



Proceedings of Supplement J. IMAB
Publications of papers presented in the Scientific Programme of the
14-th Southeast European Conference Infections and Cancer
Ohrid, North Macedonia
3-6 October 2024

SECTION DENTAL MEDICINE

Proceedings of Supplement J. IMAB
Publications of papers presented in the Scientific Programme of the
14-th South-East European Conference Infections and Cancer
Ohrid, North Macedonia
3-6 October, 2024

**Publications of presented papers in Scientific Programme of Joint Forum:
14-th South-East European Conference Chemotherapy, Infections and Cancer
and
34-th Annual Assembly International Medical Association Bulgaria (IMAB)
3-6 October 2024, Metropol Lake Resort, Ohrid, North Macedonia**

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ALLERGY TO COMMON ANTIBIOTICS AND ITS ALTERNATIVES

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ABSTRACT

An allergy is an adverse hypersensitivity of the immune system. When diagnosed early, most allergies are minor and controllable, but others can be fatal. The majority of severe cutaneous, organ-specific, and possibly deadly off-target immune-mediated drug reactions are caused by antibiotics. The aim is to categorise the prevalent allergic responses to antibiotics. Despite posing a negligible risk to patients, these responses presently constitute a worldwide threat to public health. The greatest risk factor for adverse effects is antibiotic exposure. IgE-mediated allergies cause 10% of drug reactions. Even when an IgE-mediated mechanism is incompatible with the symptoms, "allergy" is routinely used to describe any unpleasant reaction. This article describes allergic responses to popular antibiotics and what to use if you have a real allergy.

Key words: antibiotics, allergy, Penicillins, Cephalosporines, Aminoglycoside, Tetracyclines, Macrolides, Sulfonamides, Glycopeptides, Lincosamides, Fluorquinolones, Nitroimidazols,

INTRODUCTION

An allergy is an adverse hypersensitivity of the immune system. When diagnosed early, most allergies are minor and controllable, but others can be fatal. Most severe cutaneous, organ-specific, and potentially fatal off-target immune-mediated medication responses are antibiotic-related. The greatest risk factor for adverse effects is antibiotic exposure. About 10% of unfavourable antibiotic responses are IgE-mediated allergies (1). Unfortunately, even when an IgE-mediated mechanism is incompatible with the symptoms, "allergy" is often misused to characterise any unpleasant reaction. Drug intolerances are often listed as "allergy" in medical records. Medical documentation may misrepresent medication reexposure risk by casually recording all drug intolerances, including allergy, hypersensitivity, and other adverse drug reactions (ADRs), as "allergy". ADRs caused by IgE, IgG, T-cell, and other immunological factors are called "hypersensitivity." The majority of ADRs are not caused by drug-specific IgE, T-cells, or immunologic processes. True IgE-mediated allergies need sensitisation and systemic exposure (2,3,4).

AIM The aim is to systematize the more common allergic reactions to antibiotics. Although such reactions pose a minor risk to patients, they currently represent a global threat to public health.

MATERIALS AND METHODS

A database search was conducted to find literature regarding antibiotic allergies. Articles were reviewed and additional sources included to the literature review.

RESULTS AND DISCUSSION

I. β -LACTAM ANTIBIOTICS. They include groups: **Penicillins, Cephalosporins, Carbapenems, Monobactam.** They are among the most effective and safest. Allergies prevent many from using them. Use of broad-spectrum antibiotics increases side effects and antimicrobial resistance. Beta-lactamase causes penicillin allergy (5,6).

1. PENICILLINS. Penicillins include **Amoxicillin, Ampicillin, Piperacillin, Benzylpenicillin (PenicillinG)** and **Dicloxacillin.** Combination with beta-lactamase inhibitor: **Amoxicillin/Clavulanate (Augmentin), Ampicillin/Sulbactam, Piperacillin/Tazobactam.** Penicillin and derivatives are first-line surgical preventive and treatment options for bacterial infections such as tooth abscesses, ear infections, gonorrhoea, pneumonia, respiratory tract

infections, rheumatic fever, scarlet fever, skin infections, urinary tract infections caused by susceptible bacteria. Penicillin allergic responses can occur seconds, minutes, hours, days, or weeks after antibiotic use. Anaphylaxis, redness, and hives are common allergies. Patient, allergic to penicillin can safely receive a third- or fourth-generation cephalosporin. In penicillin allergy patients, clinicians avoid beta-lactamase-family drugs despite their low cross-reactivity (7,8). This is problematic since Cephalosporins, and beta-lactamase Penicillins protect against many penicillin-sensitive infections. Clindamycin is the most usual alternative preoperative prophylactic. Vancomycin, Sulfamethoxazole/Trimethoprim, Doxycycline, Clindamycin, Linezolid, Synercid, and Levofloxacin are other choices (9,10,11,12).

2. CEPHALOSPORINES. Significant Cephalosporins include: **Cefazoline** (I generation), **Cefuroxime** (II gen.), **Cefixime** (III gen.), **Ceftriaxone** (III gen.), **Cefepime** (III gen.), **Cefoperazone**, (IV gen.), **Ceftaroline** (Vgen.). Cephalosporins have a similar structure and mode of action to penicillins, but they are more resistant to the bacterial enzymes that degrade them. Cephalosporin antibiotics are widely prescribed for common infections such as skin or soft tissue infections, urinary tract infections, strep throat, ear infections, pneumonia, sinus infections, meningitis, and gonorrhea. They are also used as a first-line preventive measure for a variety of surgical operations. Allergic reactions that may be observed are skin rashes, swelling, itching, urticaria, rarely anaphylactic shock.

II. AMINOGLYCOSIDES. Representatives: **Gentamicin, Amikacin, Tobramycin, Kanamycin, Neomycin and Streptomycin.** These antibiotics are mainly used to treat urogenital infections, bronchopneumonia, skin and eye infections, bone, and joint infections. Allergic responses to aminoglycosides are rare but may manifest as cutaneous reactions or systemic reactions, including anaphylaxis. Among the assessed aminoglycosides, gentamicin had the highest incidence of allergic responses, including the greatest number of anaphylaxis cases, followed by tobramycin and subsequently amikacin. The majority of adverse response reports were observed in individuals with previous exposure to a specific dosage type of aminoglycoside (13). Alternatives are Ciprofloxacin, Doxycycline, Clindamycin, Amoxicillin, Augmentin.

III. TETRACYCLINES. Tetracyclines are: **Doxycycline, Minocycline, Oxytetracycline and Tetracycline.** Tetracyclines are used to treat various bacterial infections affecting the skin, intestines, respiratory tract, urinary tract, genitals, lymph nodes, other systems of the body, severe acne and sexually transmitted diseases (syphilis, gonorrhoea, chlamydia); illnesses obtained from direct contact with infected animals or contaminated food. Tetracycline is contraindicated for children under the age of 8. Administering this medicine during pregnancy may affect dental and skeletal development in the baby or could lead to persistent tooth discolouration in later life. Refrain from nursing when giving tetracycline. Doxycycline is recommended for people with diabetic foot infections resistant to penicillin. An actual allergy to tetracycline is uncommon; nonetheless, allergic reactions may manifest as a rash, skin lesions, and pruritus. Alternatives are Penicillin, Bactrim, Vancomycin, and Ciprofloxacin. (8)

IV. MACROLIDES. Representatives: **Azithromycin, Clarithromycin, Erythromycin, Midecamycin, Roxithromycin, Spiramycin.** Macrolides are primarily utilised for the treatment of upper and lower respiratory tract infections (rhinitis, sinusitis, tonsillitis, laryngitis, pharyngitis, bronchitis, pneumonia), skin infections, otitis, ocular infections, biliary tract infections, peptic ulcer disease, urinary tract infections, dental infections. Although macrolides are a popular antibiotic indicated in medication allergy records, only a few people have been proved to be allergic to them. They can cause mild to severe cutaneous reactions and life-threatening anaphylaxis (14). Macrolides serve as a great alternative to Penicillin in cases of allergy. Alternatives to Macrolides include Cephalalexin, Doxycycline, Clindamycin, Keflex, Metronidazole, Amoxicillin, and Augmentin.

V. SULFONAMIDES. Significant sulfa drugs include **Sulfamethoxazole/Trimethoprim, Sulfadiazine** and **Sulfisoxazole.** Sulfonamide structure is found also in diuretics (Hydrochlorothiazide, Furosemide), sulfonyleureas (Glyburide) and leprosy medicines (Dapsone). Bacteriostatic sulfonamides treat many bacterial diseases due to their broad spectrum of action.

They focus on respiratory (sinusitis, otitis, bronchitis) and urine infections. Rash, nausea, vomiting, and diarrhoea are common side effects of sulfa medicines, not allergic reactions. Rashes, hives, and swelling of the lips and mucous membranes with breathing problems are frequent allergic reactions. Patients may get a potentially extreme anaphylactic response, angioedema, Stevens-Johnson syndrome, vasculitis, serum sickness and drug fever (15). Alternatives include Augmentin for gram-positive coverage in individuals without a history of MRSA (Methicillin-resistant *Staphylococcus aureus*), Clindamycin, Levofloxacin, or Doxycycline for MRSA-infected patients (8).

VI. GLICOPEPTIDES. Significant Glycopeptide antibiotics include **Vancomycin**, **Teicoplanin** and the antitumor antibiotic **Bleomycin**. Glycopeptides are antibiotics used to treat bacterial infections, particularly those caused by gram-positive organisms and enterococcal infections that are resistant to conventional antibiotics. Vancomycin is used if infection when MRSA is suspected. Vancomycin can produce two forms of hypersensitivity reactions: 'red man syndrome'(RMS) and anaphylaxis. RMS is assumed to be an infusion-related adverse response with incidences ranging from 3.7 to 47%. This happens when Vancomycin is quickly injected or given over a short period of time and includes pruritus and an erythematous rash over the face, neck, and upper body (16). Alternative treatments for MRSA in patients with an allergy to Glycopeptides include Bactrim, Doxycycline, Linezolid, Daptomycin, Tigercycline, and Synercid (8).

VII. LINKOSAMIDES. Significant Linkosamids are **Clindamycin** and **Lincomycin**. Lincosamides are utilised as penicillin substitutes in therapy, notably for surgical prophylaxis. Clinicians prefer Clindamycin due to its better oral absorption, bioavailability, and target organism spectrum efficacy (8). Skin infections, dental infections, stomach infections, abscesses, pelvic inflammatory disease, anaerobic infections, gynecological infections, and the treatment of MRSA are the most prevalent conditions for which Lincosamides are applied. Clindamycin-related allergies are uncommon, although they do occur. The most frequent Clindamycin allergy is a delayed maculopapular exanthema; additional allergic responses include anaphylactic shock, Sweet's syndrome, and bullous eruptions. Synercid, Linezolid, Metronidazole, Imipenem, Vancomycin, Bactrim, and Doxycycline are alternatives for treating patients with Clindamycin allergy (8).

