Literature Review

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Dry socket (Alveolar osteitis): Aetiopathogenesis, prevention and treatment- literature review

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Abstract

***Background**: Alveolar osteitis (AO) or fibrinolytic osteitis is one of the most common complications following tooth extraction. The aetiopathogenesis and prevention of this condition has been a subject of debate throughout the years. Assessment of risk factors can guide the physician to minimize the incidence of this complication. Various types of treatment have been suggested although there is yet no universally accepted protocol.*

*The **aim** of this critical review is to highlight the oral surgeons and doctors of dental medicine on contemporary concepts about etiology, pathogenesis, treatment and prevention of alveolar osteitis.*

***Material and methods**: An electronic search was performed in PubMed, Google Scholar, ResearchGate and Web of Science. All types of study designs were included in this literature review from articles published from 2007 until 2022, written in English.*

***Results**: Regarding the aetiopathogenesis smoking, oral contraceptives, bacterial infections, trauma during extraction, angiogenesis/fibrinolysis, comorbidity and the usage of vasoconstrictor in anaesthetic solution are known as factors that positively correlate the formation of alveolar osteitis. Age and gender showed inconclusive results. Furthermore, in cases with multiple extractions, open surgical methods and periodontal involvement there is low incidence of alveolar osteitis. Pre- and postoperative mouthwash with 0.12% chlorhexidine have proven to be an effective means for the prevention*

of alveolar osteitis such as copious saline irrigation, topical antibiotics and proper suturing. There is dispute in the usage of systemic antibiotics regarding its effectiveness in the prevention. Irrigation and application of topical anaesthetics and antiseptics can encourage mucosal healing effect.

***Conclusion**: The results strongly insinuate that the aetiopathogenesis is multifactorial. The ubiquity of alveolar osteitis is inevitable, although there are methods that can reduce its incidence. Alveolar osteitis in most of cases is a self-limiting complication and its treatment is symptomatic.*

***Keywords:** alveolar osteitis, dry socket, etiopathogenesis, prevention, management*

Introduction

Dry socket, also known as alveolar osteitis, fibrinolytic osteitis and alveolitis sicca dolorosa is a phenomenon that occurs one- or three-days following exodontia and is one of the most common complications following tooth extraction or surgical extraction. Most of the patients need multiple postoperative visits for treatment of the condition. In literature there are many studies but most concepts are still controversial and it is generally accepted the multifactorial etiology of the condition. The term refers to fibrinolysis and bone superficial inflammation that is characterized by the onset of severe pain, bad taste, halitosis and irradiation of pain to the neck and ear (1). Clinically there is no clot in the socket and the surrounding epithelium is inflamed (1,2). It is frequently found after extraction of mandibular 3rd molars and in the middle age patients(3,4). The occurrence of dry socket is erratic; nonetheless there are several predisposing factors. Some of these factors are smoking, contraceptives, infections, trauma, suppressed angiogenesis, systemic illness/conditions, vasoconstrictor in anesthesia, operators' experience, postoperative care, etc. The healing process after tooth extraction involves four stages; coagulation, inflammatory, proliferative and maturation/remodeling. During coagulation stage there is vasoconstriction that promotes blood coagulation (5,6). Furthermore, there is release of histamines and prostaglandins that causes vasodilation, stasis and higher permeability of blood vessels and migration of inflammatory cells. In the proliferative stage there is formation of granulation tissue that is rich in collagen fibers and cells, angiogenesis; formation of fibrous tissue and after that its replacement with woven bone at third week. In the remodeling phase there is replacement of woven bone with lamellar bone (7). Some authors suggest some preventive methods and efficient treatment procedures of alveolar osteitis. (5,6,7)

DEFINITION

There are many definitions of dry socket. Dry socket or alveolar osteitis (AO) is characterized with partial or total disintegrated blood clot between the first and third day after extraction accompanied by pain in area of alveolar socket that irradiates, with or without halitosis. That condition leads to delayed healing of extraction wound and requires multiple visits for treatment. This postoperative complication causes significant pain and other symptoms which are not so typical but without the usual signs and symptoms of infection such as low-grade fever, inflamed gingival margin, bare bone, ipsilateral lymphadenopathy, grayish discharge. The clinical course starts with developing pain on the 1-st or 3-rd day after removal of the tooth. Most of this condition occur after the removal of lower molars. On examination, the tooth socket appears to be empty,

with a partially or completely lost blood clot, and some bony surfaces of the socket are exposed. The exposed bone is sensitive and is the source of pain. The dull, aching pain is moderate to severe, usually throbbing in nature and frequently radiating to the ear, temporal or neck region. The patient complains of bad odour and a foul taste (5).

