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LOCAL ANESTHETIC-INDUCED ALLERGIC REACTIONS IN DENTISTRY: CURRENT PERSPECTIVES AND KEY CONSIDERATIONS

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Abstract

Background: Local anesthetics (LAs) are frequently utilized in dentistry. Despite their generally well-tolerated nature, they can occasionally induce adverse reactions of varying types and severity. The actual prevalence of allergic reactions to these agents remains unknown. The review objectives were to evaluate the occurrence of immediate adverse events in individuals undergoing local anaesthetic injections for dental procedures, observe the frequency of anaphylactic allergic reactions among documented adverse events, and scrutinize the relationship between the atopic history of these patients and documented allergic reactions.

Materials and Methods: A thorough literature review was undertaken, examining articles discussing the utilization of local anesthetics during dental treatments in healthy patients, regardless of age. All potential reactions that could manifest during treatment following the anaesthetic administration were considered.

Results: Fourteen articles were chosen, revealing reactions not ascribable to allergic causes. The majority were mild, swiftly reversible psychogenic or vasovagal reactions. One instance was associated with deficiencies in the anesthetic technique. In two other cases, allergic causation was dismissed following skin and dosed provocative challenge tests with the anaesthetic.

Conclusion: Allergic reactions to local anesthetics are infrequent. The majority of adverse reactions tend to be psychogenic or vasovagal. Physicians and dentists must be aware of these findings to alleviate common fears and dispel myths surrounding using local anesthetics in dental practices.

Key-words: *local anesthesia; dentistry; allergic reactions; pharmacology*

Introduction

Allergic reactions in dentistry have become relevant, requiring a more in-depth analysis of the contemporary landscape and critical issues associated with using local anesthetics.[1] As patient safety remains a priority, understanding the evolving nature of allergic responses in dental procedures is crucial.

In the ever-evolving field of dentistry, the incidence of allergic reactions to various components of dental materials, including local anesthetics, has garnered increased attention. With a growing awareness of allergic sensitivities in the population, dental professionals are challenged to stay informed about the latest developments to provide optimal care.[2,3]

The timeliness of allergic reactions in dentistry lies in the increasing prevalence of allergies and the wide range of dental materials used in clinical practice. Levy ML et al.[4] discuss the Global Initiative for Asthma's perspective on transitioning to environmentally friendly respiratory inhalers, emphasizing the need for global access and ensuring patient safety. Yanagi T et al.[5] explore the association between zinc dental fillings and palmoplantar pustulosis, suggesting a potential link that warrants further investigation. Local anesthetics, essential in pain management during dental procedures, are not immune to triggering hypersensitivity reactions. To ensure patient safety and well-being, dental professionals must recognize the signs, symptoms, and risk factors associated with such reactions.[6]

Several critical issues surround local anesthetics, demanding a comprehensive understanding and proactive management.[7]

Delving into the intricate composition of local anesthetics is essential. Components such as preservatives, stabilizers, and vasoconstrictors can elicit allergic responses. Dental practitioners must be aware of these elements and their implications for patient safety. Recognition of the ability to recognize allergic symptoms promptly is paramount. From mild manifestations like itching and erythema to severe anaphylactic reactions, dentists should be proficient in identifying these signs, allowing for swift intervention and appropriate medical care.[8] Patient Assessment and Thorough patient assessment, including a comprehensive medical history, is indispensable in identifying individuals predisposed to allergic reactions. Effective communication with patients about potential risks and alternatives to specific local anesthetics is crucial for informed decision-making.[9] Considering alternative local anaesthetics or exploring anaesthesia-free approaches becomes crucial in managing patients with known sensitivities. Dental professionals should be proficient in adopting alternative strategies to ensure optimal pain control without compromising safety.[10]

