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Alveolar osteitis: the current state of knowledge

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Abstract

Introduction and purpose:

Alveolar osteitis, also known as dry socket is a common complication after tooth extraction, especially third molar extraction. Taking into consideration only third molar extractions, the prevalence of dry socket reaches even 45%. The aim of this literature review was to describe current knowledge about etiology, risk factors, treatment, and prevention of dry socket.

State of knowledge:

The symptoms of alveolar osteitis most frequently are reported between the first and third post-extraction days and they include discomfort, lancing, and intense pain which radiates to the neck and ear. The etiopathogenesis of dry socket remains unclear. However, the currently accepted hypothesis describes a loss of formed after an extraction blood clot from the alveolar socket as the main cause of this pathology. Several factors may increase the risk of dry socket and include smoking, oral hygiene, female gender, oral contraceptive drugs, and anesthesia. In the treatment of alveolar osteitis, irrigation of the socket with chlorhexidine gluconate, iodopovidone, or physiological saline followed by filling the socket with intra-alveolar dressing constitute a current fundamental procedure. Plenty of substances are currently used as an intra-alveolar dressing. Part of them exhibits only pain-decreasing features, whereas some drugs can also stimulate the regeneration of treated tissue. In the prevention, the use of alveolar osteitis warm saline, antibiotics, chlorhexidine, ozone gas, or autologous platelet therapy may be useful maneuvers.

Conclusion:

This literature review summarizes the current state of knowledge about causes, risk factors, and therapeutic and preventive methods with regard to alveolar osteitis.

Keywords: dry socket; tooth extraction

1. Introduction

Dental extractions, especially extractions of wisdom teeth are a common practice. Complications following the extractions include iatrogenic and inflammatory sequelae (e.g. dry socket) [1–5].

Dry socket was described by Blum as “post-operative pain in and around the extraction site, which increases in severity at any time between one and three days after the extraction, accompanied by a partially or totally disintegrated blood clot within the alveolar socket, with or without halitosis” [6].

The prevalence of dry socket is recorded from 1% to 4% [7], but considering the frequency of dry socket after mandibular third molar extraction, it may even be 45% [8].

The symptoms most frequently are reported between the first and third post-extraction days [2,9,10] and they include discomfort, lancing, and intense pain which radiates to the neck and ear [11]. Moreover, the pain enhances during suction or chewing [6,12–17]. In the course of dry socket covering of the alveolar socket with a yellow-gray layer consisting of necrotic tissue and erythema of surrounding mucosa are often observed. What is more, halitosis can also coexist [18].

There are three types of alveolar osteitis: dry, granulomatous, and marginal superficial. The first two types are the most popular. The dry is observed when no clots form and in the granulomatous essence is an infection that coexists with the degradation of the clot [19]. Marginal superficial is temporary and does not need treatment.

In this literature review we summarized current knowledge about etiology, risk factors, treatment, and prevention of dry socket.

2. Pathogenesis of dry socket

The etiology of dry socket still remains unclear. Currently, enhanced fibrinolytic activity is considered as the main factor of this condition by many authors [11,16,20–23]. That leads to premature loss of formed after an extraction blood clot from the alveolar socket and impairs wound healing [16]. However, the cause responsible for increased fibrinolysis has not been well-known yet. Theories, which have been proposed for an explanation for that phenomenon include excessive bone trauma and bacterial etiology. It has been suggested that necrosis of the osteoblast due to excessive bone trauma destabilizes blood clot integration [21,24]. That destabilization is probably caused by the post-traumatic release of plasminogen activators (PAs) from bone surrounding the extraction socket [22]. On the other hand, some bacteria such as *Treponema denticola* and *Bacteroides oralis*, associated with acute necrotizing ulcerative gingivitis and periodontal disease demonstrated the ability to induce fibrinolysis in vitro [21,25,26]. Such activity is also presented by bacteria from *Streptococcus*, *Fusobacterium*, and *Peptococcus* species, which have been observed in the third molar extraction socket during advanced periodontitis [21]. Activation of fibrinolysis by bacteria acts through different interactions with plasminogen, which lead to its activation [22]. A recent study by Shen et al. identified specific microbial pattern present in dry socket, which included *Parvimonas*, *Peptostreptococcus*, *Prevotella*, *Fusobacterium*, *Slackia*, *Oribacterium*, and *Solobacterium* and it differed considerably from a pattern in extraction sockets without

postoperative complications [21]. Furthermore, a case-control study conducted by Aguilar-Duran et al. [27] also demonstrated a significant difference in the composition of microbiota in dry socket compared with the control group. These studies suggest an important role of a bacterial factor in the pathogenesis of dry socket and should be considered appropriately in prevention and treatment planning.

