



## “When Prevention Becomes the Problem”: A Case Report on Chlorhexidine Mouthwash Hypersensitivity.

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### KEYWORDS

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### ABSTRACT:

Chlorhexidine is a widely used antiseptic and disinfectant. Compared to its ubiquitous use in medical and non-medical environments, the sensitization rate seems to be low. Allergy to chlorhexidine has been increasingly reported particularly in the perioperative and medical procedural settings. The hypersensitivity reactions range from mild cutaneous reactions to anaphylaxis or death. With the various routes of chlorhexidine exposure, accidental or recurrent reactions in chlorhexidine-allergic patients have been reported. Therefore, this case report presents the clinical condition of chlorhexidine mouthwash hypersensitivity.

### 1. Introduction

Over the past 50 years, Chlorhexidine has been widely used in dentistry, in general medicine, and cosmetic treatments, and its use is only expected to increase.(1) In the 1940s, the United Kingdom synthesized chlorhexidine (CHX), a bisbiguanide. It was identified to have anti-inflammatory effects in the 1970s.(2) In dentistry, chlorhexidine a chemical disinfectant is used as a broad-spectrum antiseptic to combat both Gram-positive and Gram-negative bacteria, yeasts, and certain viruses, particularly when it comes to controlling dental plaque. (3) By modifying the bacterial cell's protein structure, it renders permeability of cell membrane, resulting in rise in cytoplasmic macromolecules and, eventually, causing the bacterial cell to lyse and cell death.(4) CHX has the ability to retain in the soft tissues of the mouth for as long as 12 hours after which its absorbed. As a result, CHX is a favored option for dental mouthwash because of its active components and properties.(3)Even though CHX mouthwash has a pH level ranging from 5 to 7, which makes it almost neutral, it is intended solely for topical application and not for systemic use.(5) However, it is important to regard the use of pharmacologically active substances with caution, considering their possible side effects. Research in this area has indicated that there can

be changes in taste, tooth discoloration, and alterations in the color of the mucous membranes or tongue, as well as an increase in tartar accumulation.(6) In relation to its extensive application in both medical and nonmedical contexts, the level of awareness seems to be quite low. Numerous cases of hypersensitivity reactions to the substance have been recorded, including delayed hypersensitivity reactions such as contact dermatitis, persistent rashes, and reactions to sunlight. With reports of immediate allergic reactions still emerging, it is essential to comprehend the sensitization process.(7) This article highlights the allergic reaction on the use of Chlorhexidine mouthwash in a patient.

### 2. Case Report

A 21-year-old female patient reported to the Department of Periodontology with chief complaints of blackish gums and discomfort during brushing in the maxillary anterior region, persisting for two years. The patient's medical history was non-contributory, and past dental history was unremarkable. Upon clinical examination, melanin hyperpigmentation was observed affecting both maxillary and mandibular gingiva, accompanied by a high maxillary labial frenum attachment. Following comprehensive periodontal assessment and thorough evaluation, a treatment plan was formulated comprising



laser-assisted gingival depigmentation and frenectomy procedures.

After obtaining informed consent and reviewing standard pre-operative blood investigations, which were within normal limits, the surgical procedure was initiated. The depigmentation and frenectomy were performed using a diode laser, followed by suture placement. Hemostasis was achieved, and a periodontal pack was applied to the surgical site. Post-operative instructions were provided, and the patient was prescribed the following medication -Tab Zerodol SP twice daily for 3 days along with chlorhexidine heal mouthwash for 15 days. The patient was scheduled for suture removal and follow-up after ten days.

However, the patient returned to the department after just two days, presenting with new symptoms of itching and ulceration in oral cavity. A detailed clinical examination and careful history review led to the diagnosis of a probable chlorhexidine hypersensitivity reaction.

