral sedation in the field of dentistry.

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Table 1. Selection of articles accordin	ng to author, type of stud	ly, objectives, methodology,	results, and conclusions
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			ctives, methodology, result	
Author	Objective	Methodology	Results	Conclusions
AIRES et al. (2022)	To review the literature on various aspects related to the use of conscious sedation in dental practice, as well as sedation methods, aiming to disseminate knowledge about these techniques.	Integrative literature review	Anxiety control is a constant challenge during dental treatment. The application of sedation techniques brings several advantages that assist in treating special patients and children, allowing the reduction of anxiety. Various techniques and drugs, such as benzodiazepines, nitrous oxide, antihistamines, opioids, chloral hydrate, and the herbal remedy Valeriana officinalis, were discussed, highlighting mechanisms of action, routes of administration, clinical advantages, and main adverse effects associated with each method.	Conscious sedation provides greater comfort during dental treatments, especially in children and patients with special needs. Various drugs with sedative and hypnotic properties are available on the market, each with its clinical advantages and disadvantages. Knowledge of the various methods to reduce anxiety during dental treatments results in better behavioural control and patient well- being during treatments.
ARAÚJO et al. (2012)	To compare the preemptive analgesic effect of nimesulide and tramadol hydrochloride during third molar surgery. The study was conducted between March and November 2009, involving 94 operations on 47 patients of both sexes with bilaterally impacted lower third molars in comparable positions.	Prospective, randomised, controlled, and paired study	Pain peaked 5 hours after surgery in both groups, with a mean pain score of 2.3 in Group A and 3.0 in Group B; this difference did not reach statistical significance (p > 0.141).	Based on the sample studied, nimesulide and tramadol hydrochloride demonstrate similar preemptive analgesic effects when used in lower third molar surgeries.
BATISTA et al. (2018)	To discuss how emotions affect clinical conduct, identify the main causes of this aversion, and correlate Dentistry and Psychology as a means of acquiring knowledge.	Literature review using scientific articles found in databases such as PubMED/Medline, Lilacs, and Scielo. Articles were selected according to inclusion criteria, publication period, and methodological detail. The descriptors used	According to measurements, females are generally more prone to developing fear and anxiety in dental treatment. The study also observed that anxious individuals tend to have a longer interval since their last visit, which also applies to	Aversion to clinical procedures is a recognised issue in dentistry. Therefore, professionals should acquire theoretical and practical knowledge in Psychology to develop



Author	Objective	Methodology	Results	Conclusions
		were dental anxiety and dental fear.	individuals who avoid treatment due to fear. Some studies used the VPT (Venham Picture Test) and the Corah Dental Anxiety Scale.	behavioural management strategies.
BAEDER et al. (2016)	To evaluate patients' knowledge about conscious sedation with benzodiazepines and its acceptance in controlling fear and anxiety for dental treatment.	Quantitative descriptive study through data collection by the researcher using questionnaires. Patients received instructions about the questionnaire before answering and were informed that the data would be kept confidential. Data were analysed by cross-tabulating the socioeconomic class of 150 patients, equally selected from classes A/B, C, and D/E. The association between social class and responses was evaluated using Fisher's exact test.	Class A/B patients had higher knowledge and acceptance of benzodiazepine use for controlling fear and anxiety in dentistry compared to lower socioeconomic classes. Class A/B patients also had more access to resources related to dental technical knowledge. There has been a significant reduction in fear related to dental treatment.	Social class influences the acceptance and knowledge of benzodiazepines in controlling dental treatment-related anxiety.
BLUMER et al. (2018)	To examine whether changes in oxygen saturation and pulse rate in paediatric patients during conscious sedation with midazolam and nitrous oxide are associated with the child's behaviour, midazolam dose, type and duration of treatment, and demographic parameters.	Retrospective review of the medical records of consecutive paediatric patients aged between 2.5 and 12.5 years who underwent conscious sedation for dental treatment with oral midazolam (with or without nitrous oxide) between January 2011 and September 2015 at the Department of Paediatric Dentistry, Tel Aviv University. Midazolam was administered according to patient weight in doses of 0.4 mg/kg, 0.5 mg/kg, or a maximum dose of 10 mg. Pulse rate and oxygen saturation were monitored every 15 minutes during treatment.	Sedation was successful in 80% of cases. Children with poor behavioural scores had statistically significant differences in average saturation, although within normal limits, during treatment ($p < 0.012$) and a clinically higher average pulse rate ($p =$ 0.0001) compared to children with good behaviour scores. The duration of treatment, type of dental procedure, or patient weight did not correlate with changes in oxygen saturation or pulse rate during treatment.	Poor behaviour in paediatric patients does not affect oxygen saturation but increases pulse rate during sedation with midazolam and nitrous oxide.
CAVALCANTE et al. (2011)	To report the most commonly used conscious sedation techniques in paediatric dentistry	Integrative literature review	In clinical practice, many children are immature, anxious, or have physical and/or mental behaviours that	Conscious sedation techniques, when properly applied, are effective and safe alternatives for