VIII. FLUORQUINOLONES. Significant drugs are **Ciprofloxacin**, **Levofloxacin** and **Moxifloxacin**. Ciprofloxacin is one of the most recommended fluoroquinolones for gram-negative coverage, particularly against *Pseudomonas* spp., because to its oral bioavailability (17). Levofloxacin and Moxifloxacin are becoming more popular because of the increase in community-acquired MRSA and pneumonia infections. Fluoroquinolones are used to treat complex or recurring urinary tract infections, pneumonia, and severe diabetic foot infections that affect bone and joints. Ciprofloxacin can have major adverse effects such as tendon difficulties, nerve damage, severe mood or behaviour changes, and low blood sugar. Alternatives: Linezolid, Bactrim, Aztreonam, and Piperacillin-Tazobactam (8).

IX. NITROIMIDAZOLS. Main drugs are: **Metronidazole**, **Tinidazole**, **Secnidazole**. Nitroimidazoles are used for the treatment of anaerobic bacterial, parasite, and protozoal infections, including bacterial vaginosis, gastrointestinal infections, skin infections, meningitis, lower respiratory infections, bacterial infections, diarrhoea, and rosacea, as well as for the prevention of postoperative infections. When used with alcohol, Metronidazole can cause a disulfiram-like response. True allergic reactions to Nitroimidazoles are uncommon. Cross-reactivity may occur between Metronidazole and other imidazoles, including Tinidazole, Clotrimazole, Ketoconazole, Miconazole, and Albendazole, due to structural similarities (8). Clindamycin, linezolid, synercid, cefoxitin, and Cefmetazole serve as alternatives to Nitroimidazols.

CONCLUSION

Considering antibiotics are still among the most often prescribed medications, using them carries a risk of side effects and hypersensitivity. An essential technique for antimicrobial stewardship is the assessment of antibiotic allergies prior to the decision to use antibiotics or other alternatives. When choosing antibiotic substitutes, it is crucial to consider the patient's history of susceptibility or resistance as well as the sensitivity report.

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EVALUATION OF SKELETAL MATURITY USING MANDIBULAR SECOND MOLAR CALCIFICATION STAGES: A DIGITAL X-RAY STUDY

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ABSTRACT

Aim: The purpose of this study was to establish whether the development of second mandibular molar (tooth 37) can be used for assessment of skeletal maturity. **Material and methods:** Total of 388 digital x-rays were evaluated of 69 males and 125 females. Developmental stages of tooth 37 were assessed with Demirjian et al. (1973) method and skeletal age- Cervical vertebrae maturation (CVM) by Baccetti et al. **Results:** For both genders correlation was found between the mineralisation stages of tooth 37 and the skeletal age. For females ($r = 0,609$ $P = 0,000$); for males ($r = 0,407$; $P = 0,000$). For boys in CVM II 100 % of the studied teeth 37 were immature with prevalence of stage G ($\chi^2 = 14,579$; $P < 0,001$). In stage CVM III the mineralization dominant stage continued to be G ($\chi^2 = 22,00$; $P < 0,0001$). In stage CVM IV stage G was defined in 76,9% ($\chi^2 = 3,769$; $P = 0,052$). For girls in CVM II 100 % of the 37 were immature with prevalence of stage F 61,5 % ($\chi^2 = 20,462$; $P < 0,0001$). In CVM III the proportion of stage G was increased to 82,1 % ($\chi^2 = 61,00$; $P < 0,0001$). In stage CVM IV 95,3 % of tooth 37 were in stage G ($\chi^2 = 35,372$; $P < 0,0001$). **Conclusion:** A positive correlation found between calcification stages of tooth 37 and skeletal age gives us grounds to use its development to predict the pubertal period with great growth potential ahead.

Keywords: dental age, skeletal age, mandibular second molar, pubertal spurt, Demirjian, Baccetti

INTRODUCTION

In the planning of orthodontic treatment anticipation of growth potential of the facial skeleton is essential to ensure the successful outcome. There are wide individual variations in the timing, duration, and velocity of growth and therefore assessment of individual development stages is required. A lot of authors claimed significant correlation between calcification stages of different teeth (canines, premolars, second and third molars) and skeletal age (1, 5, 11, 13, 16, 17, 18).

AIM:

The purpose of this study was to evaluate the correlation and efficacy of using the calcification stages of mandibular permanent left second molar (tooth 37) to predict the circumpubertal growth phase in Bulgarian subjects.

MATERIALS AND METHODS:

A total of 388 digital x-rays (panoramic radiograms and lateral cephalograms) were evaluated of 194 Bulgarian children. (Table 1). Sixty-nine boys and one hundred twenty-five girls were recruited for the study. The inclusion criteria were (a) Bulgarian outpatients of age ranging from 7 to 17 years (b) mixed or permanent dentition, (c) no accompanying systemic diseases, (d) no tooth agenesis, impacted or extracted teeth 23, (e) no facial injuries, (f) no previous orthodontic treatment, (g) skeletal age CVM II, III or IV. Orthopantomograms were used to assess the development of tooth 37 into eight stages with Demirjian method (6). The skeletal maturity was assessed with Baccetti et al. method (2), based on morphological characteristics of second, third and fourth cervical vertebrae-C2, C3, C4. The target group of the present study included patients within the circumpubertal growth period (CVM stages II, III and IV), because of the importance of this period for orthodontic treatment success. Data were analyzed with Spearman's rank correlation coefficient at a significance level of $P \leq .05$.

Table 1: Studied sample including boys and girls in CVM II, CVM III and CVM IV

CVM	SEX	N	Total
CVM II	boys	38	64
	girls	26	
CVM III	boys	18	74
	girls	56	
CVM IV	boys	13	56
	girls	43	
Total	boys	69	194
	girls	125	

RESULTS:

For Bulgarian girls in pre-pubertal stage **CVM II**, observed at least a year before pubertal growth spurt 100 % of the studied tooth 37 were immature with open apical foramen and stage F dominated in 61,5 % ($P < 0,0001$) among the sample. The prevalence of stage G was 23,1%. In stage **CVM III**-the pubertal growth spurt, the number of mandibular second molars in stage G increased to 82,1 % ($P < 0,0001$) and teeth assessed in developmental stage F dropped significantly down to 14,3% of the studied subjects. During the post-pubertal stage **CVM IV** observed at least a year after the pubertal peak with limited growth potential ahead the percentage of teeth 37 in stage G climbed up to 95,3% ($P < 0,0001$). Only few of studied teeth have reached completed root development and stage H- 4,7%. For Bulgarian boys in **CVM II** developmental stage G of tooth 37 dominated in 60,5% of the studied subjects ($P = 0,001$). The number of teeth assessed in stage F is high 28,9%. In **CVM III** the number of teeth in stage G increased to 72,2% ($P < 0,0001$). The percentage of mandibular second molars in stage F dropped to 16,7%. A few subjects appeared with stage H-5,6%. In stage **CVM IV** the percentage of teeth in stage G climbed up to 76,9% ($P = 0,052$) and the number of teeth in stage H with completed root development significantly increased to 23,1%.

DISCUSSION:

The bud of second mandibular molar started to form at around 9 months after birth. The mineralization of hard tissues began at 2 ½-3 years, tooth crown formation was completed at around 7-8 years, eruption was expected at 11-13 years and root completed-14-15 years (10). Because of superimposition of the structures on the panoramic radiographs, the mandibular teeth are usually evaluated for the identification of the calcification stages instead of maxillary. Studies showed that the left and right, as well as maxillary and mandibular second molars were generally at similar stages of mineralization (9). The evidence points to an apparent positive correlation between dental and cervical vertebrae maturation (3). On the other hand, the CVM method shows a high level of correlation with the hand wrist method-a golden standard for evaluation of skeletal age (15, 19). Congenital absence of permanent mandibular second molar has been reported as a rare occurrence (8, 12). Very few literature is available in agenesis of the second permanent molar and its prevalence is ranging from 0,7-12% [4] ; 0-3,4 [7] , mandibular 4% and maxillary 0% (14). As other research (20) our study approved a high correlation between the mineralisation stages of tooth 37 and CVM stages for girls ($r = 0,609$; $P = 0,000$) and for boys ($r = 0,407$; $P = 0,001$).

CONCLUSION:

A correlation found between mandibular left second molar calcification stages and Cervical vertebral maturation stages ease the skeletal maturity evaluation with aid of a single panoramic

radiograph. In stage CVM II observed at least a year before the pubertal growth spurt with a great growth potential ahead, maturational stage F of the mandibular tooth 37 could be used as predictor of pre-pubertal peak phase for girls only. The stage G dominated phases CVM III and CVM IV for both genders during the maximum pubertal growth. Until apical foramen of tooth 37 is still opened and not completed its development, the opportunity for modification of unfavorable jaw growth is significant. The calcification stages of tooth 37 as indicator of skeletal maturity could be clinically used with caution, until this method is verified with a larger sample group.

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EVALUATION AND MANAGEMENT OF ANTIBIOTIC ALLERGY

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ABSTRACT

Antibiotic allergies to medications can cause rapid or delayed hypersensitivity. Many people think they are allergic to antibiotics, although few have serious responses. Antimicrobial stewardship requires determining actual antibiotic allergy before refraining from the drug or using alternatives. Initiate antibiotic allergy treatment with a full medication history and verified in-vivo and in-vitro allergological testing to identify the antibiotic. Prevention of suspicious antibiotic and drug responses can be achieved by patient education, prescription warning cards, and electronic medical records with built-in checks for medication allergies and ADRs. Understanding antibiotic cross-reaction research is essential for patient education. Evidence-based testing, challenge, and desensitization procedures are some of the most used methods for dealing with the problem. When advantages outweigh concerns and other antibiotics are unavailable, drug desensitisation may be considered.

Key words: antibiotic allergy, evaluation, management, evidence-based testing, drug provocation testing, desensitization procedures

INTRODUCTION

Antibiotic drug allergies can manifest as either immediate or non-immediate (delayed) hypersensitivity responses (HSRs). While non-immediate hypersensitivity reactions (HSRs) are typically non-IgE or T-cell mediated, instant reactions are typically IgE-mediated. Antibiotic allergy symptoms can be systemic (such as anaphylaxis or drug-induced hypersensitivity syndrome), cutaneous, organ-specific (such as blood dyscracias, hepatitis, or interstitial nephritis), or a mix of these. It may be fatal to experience severe cutaneous adverse responses that show up as toxic epidermal necrolysis (TEN) or Stevens Johnson syndrome. Treatment of an antibiotic allergy begins with a complete medication history and validated in-vivo and in-vitro allergological tests to identify the suspected antibiotic. Prevention of suspicious antibiotic and drug responses can be achieved by patient education, prescription warning cards, and electronic medical records with built-in checks for medication allergies and ADRs. Understanding antibiotic cross-reaction research is essential for patient education. If the advantages outweigh potential risks and other antibiotics are unavailable, drug desensitisation may be considered (1).