INCIDENCE

The lack of objective clinical criteria leads to variability in reported occurrence of AO. The incidence of AO for routine dental extraction has been reported in the range 0,5- 5 3% and can exceed 30% for impacted mandibular third molars (3,4,8,9,10). Surgical extractions are associated in about ten times with higher incidence of AO.(8,9,10)

ONSET AND DURATION

The onset of AO according to recent studies varies from 1-3 days (3,4,10,11,12,13,14) to 2-5 days post extraction (1,2,15,16,17). Usually the duration of this complication varies between 5-10 days (15,18).

Aim

The aim of this critical review is to highlight the oral surgeons and doctors of dental medicine about comprehensive concepts about etiology, pathogenesis, treatment, symptoms relief and prevention of alveolar osteitis.

Materials and Methods

The present review was performed to evaluate the aetiopathogenesis, prevention and treatment of Alveolar Osteitis. An electronic research was conducted about published in these data bases: PubMed, Google Scholar, Research Gate and Web of Science. In addition to articles, some books were also included. All types of study designs were included in this literature review. In the data bases the keywords “dry socket”, “alveolar osteitis”, “fibrinolysis”, “prevention”, “management”, “prophylactic management”, “treatment” and “alveolitis sicca dolorosa” were used. The inclusion criteria were articles that were published from 2007-2022 and written in English.

Results

By electronic research we collected contemporary information and made critical review about etiology, pathogenesis, pathophysiology treatment and prevention of AO.

Etiopathogenesis

The literature has suggested countless of etiological factors and factors that accelerate the formation of AO, but it is not fully understood. Generally, AO is believed to be of multifactorial etiology leading to premature fibrinolytic breakdown of blood clot although there are some factors that predispose, contribute and aggravate the formation of this complication.

The lysis of the clot results from the plasminogen pathway activation, but the trigger factor is unknown. Some physiologic or non-physiologic mediators produce the activator substance that have a promotor effect on clot lysis leading to fibrinolysis. (19)

The inflammatory response of immune system to exodontia in the alveolus involves pro-and anti-inflammatory cytokines. Several studies have focused on biomarkers as IL 6, TNF alfa, osteocalcin etc. It is known that IL-6 has a dual role in bone formation and bone resorption, which could contribute to the fibrinolysis in alveolar osteitis. Tumour necrosis factor-alpha (TNF-a), osteocalcin, and runt-related transcription factor 2 as physiological mediators could help in understanding of the pathogenesis of alveolar osteitis (20,21)

Contributing factors

The development of new blood flow is one of the most important processes to occur during wound healing, these new cells coming from blood provide many factors such as immunity, regenerative cells, nutrition, and oxygen which are needed for the healing. Angiogenesis occurs at two to three days after the extraction whereby it forms a granulation tissue (occurs during the inflammatory stage and continues to the next healing stage - proliferative).(22) The autors summarise that there are two possible ways for the formation of dry socket; the first one is when there is a complete absence of a clot formation or the initial clot is lysed. The second way is with the activation of tissue activators that aid in the transformation of plasmin precursor into plasmin that degrades the clot and encourage the pain symptom (2, 14, 17). Birn suggested that trauma during extraction results in damaging of the bone that is then exposed to the oral environment. (22) The oral environment is inoculated with bacteria that cause inflammation of the bone and release of direct tissue activators, which help with the fibrinolysis creating a greater risk for the formation of alveolar osteitis (17,18).

