Recent advances in the management of dry socket - A review
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ABSTRACT
Alveolar osteitis is a well-known post-extraction complication. It is commonly known as “dry socket,” a common post-operative problem that results in severe pain. The prevention methods include avoiding smoking before and after surgery; atraumatic surgery; the use of antibiotics, such as azithromycin, chlorhexidine rinse or gel, use of sutures and local hemostatic, low level laser, Alvogyl and the Salicept patch, eugenol on a gauze strip, and a thermosetting gel containing 2.5% prilocaine and 2.5% lidocaine. Plasma rich in growth factors can also be effective in the reduction of dry socket incidence. This article reviews about the new advances, drugs, and materials used for dry socket management.

KEY WORDS: Alveolar osteitis, Drugs, Dry socket, Extraction, Management, Pain

INTRODUCTION
Alveolar osteitis (dry socket) is one of the most common complications after extraction or surgical removal of tooth. It is commonly known as “dry socket.” The other terms used are alveolar osteitis, alveolitis, localized osteitis, alveolitis sicca dolorosa, localized alveolar osteitis, fibrinolytic alveolitis, septic socket, necrotic socket, alveolitis, localized osteomyelitis, and post-operative alveolitis. This condition remains as the most common post-operative problem that results in severe pain and also interferes with the healing process that takes place after a tooth extraction. Dry socket was first described by Crawford in 1896. The name dry socket is used because the socket has a dry appearance after the blood clot is lost and debris washed away. Hermesch et al. classified this complication into three types: Superficial alveolitis marginal, suppurative alveolitis, and dry socket. In 1960, Hansen described alveolitis simplex as accidental loss of the clot and the absence of pain, in addition to alveolitis sicca dolorosa and granulomatous alveolitis. Blum defined alveolar osteitis as “post-operative pain inside and around the extraction site, which increases in severity at any time between the first and third days after the extraction, followed by a partial or total disintegrated blood clot within the alveolar socket with or without halitosis.” The incidence of dry socket ranges from 0.5 to 5% for all routine extractions but can reach up to 38% for extractions of impacted mandibular third molars.

PATHOGENESIS
The pathogenesis and cause for dry socket are not clear; however, several theories have been proposed on the etiology of dry socket. They are trauma during extraction, bacterial infection, biochemical agents, and fibrinolysis. Fibrinolysis is the most accepted theory. Fibrinolysis is a normal physiological process that removes fibrin deposits by enzymatic digestion of the fibrin meshwork into smaller soluble fragments. Local increase in fibrinolysis occurs in response to bleeding. In 1973, Birn showed that fibrinolytic activity is increased in dry socket.

In a normal post-extraction site, fibrin clot is formed by thrombin and fibrinogen, and over this, the epithelium migrates. New blood vessels are formed inside the clot followed by formation of granulation tissue, and this clot degrades through the activity of fibroblast and fibrinolysis.

However, in case of dry socket, kinases are liberated during inflammation through direct or indirect
activation of plasminogen in the blood. These kinases cause lysis and destruction of the blood clot. Tissue or plasma pro-activators and activators convert the plasminogen to fibrin, which causes the dissolution of the clot by disintegration of fibrin. This plasminogen pathway activation can be of two types either direct (physiologic) or indirect (non-physiologic) activators. Direct activators are released to the alveolar bone cells after trauma. Indirect activators are released by bacteria. Direct activators are divided into extrinsic and intrinsic. Direct extrinsic activators are tissue plasminogen activators and endothelial plasminogen activators. Direct intrinsic activators include the components of plasma such as urokinase and factor XII.[3,7,8]

**RISK FACTORS FOR DRY SOCKET**

Many factors play an important role in formation of dry socket, for example, age, gender, extraction site, trauma, microorganisms, smoking, lack of operator experience, local anaesthesia with vasoconstrictors, remnants of bone or root fragments, systemic disease, radiotherapy, oral contraceptives, excessive irrigation, or curettage.