MATERIALS AND METHODS

A database search was performed to locate material on antibiotic allergies, assessment, and management. The literature review included articles and additional sources.

AIM

The primary aim of the drug allergy practice parameter has been to provide recommendations and guidance for the accurate identification and management of various drug HSRs.

RESULTS AND DISCUSSION

DIAGNOSIS OF ANTIBIOTIC ALLERGY

Skin prick tests (SPT) and intradermal tests (IDT) are the in-vivo techniques that can be used to diagnose acute allergic reactions to antibiotics (2,3). The commercially available fluorescent enzyme immunoassays (FEIA) (ImmunoCAP®, Phadia) and other in-vitro tests, which are again mostly for penicillins and cephalosporins, are less sensitive and specific than skin testing. During the year, the FEIA assay took the position of radioimmunoassays, which were previously

primarily employed to diagnose penicillin allergy (radioallergosorbent test, RAST)(4,5). The diagnosis of antibiotic allergy may be aided by flow-cytometric based basophil activation tests (BAT) (flow assay stimulation test, FAST/FlowCAST®, Buhlmann Laboratories), which measure CD69 or CD203c on drug-specific activated basophils. Up until now, researches of this test has mostly concentrated on beta-lactam allergy (6). Antibiotics, such as fluoroquinolones and vancomycin, which often induce non-IgE-mediated responses, exhibit quantifiable non-specific mast cell activation, complicating the interpretation of acute hypersensitivity skin tests (7).

Delayed IDT values are done at 24 and 72 hours for non-immediate reactions. Delays in infiltrating erythematous reactions are favourable. Antibiotic patch tests are common in Europe to diagnose non-immediate responses. Day 2, 4, and 7 tests are done (if negative on days 2 and 4). The vehicle utilized is usually petrolatum. Patch testing allergens can be made domestically or with commercial products. (Chemotechnique Diagnostics®, Sweden). Patch tests can detect delayed reactions to Amoxicillin, Cefcapene pivoxil, Clindamycin, Ciprofloxacin, Clarithromycin, Cotrimoxazole, Doxycycline, Erythromycin, Fluoroquinolones, Isoniazid, Metronidazole, Minocycline, Pristinamycin, Rifampicin, Spiramycin, Teicoplanin, and Vancomycin. Patch tests are generally helpful in maculopapular exanthema (MPE), eczema, acute generalised exanthematous pustulosis (AGEP), fixed drug eruptions (FDE) (when performed on the lesional skin), and symmetric drug-related intertriginous and flexural exanthema (SDRIFE, Baboon's syndrome). They are not very helpful in SJS/TEN and vasculitis (8,9,10).

The five most often reported adverse responses to antibiotics were associated with penicillins (42%), sulfonamides (25%), fluoroquinolones (4.3%), tetracyclines (4.2%), and macrolides (3.5%). In all contexts, adverse responses to penicillins and sulfonamides were the two most often reported. 11.88% of patients with documented adverse events exhibited sensitivity to various antibiotics (11)

MANAGEMENT OF ANTIBIOTIC ALLERGY

Antibiotic allergy management begins with a thorough medication history to identify the likely antibiotic. This includes symptoms, response timing, treatment, and relevant exposures during and after the reaction. Where applicable, examine rash description, pictures, biopsy results, drug inventory, diagnosis, laboratory findings, and imaging. ADRs include all adverse drug reactions at conventional therapeutic levels, while HSRs are immune-mediated ADRs. On- and off-target effects may have concentration-exposure correlations that vary by person due to acquired or inherited host factors. The drug-patient interaction may depend on dosage and therapy duration(1).

Skin, respiratory, and gastrointestinal issues result from mast cell activation. Vital sign problems, neck stiffness, and oedema are severer. Drug-allergen cross-reactivity has been recorded (e.g., pollen allergy sufferers who become hypersensitive to taxanes). Prior sensitisation is often required. The effects of drugs are immediate (1–6 hours). Type IV reactions (delayed reactions), are more varied and occur days or weeks following medication therapy. They include T cell-mediated symptoms including maculopapular exanthema and delayed urticaria and can affect the liver, lungs, kidneys, or haematology. IgE reactions should be quick. This represents a true allergy. According to a literature review, gastrointestinal symptoms are the second most common adverse drug response after cutaneous skin responses. Anaphylaxis occurs less commonly than both (12). Long reaction times reflect non-IgE-mediated drug allergies involving IgG, IgM, Tcells, or drug immune complexes. A gastrointestinal discomfort is not an allergy. Most indications are dose-dependent or negative and not IgE-mediated. Some people benefit from dosage adjustments (12,13).

Skin testing is needed because clinical history-based 'risk assessment' is unreliable. The patient may not remember the childhood reaction, which may have been triggered by infection or drugs. Testing is simple but rare, which may increase medicine expenses owing to frequent antibiotic prescriptions, especially for patients needing prophylactic antibiotics for scheduled procedures.

The accuracy of skin testing for most drugs is unclear. A positive skin test is a ≥ 3 mm wheal compared to the negative control for prick/puncture or intradermal tests, with a ≥ 5 mm flare (14). Drug challenge is reduced by positive skin testing.

90% of penicillin allergy sufferers can tolerate penicillin-class drugs. Several factors may cause this. Avoiding penicillin may initially lower penicillin IgE antibody susceptibility. Second, people sometimes misinterpret non-IgE-mediated cutaneous or gastrointestinal immune responses for medicine-induced IgE reactions. Penicillin allergy diagnosis requires diagnostic testing (Histamine, tryptase, allergen-specific IgE, basophil activation, and CAST ELISA), patient-reported symptoms, and expert clinical observations (15,16,17) Penicillin skin testing is highly accurate at predicting severe penicillin allergic reactions. It can rule out resistance to the β -lactam ring in other medicines. The patient's history is the best predictor of a significant response to alternative antibiotics. Penicillins and second- or third-generation cephalosporins (excluding cefamandole) cross-react similarly to other antibiotics (18).

Drug provocation testing is the gold standard for identifying the substance responsible for hypersensitivity responses. Patients with significant cutaneous systemic responses shouldn't undergo the drug challenge. It can be done in cases of mild cutaneous delayed-type reactions without systemic involvement. Provocation tests using drugs believed to have adverse effects can confirm or deny medication hypersensitivity. These tests can be performed one month after the initial drug allergic response by hypersensitive reaction centres ready to help in life-threatening situations (19). There are different protocols that are used. In the United Kingdom, it is advised that, depending on the intensity of the initial reaction, either a fraction of the dose or the entire dose be delivered on the first day, followed by a course of treatment one week later if no delayed reaction occurs (14).

The term desensitisation (DS) typically applies to IgE-mediated drug responses and describes the establishment of a temporary state of unresponsiveness to the treatment that caused the original hypersensitive reaction. DS is an innovative method for the safe reintroduction of immunogenic drugs. Non-irritating concentrations are used to skin-test individuals for rapid responses to antibiotics except penicillin. DS should only be considered when no other medicine is available or when a specific drug is necessary for treatment or more effective. In the treatment of serious infections, it is typically possible to safely provide the recommended antibiotic despite a previous history of probable antibiotic allergy. The risks and advantages of DS must be carefully assessed before starting. Algorithms for managing HSRs by DS have been defined for antibiotics, enabling certain patients to endure the problematic medication via continuous infusion without safety concerns (20). Desensitisation is the progressive administration of the medicine to which the patient has become sensitised in order to reduce immunological reactivity.

CONCLUSION

Many individuals say they are allergic to antibiotics, although few have clinically severe reactions and managing them is a common challenge in medical practice. The assessment of true antibiotic allergy before deciding not to use the medicine or other alternative antibiotics is an important tool in antimicrobial stewardship. Comprehensive documentation of the adverse reaction will assist in future instances when analogous drug therapy is required. Evidence-based testing, challenge, and desensitization procedures are some of the most used methods for dealing with the problem.

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IMPACT OF SCARLET FEVER UPON THE ORAL HEALTH IN CHILDREN. A CASE REPORT

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ABSTRACT

Infections caused by Group A Streptococcus are characterized with the synthesis of erythrogenic exotoxin A. The aim of the study is to investigate the impact of scarlet fever upon the oral health in children in the context of a case report. The subject of the study is a female at the age of 9 years. The girl suffered from the infectious disease of scarlet fever twice till the moment. For the purpose of the study are applied the epidemiological index of tooth decay dft/DMFT, clinical indices of PLI, GI, PBI. A laboratory test of determination of the rate of Antistreptolysin O Titer is implemented. It concerns a clinical case of caries-non-resistant mixed dentition, with a moderate generalized plaque-induced gingivitis. There was recorded a considerably high value of the Antistreptolysin O Titer (685.18 IU/ml) of the patient on the onset of the relapse of scarlet fever. Approximately a month later, parallel to the decrease of the value of the Antistreptolysin O Titer (542.50 IU/ml), the dental therapeutic procedures have helped to mitigate the clinical signs of the oral infection and complaints of the child concerning dentes 55 and 65. Professionals in Dental medicine have to take into account the early symptoms of scarlet fever. The adequate diagnostic and therapeutic interdisciplinary approach, in accordance with individual needs, is essential for minimizing the risk of local and systemic complications, including prevention of the deterioration of the oral health status in children.