Local anesthetics (LAs) are frequently employed in dentistry to facilitate dental procedures and ensure the comfort of patients undergoing painful techniques.[11] While generally well-tolerated, LAs can trigger adverse reactions of various types and severity. These reactions may stem directly from LAs (such as allergic/idiosyncratic reactions), their dosages (resulting in toxic reactions or overdoses), or psychogenic/vasovagal factors, such as fear and

anxiety related to the anesthetic/dental procedure.[12]

Other substances associated with LAs, including antioxidants, preservatives, and norepinephrine, can also induce adverse reactions or even allergic responses.[13]

The true incidence of allergic reactions to LAs is not precisely known. In some articles, these reactions are considered rare, with an incidence of less than 1% of all adverse reactions to LAs. However, any adverse reaction occurring after an anesthetic procedure, during medical or dental treatments, is often initially attributed to an "allergic cause."[13]

This can cause concern and anxiety for the patient, dentist, and physician. Consequently, individuals with other adverse reactions are mistakenly diagnosed as allergic, leading to complications in future therapeutic management. In some cases, treatments requiring LA injections may be delayed, and surgical procedures may be performed without anesthesia, or conversely, patients may undergo general anesthesia with its associated risks.[12–14]

Numerous articles in the literature report allergic reactions to LAs, often linked to isolated cases or groups of subjects with previous adverse reactions. Currently, no published prospective studies assess the incidence of allergic or adverse reactions to LAs in dentistry. For this reason, a multidisciplinary group comprising dentists and allergists decided to conduct a study to investigate and clarify these issues.[11–14]

The objectives of this study were estimate the immediate incidence of adverse events in subjects who received an LA injection during dental therapy, evaluate the incidence of immediate allergic reactions among adverse events and analyze the correlation between allergic reactions and previous atopic antecedents.[14]

Materials and methods

This review conforms to the guidelines outlined in the Preferred Reporting Items for Systematic Review (PRISMA), as depicted in Figure 1.

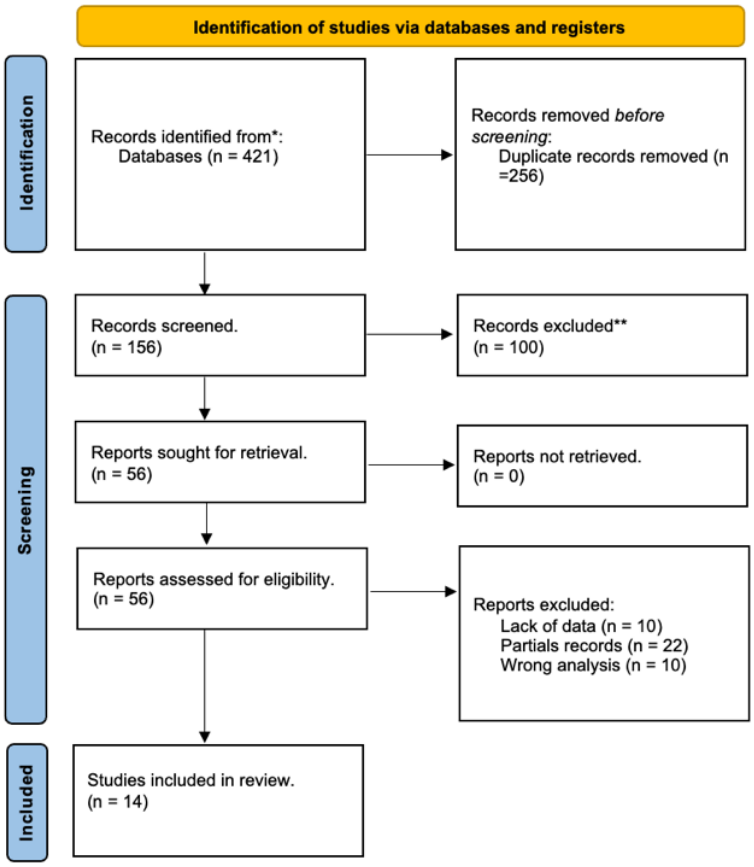

Figure 1. *Search strategy flow chart*

The primary research inquiry was formulated using the PICO (Population, Intervention, Comparison, Outcomes) structure. In conducting this systematic review, an effort was made to investigate the question: "Does the utilization of local anesthetics carry the potential risk of anaphylaxis in individuals undergoing dental procedures?" All studies that met the subsequent inclusion criteria were taken into consideration: (I) Written in English, (II) Published between 2000 and June 2022, (III) Studies examining the correlation between allergic reactions and local anesthetics, (IV) Studies involving adults aged 18 and above, (V) Epidemiological studies focusing on adults, (VI) Randomized studies involving adults.

