Open Access Article

Ann. Acad. Med. Siles. (online) 2024; 78: 269–275
eISSN 1734-025X
DOI: 10.18794/aams/189387
www.annales.sum.edu.pl

PRACA POGLĄDOWA
REVIEW

Interdisciplinary approach of odontogenic infectious foci – a literature review

Zębopochodne ogniska zakażenia w ujęciu interdyscyplinarnym – przegląd piśmiennictwa

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ABSTRACT

Odontogenic foci are bacterial inflammatory changes, whose primary center is located in the area of the causal tooth. Various mechanisms result in the formation of secondary foci or systemic infections. Reliable diagnostics and elimination of the aforementioned foci are essential in the process of preparing patients qualified for ophthalmic surgery, organ transplants, dialysis, and anti-cancer therapy. Particular vigilance should also be exercised in the cases of patients with cardiovascular disease, especially those at high risk of infective endocarditis due to cyanotic congenital heart disease or an implanted valve prosthesis. The review paper presents the justification for conducting in-depth diagnostic and therapeutic procedures in the aforementioned groups of patients, citing methods for identifying the foci as well as methods for their elimination. The basic and overarching goal of the presented actions is to avoid complications in the form of severe infection and death.

KEYWORDS

dentistry, infection prophylaxis, odontogenic infectious foci, general disease

STRESZCZENIE

Ogniska zębopochodnego zakażenia to bakteryjne zmiany zapalne, których pierwotny ośrodek zlokalizowany jest w okolicy zęba przyczynowego. Za pośrednictwem różnych mechanizmów powodują powstawanie narządowych ognisk wtórnych lub infekcji ogólnoustrojowych. Rzetelna diagnostyka i eliminacja wspomnianych ognisk jest niezbędna w procesie przygotowawczym pacjentów kwalifikowanych do operacji okulistycznych, przeszczepów narządowych, dializoterapii, a także terapii przeciwnowotworowej. Szczególną czujność należy zachować także w przypadku pacjentów z chorobami sercowo-naczyniowymi, zwłaszcza obciążonych wysokim ryzykiem infekcyjnego zapalenia wsierdzia

Received: 23.11.2023 **Revised:** 21.05.2024 **Accepted:** 27.05.2024 **Published online:** 25.10.2024

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Publisher: Medical University of Silesia, Katowice, Poland

z powodu siniczej wrodzonej wady serca czy wszczepionej protezy zastawkowej. W pracy przedstawiono zasadność dogłębnego postępowania diagnostyczno-terapeutycznego u wspomnianych grup pacjentów, przytaczając metody identyfikacji ognisk oraz sposoby ich eliminacji. Podstawowym i nadrzędnym celem przedstawionych działań jest uniknięcie powikłań w postaci ciężkiej infekcji i zgonu.

SŁOWA KLUCZOWE

stomatologia, profilaktyka infekcji, zębopochodne ogniska zakażenia, choroba podstawowa

INTRODUCTION

Odontogenic foci are bacterial inflammatory changes located in a small space called the primary focus, which in this case is the tooth. They can cause secondary foci located in the periphery, including all of the organs and implants in the human body, especially in the head and neck region [1]. The main potential odontogenic foci are periapical inflammatory changes, teeth with deep caries penetrating to the pulp chamber, endodontically treated teeth with unfilled canals, roots left behind, pulpless or dead pulp teeth, as well as teeth with a surrounding cyst [2,3]. Inflammatory processes during a complicated tooth eruption or accompanying foreign bodies left behind are also significant pathogenic factors [4]. According to the literature, even 90% of the primary foci are located within the head, and 80% have a source in the middle ear, paranasal sinuses, but above all, in the oral cavity, tonsils, teeth and periodontal tissues [4]. Because of the organism's protective functions, which prevent the development of infection, odontogenic foci can remain latent. During predisposing factors such as trauma, hypothermia, stress, acute viral infection, immunodeficiency or immunosuppression and aggressive therapy, the focus of latent infection may be activated or exacerbated and finally lead to septic complications [1,5,6,7,8,9].