Key words: scarlet fever, oral health, impact, children

INTRODUCTION

The clinical manifestation of acute streptococcal pharyngitis associates with a considerably high risk of non-suppurative and suppurative complications (1). Infections caused by Group A Streptococcus (GAS) are characterized with the synthesis of erythrogenic (named as pyrogenic) exotoxin A. The greatest rate of distribution of Streptococcus pyogenes pharyngitis concerns children between 5 and 15 years of age (2, 3). Topical complications include peri-tonsillar or retropharyngeal abscess. Immune responses to streptococcal infection provoke the initiation and aggravation of non-infectious auto inflammatory complications (4). The streptococcal pyrogenic exotoxins lead to serious general manifestations of streptococcal toxic shock syndrome based on their active role of super antigens. These super antigens induce a great number of T cells to secrete cytokines in an antigen-independent way (5). It was established that streptococcal pyrogenic exotoxins (SPEs) intensify the IL-1 β -mediated inflammatory process and the chemotaxis of neutrophils. Some researchers assume that streptococcal pyrogenic exotoxins play an important role for the activation of an IL-1 β -driven neutrophil response (6). There are strong interrelations between common health and oral health which require the implementation of an interdisciplinary approach in the diagnostic, therapeutic and prophylactic procedures regarding various noxae, including scarlet fever (7). It was ascertained that between 3% and 5% of the untreated or not efficiently treated clinical cases of that infectious disease can aggravate into severe long-term complications such as hepatitis, glomerulonephritis, rheumatic heart disease (7). Super antigens released by the GAS, respectively Streptococcus pyogenes, lead to overstimulation of the immune system and reactions of enhanced hypersensitivity manifested by the symptoms of sandpaper-like skin rash, high fever and sore throat, petechiae localized on the palate. A pathognomic extraoral manifestation is a red face, with pallor surrounding the nasolabial triangle (sign by Filatov) (7). Typical intraoral symptoms are enlarged tonsils with suppurative collection, as well as tongue alterations, the so-called "strawberry tongue" and "raspberry tongue". The first characterizes with a white-colored coating on the dorsal surface of

the tongue with outstanding fungiform papillae. The typical traits of “raspberry tongue” concern edema and hyperemia, accompanied by desquamation of the keratinized epithelium of the filiform papillae related to the inflammatory process (7). The aim of the study is to investigate the impact of scarlet fever upon the oral health in children in the context of a case report.

CASE DESCRIPTION

The subject of the study is a female at the age of 9 years. Regarding the anamnestic data, the girl has suffered from the infectious disease of scarlet fever twice till the moment, without any accompanying common health disorders and no established allergic reactions. A declaration of an informative consent is signed by a parent of the patient. The child’s mixed dentition corresponds with her age. For the purpose of the study are applied the epidemiological index of tooth decay dft/DMFT, clinical indices of Plaque Index Silness-Löe (PLI) and Gingival Index Löe-Silness (GI), recorded by the means of these Ramfjörd teeth: 55, 22, 64, 36, 42 and 84. For the evaluation of the gingival health status is used also the Papilla Bleeding Index by Saxer and Mühlemann, assessing the rate of distribution and degree of severity of gingival inflammation. The para-clinical tools of the image diagnostics of an ortho-pan-tomography and a laboratory test of determination of the rate of Antistreptolysin O Titer are implemented. The index of dft equals to 66.67% due to four primary teeth with fillings, 2 primary teeth with fillings and secondary caries and both of the upper second primary molars with the diagnosis of Periodontitis Chronica Granulomatosa Diffusa sine Abscessus submucosus. The index of DMFT amounts to 36.36% related to non-cavitated lesions of caries incipience on the vestibular surfaces of permanent lateral and central incisors on the upper jaw. The upper right first permanent molar was extracted because of an unsuccessful treatment of a complicated carious lesion. It concerns a clinical case of caries-non-resistant dentition. We calculated $PLI=1.83$ corresponding to a state of unsatisfactory oral hygiene, explained with the lack of regular usage of fluoridated tooth paste, mouth wash and interdental floss, related to the disturbed general health in the post-infection period of suppressed immunity. The $GI=1.71$, $PBI=2.08$ and $PBI=80\%$. These figures are in accordance with the condition of a moderate generalized plaque-induced gingivitis. There was recorded a considerably high value of the Antistreptolysin O Titer (685.18 IU/ml; the norm up to 250.00 IU/ml) of the patient in our clinical case report with the onset of the relapse of scarlet fever. Approximately a month later, there has been a decrease of the value of the Antistreptolysin O Titer equal to 542.50 IU/ml.

DISCUSSION

The punctual diagnosis of scarlet fever and its precise treatment serve as key prerequisites for prevention against deterioration of general and oral health status of individuals (7, 8, 9). There can be one or multiple relapses of that infectious disease through human lifespan based on the variety of genes of GAS related to the synthesis of a diversity of pyrogenic toxins (10]. There were recorded patients with three or four episodes of recurrence of scarlet fever. Some researchers focus on up to nine new pyrogenic toxin modifications which induce multiple episodes of scarlet fever (11). These establishments correspond with our clinical case of a recurrence of scarlet fever in a period of approximately one year. Under such conditions the role of a multidisciplinary team is essential for the prevention of complications (12). Among the other suppurative complication such as otitis media, sinusitis and meningitis, Streptococcal bacteremia is a severe pathological state of impinged innate and adaptive immune reactions towards infections (12, 13, 14, 15). There was recorded a considerably high value of the Antistreptolysin O Titer (685.18 IU/ml) of the patient in our clinical case report on the onset of the relapse of scarlet fever. Simultaneously, both of the upper second primary molars, respectively the previously endodontic treated and filled dentes 55 and 65 were diagnosed with Periodontitis Chronica Granulomatosa Diffusa sine Abscessus submucosus. Approximately a month later, parallel to the decrease of the value of the Antistreptolysin O Titer (542.50 IU/ml), the therapeutic procedures have helped to mitigate the clinical signs of the oral infection and

complaints of the child related to dentes 55 and 65. Scientists accentuate that efficient treatment corresponds to the level of education of children and their parents about antibiotics, hand and personal hygiene in order to prevent transmission of the bacteria to other people (12). Enhancement of the individual, family and society healthcare is the key of success in overcoming the disease and its detrimental consequences (12, 13, 14, 15, 16). In 2022 WHO reported that children under the age of 10 years are most affected by scarlet fever. The subject in our study is at the age of nine years, which corresponds to that establishment (14). Parallel to the dental procedures, the child went for consultations with an oto-rhino-laryngologist, nephrologist, rheumatologist and general practitioner to be excluded any general complications. In the context of their investigations, Engelberger et al. compared the recordings of clinical indices and histological tests for evaluation of the degree and severity of inflammation of gingival tissue with the obtained results based on the Papilla Bleeding Index scores. There was ascertained a definite correlation between the elevated PBI values and the increased absolute amount of inflammatory infiltrate parallel to the clinical manifestation of zones of a moderate and severe gingivitis (17). Taking into consideration the established clinical parameters for assessment of the state of gingival tissue, we recorded the rates of PLI, GI, PBI.

CONCLUSION

The primary prophylaxis and prevention of diseases has to be prioritized in worldwide scales. Professionals in different scopes of Dental medicine have to take into account the early symptoms of scarlet fever. The adequate and precise diagnostic and therapeutic interdisciplinary approach in accordance with individual needs is essential for minimizing the risk of local and systemic complications, including prevention of the deterioration of the oral health status in children.

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ANXIETY AND DENTAL PHOBIA

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ABSTRACT

Visiting the dentist is often associated with fear or anxiety of the patient. Patients with dental anxiety delay or avoid dental care, which will further worsen their oral health. Dental anxiety affects the quality of life, affects the patient's behavior and health status. It can manifest as fear, aggression, tension and emotional instability, which in turn cause changes in sleep, work and relationships with others. The greatest anxiety is caused by the fear of pain during dental treatment. The terms “dental anxiety” and “dental phobia” are used synonymously. Today, dental anxiety is distinguished from dental phobia. It is possible to measure the level of subjective anxiety using the Dental Anxiety Scale (DAS). The scale allows the differentiation of patients into three categories: patients without anxiety, patients with moderate anxiety and patients with high anxiety, such as those suffering from dental phobia. Their correct differentiation is important for choosing the appropriate treatment approach. There is no universally effective way to manage dental anxiety. Psychotherapeutic strategies, pharmacological interventions or a combination of both are used.

Keywords: Anxiety, Dental phobia, Dental anxiety scale, Oral health, Psychotherapis,

INTRODUCTION

Dentistry and oral health are at the core of a person's overall health. This is often underestimated due to socio-economic reasons or fear. There is a “dynamic vicious cycle” linking dental anxiety to poor oral health. Patients with dental anxiety delay or avoid dental care, which will further worsen their oral health. The progressive deterioration of untreated oral diseases, combined with feelings of guilt, shame or inferiority, contribute to further increases in dental anxiety, and the vicious cycle continues (1, 2, 3). People who suffer from dental phobia (a disproportionate fear of dental treatment) exhibit psychological and physiological symptoms during procedures that make dental treatment difficult or impossible (4). Patients with dental phobia are a specific group of people who have poor dental health due to avoidance of timely dental treatment (5). People with dental phobia often have more active dental caries and fewer teeth (6). Dental fear is a feeling that is provoked by a real, concrete stimulus (e.g., needles or burs), whereas in anxiety the threat is unclear or not immediately apparent. The emotional reactions of individuals are practically the same in both situations, which is why the terms "dental anxiety" and "dental phobia" are used as synonyms in the literature (7).

AIM

The purpose of this study is to analyze information about the prevalence and differentiation of the individual categories of dental anxiety and phobia.

MATERIALS & METHODS

Information was gathered from literature searches on the internet in databases such as PubMed.

RESULTS

The term “dental anxiety” was first used by Coriat (8), who defined it as an excessive fear of any dental procedure, from dental prophylaxis to any dental surgery. Coriat suggests that fear of the dentist is anticipatory anxiety because it stems from fear of real danger and expected unknown danger. Etiologically, fear of dental treatment can be divided into two large groups: “Exogenous” fear, caused by one's own traumatic experience and/or fear arising from a past experience of a

family member or friend. The second group includes the so-called "endogenous" fear, which is associated with internal factors such as personality traits such as anxiety, neuroticism and/or heredity. Patients with high levels of dental anxiety often attribute their anxiety to their experience of traumatic past dental treatment. When traumatic dental treatment occurred in childhood, this has a lasting effect on dental phobia as the individual grows up. Dental phobia exhibits features of a mild form of posttraumatic stress disorder (9). Dental anxiety or dental fear is estimated to affect approximately 36% of the population (8), and according to another study, it affects 15.3% of adults and 25.8-36.5% of preschool and school-age children (10). The prevalence of dental fear in adults is higher among women (2), while in childhood it is equal among girls and boys (7). Dental anxiety is common and occurs before, during, or after dental treatment (11). Dental anxiety is a negative emotion that is created in response to dental treatment (12). Dental anxiety affects the quality of life, affects the behavior and health of the patient. It can manifest as fear, aggression, tension and emotional instability, which in turn cause changes in sleep, work and relationships with others. It has been found that age, gender, level of education, as well as the frequency of dental treatment have a direct effect on the patient's anxiety state. The greatest anxiety is caused by the fear of pain during dental treatment. The terms "dental anxiety" and "dental phobia" are used as synonyms. Today, dental anxiety is distinguished from dental phobia. According to the International Classification of Diseases (World Health Organization ICD-10 Version 2015), dental phobia is a recognized disease that is accompanied by an overwhelming fear of objects and situations, leading to avoidance and postponement of a visit to the dentist (13). Unlike dental anxiety, patients with dental phobia need psychotherapy before dental treatment. Subjective dental phobia is accompanied by objective physiological symptoms (increased muscle tension, rapid pulse (tachycardia), sweating, stomach pain), immobility and panic. It is possible to measure the level of subjective anxiety using the Dental Anxiety Scale (DAS). The scale allows the differentiation of patients into three categories: patients without anxiety, patients with moderate anxiety and patients with high anxiety, such as those suffering from dental phobia. Patients with dental phobia have reduced salivary secretion, which further worsens their oral health and increases the caries index. The Modified Dental Anxiety Scale (MDAS) is a reliable and clinically useful instrument for assessing dental anxiety. The MDAS is an extension of the Corah Dental Anxiety Scale, improving it by including a question about the administration of local anesthesia and recording potential responses to each question on a Likert scale ranging from "anxious" to "extremely anxious" (3).