Some proteins, such as tumor necrosis factor-alpha (TNF- α), osteocalcin (OCN), and Runt-related transcription factor 2 (Runx2) may be engaged in the process of bone healing after tooth extraction. It has been observed that the level of TNF- α , a pro-inflammatory cytokine, was increased in an animal model of the post-extraction socket with a delayed healing process [28]. That overexpression was also associated with bone resorption and a decrease in new bone formation [29]. Moreover, TNF- α increases pain sensitivity through the direct impact on nociceptive neurons [30,31]. However, apart from TNF- α , many other pro-inflammatory cytokines may influence the intensity of pain in alveolar osteitis. On the other hand, Runx2 constitutes one of the pivotal regulators of osteoblastogenesis. Runx2 is responsible for the upregulation of genes promoting osteoblasts differentiation such as genes of type 1 collagen (COL-I), alkaline phosphatase (ALP), osteopontin (OPN) and mentioned before OCN [32]. As a matter of fact, lower expression of Runx2 and OCN have been observed in animal models of dry socket [28]. Thus, decreased levels of Runx2 and OCN can affect the process of bone formation. Therefore, these molecules may be used as indicators in the evaluation of dry socket to better understand its pathophysiology.

3. Risk factors

Several factors may increase the risk of dry socket. Some of them are modifiable, thanks to which reducing the risk of this complication is possible.

Oral hygiene

There was found that bacterial infections might increase the likelihood of developing dry socket [33,34]. Egauvoen [35] came to the conclusion that the risk of dry socket was higher in patients with poor oral hygiene. Chuang et al. [36] came to a similar claim. Moreover, Parthasarathi et al. [10] pointed to the evidence that periodontal diseases which led to extraction improved the risk of dry socket. It might be caused by the presence of bacteria.

Smoking

Al-Belasy [37] found that the riskiest is smoking on the same day as extraction, smoking the day after is safer. What is more, people who smoke more per day have a greater risk of dry socket. Halab et al. [38] observed that smoking 5 or more cigarettes per day has an important influence on occurring of dry socket. Beit [39] also showed that smoking increases the risk of dry socket. Moreover, nicotine has an influence on the release of catecholamine, microvascular occlusion and reduced tissue perfusion [40]. Smoking-related factors such as heat and suction might delay healing [41].

Gender

Many research works found a correlation between gender and a higher risk of dry socket. It is suggested that women are more vulnerable to this complication after extraction [35,42–45]. On the other hand, many authors showed that there is no connection between gender and the development of dry socket [2,9,46–48]. Patients who had menstrual periods had a lower risk of dry socket [49]. This discrepancy may be due to factors such as smoking,

antibiotic prophylaxis, and level of estrogen [14,46,49].

Oral contraceptives

Some authors do not find a correlation between OC and dry socket [2,9,10,34], but some authors showed that women taking OC have a higher risk of post-extraction complications [49,50]. Bienek et al. [45] found that women who were using OCs had an increased likelihood of AO. A similar conclusion came from Xu JL et al. in a meta-analysis that showed a 2-fold higher risk of alveolar osteitis. Research taken by Almeida et al. [51] suggested a greater likelihood of AO among females who were using OC. Oral contraceptives include estrogen, which might raise fibrinolysis of plasma [13,16].

Anesthesia

Eshghpour and Nejat [52] observed that epinephrine might increase fibrinolysis and weaken healing. If extraction is complicated and lengthier and needs more anesthesia more vasoconstrictor is needed, which led to a higher risk of AO [53].

Other risk factors

Some studies find a link between excessive curettage [33], root fracture, alveolar bone fracture [51] and the development of dry socket. Moreover, surgical extraction has a higher risk of AO than non-surgical cases [48]. Also, the experience of surgeons may have an influence on complications after extraction, it is related to faster and less traumatic operations [9,42,54–56]. Surgeries that were performed by dental students had more complications than extractions that were taken by dentists. What is more, the mandible has a greater bone density which may result in a greater risk of the dry socket in this area [57]. Moreover, mental stress can be also classified as a risk factor that increases the likelihood of developing a dry socket because of the possibility of fibrinolytic activity [58].