In an interdisciplinary approach, the problem of odontogenic infectious foci is widely discussed in the available scientific base. The elimination of sources of dental infection often becomes one of the main elements determining the effectiveness of treating the disease, which is why the issue is fundamental.

In this paper, we will consider specific groups of patients in detail and present the cause-effect relationship in addition to the available detection and elimination methods of the odontogenic foci.

DISCUSSION

Mechanisms of the formation of secondary foci of primary odontogenic origin

Researchers distinguish three main mechanisms by which a focus located in the oral cavity gives rise to a secondary focus. These include metastatic infection, metastatic damage and metastatic inflammation. Metastatic infection is caused by bacteria entering the bloodstream during dental procedures (e.g. tooth extraction) or as a result of periodic release from the primary focus in the oral cavity (e.g. periodontal pocket). Once the bacteria have colonised a site convenient for their growth, such as a pacemaker, they multiply and can cause an infection.

Another mechanism is metastatic damage, which is caused by the entry of bacterial endo- and exotoxins into the bloodstream. Bacterial endotoxins are potent toxins released during the breakdown of a bacterial cell. Exotoxins are highly immunogenic lipopolysaccharides of Gram-negative bacteria, which are antigens and therefore able to induce an immune response of the organism. The third means of spreading dental infection is metastatic inflammation. The essence of this process is the entry of a soluble antigen into the bloodstream, where it reacts with specific antibodies, resulting in the formation of a macromolecular complex. The formed complexes are deposited in the body and can cause inflammatory responses of varying severity [10].

Patient groups requiring exclusion of the presence of dental foci

Patients at high risk of cardiovascular disease

Patients at high risk of cardiovascular disease represent one of the largest groups of patients in the dental surgery. Each time, patients in this group should undergo a thorough diagnostic procedure to effectively confirm or exclude the presence of dentally derived foci of infection [11].

One of the conditions to be concerned about when there are oral primary foci of infection is infective endocarditis (IE), known as intravascular infection. It can also involve the heart valves and an implantable prosthetic valve, leading to regurgitation and subsequent severe heart failure [12]. A particularly high risk of IE applies to patients with artificial heart valves (including those implanted subcutaneously) as well as patients in whom an artificial material was used to repair their own valve. Patients with the presence of a congenital cyanotic heart defect and a history of an episode of IE are also at risk of developing IE [13].

Numerous studies confirm that the oral cavity and teeth are the most common primary foci of infectious diseases like IE, providing a habitat for many species of bacteria, such as *S. sanguis*, *S. mitis*, *S. salivarius*, *S. mutans*, or *S. aureus*, often isolated cases in this disease. For this type of infection, in the material taken from the odontogenic primary focus and the focus of IE, a correlation is found in the scope of the examined microflora. Among the etiological factors, bacteria of the genus *Streptococcus* and *Staphylococcus* are particularly indicated.

In the acute form of IE, *Staphylococcus aureus* is most often isolated from the natural valve and *Staphylococcus epidermidis* from the implanted valve. In the subacute form, coagulase-negative staphylococci, the aforementioned streptococci of the oral flora, *Enterococcus* and Gram-negative bacteria are predomine [12].

The problem of IE also includes a significant risk of mortality. In the case of patients in whom microorganisms have invaded the natural structures of the heart, the mortality rate is estimated at approx. 15%, while in the case of patients with prosthetic valves, it increases to approx. 60%. Therefore it is essential to implement the described diagnostic and therapeutic procedures aimed at removing the primary infectious foci and protecting against the spread of microorganisms in the body [14].

Patients qualified for organ transplantation

Another group of patients in whom a particularly careful diagnosis and elimination of dental foci should be initiated are patients qualified for transplantation. On the basis of medical reports on patients with renal failure and a renal transplant operation planned as a result, we will discuss the validity of eliminating the odontogenic foci. Currently, a kidney transplantation is considered the procedure with the highest success rate in the treatment of severe failure of this organ, but as a method with a risk of rejection of the transplanted organ and death of the patient, it requires special care and a reliably managed convalescence combined with immunosuppressive management.