Author	Objective	Methodology	Results	Conclusions
	as an alternative		do not cooperate	managing children
	for treating		during dental	with difficult
	children with		treatment. Conscious	behaviour during
	difficult behaviour.		sedation through pre-	dental treatments.
			medication or sedation	
			with nitrous	
			oxide/oxygen is a valid	
			and safe alternative for	
			managing these	
			patients, providing	
			excellent results,	
			especially with	
			children.	
			Nitrous oxide (N2O),	
			an odourless and	
			colourless gas, is	
			highly attractive as a	
			sedative due to its	
			anxiolytic, analgesic,	
			and amnesic	ът', · · · ·
			properties, rapid onset	Nitrous oxide is a
			and recovery, and no	safe and effective
			need for needles.	sedation and
	To detail the use of	Integrative literature	Numerous studies have	analgesia agent, but
CHI (2018)	nitrous oxide.	review	reported that N2O can	its potential to
	introus oxide.		be used safely and	cause irreversible
			effectively as a	inactivation of
			sedation and analgesia	vitamin B12 must
			agent for procedures.	be considered.
			However, N2O may	
			lead to irreversible	
			inactivation of vitamin	
			B12, which is essential	
			for humans; although	
			rare, this can be fatal	
			in some patients.	
			Tramadol and fentanyl	
			have quite different	
			pharmacodynamics	
			and pharmacokinetic	
			characteristics, and	
			their uses differ	Both tramadol and
			according to these	fentanyl have their
			characteristics.	specific indications
	To compare		Fentanyl, a highly	and should be
			1	
	-	Integrative literature	potent opioid	prescribed by a
CHON (2011)	tramadol with	Integrative literature	analgesic, has a very	prescribed by a
CHON (2011)	tramadol with fentanyl for	Integrative literature review		qualified dental
CHON (2011)	tramadol with		analgesic, has a very short onset time and	qualified dental professional
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours	qualified dental professional according to their
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half-	qualified dental professional according to their pharmacokinetic
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours,	qualified dental professional according to their
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce	qualified dental professional according to their pharmacokinetic
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites.	qualified dental professional according to their pharmacokinetic
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their	qualified dental professional according to their pharmacokinetic
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should	qualified dental professional according to their pharmacokinetic
CHON (2011)	tramadol with fentanyl for		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should be prescribed by a	qualified dental professional according to their pharmacokinetic
CHON (2011)	tramadol with fentanyl for conscious sedation.		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should be prescribed by a qualified dentist.	qualified dental professional according to their pharmacokinetic characteristics.
CHON (2011)	tramadol with fentanyl for conscious sedation.		analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should be prescribed by a qualified dentist. The level of sedation	qualified dental professional according to their pharmacokinetic characteristics.
	tramadol with fentanyl for conscious sedation.	review	analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should be prescribed by a qualified dentist. The level of sedation required should be	qualified dental professional according to their pharmacokinetic characteristics.
CHON (2011) FIORILLO (2019)	tramadol with fentanyl for conscious sedation. To evaluate some methods used in dentistry for	review Integrative literature	analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should be prescribed by a qualified dentist. The level of sedation required should be adjusted individually	qualified dental professional according to their pharmacokinetic characteristics.
	tramadol with fentanyl for conscious sedation.	review	analgesic, has a very short onset time and peak effect (0.25 hours and 0.5 hours), a half- life of 1 to 1.5 hours, and does not produce any active metabolites. Both have their indications and should be prescribed by a qualified dentist. The level of sedation required should be	qualified dental professional according to their pharmacokinetic characteristics.