Symptoms of dental fear, dental anxiety, and dental phobia can be categorized into "physiological responses," "behavioral responses," and "cognitive responses." Most patients exhibit a fight-or-flight response, which is an automatic physiological response to stressful situations and is manifested by increased heart rate, blood pressure, and sweating. Other patients report dizziness, abdominal pain, and vomiting that occur before and during dental treatment. Additionally, most patients with dental fear and anxiety have not been able to sleep well at night or have had nightmares (11). Patients with dental phobia seek alternatives to deal with their dental problems themselves, so as to reduce the need to visit the dentist.

There is no universally effective way to manage dental anxiety. Psychotherapeutic strategies, pharmacological interventions, or a combination of both can alleviate anxiety in patients in the dental office. Psychotherapeutic management strategies modify patient behavior through learning and are minimally invasive with zero or negligible side effects. These therapies include muscle relaxation, hypnosis, acupuncture, distraction, and desensitization. Pharmacological approaches include the use of relative analgesia (nitrous oxide), conscious intravenous sedation, or oral sedation (11). The use of music as a distraction method has been shown to have beneficial effects on the patient, such as reducing blood pressure, heart rate, respiratory rate, and heartbeat. Hypnosis is a psychological method that can modulate the neural circuitry of fear and anxiety. Hypnotherapy is an older, noninvasive intervention that uses audio recordings with or without "relaxing music" to reduce patients' fear and pain during treatment. Hypnotherapy can be used

as a stand-alone anxiolytic intervention or as an adjunct to other methods. Hypnosis also requires specialized training, as it can lead to a loss of trust between the dentist and the patient during the treatment process if used inappropriately (14). Aromatherapy is one of the most effective non-pharmacological techniques for anxiolysis and relaxation. Essential oil aromas (orange, chamomile, lavender, lemongrass) are used to influence the mood/emotions of patients. Aromatherapy can affect pain and anxiety. Auricular acupuncture is a minimally invasive technique that can reduce general and preoperative anxiety. Many patients become anxious due to loss of control or lack of understanding during treatment. Therefore, explaining the upcoming procedure and discussing expectations, concerns, and safety measures can alleviate anxiety.

One way to treat patients with dental phobia is minimally invasive oral surgery (MIOC), which consists of four interrelated stages. In the first stage, the patient's disease state and anxiety state are identified and diagnosed. In the second stage, an individual treatment plan is developed that is based on the prevention of dental diseases. In the third stage, a minimally invasive surgical approach is undertaken to restore the teeth while preserving the tooth substance and limiting the use of stimuli that can provoke fear (e.g., rotating instruments) when possible. In the final fourth stage, a review is performed to reassess the patient's oral health care behavior, sensitivity levels, and fear (6).

Pharmacological methods of treating patients with dental phobia include premedication, sedation, and general anesthesia. Benzodiazepines have anxiolytic effects, but there is insufficient data on their effect when taken orally, since in most studies they are taken intravenously (15). However, taking midazolam orally preoperatively leads to a decrease in anxiety, as the maximum absorption of midazolam in the blood can be achieved after 30 minutes only on an empty stomach and mandatory monitoring of pulse and oxygenation. Moderate sedation/analgesia ("conscious sedation") is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, alone or with mild tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. The most widely used pharmacological combination is benzodiazepines and barbiturates (16). General anesthesia is a drug-induced loss of consciousness during which patients cannot be aroused even by painful stimulation. The ability to maintain independent ventilatory function is often impaired. Patients require assistance to maintain a patent airway and may require positive pressure ventilation because spontaneous ventilation is suppressed due to drug-induced depression of neuromuscular function. Cardiovascular function is maintained (5). Patients with severe dental phobia should see a psychologist or psychotherapist as soon as possible. With the support of a psychologist, the patient will be able to slowly change their beliefs, emotional and cognitive reactions, and thoughts related to the perception of the feared stimuli (17).

CONCLUSION

Despite the progress of modern dentistry, dental anxiety and dental phobia are still relatively common in dental practice. Recognizing the symptoms and distinguishing them is important for choosing the right approach during the treatment of such patients. There is no universally effective way to manage dental anxiety and phobia, but the combination of psychotherapeutic and pharmacological approaches gives satisfactory results.

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DEVELOPMENT OF MANDIBULAR THIRD MOLAR AS AN INDICATOR OF SKELETAL MATURATION

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ABSTRACT

Aim: The purpose of this study was to establish whether the development of the third mandibular molar can be used as an indicator of skeletal maturation. **Material and methods:** 388 digital roentgenographs were evaluated of 194 children in CVM II, III and IV. Mineralization of tooth 38 was assessed with Demirjian et al. method and skeletal age with Baccetti et al. method. **Results:** A moderate positive correlation was found between the mineralisation stages of tooth 38 and skeletal age for girls ($r=0,448$; $P=0,000$) and for boys ($r=0,481$; $P=0,000$). For boys in skeletal age CVM II, 2/3 (63.6%) of the examined teeth 38 were in stage D. In CVM III and CVM IV the proportion of teeth 38 in stage D continued to prevail in almost the same percentage -respectively - 68.5% and 69.2%. For girls in stage CVM II, in 30% tooth 38 has completed crown development - stage D, but in 35% stage C was observed. During CVM III, the proportion of stage D doubled and reached 58%. Stage - CVM IV was dominated in 75% by stage D of tooth 38. **Conclusion:** The results from the study of dynamics of mineralization of tooth 38 does give us grounds to use the development of tooth 38 as an indicator of skeletal maturation. The skeletal age CVM II, III and IV are dominated in majority of both genders by the same stage D.

Keywords: dental age, left mandibular third molar, skeletal maturity, pubertal spurt, Demirjian, Baccetti

INTRODUCTION

The assessment of the skeletal age of children is important for the beginning of orthodontic corrections of maxillo-facial deformities, the prognosis of treatment results and their long-term stability. Some authors claimed significant correlation between calcification stages of different teeth (canines, premolars, second and third molars) and skeletal age (1, 3, 6, 7, 8, 10, 11, 12, 13).

AIM

The purpose of the study was to establish whether the dynamics of development of the third mandibular molar can be used as an independent indicator of skeletal maturation and to assess the correlation between the skeletal age CVM II, III, IV and mineralization stages of tooth 38.

MATERIAL AND METHODS

One hundred and ninety-four subjects aged 7-17 years with mixed and permanent dentition were recruited. The children were in skeletal age CVM II, III or IV. 388 radiographs were assessed. All subjects included in this study were outpatients in Orthodontic Department, Dental Faculty - Medical University "Prof. Dr. Paraskev Stoyanov" Varna. The inclusion criteria for the studied sample were (a) Bulgarian outpatients of age ranging from 7 to 17 years (b) mixed or permanent dentition, (c) no accompanying systemic diseases, (d) no tooth agenesis or extracted teeth 23, (e) no facial injuries, (f) no previous orthodontic treatment, (g) skeletal age CVM II, III or IV. From the initially selected 194 subjects, one hundred seventy-two children, of which 62 boys and 110 girls, met the inclusion criteria. Orthopantomographs (OPG) were used to assess the development of tooth 38 into eight stages with Demirjian method (4) (Fig. 1). The skeletal maturity was assessed on teleoroentgenographs (TRG) with Baccetti et al. method (2), based on morphological characteristics of second, third and fourth cervical vertebrae-C2, C3, C4. All radiographs were digital, obtained with Planmeca ProMax 2D Unit (Planmeca OY, Asentajankatu 6, FIN-00880 Helsinki, Finland). Exposer time was 16 sec, 13 mA, 68 KV. The visualization of the 2D images

was made with ROMEXIS software allowing magnification of the image in case of need of more accurate assessment. Data were analyzed with Spearman's rank correlation coefficient at a significance level of $P \leq .05$. The study obtained a positive assessment by the Committee on The Ethics of Research (KENI) at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.



Fig.1 Stages of calcification of tooth 38 by Demirjian (1973) (14)

RESULTS

A moderate positive correlation was found between the mineralisation stages of tooth 38 and skeletal age for girls ($r=0,448$; $P=0,000$) and for boys ($r=0,481$; $P=0,000$). For Bulgarian males in stage CVM II, 2/3 (63.6%) of the examined teeth 38 have completed crown development - stage of mineralization D. In skeletal age- phase CVM III – the peak of pubertal growth (2), the number of teeth 38 that have completed their crown formation increased slightly to 68.5%, but nearly 20% of the studied male subjects appeared, where the mandibular third molars were with formed root furcation and beginning of development of tooth roots- stage E. In stage CVM IV -a year after the peak of puberty (2), the proportion of teeth 38 in stage D continued to prevail in almost the same percentage - 69.2% among the sample. For studied Bulgarian females in stage CVM II, only 30% of the examined third mandibular molars - teeth 38 were assessed with completed crown development - stage D. In the same skeletal age, the proportion of teeth with more immature crown development- stage C, was slightly increased to 35%. During puberty peak – skeletal age CVM III, the number of teeth that have reached stage D doubled, reached 58%. Compared to the boys no stage E was examined. The skeletal age CVM IV phase was dominated in 75% by mineralization stage D of tooth 38 with formed and shaped crown to the Enamel-Cement border.

DISCUSSION

The study of the stages of mineralization of different teeth (23, 33, 35, 37, 38) and their correlation with skeletal maturation is of interest to many authors in the research for indicators of skeletal age. (1, 6, 7, 8, 9, 11, 13). Engstrom et al. in 1983 pioneered a survey correlating the mineralization stages of mandibular third molar with skeletal age evaluated by hand wrist radiographs (5). He concluded that during the beginning of pubertal growth the third mandibular molar showed completed crown formation in majority of the subjects. During the pubertal peak the lower third molar crown was still incomplete in some subjects, but it had already attained full root length in others. However, during the pubertal growth peak the lower molar crown mineralization was completed in majority of the subjects. When the epiphyseal union was assessed in the end of pubertal growth the crown was completed only in one third of the studied subjects and rarely had the root developed in one third length (5). The results of our study, although using another method for skeletal age assessment-CVM-Baccetti method (2), more popular among the orthodontists, showed similar results. An average degree of correlation was examined between the stages of mineralization of tooth 38 and the stages of bone age CVM II,

CVM III, CVM IV ($r = 0.48$ for boys and $r = 0.45$ for girls). The established moderate correlation does give us grounds to predict, like other authors the pubertal growth period for the purposes of orthodontic treatment planning by the degree of morphological maturity of tooth 38 (1, 3, 11, 12, 13). Some authors suggested a strong correlation between third molar development and skeletal maturity in their research (in males: $r=0.88$, $P<0.001$; in females: $r=0.77$ for maxillary third molar and 0.89 for mandibular third molar, $P<0.001$) (12).