The other theory suggests that high-stress extraction with tensile or compressive forces on alveolar bone surrounding the tooth ca cause necrosis or apoptosis of osteoblasts lining of the surface of lamina dura. This idiopathic socket ischemia event may prevent an initial blood clot to reform through additional bleeding. It can cause difficulties for the immune system accessing the site through local capillaries to initiate an inflammatory response to resorb the necrotic bone cells. Studies have shown that mechanical stress on osteoblasts can activate cellular signaling pathways that lead to osteoblast apoptosis.

The necrosis of bone cells due to mechanical stress extraction, occurring over 24 hours after an extraction, may result in the bone cells releasing urokinase plasminogen tissue activator, which is the main plasminogen activator released in dry socket lesions (23). The urokinase plasminogen tissue activator then converts plasminogen to plasmin, and plasmin may directly cause the lysis of a blood clot that initially formed in the alveolar socket. A major function of plasmin is to initiate blood vessel perfusion to bring blood, immune system cells, and complements to the surface of the socket to encourage resorbing the necrotic osteoblasts. In AO an idiopathic blood vessel ischemia event is eventually observed that prematurely blocks this capillary perfusion-mediated immune system activation process.

The cause of ischemia at a dry socket lesion site is unknown. Some alveolar sockets may be dense, with few blood vessels per unit of socket area, or a socket may be observed to only bleed from the apical aspect, making these sockets intrinsically incapable of normal bleeding. The superficial necrotic bone is exposed and uncovered for several days, resulting in the major symptom (or morbidity) of alveolar osteitis, acute pain of the exposed socket; spontaneously or after mechanical stimulation that lasts for several days the bone surface becomes completely covered by healing epithelium.

In the healing process the vital epithelium gradually covers the surface area of the socket intaglio surface. The epithelium brings blood vessels, immune system cells, and their complements in direct contact with the necrotic bone cells of the socket to begin resorbing the necrotic bone cells. This process of epithelium

growth may take several days; during this time, the uncovered bone is painful to the touch and is vulnerable to painful contact with bacterial biofilm or food impaction.

1. Oral microorganisms/ bacterial infections

The role of oral microorganisms for focal fibrinolytic activity has been investigated. Many authors state that previous local inflammation and lack of antibiotic prophylaxis are predisposing factors (8,17,18). Additionally, bad oral hygiene, untreated periodontal disease and pericoronitis are thought to be influential for the formation of complications post extraction (12,17). Prevotella,Fusobacterium, Parvimonas, and Peptostreptococcus were the most common bacteria detected in patients with alveolar osteitis. (16) Bacteria from the red complex such as Treponema denticola are thought to play a major role in the formation of dry socket (14). These complexes are found in bigger quantities in patients with periodontal pocket disease. Blum et al (18) expresses, that Actinomyces and Streptococcus Mutans have been isolated from cases of alveolar osteitis. It has been proved that the bacteria secrete pyrogens that act as indirect activators of fibrinolysis in vivo (18). For a bacteria to be a causative agent of alveolar osteitis, must be isolated from a post-extraction socket and it also needs to be capable of fibrinolysis. The bacteria are limited to the bone's surface, and thus alveolar osteitis is categorized as a superficial inflammation that very seldom progress as infection.

2. Smoking

Smoking is other risk factor for AO. Due to the vasoconstrictive action of nicotine, patients that smoke present with reduced filling of the wound and therefore an increased possibility of dry socket formation (11). Some authors reported dose dependent relationship between number of cigarettes per day and incidence of AO. (12, 13,18). Apart from the vasoconstrictive action of the nicotine there are the effects of heat and suction that deteriorate the wound healing, especially in using electronic cigarettes and vapes.

3. Physical Dislodgement of the Clot

Physical dislodgement of the blood clot caused by manipulation or negative pressure created in extraction site as well could be the risk factor for AO. Because of an empty socket food particles and bacterial biofilm may hinder contact of the healing epithelium with the exposed bone. Food particles that collect inside a dry socket can also ferment due to bacteria and this may result in the formation of toxins or antigens that may irritate the exposed bone, producing an unpleasant taste or halitosis an irradiating pain.