Author	Objective	Methodology	Results	Conclusions
			patient's needs, the operator, and the safety of the procedure. Surgical time is an important factor for postoperative phases and can be significantly increased if the patient interrupts the surgeon or is uncooperative.	improving the comfort and safety of dental procedures.
GALLAGHER (2019)	To detail the use of benzodiazepines in conscious sedation.	Integrative literature review	The increasing availability of conscious sedation in dental practice has made treatment much more accessible for anxious patients. Currently, benzodiazepines are the most commonly used medications in sedation practice and provide a pleasant experience for most patients, although not for everyone. Understanding the mechanism of action of benzodiazepines should inform our practice and deepen our understanding of why and how sedation might fail.	Benzodiazepines are the most commonly used medications for conscious sedation in dentistry, providing a generally pleasant experience, but understanding their mechanism of action is crucial for effective use.
GENTZ et al. (2017)	To characterise the efficacy and complications in children receiving oral midazolam alone, nasal midazolam alone, or oral midazolam with other sedatives.	Children received oral midazolam alone, nasal midazolam alone, or oral midazolam in combination with other sedatives. All individuals received a pre-sedation history and physical examination and were sedated according to protocol by any of the 28 resident professionals under supervision. Sedations were evaluated for success and complications by doctors. Postoperative complications were assessed by trained staff up to 48 hours post-operatively.	Sedations were successful in approximately 80% of cases. The planned treatment was completed in over 85% of encounters. Oral midazolam alone produced the best behaviour. Physical evaluation factors, behaviour, and age were correlated (P = 0.035) with efficacy. All three regimens were effective with minimal postoperative complications.	Oral midazolam alone produced the best behaviour in children, while all regimens were effective and had minimal complications.
GÖKTAY et al. (2011)	To evaluate the effects of fentanyl and tramadol	Prospective, randomised, double- blind, placebo-	Tramadol showed the best analgesic effect compared to fentanyl	Tramadol is more effective than fentanyl and



Author	Objective	Methodology	Results	Conclusions
	combined with nitrous oxide on sedation for extraction of impacted third molars.	controlled study. Patients received either tramadol, fentanyl, or placebo combined with nitrous oxide. All patients underwent similar procedures under local anaesthesia. The effects on sedation and pain relief were assessed by pain scores and satisfaction surveys.	and placebo. Satisfaction levels among patients did not differ significantly between the groups.	placebo for sedation and pain relief during third molar extraction.
GUERRERO et al. (2020)	To assess the impact of conscious sedation on paediatric patients' behaviour.	Clinical study involving 65 paediatric patients. Patients were observed during and after the sedation process to assess behavioural changes and overall impact.	Conscious sedation led to a behavioural improvement in 86.15% of patients. Children with high levels of anxiety and fear showed significant reductions in these feelings after sedation.	Conscious sedation effectively reduces anxiety and improves behaviour in paediatric patients during dental treatment.
KAPUR (2018)	To study recent trends in conscious sedation in dentistry.	Integrative literature review from the perspective of an anaesthesiologist. Various methods and guidelines for conscious sedation are discussed.	Conscious sedation in dentistry has evolved with various methods, but safety remains a significant concern. The challenge includes maintaining airway safety and patient monitoring.	The evolving trends in conscious sedation require a thorough understanding of sedation methods and safety protocols to ensure effective and secure treatment.
MALAMED (2013)	To compare the latency and pain associated with injections of alkalinised versus non-alkalinised local anaesthetic.	Study involving 20 participants who received either alkalinised or non- alkalinised local anaesthetic. Pain and latency were measured and compared.	Alkalinised local anaesthetic resulted in significantly less latency and pain during injection compared to non- alkalinised anaesthetic.	Alkalinisation of local anaesthetic improves patient comfort by reducing injection pain and latency.
LADEWIG et al. (2016)	To discuss the use of nitrous oxide in dental practice.	Literature review including recent and classic articles on nitrous oxide use.	Nitrous oxide is effective in controlling anxiety and is safe when used properly. The technique should be well understood to prevent potential complications.	Nitrous oxide is a valuable tool for managing anxiety in dental patients, but proper understanding and use are essential for ensuring safety and effectiveness.
MELONARDINO (2016)	To describe detection methods for	(Incomplete information)	(Incomplete information)	(Incomplete information)