2.1 Search strategy and exclusion criteria

Two reviewers independently conducted a literature search using search engines like Pubmed, EMBASE, and Web of Science, employing keywords such as ('allergic reactions' and 'local anesthesia') or ('lidocaine' and 'anaphylaxis'). The exclusion criteria comprised the presence of additional pathologies in adult patient samples, animal studies, in vitro studies, studies not in English, systematic reviews with meta-analysis, letters, dissertations, and abstracts (Table 1).

Table 1. Search strategy with Mesh Term

PubMed
anaphylaxis AND local anesthesia ("allergic reactions"[MeSH Terms] OR ("allergic reactions"[All Fields] AND "local anesthesia"[All Fields]) OR "anaphylaxis"[All Fields]) AND ("local anesteshia"[All Fields] OR "anaphylaxis"[MeSH Terms] OR ("allergic reactions"[All Fields] AND "local anesthesia"[All Fields]) OR " dentistry"[All Fields])
Web of Science
(allergic reactions) AND (lidocaine) (ALL FIELDS)
Scopus
(local anesthesia) AND (allergic reactions) TITLE ABS KEY

2.2 Selection criteria and Data extraction

Figure 1 illustrates the complete process of article selection and search strategy. The investigation resulted in 421 articles. Initially, two authors independently evaluated the identified studies to ensure they met the inclusion and exclusion criteria. Following that, the full texts of these articles underwent examination. Most of these studies were excluded as they did not investigate the connections between local anesthetics employed in dentistry and allergic reactions. After eliminating duplicate records and those needing to meet the inclusion criteria, 14 publications were ultimately chosen.

Results

In the analysis of various studies included in the aforementioned review, a total of 2100 patients were assessed. The average age was 25.4 years, with a majority of females comprising 70% (n = 1470) and males 30% (n = 1260). The local anesthetics utilized in the chosen studies encompassed four types: mepivacaine, lidocaine, articaine, and procaine, all currently used in our country.[14,15] Only 5% of the population exhibited allergic conditions such as asthma, rhinitis, or insect sting anaphylaxis, and 1.4% (n = 13) reported adverse events following the administration of local anesthesia during dental procedures.[1,2,16,17] Among the study sample, 15 adverse reactions were identified, representing 0.5% of the total.[18] Of these reactions, 78% occurred in females (n = 15) and 22% in males (n = 5). 14 of the 15 patients with adverse reactions had previously undergone local anesthesia, and 12.7% experienced a similar adverse reaction on a previous occasion. A

topical anaesthetic was applied in four instances out of 15 before the local anesthesia injection.[19] Additionally, 78% (n = 17) of the population used vasoconstrictors with the administered local anesthesia. The infiltrative technique was employed in 50% of cases, regional anesthesia in 17% of patients (n = 5), and 22% (n = 6) received both infiltrative and regional anesthesia.[20]

Despite mepivacaine being the most frequently used local anesthetic and exhibiting the highest number of adverse reactions, the percentage of reactions did not surpass those associated with other types of anesthetics.[16,21]