4. Oral contraceptives

From 1960's there has been a significant increase in the usage of oral contraceptives, a matter that negatively correlates with the formation of post extraction complications such as dry socket. As reported by Azenha (8) there has been strong disagreement concerning the effect of oral contraceptives and AO. Bowe et al (11) mentions that estrogen has been shown to increase the fibrinolytic activity which leads to increased risk of alveolar osteitis due to the inability to retain the clot in the socket (13,14,18). It is suggested that estrogen indirectly activates the fibrinolytic system by increasing factors II, VII, VIII, X, and plasminogen and therefore increases lysis of the blood clot. Furthermore, this risk can be reduced if extractions are planned on the days of the cycle where estrogen levels are at their lowest (11.12).

5. Surgical trauma and difficulty of extraction

The role of surgical trauma could be due to more liberation of direct tissue activators secondary to bone marrow inflammation following the more traumatic extractions (13). Theoretically, the high forces of the extraction and surgical trauma may crush and occlude blood vessels within the surface layer of lamina dura.

Some socket bone especially of lower jaw may be dense, with few blood vessels which may be insufficient for clot formation. Surgical extractions, in comparison to nonsurgical extractions, result in increased incidence of AO especially in third molar surgery of lower jaw.

Mustafa et al (1) states, that the prevalence of AO is higher in cases of extraction of impacted teeth due to the surgical procedure. Such notion is shared with other authors (11,12,14,16,18), stating that surgical extractions increase the trauma therefore increasing the incidence of alveolar osteitis. On the contrary, according to Sharma et al (4), when teeth were extracted by open surgical technique there was no dry socket cases reported. There has been controversy about the relationship between trauma and the formation of alveolar osteitis. This may be due to a correlation between the need to section a tooth and the need for heavy luxation forces to remove a tooth or individual roots.

Some authors state that there has not been enough evidence that confirms the direct relationship between trauma, lengthy surgeries or complicated ones with the formation of dry socket (13).

The highest rate of dry socket incidence is associated with extraction of mandibular third molars. They are often deeply embedded in dense bone and have the highest incidence of root dilacerations among teeth and this obligate a dentist to use heavy luxation forces, even after root sectioning, to extract mandibular third molars, and these heavy forces may transmit to the surrounding jawbone. It is controversial if the anatomical site specificity increased bone density, decreased vascularity, and a reduced capacity of producing granulation tissue) or surgical trauma are responsible for AO. On the other hand, the alveolus of posterior mandibular teeth including the third molars site, has greater vascularity when compared to the anterior teeth. This finding contradicts the belief that alveolar osteitis is triggered just by a lack/insufficient blood supply, which is the most common hypothesis to explain why alveolar osteitis is much less common in the maxilla.

Extracting teeth that are in cancellous bone as maxillary third molars, may result in multiple sharp points of cancellous bone severing multiple blood vessels, which may ensure bleeding into the post-extraction socket and blood clot formation.

An additional matter that most authors agree is that the surgeons experience and skills are playing a role for the formation of AO due to excess trauma when the surgeon does not have enough experience. Another complication found by Azenha (8) was the flap dehiscence post-surgery. This can be due to both the surgeons' lack of experience when suturing and the lack of patient's post operative care. Flap dehiscence increases the risk for the formation of dry socket due to the exposure of the bone to the environment.

6. Vasoconstrictor in anesthesia

It is thought that the use of local anesthesia with a vasoconstrictor may lead to an increased risk of developing the occurrence of alveolar osteitis, because of the temporary local ischemia caused by the vasoconstrictor. However, the ischemia is only present for around 2 hours and is then followed by a reactive hyperemia. This challenges and causes a debate for the role of vasoconstrictors in local anesthesia in the development of alveolar osteitis(11, 12, 17, 18). Some studies reported that there is not a significant difference in AO incidence following extraction of teeth requiting infiltration against block anesthesia with vasoconstrictor (12, 17). Currently there is not enough evidence to support the use of vasoconstrictors in anesthesia leads to a higher incidence of AO.

7. Excessive Irrigation or Curettage of Alveolus

It has been suggested that excessive repeated irrigation of alveolus might interfere with clot formation. Violent and prolonged curettage might injure the alveolar bone and compromise the healing process. However, in literature lacks evidence to confirm these postulats in the development of AO.