CONCLUSION

The successful treatment of skeletal dentofacial deformities and anomalies includes the modification of the unfavorable growth of the maxillofacial structures. The optimal timing for this purpose is puberty growth in the skeletal age CVM II, CVM III, CVM IV according to Baccetti (2). The study of the degree of mineralization of tooth 38 in Bulgarian girls and boys does give us grounds to use it as an indicator for puberty period. The same degree of development of the third mandibular molar prevails in both sexes - stage D. During pubertal peak the lower third molar crown mineralization was completed in majority of the male and female subjects.

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FIBEROPTIC NASOPHARYNGOSCOPY WITH MULLER'S MANEUVER AND ITS IMPLEMENTATION IN CASES OF THE SYNDROME OF OBSTRUCTIVE SLEEP APNEA AND SNORING

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ABSTRACT

Introduction: The Syndrome of Obstructive sleep apnea and snoring (SOSAS) is a disease in which total or partial obstructions of the upper airways occur during sleep, leading to awakenings. Patients suffer from, nowadays widespread, syndrome of SOSAS. In 1983 Borowieck and Sassin first described fiberoptic nasopharyngoscopy using Muller's maneuver in the evaluation of patients with obstructive sleep apnea. **Aim:** To review the literature, dedicated to the use of fiberoptic nasopharyngoscopy, with the application of Muller's maneuver for the diagnosis of patients with obstructive sleep apnea and snoring syndrome. **Material/Methods:** For the period September 2023 – September 2024 in the databases PubMed, Bio Med Central, Science Direct, Scopus, Web of Science, Embase, a systematic analysis of scientific publications, investigating the application of fiberoptic nasopharyngoscopy, implementing Muller's maneuver, for the diagnosis of patients with SOSAS, was executed. **Results:** Authors reached the conclusions that fiberoptic nasopharyngoscopy using Muller's maneuver is an easy-to-use technique that is time-efficient and widely accessible to patients suffering from SOSAS. As a disadvantage of fiberoptic nasopharyngoscopy using Muller's maneuver authors describe its invasiveness, subjectivity in relation to patients regarding the control of inspiratory effort. **Conclusion:** SOSAS is a widespread disease among the population and is often left undiagnosed. For that mentioned reason, OSA must be diagnosed in time and treatment undertaken, returning patients' normal life, reducing the risk of death and motor vehicle accidents.

Keywords: obstructive sleep apnea and snoring syndrome, fiberoptic nasopharyngoscopy, endoscopy

INTRODUCTION

The Syndrome of Obstructive sleep apnea and snoring (SOSAS) is a disease, widely spread among the population, which often remains unnoticed in its early development. Irreversible consequences for human health can be present. In SOSAS complete or partial collapses of the airways occur during sleep, resulting in awakenings (1). Patients with obstructive sleep apnea (OSA) experience breathing cessations and subsequent restoring of breathing during sleep. These pauses in breathing can be repeated from 5 to 30 times or more per hour (2,3,4). Breathing cessations lead to a poor supply of oxygen to the body. The brain receives a signal of danger and the patient wakes up. Latter can happen repeatedly during the night. The sleeping person is not aware of his or her awakenings, but morning and daytime tiredness, sore and dry throat, headache co-occur. In the presence of sleep apnea, a person experiences difficulties concentrating, often falls asleep suddenly, has cognitive problems and is not fully productive at work (2,3). Three types of sleep apnea are described in the scientific literature - obstructive sleep apnea, central sleep apnea and complex or mixed sleep apnea (3,4). The most widespread is the OSA, a disease that affects more men than women, but after the onset of menopause, the number of women affected increases significantly. Every fifth man and every tenth woman suffer from sleep apnea (SA) (3,4). Apnea is defined as a cessation of breathing for more than ten seconds. In 1983, Borowieck and Sassin first described fiberoptic nasopharyngoscopy implementing Muller's maneuver in the evaluation of patients with OSA.

AIM

To review the literature on the implementation of fiberoptic nasopharyngoscopy with Muller's maneuver for the diagnosis of patients with obstructive sleep apnea and snoring syndrome.

MATERIAL AND METHODS:

For the period Sept 2023 – Sept 2024 in databases PubMed, BioMedCentral, ScienceDirect, Scopus, Web of Science, Embase, a systematic analysis of scientific publications, investigating the application of fiberoptic nasopharyngoscopy, implementing Muller's maneuver, for the diagnosis of patients with OSA, was executed.

RESULTS

SA is a disease that, undiagnosed and untreated in time, impacts the organism, the efficiency at the person's workplace and the quality of life. A close relationship exists between certain general diseases and SA (7,8,9,10). Timely diagnosis and proper treatment of OSA have a beneficial effect on patients' quality of life (4,5,6).

Polysomnography is the study that establishes the presence or absence of sleep apnea. It is carried out using a device that tracks several indicators of patient's sleep (6,18,19). Currently, polysomnography is the gold-standard for determination of presence or absence of SA (20,21,22). Under video surveillance, high-sensitive, specialized sensors and electrodes are placed on specific predetermined locations of patient's head and body and sleep is examined - its different phases, number and duration of awakenings, brain activity, eye movements, muscle tone, heart activity, oxygen in the blood and the pulse rate, the movements of the lower limbs, body position, respiratory effort, respiratory flow and snoring time and index (14,15,16,21). The test gives a result based on the number of apneas at night, if they are up to 5, there is no presence of OSA, from 5-15 – mild OSA case, 15-30 apneas – moderate OSA case and severe sleep apnea – in cases of more than 30 apneas (21,22,23,24). The test can be performed at home (17,18,21). As a result of the literature review, authors reached to the conclusions that fiberoptic nasopharyngoscopy using Muller's maneuver is an easy-to-use technique that is effective and accessible to patients suffering from OSA (28,29). As a disadvantage of fiberoptic nasopharyngoscopy with Muller's maneuver, authors describe its invasiveness, subjectivity in the attitude of patients regarding the control of inspiratory effort, and untimely reproduction of the apneic episodes (30,31).

DISCUSSION

There is a close relationship between SA, cardiovascular disease, heart attack, stroke, and sudden death syndrome. The degree of danger depends on the frequency and type of apneic episodes - apneas and hypopneas. People with cardiovascular disease are at greater risk of mortality. Higher mortality rates are generally observed in sufferers from sleep apnea (3,9,10,11,12).

Fiberoptic nasopharyngoscopy using Muller's maneuver can be performed on patients in the supine or sitting position. In this diagnostic procedure, a patient with a history of OSA and snoring syndrome is subjected to a forced inspiratory effort. By inserting a flexible fiberoptic device into the hypopharynx of a patient with OSA, the examiner can observe the collapse of the airway. Fiberoptic nasopharyngoscopy using Muller's maneuver is used to determine the cause of sleep apnea and establish the exact location of the obstruction. When using fiberoptic nasopharyngoscopy with Muller's maneuver, a positive test result means that the site of upper airway obstruction is likely below the level of the soft palate. During the examination with the fiberoptic nasopharyngoscope, which is in the retrolingual area, a lateral and anterior-posterior narrowing of the pharyngeal walls can be observed. (25,26).

The authors share the opinion that despite the availability of Muller's maneuver, it is a presumptive and non-specific method for the diagnosis of obstructive sleep apnea to determine the exact localization of the obstruction of the upper respiratory tract. Fiberoptic

nasopharyngoscopy with Muller's maneuver is used to determine the severity of the respiratory disorder and obstruction.

Ritter et al. in 1999 published a scientific study with a quantitative analysis of fiberoptic nasopharyngoscopy using Muller's maneuver, implementing a software to measure the area and diameters of the retropalatal and retroglossal areas (27). When performing Muller's maneuver, a pressure sensor is applied to monitor the patient's inspiratory effort. By applying the sensor to monitor patients' inspiratory effort, the subjective factor in the patient and the examiner is excluded. Fiberoptic nasopharyngoscopy was performed in ambulatory patients, either supine or sitting. A decrease in the area and diameter of the retropharyngeal and retroglossal regions was observed in the retropalatal region compared to baseline values.

Alleviation of SA symptoms affect the comorbidity present (3,6). Weight loss, healthy diet and lifestyle have a positive effect on sleep quality. The accumulation of extra pounds affects the structure of the upper respiratory tract (5,6). Dental intraoral appliances, called mandibular advancement devices (MADs), assist breathing by pulling or pushing the mandible forward and thereby providing a wider opening for air intake during sleep. MADs can be combined with Continuous Positive Airway Pressure (CPAP) devices. The latter provide constant air pressure by the mask present on the nose and/or mouth (32,33,34). Those devices are effective but can be used as well alone for moderate to severe cases of SA. Research shows that after treatment with CPAP devices, heart health improves, the risk of stroke decreases, blood pressure decreases, daytime sleepiness decreases, and the number of accidents caused by SA and falling asleep at the wheel respectively decreases (3,11,34).

CONCLUSION

SA, a common condition, is often undetected. Causes cardiovascular illnesses, heart attack, stroke, sudden cardiac death, etc. For these reasons, OSA must be identified and treated early to reduce mortality and car accidents. Patients' quality of life can be restored by the latter.

ACKNOWLEDGMENTS

The project is implemented under contract No.BG-RRP-2.004-0009-C02 and is financed by the EU -Next Generation EU, through the National Plan for Recovery and Sustainability of the Republic of Bulgaria under procedure BG-RRP-2.004 - Creation of a network of research universities.

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FLAP DESIGNS FOR PERIODONTAL REGENERATIVE THERAPY

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ABSTRACT

Flap design and suturing technique are key aspects in influencing outcomes in periodontal regenerative therapy. The soft tissues overlying the bone defects are fundamental in preventing postoperative infection and, consequently, contamination of the biomaterials used (barrier membranes, bone repair materials and/or biologic agent) and the blood clot. Primary wound closure, excellent angiogenesis, barrier function for a sufficient duration, bone defect distensibility, and a stable blood clot are the bio-clinical principles that predict regeneration therapies. Surgical design, flap management, and suturing technique affect predictable regenerative treatment. Every regeneration treatment requires proper flap design. Primary wound closure prevents surgical complications. The new procedures being developed are aimed at fully preserving marginal tissue. Currently, papilla-preserving flap designs and closure procedures are the conventional methodology for regenerative periodontal surgery.