The majority of adverse reactions were characterized as mild, rapid, and spontaneous, not requiring medication. Psychogenic or neurovegetative reactions were promptly reversed within 30 minutes after the administration of anesthesia (Table 2). One patient experienced inflammation, itching, and a tingling sensation on the facial area innervated by the lower dental nerve, where the dentist applied regional infiltration of local anesthesia (mepivacaine).[17] These symptoms were linked to complications arising from the local anesthetic technique. [10]In another case, eyelid edema occurred 8 hours after the injection of local anesthesia (articaine) without additional clinical manifestations. Similarly, another case presented eyelid edema 5 hours after the injection of local anesthesia (procaine) without associated clinical symptoms.[22] Clinical and skin tests, along with the provocative dose challenge test using local anesthesia, indicated an absence of allergic mechanisms, and subsequent administration by the dentist was well tolerated. In a separate case involving a 28-year-old patient, eyelid and periocular edema, urticaria, itching on the abdominal surface, and cough were observed.[22,23] These symptoms manifested 4 hours after the injection of 2% lidocaine associated with vasoconstrictors using the infiltrative technique. The patient was treated with antihistamines and corticosteroids, resulting in improvement within 12 hours. Subsequently, the patient was referred to an allergist for further examination.[2,24–26]

According to the patient's clinical history, no medications were taken prior to the anesthetic procedure. The dentist utilized latex gloves, cleaned the area with acid, and employed methacrylate resins during the treatment.[20,27]

Discussion

There are two categories of local anesthetics distinguished by their varying chemical properties and sensitization potential.[27] The first group comprises esters of benzoic acid, such as benzocaine, chloroprocaine, cocaine, piperocaine, procaine, propoxycaine, and tetracaine. Para-aminobenzoic acid, a metabolite of these compounds, can induce hypersensitivity. These anesthetics exhibit cross-reactivity due to their chemical similarity to other antigenic compounds. [28]The majority allergic reactions documented in recent literature, particularly those related to procaine, are attributed to this group. The second category consists of amides, namely lidocaine, mepivacaine, articaine, bupivacaine, and prilocaine. These exhibit low sensitization potential and do not cross-react with each other, making them the most widely used today.[29,30]

Our study involved a significant number of individuals requiring local anesthetic injections, with a very low incidence of adverse reactions (0.5%).[31,32] Importantly, none of these reactions stemmed from allergic mechanisms. These findings align with the perspective of other researchers who consider allergy a rare complication of local anesthetics. Dentists and physicians frequently encounter such scenarios.[33] Some cases lack an explanation for their etiology, while others can be linked to adverse reactions from prescribed drugs for dental issues (antibiotics, non-steroidal anti-inflammatory drugs) or substances used by the dentist during treatment procedures (latex, resins, etc.).[34]

his evaluation relied on the analysis of eight Randomized Controlled Trials (RCTs) investigating the incidence of adverse reactions in pediatric dentistry when using articaine and lidocaine. The findings indicate that articaine demonstrates comparable safety in children, with no significant differences in postoperative pain, soft tissue injury, or edema compared to lidocaine. While there is no dedicated review on adverse reactions between these drugs in dental practice, subgroups analysis from some literature in the meta-analysis aligns with our study's results, indicating a consistent lack of difference in adverse reaction rates between the two local anesthetics.[35–37]

It's crucial to note that a narrative review covering various adverse events related to local anesthesia suggests the need for more clinical trials to enhance

the reliability of this review's outcomes. Additionally, two studies included age groups below 4 years, contrary to the manufacturer's recommendation not to use articaine in children under 4 years. Despite this, many dentists already use articaine in children under 4 years, supported by positive safety and efficacy results from previous studies. However, more clinical trials are warranted to strengthen these conclusions.[38–41]

The study emphasizes that different methods influence the efficacy of anesthesia. Mandibular molars often require Inferior Alveolar Nerve Block (IANB), associated with complications, while local infiltration anesthesia is commonly used in the maxilla and anterior mandible. The study results suggest that articaine and lidocaine have similar safety profiles, but the choice between them may depend on the specific anesthesia technique employed.[39,40]

Concerning anesthetic concentrations, articaine is commonly used in 2% and 4% concentrations. Limited studies compare these concentrations, with one indicating that concentration mainly affects the duration of anesthesia, showing no significant differences in other aspects.[41]