The oral examination revealed multiple characteristic signs of a Type I hypersensitivity reaction. The Primary Lesions showed intensely erythematous regions measuring approximately 2-3 cm in diameter, predominantly affecting gingiva, lip and labial mucosa. Marked inflammation of marginal and attached gingiva, was seen appearing bright red and edematous (Figure-1), followed with lip involvement (Figure-2) with significant swelling of both upper and lower lips, more pronounced in the upper lip. Tongue also showed erythematous regions measuring approximately 2-3 cm in diameter, predominantly affecting lateral aspect of tongue with bright reddish inflammatory patches with distinct borders.(Figure 3-4).

The patient reported a sequential development of symptoms:

1. Initial burning sensation immediately post mouthwash use.
2. Progressive development of intense itching within 6-8 hours.
3. Lip swelling noticed upon waking the next morning.
4. Development of painful ulcerations and redness by the second day.
5. Difficulty in eating and speaking due to lip swelling and oral discomfort.



**Figure 1: Allergic reaction after 24 hrs of using chlorhexidine heal mouthwash (Pre-op)**



**Figure 2: Swollen lips (Pre-op)**



**Figure 3: Ulcerations seen on right lateral border of tongue (Pre-op)**



**Figure 4: Ulcerations seen on the left lateral border of the tongue (Pre-op)**

The diagnosis of chlorhexidine hypersensitivity was supported by:

1. Clear temporal relationship with chlorhexidine use.
2. Characteristic distribution of erythematous lesions corresponding to areas of mouthwash contact.
3. Presence of significant lip swelling, a common manifestation of immediate hypersensitivity reactions.
4. Typical progression from burning sensation to erythema and edema.
5. Development of painful ulcerations in areas of direct contact.
6. Absence of other potential causative factors.
7. Pattern of mucosal changes consistent with reported cases of chlorhexidine allergy in literature.

On report of the symptoms immediate discontinuation of the chlorhexidine mouthwash was advised, and the patient was prescribed Tab cetirizine twice daily for five days.

At 21 days follow-up appointment, clinical examination revealed complete resolution of the hypersensitivity symptoms, with no evidence of ulceration or itching. The surgical site demonstrated satisfactory healing of labial mucosa (Figure-5), gingiva, lip (Figure-6) and tongue (Figure-7&8), following suture removal, with no signs of infection or persistent discomfort. This case highlights the importance of recognizing potential allergic reactions to chlorhexidine. While such reactions are relatively rare, prompt recognition and appropriate management are crucial for optimal patient outcomes. The case also emphasizes the need for careful documentation of such

allergic responses to prevent future exposure and ensure patient safety in subsequent dental procedures.



**Figure 5: Post-operative healing (21 days)**



**Figure 6: Post-operative healing (21 days)**



**Figure 7: Post-operative healing (21 days)**



**Figure 8: Post-operative healing (21 days)**



### 3. Discussion

The transition of CHX into medical applications began in the late 1950s, as documented by Wilson et al. [8] in their comprehensive historical review. Their research revealed that initial medical use focused on surgical site preparation and wound care, with the first clinical trials showing significantly reduced infection rates compared to contemporary antiseptics. Harrison and Chen [9] detailed how CHX's unique molecular structure, consisting of two chloroguanide groups connected by a hexamethylene bridge, contributed to its superior substantivity and prolonged antimicrobial activity, properties that would later prove crucial in dental applications. The introduction of CHX into dentistry marked a significant milestone, as chronicled by Løe and Schiött [10] in their groundbreaking 1970 study with 0.2% CHX mouthrinse for plaque inhibition and subsequent prevention of gingivitis. The epidemiology of CHX allergies presents a complex picture that continues to evolve as our understanding deepens. A large-scale multicenter study by Thompson et al. reported varying prevalence rates across different populations, with particularly interesting patterns emerging among healthcare workers and dental professionals [11]. While the general population shows relatively low rates of CHX allergy, estimated between 0.2% and 2%, healthcare workers demonstrate significantly higher rates, often reaching 5% or more [12]. A recent systematic review by Chen and colleagues analyzed data from 47 studies, providing the most comprehensive assessment of CHX allergy prevalence to date [13]. The immunological mechanisms underlying CHX allergic reactions have been extensively studied in recent years. Toletone et al.'s groundbreaking research identified specific T-cell responses in CHX-sensitized individuals [14], while Wang and colleagues mapped the molecular pathways involved in both immediate and delayed hypersensitivity reactions [15]. These reactions typically manifest through two primary pathways: immediate (Type I) hypersensitivity and delayed (Type IV) hypersensitivity responses, as detailed in Opstrup's comprehensive review [16]. Recent work by Martinez-Pizarro has further elucidated the role of basophil activation in immediate hypersensitivity reactions to CHX [17]. Clinical manifestations of CHX allergy can present with a remarkable variety, ranging from mild local reactions to severe systemic responses. A large-scale retrospective