Keywords:

Flap designs, regenerative therapy, periodontology, primary closure

INTRODUCTION

The soft tissues overlying the bone defects are of fundamental importance in preventing postoperative infection and contamination of the used biomaterials (barrier membranes, bone repair materials and/or biological agent) and blood clot (1).

Postoperatively sutured soft tissues overlying bone defects inevitably shrink during the early healing phase. This often results in membrane exposure and/or exfoliation of the bone repair material with subsequent contamination of the biomaterials and blood clot located within the defect (2,3,4,5). On the other hand, when the primary wound closure in the interdental area is compromised - subsequently interdental craters are extremely common (1).

Because of all the postoperative complications described above, different surgical approaches have been developed regarding flap design and suturing technique. The goal was to find an optimal protocol providing primary closure.

AIM

The aim of the present study was to review and summarize the most common Flap Designs used in periodontal regenerative therapy today.

MATERIALS AND METHODS

The databases utilized were Google Scholar, ResearchGate, and PubMed to identify pertinent scientific publications published in English up to 2024, employing keywords such as "Flap designs," "Regenerative therapy," "Periodontology," and "Primary closure." An comprehensive examination of the literature was performed. Relevant papers were identified for analysis, and their references were examined for more related research following a thorough review of the reference list.

RESULTS AND DISCUSSION

The main bio-clinical principles on which the predictability of regenerative procedures depends are primary wound closure, good angiogenesis, barrier function for a sufficient period of time, provision and maintenance of bone defect distensibility and last but not least - a stable blood clot (6).

Predictable regenerative therapy is closely related to surgical design and flap management and suturing technique. Proper flap design is very important in every case of regenerative therapy. This ensures primary wound closure, preventing postoperative complications (7, 8).

In 1995, Cortellini et al. found that the incidence of complications associated with postoperative barrier membrane exposure could be dramatically reduced with the use of access flaps particularly engineered to maintain interdental tissues (the modified papilla preservation procedure) (9). The first papilla preservation approach was developed by Takey et al. in 1985 and is employed to avert soft tissue collapse and to sustain stability during the regeneration phase (10).

The new procedures being developed are aimed at fully preserving marginal tissue. The aim is to provide primary wound closure after a regenerative procedure. The flap designs aimed to attain passive primary closure and superior wound stability. Currently, papilla-preserving flap designs and closure procedures are the conventional methodology for regenerative periodontal surgery (11).

Modified Papilla Preservation technique (MPPT)

The Modified Papilla Preservation Technique (MPPT) was created to enhance regeneration space and to secure initial flap closure in the interdental area. This technique is used when the width of the interdental area is at least 2mm (12).

The technique - two sulcular incisions are made vestibularly in the area of the teeth adjacent to the defect. These incisions are extended towards the interdental space of the defect and reach their palatal surface. The papilla is not cut! A horizontal incision is made vestibularly to the base of the papilla. Next, the flap is dissected from vestibular to palatine (the flap passes under the interdental contact) (13).

Simplified Papilla Preservation Flap (SPPF)

This technique was developed to overcome some problems associated with MPPT, namely difficult application in narrow interdental spaces and difficult application in distal areas of the dentition. SPPF is applied in cases where the interdental space is narrower than 2mm (14).

The technique - sulcular incisions are made vestibularly and orally in the area of the teeth adjacent to the defect. An oblique incision is made in the interdental space. The oblique incision starts from the vestibular corner of the tooth with the bony defect to the mid-proximal point of the adjacent tooth. Thus, the interdental papilla is divided into one vestibular and one oral part (14).

Minimally Invasive Surgical Technique (MIST)

A technique developed to further preserve wound stability. This type of technique is minimally invasive. This means that minimal incisions are made, very little flap is removed and the soft and hard tissues are worked extremely gently. It is usually applied in regenerative procedures with enamel matrix derivative (EMD). The limitations of this technique are related to the reduced visibility of the operative field and the need for extremely gentle handling of the microsurgical instruments under the microscope (15, 16).

The technique - the incisions are mandatory sulcular. In the medio-distal direction they are minimally extended. The interdental incision may be MPPT or SPPF depending on the width of the space between the teeth. Vertical incisions are avoided. Periosteal incisions are never performed with this technique. Flap suturing is done with single O-shaped sutures (15).

Modified- Minimally Invasive Surgical Technique (M-MIST)

The stability of the flap is further improved. Secures and maintains the bone defect space independently (16, 17).

The technique - Characterized by extremely small interdental access (16).

Single Flap Approach (SFA)

The next stage of microsurgery is the introduction of a single flap procedure (either vestibular only or oral only) (17, 18). The utilization of the SFA is warranted just when the expansion of the intraosseous defect is mostly from the buccal or lingual/palatal side, and access from a single

side permits sufficient surgical debridement of the intraosseous lesion and the radiographic area impacted by the defect (11).

Entire Papilla Preservation technique (EPPT)

In 2017, Aslan et al. presented an innovative surgical approach - the entire papilla preservation technique. This innovative design offers an unaltered gingival area above the intraosseous defect, with the interdental papilla fully retained (19, 20).

CONCLUSION

Primary closure of the wound after periodontal regenerative procedures is of utmost importance, as this would ensure the stability of the blood clot and activation of all biological processes associated with subsequent regeneration of the defect.

The new procedures being developed are aimed at fully preserving marginal tissue. Currently, papilla-preserving flap designs and closure procedures are the conventional methodology for regenerative periodontal surgery.

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MANAGEMENT OF AN OROANTRAL COMMUNICATION USING A NON-RESORBABLE PTFE MEMBRANE (OPEN BARRIER MEMBRANE TECHNIQUE)

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ABSTRACT: Oroantral communications (OACs) are abnormal openings between the oral cavity and the maxillary sinus. They can be caused by the extraction of maxillary premolars and molars, trauma, tumors, infections, and so on. An untreated OAC develops into an oroantral fistula – a pathologic pathway covered with epithelium that persists until its surgical removal and defect closure. Although small OACs can heal spontaneously, bigger defects require surgical management with different soft-tissue flaps, bone grafts, or synthetic materials. However, some of the most effective methods utilize flap advancement, which can cause severe tissue deficiency and difficulties in subsequent tooth restoration. This case report presents a minimally invasive approach for the management of OAC using dense polytetrafluoroethylene (d-PTFE) membranes without flap advancement. D-PTFE membranes are barrier membranes that do not require complete coverage (open barrier technique) and can be used for socket preservation.

Keywords: oroantral communication, oroantral fistula, barrier membrane, dense polytetrafluoroethylene membrane, open barrier membrane technique

INTRODUCTION

Oroantral communications (OACs) are pathological communications between the oral cavity and the maxillary sinus, with an incidence of about 10%. The most common cause of OAC is the extraction of a premolar or molar whose roots are in close anatomic proximity to the sinus floor or the presence of periapical pathology spreading to the sinus floor. Other possible causes include trauma, tumors, infections, osteoradionecrosis, and iatrogenic causes. If left untreated OAC can develop into an oroantral fistula and cause chronic sinus inflammation (1). Small defects (< 2-3 mm) often heal spontaneously, while larger defects require surgical closure (2). The treatment success depends not only on the defect size but also on the number and integrity of the socket walls and the socket's depth. Different treatment methods have been suggested through the years, most commonly utilizing advancement flaps from the buccal and/or palatal mucosa, the buccal fat pad, and combined flaps (2). However, flap advancement can cause severe tissue deficiency and difficulties in dental rehabilitation. This necessitates the development of novel techniques that can eliminate the aforementioned limitations. In recent years, various natural and synthetic biomaterials have been introduced and adopted for implant dentistry, oral surgery, and periodontology (3, 4, 5, 6). Some of them have demonstrated promising results in the management of oroantral communications.

CASE REPORT

A 61-year-old male visited the Department of Oral Surgery, at the Faculty of Dental Medicine, Medical University of Varna, Bulgaria in October 2024 for the extraction of FDI (The Fédération Dentaire Internationale) teeth #25, 26, and 27. The clinical examination revealed root remnants in teeth #25 and 26 and third-class mobility in tooth #27 (Miller's classification). The panoramic radiograph displayed severe bone resorption around tooth #27, indicative of advanced periodontal disease (fig.1.)



Fig.1. Preoperative orthopantomogram

The patient had no comorbidities or allergies and did not take any systemic medication. This study was conducted in accordance with the Declaration of Helsinki. A written informed consent was obtained from the patient before the procedure. The extractions were performed under local infiltration anesthesia with 3,6 ml Articaine, 4%. The nose-blowing test confirmed the suspected OAC in the socket of tooth #27. The socket walls were carefully debrided and irrigated with saline. The OAC was observed and its size was evaluated to be about 5 mm. (fig.2A.) Then the marginal bone was deperiostated by undermining the gingival margins with a periosteal elevator until buccal and palatal full-thickness pockets were created. The d-PTFE membrane (Permamem®, Botiss Biomaterials GmbH) was cropped and shaped to seal the socket orifice, exceeding 3-5 mm of the socket walls under the periosteum (fig.2B). The membrane covered the socket orifice and was stabilized by interrupted crossed mattress sutures with a 5/0 polyamide material without penetrating the membrane. (fig.2C.)

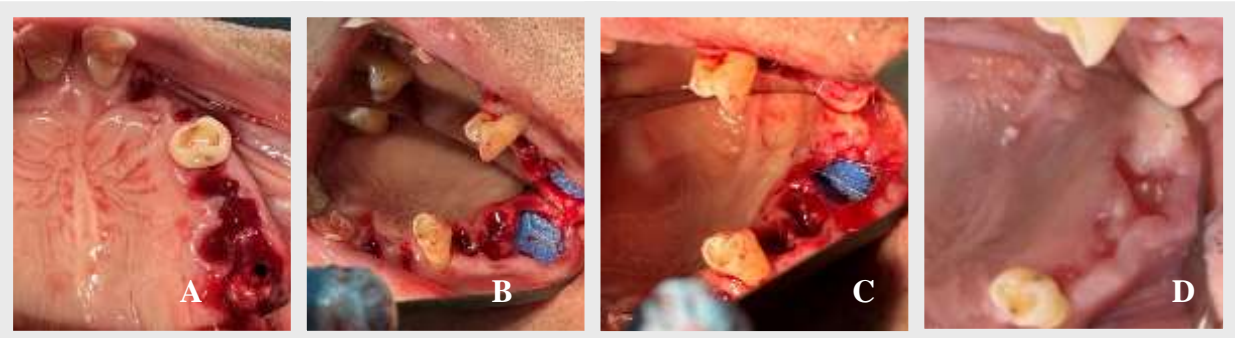


Fig.2. Open barrier technique for management of OAC with a d-PTFE membrane:
A – clinical view of the OAC; B – closure of the socket orifice with a d-PTFE membrane;
C – sutured gingival margin of the socket; D – socket orifice one week after membrane removal.