The immunosuppressive effect can be achieved both by the use of pharmacological agents and by exposure to X-ray waves, e.g. during radiotherapy of oncology patients. Immunosuppression can also be induced by factors such as stress, temperature, infections or even air pollution [15]. In clinical transplantation practice, immunosuppressive preparations affecting cellular and humoral immune responses are distinguished. During modulation of the humoral response, deficiencies of IgG, IgA and IgM class antibodies can be observed, as well as the cessation of cytokine and lymphokine production. The effects on the cell-type response are more commonly noted and result in an impaired lymphocyte T function in addition to their reduced amount. This type of immunosuppressive effect can be achieved by eliminating lymphocytes, blocking the circulation of lymphocytes, or blocking the signalling pathway in the mechanism of lymphocyte activation. All this increases the body’s susceptibility to severe infections, which in turn escalate the incidence of treatment failures and even the risk of death of the patient [15,16]. Although the method is constantly being improved, severe systemic infections, also due to dental causes, are the second most common cause of treatment failure.

The first reports confirming the validity of the diagnosis and elimination of odontogenic foci in patients immunosuppressed after kidney transplantation date back to 1982. Three transplant recipients developed a high fever, which subsided after the removal of asymptomatic but showing features of primary infectious foci – dental foci [17]. Research by Sarmento et al. [17] from 2020 showed that 32% of kidney transplant patients whose oral hygiene before and after transplantation was defined as very poor underwent treatment in a hospital ward as a consequence of a severe systemic infection caused by periodontal foci. In the context of the legitimacy of conducting a reliable diagnostic and therapeutic procedure in patients qualified for transplantation, noteworthy is the research of Hansen et al. [18] from 2021. These studies raise issues about the dental care of a patient with blood cancer before hematopoietic stem cell transplantation (HSCT) and odontogenic complications that developed in two transplant recipients. The examined patients had asymptomatic infectious foci in the oral cavity, which had not been eliminated before starting the treatment. These foci were periapical changes visible in the X-ray image. In the following stage, they caused abscesses and required intensive treatment, as well as the implementation of antibiotic therapy.

Oncologic patients

In the case of cancer therapy, the implemented treatment causes immunosuppression and exposes patients to dangerous complications resulting from any infections. Chemotherapy of haematological malignancies causes myelosuppression, i.e. damage to bone marrow cells, and increases the susceptibility of patients to severe systemic infections [19]. According to recommendations, each potential odontogenic focus should be eliminated before starting radiotherapy or chemotherapy [10].

Researchers are also interested in the effect of anticancer therapy on oral cavity colonisation by *Lactobacillus* and *Streptococcus* bacteria. An increase in the colonies of both strains during radiotherapy of head and neck tumours was demonstrated. Nevertheless, statistically significant results were not always obtained, and no consistent pattern was observed. Hence, further work is needed to systematise this issue clearly [20]. According to previous studies, no increase in the colonies of the bacteria mentioned above resulted from chemotherapy, and their levels remained unchanged or reduced. Colony reduction was observed during the induction and treatment phases of anticancer chemotherapy, probably owing to the antimicrobial effect of some cytotoxic substances used during the therapy [20].

In the case of patients with cancers in the oral cavity, it has been proven that the biofilm on the surface of the mucosa affected by cancer shows a predominance of bacterial species characteristic for inflammatory surfaces, thus it seems reasonable to consider a tumour in the oral cavity as an inflammatory focus [10].