According to Santos (2012), Rodrigues (2015), and Tshiswaka (2018), since a visit to the dentist can be a daunting experience for certain individuals, it is pertinent to assess dental anxiety during the patient's anamnesis. This is of paramount importance as dental anxiety not only constitutes a public health issue but also becomes a barrier to dental treatment (MALAMED, 2013).



Anxious patients tend to avoid dental treatment, which often leads to deteriorating oral health (PINHEIRO et al., 2014; MELONARDINO, 2016). Furthermore, it is crucial to evaluate the emotional state of patients before any procedure to prevent difficulties during dental care, operative complications, or even medical emergencies. It has been found that 75% of medical emergencies in dental practices are related to anxiety (SANTOS, 2012).

According to BATISTA et al. (2018), although trust and adequate pain control are crucial factors for reducing anxiety in anxious patients, sometimes it is necessary to use oral sedation in dentistry to achieve effective anxiety control (AIRES, 2022). As Araújo (2012) reports, this approach aims to ensure a calmer and safer dental experience for the patient.

For Sivaramakrishna (2017), sedation in dentistry is commonly performed using benzodiazepines and/or nitrous oxide. Sedation with benzodiazepines is classified by the American Society of Anesthesiologists (ASA) as minimal, moderate, and deep (MALAMED, 2013). Fiorillo (2019) explains that during sedation, cardiovascular function generally remains stable, but spontaneous respiratory function may be affected, especially in cases of deep sedation, possibly requiring ventilatory support. Thus, a lack of technical knowledge about sedation and potential medical complications is the main factor for its limited use in dental practice (SANTOS, 2012).

According to Baeder (2016), Blumer (2018), and Cavalcante (2011), the ideal anxiolytic should be rapidly absorbed, have a quick onset of action, a high therapeutic index, and should not cause psychomotor impairment. However, not all single drugs possess all these desirable attributes. The complexity of possible negative effects and lack of information may be reasons for the reluctance to accept the use of benzodiazepines. Nonetheless, these medications have few adverse effects and are minimally toxic, especially in short-duration treatments such as those used in dentistry, exemplified by midazolam (CHI, 2018; CHON, 2011).

Oral sedation has advantages and disadvantages that need to be considered when compared to other techniques such as inhalation sedation. Chi (2018) and Chon (2011) highlight the advantages of oral sedation, including its convenience of administration via oral intake, which is easier and less invasive than the administration of inhalation gases. This can be particularly useful for patients who fear needles or masks; its ability to reduce anxiety, as it can help alleviate anxiety and fear associated with dental procedures, providing a state of relaxation and comfort; its prolonged effect: depending on the dosage and type of medication used, oral sedation can have a longer-lasting effect compared to inhalation sedation, which can be beneficial for longer procedures; and also its less invasive monitoring, as compared to inhalation sedation, oral sedation may require less constant monitoring of vital signs, as the medications are administered orally and do not directly affect the respiratory tract.

Authors such as Sivaramakrishna (2017) and Malamed (2013) highlight several disadvantages of oral sedation, including variability in absorption. This method can lead to individual

differences due to factors such as metabolism and gastric content, making the effects of sedation less predictable compared to inhalation sedation. Another characteristic is the delayed onset of effect, as oral sedation generally takes longer to produce effects compared to inhalation sedation, which has a quicker onset. Patient cooperation is also necessary, as some individuals may have difficulty swallowing pills or liquids, which can hinder the effective administration of oral sedation.

It is important to emphasize that the choice between oral sedation and inhalation sedation will depend on the individual needs of the patient, the type of procedure to be performed, and the healthcare professional's assessment. Both techniques have their own merits and challenges, and the decision should be based on a comprehensive evaluation of the risks and benefits for the patient.