A postoperative CBCT was conducted and confirmed a defect size of almost 5.5 mm and substantial loss of the alveolar bone height (fig.3.) The postoperative care included the prescription of amoxicillin 875 mg + clavulanic acid 125 mg (twice daily for 7 days), ketoprofen 50 mg (2-4 times daily if needed), probiotic, antihistamine, nasal decongestant, and 0.12% chlorhexidine solution for mouth rinsing (twice daily for 15 days). Dietary, hygiene, and sinus precautions instructions were given. The sutures were removed after 2 weeks, and the membrane was removed after 4 weeks (day 28). Healing was uneventful. (fig. 2D)

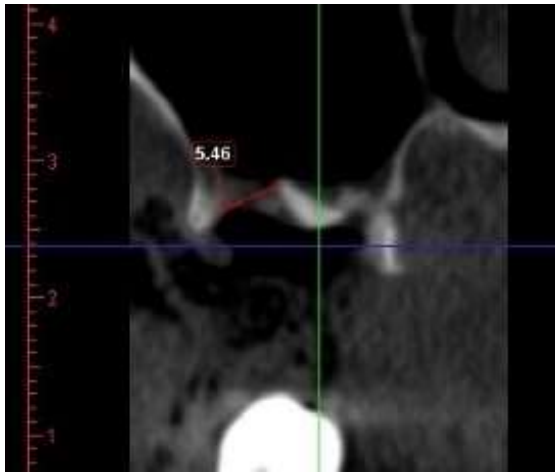


Fig.3. Postoperative cone-beam computed tomography image of the OAC.

DISCUSSION

The management of OACs should be immediate (within 48) to avoid complications. Some OACs can heal spontaneously if the socket allows for clot retention. Otherwise, surgical closure should be performed (7). Although effective, the methods with advancement flaps create unfavorable conditions for implant and prosthodontic rehabilitation. Furthermore, these techniques are technically challenging and deteriorate the patient's quality of life in the postoperative period. Therefore, bone and soft-tissue grafts and alloplastic materials have recently gained popularity (8, 9, 10). Dense PTFE membranes are non-resorbable microporous barriers used for guided bone and tissue regeneration (11, 12). They can be partially exposed to the oral cavity and do not require flap advancement. Thus, d-PTFE membranes allow for both bone and soft tissue preservation. Lee was the first to describe OAC closure with a d-PTFE membrane (13). However, he combined the method with advanced soft-tissue flaps. Yotsova et al. and Scavia et al. have recently reported the successful application of the open barrier technique (11, 14). The method can combine the surgical closure of the defect with alveolar ridge preservation at the same time (14). As in the present article, these results have been based only on case reports and series. Further studies, including randomized clinical trials, would be beneficial to evaluate the technique, the amount of remaining bone and soft tissues after its application, and its advantages and limitations.

CONCLUSION

Advancement flaps have been widely used for OAC closure through the years. Their major limitations are shallowing of the vestibule, loss of the attached gingiva, and displacement of the mucogingival junction. A minimally invasive approach using dense d-PTFE membranes without flap advancement was presented. It aims to successfully treat this complication and facilitates the subsequent implant placement and/or prosthetic restoration. Further research is necessary to validate their superiority to the conventional methods.

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ORAL PYOGENIC GRANULOMA - MODERN TREATMENT APPROACHES

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ABSTRACT

Pyogenic granuloma is a benign proliferation of connective tissue that can be found most commonly in the oral cavity of pregnant women. This lesion usually arises in response to various stimuli - chronic local irritation, trauma, or with hormonal imbalance. Current therapeutic approaches for oral pyogenic granuloma include nonsurgical (debridement with excellent oral hygiene, sclerotherapy, corticosteroid injection) and surgical procedures (conservative surgical excision, cryosurgery and laser surgery). Although pyogenic granuloma does not always necessitate immediate treatment, there are a variety of nonsurgical and surgical options available today. As a result, clinicians must not only be familiar with each therapeutic approach, but also be able to determine when it is necessary to use it.

Keywords: Oral pyogenic granuloma, Granuloma gravidarum, Pregnancy lesions, Treatment

INTRODUCTION

Pyogenic granuloma is a benign proliferation of connective tissue that can be found on the skin and mucous membranes, but most commonly in the oral cavity in pregnant women or in cases of hormonal imbalances. It is evident that oral and general health are in a close relationship (1). It is characterized by hyperplasia of granulation tissue, extremely rapid growth, high risk of bleeding and lack of pain (2, 3).

This lesion was first described by Poncet and Dor in 1897. In their study, the authors described four cases of "vascular tumors", which they also called "Botrichomycosis hominis"(4).The term "pyogenic granuloma" was introduced at a later stage, but is considered to be extremely incorrect, as it is not an infectious process, and histologically it does not have the characteristic picture of true granulomas (5). In connection with the controversy over the true nature of pyogenic granuloma, various names for this lesion have emerged over the years (6). Differential diagnoses include various benignant and malignant lesions, including gingival metastases (7).

Current treatment approaches for oral pyogenic granuloma include non-surgical (debridement with excellent oral hygiene, sclerotherapy, corticosteroid injection) and surgical procedures (conservative surgical excision, cryosurgery and laser surgery) (6, 8, 9).

AIM

The aim of this review is to present modern treatment approaches of pyogenic granuloma by reviewing the scientific literature.

MATERIALS AND METHODS

For pertinent scientific articles published in English up to 2024, Google Scholar, Research Gate, and PubMed were examined. Keywords such as "Oral pyogenic granuloma," "Gramuloma gravidarum," "Pregnancy lesions," and "Treatment" were utilized. A comprehensive review of the literature was done. After carefully reviewing the reference list, pertinent papers were identified for analysis and their references were examined for more relevant research.

RESULTS AND DISCUSSION

Current treatment approaches for oral pyogenic granuloma include non-surgical (debridement with excellent oral hygiene, corticosteroid injection, sclerotherapy) and surgical procedures (conservative surgical excision, cryosurgery and laser surgery) (6, 8, 9).

Non-surgical methods

In 2012, a study was published suggesting the most minimally invasive approach to managing pyogenic granuloma. This method is based on perfectly performed debridement of the tooth root surfaces in the area where the lesion is located and excellent personal oral hygiene on the part of the patient. Chandrashekar, in the patient's first visit performs an initial debridement, gives instructions for excellent oral hygiene and schedules a follow-up appointment for his patients in a week. In case he does not find any regression of the lesion after one week - three visits in three consecutive weeks follow, during each visit he again performs debridement in the area. Throughout this period he ensured his patients maintained strict personal oral hygiene and regular use of the 0.12% chlorhexidine frogging solution. At the end of his study, the author concluded that this minimally invasive approach would be appropriate in cases of pyogenic granuloma of relatively small size (10).

In 2006, a case of oral pyogenic granuloma recurring repeatedly after conventional surgical excision was published. The authors took a first-time approach with corticosteroid injection into the lesion, which proved successful subsequently (11). In 2015, Bugshan et al. published their study applying the same treatment. The team concluded that corticosteroid treatment is accepted as an alternative for recurrent pyogenic granulomas (12). It is still unclear how precisely corticosteroid medication acts (8).

Sodium tetradecyl sulfate sclerotherapy is an established therapeutic option for patients with pyogenic granuloma. This technique is easy to perform and does not result in scar formation, but repeated visits to the treating physician are necessary. The curative effect of this method is due to all the specific (damages endothelial cells and obliterates the lumen of blood vessels) and nonspecific effects (tissue necrosis) of sodium tetradecyl sulfate. Adverse effects of this type of treatment are associated with allergic manifestations to sodium tetradecyl sulfate, adjacent tissue necrosis and hyperpigmentations (13). In 2018, a study was published using the same approach in 40 patients with oral pyogenic granuloma. The team concluded that Intralesional sclerotherapy is an extremely effective non-surgical method in the treatment of oral pyogenic granuloma (14).

During pregnancy, dealing with oral pyogenic granuloma is a serious challenge. In general, it is recommended that if the lesion is painless and does not traumatize and bleed on chewing, the patient's fundus should be monitored and the only thing to recommend to the patient is strict personal oral hygiene (15). However, when the lesion causes problems for patients, conventional surgical excision is required (16, 17).

Surgical methods

In 2023, Lomeli Martinez et al. published their study in which it can be clearly seen that for the last 25 years or so the main methodology used has been conventional surgical excision [8]. Essentially, conventional surgical excision involves complete removal of the lesion, with incisions extending to the periosteum and about 2mm into the area of the soft tissue border. In case there are teeth adjacent to the lesion, it is extremely important to treat them supra and subgingivally by debridement. Last but not least, it is necessary to remove any irritating factors (most often iatrogenic plaque-forming factors) located in the vicinity of the lesion. All of the above aims to reduce the risk of recurrence of pyogenic granuloma (6, 8, 18).

Cryotherapy is a safe, easy to operate and low cost therapeutic option in the treatment of patients with pyogenic granuloma. It enables the pathology to be resolved without causing severe scarring. Compared to collagen fibers, endothelial cells can be more susceptible to cryotherapy (19).

In recent years one can encounter many studies in the literature that deal with pyogenic granuloma using **laser surgery** (3, 20, 21). The benefits of using the laser include a suture-free procedure with little postoperative pain, sterile conditions, cutting accuracy, and better visualization of the surgical site because it seals the blood vessels and nerve bundles, preventing bleeding throughout surgery (20, 21). As an addition, it can be reported that when working with a laser, instant disinfection of the wound occurs, thanks to their antibacterial effect. This would ensure the minimization of the risk of postoperative infection, as well as a faster healing process (21).

In conclusion, pyogenic granuloma is a lesion that recurs in about 15% of cases. Most often, this is associated with its inaccurate removal during surgical interventions or failure to eliminate etiological factors (22, 23). In 2015, Frumkin et al. proposed a protocol to prevent recurrence in patients with pyogenic granuloma. This protocol is conservative and involves the removal of etiologic factors in close proximity to the area where the pyogenic granuloma developed and patients' adherence to extremely high personal oral hygiene (24).

CONCLUSION

This study reviews all current treatment approaches for patients with pyogenic granuloma. Pyogenic granuloma does not always require urgent therapeutic measures. However, today, we have a palette of different nonsurgical and surgical treatments. It is for this reason that it is essential that clinicians not only know each therapeutic approach, but also be able to assess when it needs to be implemented.

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**Supplement J of IMAB
14-th South-East European Conference Infections and Cancer 2024**

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