Ophthalmic patients

Observations by teams comprising dentists and ophthalmologists confirm the association between the presence of odontogenic foci and inflammatory eye diseases. The ocular region is a frequent secondary focus of dental infections. According to the literature, the means of spreading the infection include the blood-borne path and the path related to the specific structure of the anatomical structure of the facial bones [5,21].
The likely mode of spreading infection by the blood-borne path is retrograde drift through the ocular veins. At the medial angle, the superior and inferior ocular veins join the angular and facial veins. The inferior ocular vein passes through the inferior eyelid crevice and then connects with the winged venous plexus. These veins do not have valves and are therefore not immune to the spread of infection through them. The lack of valves along with the anastomosis of the orbital veins with the face, nasal sinuses and pterygopalatine fossa, create the conditions for blood to flow in three directions: to the palatal fossa, the pterygopalatine fossa and the cavernous sinus. Through this vascularisation system, infection can spread from the oral cavity and from the paranasal sinuses to the orbit and further to the individual vessels of the eyeball [5].
To comprehend the nature of the spread of a dental infection, it is also important to note the specific anatomy of the facial bones. The roots of the molars and premolars are located in the vicinity of the maxillary sinus floor. We also observe cases in which the apexes of these groups of teeth are already in the lumen of the sinus. An inflammatory process in or around a tooth can move directly into the sinus and then migrate to the eyeball via the orbital floor bones, the ethmoid sinus or the infraorbital canals. Cases have also been reported in which infection of the maxillary lateral teeth has spread to the infratemporal and pterygopalatine fossa, and ultimately into the orbit via the inferior orbital fissure. The dental infection path can also lead through the soft tissues of the face and terminate in the periorbital tissues [20]. Dental foci not only cause secondary foci associated with eye disease, but also aggravate already ongoing inflammatory processes and may provoke their recurrence [5].

Diagnosis of odontogenic foci

In-depth diagnostics of odontogenic foci is based on subjective and objective examination, as well as additional tests, including most of all X-ray images.

Subjective and objective examination

The patient should be interviewed for any pain associated with the teeth each time. To avoid misclassification of a tooth with dentine hypersensitivity as a potential odontogenic focus, the patient should determine the nature of the pain, when it occurs and whether there is a provoking factor. During an intraoral examination, pulp vitality tests should be performed using a cotton swab soaked in ethyl chloride or a Doppler flowmeter. This study is considered the most reliable, especially for younger people. The condition of the periapical tissues should also be assessed using the Owiński test, Smreker's test and the percussion test [22].

Additional tests

Clinical examinations are insufficient to determine the suspicious causal tooth, unquestionably the focus of odontogenic infection; therefore, it is necessary to take an X-ray. In order to assess a specific tooth, a dental photo is taken. To assess the condition of all teeth, it is recommended to take an orthopantomographic picture, but cone beam computed tomography has the most significant diagnostic value [23]. The disadvantages of X-rays are primarily artefacts and disturbances in the anterior segment (mainly in orthopantomographic images) and the need to use a stabiliser and immobilise the patient, which in many clinical situations is difficult or even impossible. There are also situations when roentgen diagnostics are prohibited. An example of a patient for whom X-rays are not recommended is a pregnant woman. In addition, according to the literature, for thinning in the bone to be visible on an X-ray, the loss of mineral substances must be 30–50% [22]. Due to these limitations, a diagnostic method with greater sensitivity and specificity, which is not burdened with so many disadvantages, is still being sought.
In the latest reports, research centres see diagnostic value in thermal imaging, the results of which are analysed on the obtained thermograms. This method is described as entirely non-invasive and painless and can be carried out in all groups of patients. The advantage of thermography is also its sensitivity. There are devices available on the market with an accuracy of $< 0.05°C$, which allows the detection of even the most minor temperature differences between the healthy area and the odontogenic focus. Despite many advantages, the presence of prevalent diseases and local lesions should always be considered, as well as the effect of the medicines taken by the patient. These factors may affect the course of the inflammatory process, blood circulation and consequently cause a change in the temperature of the examined area in the oral cavity.
Aboushady's et al. [24] 2021 study demonstrated the usefulness of thermal imaging in diagnosing and

differentiating inflammatory changes in periapical tissues. In these studies, three groups of foci were determined and defined successively as: AA (acute periapical abscess) occurring in the form of widening of the periodontal ligament and without a radiolucent lesion in the periapical region; CA (chronic periapical abscess) in the form of a radiolucent lesion in the periapical region, closely related to the root of the causal tooth, and AAP (acute pulpitis with apical periodontitis) defined as periodontitis with widening of the periodontal ligament and loss of bone lamella. The results showed an increase in temperature in the area of odontogenic foci when taking pictures with a thermal imaging camera for 5 minutes. The most significant rise in temperature was recorded in the focus designated as AA, i.e. acute inflammation of periapical tissues [24].