4. Current methods in the treatment of dry socket

In the treatment of alveolar osteitis, irrigation the socket by chlorhexidine gluconate, iodopovidone or physiological saline followed by filling the socket with intra-alveolar dressing constitutes a current fundamental procedure [59–62]. Irrigation of the socket removes necrotic tissue, clot debris, bacterial material, or food particles from the socket [63]. The irrigation procedure has a key role but is insufficient treatment for pain relief without intra-alveolar dressing [64,65].

The intra-alveolar dressing should be resorbable and durable in the same time, which should ensure the protection of bone from bacterial infiltration, food entering, and painful mechanical stimuli [24]. The most commonly used medicament for this purpose is Alvogyl®, which contains eugenol - for analgesic action, iodoform - for antimicrobial action, and butamben - for anesthetic action, as active ingredients. [66] Alvogyl gives a soothing effect and rapidly relieves pain symptoms [64,66]. The reduction of pain by eugenol results from the inhibition of TNF- α and the modulation of the glutamatergic receptors and opioid system [67]. Other substances currently used for intra-alveolar dressing in the treatment of dry socket include hyaluronic acid, vitamin C dressings, turmeric acid, honey, rifampicin, and penghawar jambi [62,68–72].

However, the above-mentioned methods of treatment do not demonstrate regenerative character, but only ensure pain relief and protection of wound. Currently, there are many

therapeutic approaches, which focus on the regenerative aspect of dry socket treatment. These methods, enhancing the natural regenerative properties of cells, include platelet-rich fibrin or plasma (PRF/PRP) therapy, concentrated growth factor (CGF) therapy, low-level laser therapy (LLLT), and low-intensity pulsed ultrasound therapy (LIPUS) [63,73–76].

Autologous platelet therapy has constantly gained popularity in the last decades in many medical fields, such as maxillofacial surgery or esthetic medicine [77,78]. Primarily, platelet-rich plasma (PRP) was used in this method of treatment. Rutkowski et al. [79] demonstrated PRP applied at the extraction site as a potentially effective agent in the prevention of dry socket. However, this application should be more investigated in further clinical trials [80]. Platelet-rich fibrin PRF is the next-generation agent representing autologous platelet treatment. The PRF therapy enhances tissue healing and significantly decreases pain symptoms occurring in alveolar osteitis. The increase of tissue healing is achieved through releasing of growth factors including interleukin-1 (IL-1), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and transforming growth factor (TGF), and TNF- α , which increase angiogenic and fibroblastic activity [6,62,63]. On the other hand, pain control is obtained through the secretion of some molecules such as opioid peptides, interleukins, and insulin-like growth factor type 1 (IGF-1) [81]. The newest autologous plasma therapy agent – CGF also acts through the secretion of multiple growth factors, which may provide tissue regeneration [82]. In a recent study, Keshini et al. [66] evaluated the outcome of treatment of alveolar osteitis with PRF dressing compared with conventional Alvogyl dressing. In a group of patients treated with PRF, improved wound healing has been observed and pain control was comparable with that achieved in the group treated with Alvogyl. The effectiveness of dry socket treatment with PRF has been proven by other clinical studies [83–86]. Moreover, PRF is inexpensive, biocompatible, and simple to obtain method of treatment, because it is derived from the patient's own blood [87]. Therefore PRF represents a viable treatment alternative for conventional medications used in dry socket therapy.

LLLT is another potential method of treatment that may significantly decrease the pain in dry socket. In stomatology, used wavelengths range from 635 to 950 nm [88]. LLLT acts through photochemical reaction, which promotes the production of PDGF, the proliferation of fibroblasts, collagen production, and bone regeneration without thermal tissue damage [7,89,90].

Given the significant role of a bacterial factor in the pathogenesis of dry socket, antibacterial agents also should be considered in the therapy of this pathology. Indeed, many of them are used in the clinical management of dry socket and include tetracycline, metronidazole, azithromycin, amoxicillin, and lincomycin [11]. These drugs can be used both for treatment and prevention of dry socket. The preventive aspect of antibacterial agents has been discussed in section 5. of this paper. It has been demonstrated that some antimicrobials, such as tetracycline exhibits also have proangiogenic features. Tetracycline can stimulate new bone formation, and osteoclast activity suppression, enhance the expression of vascular endothelial growth factor (VEGF), and promote revascularization of tissues [91]. These additional characteristics favor tetracycline among other antimicrobials in terms of regenerative aspects of alveolar osteitis therapy. Recently, Cebi evaluated the outcomes of dry socket treatment with intra-alveolar irrigation with clindamycin and rifampicin compared with sterile saline [62]. The use of clindamycin and rifampicin was superior to the use of physiological saline in terms of alveolar mucosa healing. Moreover, clindamycin demonstrated a greater reduction of pain than rifampicin and saline. Antibiotics for dry socket treatment are often administered locally into the alveolar socket, in the foam form. The systemic route of administration should be limited to patients with immunosuppression [13,16,63,83,92]. However, the use of systemic antibiotics should not replace the intra-alveolar antibacterial treatment [63].