Several limitations should be considered, including a relatively small sample size, insufficient data for subgroup analysis, variations in the injection approaches of the two anesthetic drugs, and the reliance on patient or parent-reported, rather than clinically verified, adverse reactions.[40,41] These factors may impact the review's robustness, highlighting the need for more extensive research and multifactorial analyses to validate the conclusions, especially regarding potential confounding factors associated with anesthetic safety.[42]

Several manuscripts have been conducted about allergies and dentistry over the years. Fuchs et al.[43] explored ChatGPT's utility in dentistry and immunology, finding version advancements improved accuracy, with priming boosting early model performances. Priming's effectiveness varied by field, underscoring LLMs' dependency on training data. Caution is advised in healthcare applications due to inherent limitations. Tanwar et al. [44] discussed a rare case of titanium allergy post-dental implant, underscoring the biocompatible metal's potential for adverse reactions. The study emphasizes the need for awareness and diagnostic readiness for such allergies in implant dentistry.

Henderson et al. [45] delved into the rarity of local anaesthetic allergies in dentistry, highlighting the importance of distinguishing true allergies from other causes of similar symptoms for proper management. Mohr [46] addressed latex allergy's relevance in dentistry, highlighting its potential for serious reactions and the importance of awareness and preventive measures among dental professionals. Baluga et al.[47] evaluated the incidence of adverse reactions to local anesthetics in dentistry, revealing a very low occurrence of true allergic reactions and highlighting the predominance of psychogenic or vasovagal reactions. Chin et al. [48] reported a serious latex allergy reaction in a dental patient, emphasizing vigilance and appropriate management to prevent severe allergic responses in the dental setting. Suzuki et al. [49] presented a method using an x-ray fluorescence spectroscope for detecting allergen metals in dental restorations, advocating allergen elimination as an effective treatment for metal allergies in dentistry. Munksgaard et al. [50] contrasted toxicological concerns with allergy risks in restorative dentistry, noting low side-effect frequency among patients and occasional allergic reactions among dental staff. Vozza et al. [51] conducted a clinical study on latex allergy and desensitization in dentistry, suggesting percutaneous desensitization as an effective, safe treatment for latex-allergic patients, requiring further validation.

For certain individuals, dental treatment is a major source of stress.[32,52] Throughout the process, patients confront situations causing distress or fear, including the use of aggressive instruments (needles, forceps), painful procedures in sensitized areas, disruptive auditory stimuli (turbines, motors), unpleasant-tasting or odorous substances, and the need to maintain uncomfortable positions for extended periods.[53–56] The dental condition prompting the visit, the dentist's procedural techniques and the psychological susceptibility of some patients can trigger psychogenic or vasovagal reactions during treatment.[5,57–59] Symptoms such as anxiety, deep breaths, pallor, sweating, nausea, chills, confusion, and loss of consciousness may manifest in such situations.[55,56] Placing the patient in a supine or Trendelenburg position can lead to improvement within a few minutes. [16,17,21] A significant proportion (88%) of adverse reactions in our study were attributed to these psychological factors. Four patients

with similar reactions during previous dental treatments exhibited signs of psychological vulnerability.[60,61] Our results are consistent with other authors who assert that psychological reactions are the most common adverse effects following local anesthesia injections.[2,24–26,62]

Conclusion

This study results, as well as other investigators' opinions, orient us to the idea that allergic reactions to LAs are very rare and that most of the adverse events have a psychogenic cause. The physician and the dentist should know these facts, should be able to reassure their patients and prepare them to minimize the frequent fears that are built around the LA use.

Declarations

Authors' contributions:

Conceptualization AR, AMP, CA; methodology AR, CA; software, AMP, V.R., AP; validation, CA; writing—original draft preparation, CA, V.R., AR, AMP; writing—review and editing, LF, AH and AR; visualization, CDA, AH and RDA; supervision, GC and CA; project administration, CA; All authors have read and agreed to the published version of the manuscript.

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

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