Elimination of dental foci – current recommendations

Immunocompromised patients

Prophylaxis of surgical site infections

According to the recommendations of the Polish Dental Society (PTS) Task Force Group and the National Programme for Antibiotic Protection (NPAO) on the use of antibiotics in dentistry, the basis for the prevention of surgical site infections in the oral cavity is the maintenance of adequate oral hygiene and absolute adherence to the principles of asepsis and antisepsis of perioperative care. The decision to apply antibiotic therapy should be justified and routinely is not recommended in immunocompetent patients. Antibiotic therapy is recommended in immunocompromised patients after consultation with the treating physician [25]. This group includes patients with haematological diseases and congenital or acquired immune deficiencies, patients taking immunosuppressive, cytotoxic or corticosteroid drugs in addition to patients with long-standing and unregulated metabolic disease [13]. It is recommended to use antibiotic prophylaxis in the 'one-shot' system – the administration of a single antibiotic dose 30––60 minutes before the planned procedure.
The first-line of treatment is amoxicillin without clavulanic acid administered at a dose of 2000 mg, and in patients allergic to penicillin antibiotics, cefazolin at a dose of 1000 mg or clindamycin at a dose of 600 mg. In children, the antibiotic of first choice is amoxicillin without clavulanic acid administered at a dose of 50 mg/kg b.w., and in children allergic to penicillin antibiotics – cefazolin at a dose of 50 mg/kg b.w. or clindamycin at a dose of 20 mg/kg b.w. [25].
In contrast to immunocompetent patients, in immunocompromised patients, antibiotic administration should be considered for the following procedures: endodontic and periodontal surgery, prophylaxis of facial skin or oral mucosal wound infections and the prophylaxis of infections in maxillofacial fractures [13].

Prophylaxis of odontogenic infections

The major part of the treatment of odontogenic infections is local treatment in the form of drainage of the purulent focus and removal or endodontic treatment of the causative tooth. In immunocompromised patients, it is recommended to initiate antibiotic therapy after consultation with the attending physician. For empirical therapy, the first-line drug is amoxicillin without clavulanic acid at a dose of 500 mg every 8 hours or 750–1000 mg every 12 hours in adults. In children, the dose depends on body weight (up to 40 kg: 20–40 mg/kg b.w./day in 3 divided doses; above 40 kg: dosage as in adults). In patients allergic to penicillin, clindamycin is used in a single dose not exceeding 300 mg, taken every 6–8 hours. To monitor the course of treatment, the patient should attend a follow-up appointment 48–72 hours after the beginning of the therapy. The treatment should be continued until the patient's general condition has normalised. If no improvement is observed 72 hours after starting antibiotic therapy, a second-line antibiotic should be considered and the effectiveness of drainage of the purulent focus should be assessed [13].

Patients at high risk of cardiovascular disease

According to the recommendations of the European Society of Cardiology (ESC) Task Force Group, for patients at high and indirect risk of IE, increased oral hygiene and regular dental check-ups twice a year are recommended [26].
Before surgical procedures involving disruption of the oral mucosa and procedures involving intervention in the gingival or periapical region, adults should be given amoxicillin or ampicillin at a dose of 2000 mg orally or intravenously 30–60 minutes before the procedure. For those allergic to penicillin, one of the following selected substances should be administered p.o./i.v.: 600 mg of clindamycin, 2000 mg of cephalexin, 1000 mg of cefazolin or 1000 mg of ceftriaxone. In the case of children, we consider administering the same antibiotics, taking into account an allergy to penicillin, but we have to remember to appropriately adjust the dose to the child's body weight (amoxicillin, ampicillin, cephalexin, cefazolin and ceftriaxone at a dose of 50 mg/kg b.w.; clindamycin 20 mg/kg b.w.).
Antibiotic prophylaxis is not recommended in the case of other valvular defects, congenital heart defect, in patients after a history of myocardial infarction, stroke, by-pass or with implanted pacemakers [13].