5. Prevention

There are several ways to prevention from the development of dry socket. The most popular methods are included: chlorhexidine, antibiotics, and warm saline mouth rinse. Ozone gas, platelet-rich plasma, and platelet-rich fibrin due to their properties may be applied to prophylaxis.

Chlorhexidine

Chlorhexidine is available as a solution and gel.

Shepherd [93] and Sridhar et al. [94] in their works concluded that using CHX gluconate solution before and after surgical extraction has a preventive effect on the development of dry socket. Metin et al. [95] showed that satisfactory is using 0.2% CHX solution only after extraction for 7 days. Similar results were published by Caso et al. [92]. According to Delilbasi et al. [96], the efficiency of chlorhexidine solution can be improved by adding amoxicillin with clavulanic acid.

CHX gluconate gel 0.2% is characterized by higher bioadhesive properties and is more effective than CHX gluconate solution 0.12% Hita-Iglesias et al. [97]. What is more, the results of the meta-analysis showed that using topical metronidazole and CHX gel is effective in reducing AO [98].

Warm saline mouth rinse

It has been proven that warm saline mouth rinse has the same effectiveness as 0.12% CHX solution in the prevention of AO after third molar extraction ($P=0.648$) [99].

Antibiotics

Arteagoitia et al. [100] showed that amoxicillin with clavulanic acid has an influence on reducing the occurrence of dry socket. Moreover, it was proved that application only amoxicillin does not reduce the incidence of AO. However, Olusanya et al. [101] claimed that amoxicillin may be efficient not only in reducing AO but also in the prevention of trismus and swelling.

Sanchis et al. [102] found that using tetracycline has no influence on the development of AO. On the other hand, Hedström and Sjögren [25] concluded that tetracycline might decrease the risk of dry socket. What is more, it was concluded that tetracycline shows proangiogenic effects and encourages osteoblastic bone formation [91,103]. Øyri et al. [104] presented in their clinical trial that patients after third molar extraction with an oxytetracycline-impregnated drain had about 6 times less incidence of dry socket than the control group.

Both metronidazole [105] and azithromycin [106] do not have a significant influence on reducing the appearance of AO. However, Bascones-Martinez et al. [107] found that azithromycin might reduce alveolar osteitis more effectively than saline in the population of women using OCs and tobacco.

Ozone gas

It has been proven that O₃ has properties to stimulate angiogenesis [108,109]. Moreover, ozone gas has an influence on oxygen metabolism and the antioxidant defense system [110]. It has been found that O₃ has a bactericidal action [111,112]. Thanks to its properties and effect ozone gas is recommended to improve healing and reduce the risk of DS [113].

Platelet-rich plasma (PRP)

PRP encourages angiogenesis, chemotaxis, and cell proliferation because of including growth factors [114,115]. What is more, PRP contains intra- and extra-platelet components. All of these elements help tissue regeneration [116,117]. Rutkowski et al. [79] concluded that using PRP may reduce complications in the form of a dry socket. However, Barona-Dorado et al. [80] suggested that more clinical trials are needed.

Platelet-rich fibrin (PRF)

PRF which contains leukocytes, cytokines, and platelets, improves clot formation [118,119]. Eshghpour et al. [120] found that PRF has usage in reducing the development of DS.

6. Conclusion

This literature review summarizes the current state of knowledge about causes, risk factors, and therapeutic and preventive methods with regard to alveolar osteitis. A dry socket is one of the most common complications after tooth extraction, especially the third mandibular molar. Currently, enhanced fibrinolytic activity is considered the main factor of this condition. There are known risk factors that increase the likelihood of this complication occurring. Patients should be informed about them and pay particular attention to those that are affected. Especially when it comes to smoking, rinsing the mouth intensively, or taking oral contraceptives. There are several ways to prevent and treat. Preventive prescription of antibiotics is not recommended due to the numerous side effects. PRF appears to be the best option for prevention and treatment. Due to the lack of generalized treatment guidelines, the choice of the appropriate method depends on the dentist after considering the advantages and disadvantages of each technique of treatment. Further research is necessary to unify and find the best treatment option.

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