Despite the increased focus on educational and preventive measures in dentistry, the dissemination of new techniques remains a challenge, which may explain the reluctance towards new protocols. It is observed that more informed patients, who regularly visit the dental office and are treated by professionals who conduct anamnesis and monitor vital signs, tend to have better acceptance of sedation procedures. Basic Life Support training is a vital component of dental practice, especially when performing oral sedation. Basic Life Support (BLS) training enables the dentist to be prepared to handle emergencies, protecting patient life and well-being, fulfilling ethical and legal responsibilities, and ensuring the quality and safety of the care provided (GALLAGHER, 2016; GENTZ, 2017).

The American Society of Anesthesiologists (ASA) recommends that the practice of monitoring patients with pulse oximetry during oral sedation is of utmost importance to ensure patient safety and to detect any systemic changes that may occur during the procedure. Pulse oximetry is a non-invasive and highly effective method for measuring blood oxygen saturation, which provides vital information about the patient's respiratory health. The significance of this practice can be highlighted by the following points: early detection of hypoxemia: pulse oximetry allows for continuous monitoring of blood oxygen saturation. This is crucial during oral sedation as any changes in respiratory function can lead to hypoxemia (low blood oxygen levels). Early detection of hypoxemia enables immediate intervention to correct the issue before it becomes severe. For identifying respiratory problems, pulse oximetry helps quickly detect any respiratory compromise, allowing for adjustments in sedation as necessary. Additionally, it prevents severe complications such as brain damage, organ failure, and even death, and provides peace of mind for both the healthcare professional and the patient. Finally, it meets safety standards, as regulatory bodies and health associations recommend or require the monitoring of oxygen saturation during sedation procedures. The use of pulse oximetry demonstrates the professional's commitment to the highest standards of patient safety and care (MALAMED, 2013; BLUMER, 2018).



Drug interactions between oral sedatives and other daily or regular medications of patients can have significant implications for the safety and efficacy of treatment (GALLAGHER, 2016). It is crucial to consider these interactions when prescribing or administering oral sedatives. Some of the primary drug interactions that may occur include:

Alcohol: Concurrent use of alcohol with oral sedatives, such as benzodiazepines, can enhance the central nervous system depressant effects, leading to profound sedation, reduced reflexes, and an increased risk of respiratory depression. This combination can be hazardous and should be avoided.

Other central nervous system depressants: Medications such as opioids, barbiturates, and other tranquilizers can potentiate the sedative effects of oral sedatives, increasing the risk of excessive drowsiness, respiratory depression, and unwanted side effects.

Antihistamines: When combined with oral sedatives, antihistamines can elevate the risks of excessive sedation and diminished cognitive function.

Antihypertensive medications: Interaction between oral sedatives and antihypertensive drugs may cause a reduction in blood pressure. When used in conjunction with antihypertensives, the risk of severe hypotension may increase.

Anticonvulsants: Patients using anticonvulsant medications may experience interference with the desired effects of oral sedatives, potentially diminishing their effectiveness (FIORILLO, 2019; GENTZ, 2016).

It is essential for dentists and other healthcare professionals to conduct a thorough review of the patient's medication list before prescribing oral sedatives. Open communication between the patient and the healthcare professional is vital for identifying and managing potential drug interactions. In cases of doubt or concern, it is advisable to consult a pharmacist or physician for specific guidance on potential drug interactions.

FINAL CONSIDERATIONS

Oral sedation is an approach that provides increased comfort during dental procedures, particularly for children and patients with special needs. There are various medications available on the market with sedative properties, each with its own clinical advantages and disadvantages. Research on oral sedation has the potential to expand the use of different techniques among a broader range of professionals. Therefore, understanding the various methods available to reduce anxiety related to dental treatments is crucial for alleviating the fear associated with procedures, improving behavior management, and promoting patient well-being. Given that conscious sedation is an excellent alternative for managing anxiety and fear during dental treatment, the appropriate use of benzodiazepines and nitrous oxide can create a more tranquil and comfortable environment for patients.



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