Oncologic patients

In the case of oncology patients, the adopted treatment method, the location of the lesion and the time between the detection of the lesion and the initiation of therapy play a key role. These factors determine the choice of prophylactic treatment regimen in the context of dental foci. In the case of patients who are to undergo radiotherapy for head and neck cancer, a dental examination prior to treatment can prevent the emergence of complications during the anti-cancer treatment, which could hinder or delay the therapy [27,28]. The task of a dentist is to make the patient aware of the importance of fluoride prophylaxis in minimising the incidence of caries disease and decide on the eligibility of teeth for extraction before the beginning of the treatment since during and after radiotherapy there is a risk of osteonecrosis, which is a frequent complication of surgery in patients after radiotherapy [29,30].

For patients being prepared for radiotherapy of the head and neck region, the extraction of teeth showing signs of pulp disease and/or periodontal disease is recommended. Radiotherapy causes metabolic changes and impaired tissue perfusion, which in turn results in a reduction in the effectiveness of drugs on the area and ineffectiveness of the applied antibiotic therapy targeted at the odontogenic foci. It should be remembered that an absolute contraindication to tooth extraction is the contact of a tooth with a malignant tumour as the procedure risks the spread of the neoplastic process [31]. In order to maintain oral health, periodontal treatment is recommended before, during and immediately after radiotherapy for head and neck cancer and/or chemotherapy. In addition, the use of fluoride-containing products is recommended in order to prevent the development of caries in patients undergoing radiotherapy for head and neck cancer. Apart from the fluoride prophylaxis, it is recommended to rinse the mouth with a chlorhexidine solution (CHX) with a concentration in the range of 0.12–0.2% once or twice a day, which has the effect of reducing plaque accumulation and the number of SM colonies. Nonetheless, possible side effects of CHX in the form of tooth discolouration, tartar and taste disturbance should be taken into account [20]. Antibiotic prophylaxis corresponds to recommendations for immunocompromised patients.

In patients who have undergone maxillofacial surgery, it is recommended to routinely administer an antibiotic before procedures involving the maxillary bones, such as tooth extractions, endodontic periodontal surgery or procedures on the alveolar process. In this case, short-term prophylaxis is employed, commencing on the day before the surgery and continuing for 3 consecutive days. The antibiotic of choice is amoxicillin with clavulanic acid at a dose of 1000 mg (875 mg + 125 mg) every 12 hours in adult patients and 45 mg + 6.4 mg/kg. b.w./day in children. In cases of allergy to penicillin antibiotics, clindamycin at a dose of 300 mg every 8 hours in adults or 8–16 mg/kg/day in 3–4 divided doses in children is used. Additionally, in patients who have undergone radiotherapy in the maxillofacial area, it is recommended that an antibiotic be administered prior to endodontic treatment (choice of antibiotic and dosage in accordance with recommendations for the antibiotic prophylaxis of IE) [13].

CONCLUSIONS

Based on the literature review, odontogenic lesions in an interdisciplinary approach are pervasive. Their diagnosis and elimination significantly affect the course of the primary disease and the treatment process, which is often crucial for the patient's health and life.

Author's contribution
Study design – J. Cabon, K. Ziaja
Data collection – J. Cabon, K. Ziaja
Manuscript preparation – J. Cabon, K. Ziaja, A. Zawilska, A. Trzcionka
Literature research – J. Cabon, K. Ziaja
Final approval of the version to be published – A. Zawilska, A. Trzcionka

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