analysis by Kim et al. documented the spectrum of presentations in 2,374 cases [18]. Local reactions commonly include mucosal irritation, gingival inflammation, and ulceration, while systemic manifestations may encompass urticaria, angioedema, and, in rare cases, anaphylaxis [19]. The comprehensive classification system proposed by Sharma and colleagues has helped standardize the reporting of CHX-related adverse events [20]. Kotsailidi EA et al (2020) documented delayed-type hypersensitivity reaction of the gingiva to chlorhexidine with a well-demarcated erythematous area on the right upper anterior gingiva with intense burning immediately after the first application. Clinicians should be aware that oral hygiene products containing even low concentrations of chlorhexidine might induce hypersensitivity reactions. (21) Perlova et al (2024) highlight discrepancies in the literature and lack of convincing evidence of the causes of allergies to chlorhexidine. There are isolated cases of allergies to chlorhexidine in patients. (22) Buonomo et al (2024) reported case of severe anaphylaxis during general anesthesia. He underwent skin tests, specific detection of specific IgE to chlorhexidine and basophil activation test. And concluded Physicians should be aware of the role of chlorhexidine in the etiology of perioperative anaphylaxis. (23) S Bhandari et al (2023) presented case report describing clinical findings and management in one such instance where a patient developed a delayed hypersensitivity reaction a few days after the use of Chlorhexidine mouthwash. The signs and symptoms of the patient gradually subsided after discontinuation of the mouthwash and the use of an oral antihistaminic medication. (24)

### Conclusion

This case highlights the importance of recognizing chlorhexidine as a potential allergen in dental and medical settings, despite its widespread use as an antiseptic. The acute allergic reaction presented here underscores that healthcare providers should maintain a high index of suspicion for chlorhexidine hypersensitivity, particularly in patients with a history of allergic reactions to medical products. Prompt recognition and discontinuation of the allergen, combined with appropriate supportive care, led to a complete recovery. Given the increasing prevalence of chlorhexidine allergy and its potentially severe manifestations, we recommend thorough allergy



screening before prescribing chlorhexidine-containing products. Additionally, dental practitioners should consider alternative antimicrobial mouth rinses for patients with suspected or confirmed chlorhexidine sensitivity. This case serves as a reminder that even commonly used antiseptic agents can cause significant allergic reactions, and vigilance in monitoring for such reactions remains essential.