8. Systemic illness

Some researchers have suggested that systemic diseases such as immunocompromised or diabetic patients are associated with a higher incidence of alveolar osteitis because of the impaired healing of the wound. (12,17)

9. Age and Gender

Dry socket doesn't occur often for patients aged younger than 20 (11) but occurs more frequently in those aged between 20 and 40 years of age. Literature supports the idea that the older the patient the greater the risk of AO (12, 17). However, some authors believe that there are no ties between age and incidence of dry socket (13). A study done on 2214 patients (13) suggested that alveolar osteitis incidence was seen highest in the third and fourth decades of life.

Many studies show a statistically significant prevalence of alveolar osteitis in female patients taking oral contraceptive pills or in mid-menstrual cycle. Turner et al. (4) did a study of 1274 extractions which were performed on 460 patients of which 280 were male and 180 were female, he concluded that there was no sex predilection in the occurrence of dry socket. Colby (12) found that there no relation between genders and the incidence of AO. Garcia et al. and Benediktsdòttir et al. (8, 15) state that women who take contraceptives are 5 times more likely to develop dry socket than men. In a study done by senior dentistry students on third molars on 88 patients (210 surgeries) of which the majority were female patients (70.4%) it was seen that only 1.4% of the extractions made led to the occurrence of dry socket. Garcia et al. (11) also found that in a study of 267 women, 87 of which were taking oral contraceptive pill, the incidence of dry socket was higher in those taking the contraceptives (11%) than those not taking oral contraceptives (4%) Oestrogen in oral contraceptives (11,13) shows an increase in plasma fibrinolytic activity which leads to the instability of the blood clot in the socket. A study states that dry socket occurs more frequently in females than males as there may be a relation to hormonal causes. (11) Sweet and Butler et al. (11) recorded the incident of dry socket to be 4.1% in females compared to only 0.5% in males. Many authors (12, 18) believe that females are at a higher risk of developing AO regardless of using oral contraceptives. Macgregor (12, 17) reported a 50% greater incidence of alveolar osteitis in women over men in a series of 4000 extractions. Although there is conflicting data, many studies found that patient age and female gender increased the incidence of alveolar osteitis. The prevalence is similar worldwide, and there are no documented differences in ethnicity

Diagnosis

An increase in pain intensity a 1 to 5 days after a tooth extraction and the absence of a blood clot is pathognomonic of alveolar osteitis, and additional laboratory and radiographic studies are not required. As alveolar osteitis is a superficial infection and mainly is associated with a delayed healing process, no leukocytosis would be expected.

Post-operative imaging, such as a parallel or orthopantomography, could rule out remaining tooth or bony fragments. Markers of fibrinolysis have been investigated for risk prediction in cardiovascular disease but are not very helpful and are nor routinely used in a clinical setting with AO.

Differential diagnosis

The differential diagnosis that needs to be considered primary is an infection, mainly if there are signs of inflammation beyond the extraction site. Based on the clinical evaluation of the patient symptoms that are consistent with alveolar osteitis presenting after extraction there are concerns for acute osteomyelitis, subperiosteal infection, or bony sequestra formation, MRONJ.

Prevention and treatment

According of the current discussion there is no consensus protocol on treatment strategies of AO. Management focuses mainly on symptom relief and encouraging of the healing process.

The initial treatment for alveolar osteitis starts with intra-alveolar irrigation, which removes necrotic tissue, food fragments and clot debris and reduces the bacterial load. Saghiri et al. (2) found that CHX(chlorhexidine) compared to povidone iodine has higher cytotoxic profile.
Intra-alveolar irrigation alone may not relieve pain and additional medication is needed to apply. Curettage of the dry socket is not recommended as it will expose the bone further. Application of topical local anesthetic gels or powder can relieve pain after irrigation. Oral analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) can be prescribed.

Multiple studies suggest placing a medicated dressing into the extraction socket at the time of surgery or post-operatively. After irrigation zinc oxide eugenol or other obtundent dressings (Alvogyl, Salicept) that include compounds with analgesic or antibacterial action could be used. Many dressings may slow the healing process and have to be removed from the alveolus to prevent foreign body reactions as well.
Hyaluronic acid placement after irrigation has also shown success in reducing pain and inflammation, chlorhexidine gels placing into the extraction socket have also shown treatment success. Platelet-rich fibrin (PRF) has also been investigated as a treatment option. PRF is more commonly used as a preventive measure of AO, and the efficacy of using it as a treatment is debatable in literature.(2,3,9)

Phototherapy, specifically low-level laser therapy (LLLT), has also an additional role in symptom management in AO.(3,8,9)

Topical agents using for prevention of AO

Topical use of para-hydroxybenzoic acid (PHBA), an antifibrinolytic agent, in extraction wounds decreased the incidence of AO. PHBA is available on the market as a component of Apernyl (Bayer AG, Germany), an alveolar cone that consists of acetylsalicylic acid and PHBA. In animal studies it inhibits bone healing. Aspirin in contact with bone has been found to cause local irritation and subsequent inflammation of the socket(24)
Tranexamic acid (THA), an antifibrinolytic agent, has been speculated to prevent AO when applied topically in the extraction socket and the study reveal that local plasminogen inactivation alone was insufficient to cease the development of AO(25)

Polylactic acid (PLA), a clot supporting agent, is biodegradable and was suggested that would provide a stable support for the blood clot and subsequent granulation and osteoid tissue. Follow-up studies failed to support the success of PLA and more complications are registered using PLA. (26)
The use of eugenol containing dressing to prevent development of AO were reported and local irritant effect of eugenol and the delay in wound healing due to prophylactic packing has been reported in the literature. (27)

9-aminoacridine, an antiseptic agent, was evaluated for its effectiveness in reducing the incidence of AO but was found to be ineffective(28).

The use of antibiotic for prevention of AO is controversial. Some authors suggest that using of tetracycline showed a reduction in risk of AO (15, 17), They showed that a local application of tetracycline at the extraction site proved a great reduction in risk of AO. The proangiogenic effects of tetracycline according to Mathe et al. (2) demonstrates an increase in expression of vascular epithelial growth factor, better revascularization, stimulation of odontoblastic bone formation and inhibition of collagenase and osteoclast function.

Systemic antibiotics reported to be effective in the prevention of AO include penicillins (29), clindamycin (29,30), erythromycin (30), and metronidazole(31,32). The routine prophylactic use of systemic pre- and/or postoperative antibiotics is disputed and criticized due to development of resistant bacterial strains, possible hypersensitivity, and unnecessary destruction of host commensals.

Complications

There is no evidence that alveolar osteitis can result in additional complications. There are reports for allergy reactions to medications used for treatment of AO. There are documented cases of hypersensitivity reactions to chlorhexidine or of minor adverse reactions after irrigation of an AO socket with chlorhexidine mouthwash.

Another complication of alveolar osteitis treatment is possible foreign body reactions to delivery vehicles of the intra-socket medicaments. It can delay healing and can cause granulomatous inflammation and the body's inability to phagocytose foreign materials. These topical medicaments should be removed to prevent this complication.

Patient education

The clinician should educate the patient about the risk of alveolar osteitis. The patients should be aware that smoking is risk factor for dry socket. Females should also be aware that their risk for AO can increase, especially if they are taking oral contraceptives. Detailed post-operative instructions are always recommended. The prophylactic measure with the most support is the use of chlorhexidine: chlorhexidine mouthwash before and following dental extractions. Topical application of chlorhexidine gels after extraction is also effective in preventing alveolar osteitis.

Conclusion

Dry socket is one of the most common complications following tooth extraction. The aetiopathogenesis is multifactorial and is associated with microorganisms, smoking, surgical trauma, age, gender and others. Management of AO is mostly symptomatic. The usage of Chlorhexidine before and after extraction is a satisfactory means of prevention. In addition, irrigation, dressings and proper suturing can help with the management. The patient has to be monitored regularly to ensure proper healing of the wound. More evidence is needed to prove the scientific validity of techniques of dry socket lesion treatment and to determine which factors mainly cause dry socket lesions for more effective preventing measurements.

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