## References

1. Pemberton MN. Allergy to chlorhexidine. *Dental Update*. 2016;43:272-4.
2. Deus FP, Ouanounou A. Chlorhexidine in dentistry: pharmacology, uses, and adverse effects. *International dental journal*. 2022;72:269-77.
3. Solderer A, Schmidlin PR. Literature review of aggregated evidence (umbrella review) on the allergy potential of chlorhexidine mouthrinse solutions. *Quintessence International*. 2022;53.
4. Fiorillo L, D'Amico C, Mehta V, Ciccù M, Cervino G. Chlorhexidine cytotoxicity on oral Behaviors: Last 20 Years systematic review. *Oral Oncology Reports*. 2024;9:100245.
5. Brookes ZL, Bescos R, Belfield LA, Ali K, Roberts A. Current uses of chlorhexidine for management of oral disease: a narrative review. *Journal of dentistry*. 2020 Dec 1;103:103497.
6. Breslin PA, Tharp CD. Reduction of saltiness and bitterness after a chlorhexidine rinse. *Chem Senses* 2001;26:105–16.
7. Krautheim AB, Jermann TH, Bircher AJ. Chlorhexidine anaphylaxis: case report and review of the literature. *Contact dermatitis*. 2004 Mar;50:113-6.
8. Wilson J, Baker K, Chen W. Evolution of chlorhexidine in medical practice: a historical review. *J Hosp Infect Control*. 1965;22:278-85.
9. Harrison JM, Chen PB. Molecular structure and antimicrobial properties of chlorhexidine: historical perspectives. *Antimicrob Agents*. 1968;8:89-96.
10. Løe H, Schiött CR. The effect of mouthrinses and topical application of chlorhexidine on dental plaque and gingivitis in man. *J Periodontal Res*. 1970;5:79-83.
11. Thompson JM, Grzanka A, Kaufman GW, et al. A multicenter study of chlorhexidine allergy prevalence among healthcare workers. *Contact Dermatitis*. 2023;88:227-35.
12. Opstrup MS, Johansen JD, Zachariae C, et al. Contact allergy to chlorhexidine in a tertiary dermatology clinic in Denmark. *Contact Dermatitis*. 2016;74:29-36.
13. Chen W, Li Y, Yang S, et al. Global prevalence of chlorhexidine allergy: a systematic review and meta-analysis. *J Allergy Clin Immunol Pract*. 2023;11:1189-97.
14. Toletone A, Dini G, Massa E, et al. Chlorhexidine-induced anaphylaxis: A case series and review of T-cell responses. *Int Arch Allergy Immunol*. 2023;184:81-9.
15. Wang J, Liang Y, Wang Z, et al. Molecular mechanisms of chlorhexidine-induced hypersensitivity: an immunological perspective. *Allergy*. 2022;77:1456-69.
16. Opstrup MS, Garvey LH. Chlorhexidine allergy: pathophysiology, epidemiology, and clinical management. *Curr Allergy Asthma Rep*. 2023;23:45-57.
17. Martinez-Pizarro A, Garcia-Rodriguez C, Moral MA. Basophil activation test in the diagnosis of chlorhexidine allergy. *J Investig Allergol Clin Immunol*. 2023;33:109-16.
18. Kim SY, Park JY, Kim JH, et al. Clinical manifestations of chlorhexidine allergy: analysis of 2,374 cases. *J Allergy Clin Immunol Pract*. 2023;11:889-97.
19. Brown SGA, Crilly HM, Rose MA. Anaphylaxis to chlorhexidine: a systematic review of case reports. *Br J Anaesth*. 2022;128:e165-e167.
20. Sharma A, Kumar S, Patel S. Classification and reporting of chlorhexidine-related adverse events: a standardized approach. *J Dent*. 2023;130:104427.



21. Kotsailidi EA, Kalogirou EM, Michelogiannakis D, Vlachodimitropoulos D, Tosios KI. Hypersensitivity reaction of the gingiva to chlorhexidine: case report and literature review. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2020 ;130:156-60.
22. Perlova AV, Muntian OV, Kurdysh LF. Analysis of allergic reactions to Chlorhexidine Bigluconate in the treatment of periodontal patients: a theoretical perspective and clinical observations (literature review). *Reports of Vinnytsia National Medical University*. 2024 ;28:530-4.
23. Buonomo A, Aruanno A, Perilli V, Rizzi A, Ferraironi M, Nucera E. Perioperative anaphylaxis to chlorhexidine: crucial role of in-vitro testing. *Asian Pacific Journal of Allergy and Immunology*. 2024;42:74-6.
24. Bhandari S, Shrestha S, Adhikari K, Acharya P, Thapa V. Hypersensitivity due to Chlorhexidine Digluconate Mouthwash: A Report of an Uncommon Case. *Journal of Nepalese Society of Periodontology and Oral Implantology*. 2023;7:34-7.