**Age**

Dry socket occurrence is higher in the age group of 21–30 years. They are some studies which concluded that the surgical removal of impacted mandibular third molars should be carried out well before the age of 24 years since older patients are at greater risk of postoperative complications in general.[2,3,9]

**Gender**

Dry socket occurs more common in females than males due to hormonal changes. Sweet and Butler (1938) showed that the occurrence of dry socket in females is 4.1% compared to males. In South Asia, male consumes more alcohol and tobacco as compared to female, yet the occurrence is more in female.[3,7,9,10]

**Extraction Site**

Dry sockets occur more frequently in the mandible than the maxilla due to thick cortical bone, resulting in poor perforation of blood supply the mandible. An incident of dry socket is more common in mandibular third molar region. Increased bone density, decreased vascularity, and reduced capacity of producing granulation tissue are responsible for the site specificity.[2,3,9,11]

**Trauma**

Difficult extractions occur in older and dense bone which may have a decreased vascularity. Birn proposed that trauma from extraction or aggressive curettage can cause the inflammation which leads to the release of cell mediators. This may lead to fibrinolytic activity. Physical dislodgement of the blood clot due to manipulation or negative pressure created through sucking on a straw or trauma would be a major contributor to dry socket.[2,3,11]

**Smoking**

Smoking decreases the neutrophil chemotaxis and phagocytosis, which in turn stops the production of immunoglobulin. Smokers have a higher incidence of dry socket that is 12% than in non-smokers (4%), but there is a strong association between the amount of smoking and the occurrence of dry socket. Studies reported that among patients with a total of 400 surgically removed mandibular third molars, those who smoked half-pack of cigarettes per day had four-to five-fold increase in dry socket compared to non-smoking patients.[3,11]

**Vasoconstrictors**

Vasoconstrictors in the local anesthetizes used for extraction may also contribute to the formation of dry socket. Studies suggested that the use of local anesthesia with vasoconstrictors increases the incidence of dry socket. Vasoconstrictors cause temporary local ischemia which increases the risk of developing alveolar osteitis. Lehner found that dry socket frequency increases with infiltration anesthesia because of temporary ischemia. However, some studies showed that ischemia lasts for 1–2 h and is followed by reactive hyperemia, which makes it irrelevant in the disintegration of blood clot. It is recently accepted that local ischemia due to vasoconstrictor in local anesthesia has no role in the development of dry socket.[3]

**Systemic Disease**

Studies suggested that systemic disease could be associated with dry socket. Immunocompromised or diabetic patients being prone to development of dry socket due to altered healing.[2,11]

**Microorganisms**

Bacteria may also play a contributing factor in the etiology of dry socket. Most studies support that bacterial infections are a major risk for the development of dry socket. The frequency of dry socket increases in patients with poor oral hygiene and pre-existing local infection such as pericoronitis and advanced periodontal disease. Delayed healing may occur due to the presence of microorganisms such as *Enterococcus*, *Streptococcus viridans*, *Bacillus coryneform*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Citrobacter freundii*, and *Escherichia coli*. Nisan et al. (1983) proposed that the anaerobic bacteria *Treponema denticola* showed plasminogen like fibrinolytic activity.[2,3,11]

**Lack of Operator Experience**

Many studies claim that operator’s experience is a risk factor for the development of dry socket. Larsen concluded that surgeon’s inexperience could be related...
to trauma during the extraction, especially surgical extraction of mandibular third molars.

**Bone/Root Fragments Remaining in the Wound**

Many studies suggest that bone or root fragments and debris in the extraction socket could lead to disturbed healing and contribute to the development of dry socket. Simpson showed that small bone/root fragments are commonly present after extractions and these fragments do not cause complications as they are often externalized by the oral epithelium. \(^4\)

**Oral Contraceptives**

Certain studies prove that the dry socket is more common in females than males. It is 3 times more common in female than male. Women on oral contraceptives are more prone than those who are not taking them. Increase in use of oral contraceptives positively correlates with the incidence of dry socket. Certain hormones like estrogens play a significant role in increasing fibrinolytic process, and it is proved to indirectly activate the fibrinolytic system and therefore increase lysis of the blood clot. \(^5\)\(^6\)

**Radiotherapy**

Radiotherapy to the head and neck results in a decreased blood supply to the mandible. \(^3\)

**INCIDENCE**

The incidence of the dry socket has been reported as 3–4% following routine dental extractions ranging from 1% to 45% after the removal of mandibular third molars. The incidence of dry socket is 10 times more in mandible when compared to maxilla ranging from 1 to 4% of extractions; dry socket may affect women in a ratio of 5:1 with respect to males. The incidence of dry socket is 10 times more in mandible when compared to maxilla ranging from 1 to 4% of extractions. Dry socket may affect women in a ratio of 5:1 with respect to males due to changes in endogenous estrogens which occurs during the menstrual cycle. These estrogens activate the fibrinolytic system in an indirect way in females. This great variability in the reported incidence of dry socket is largely due to differences in diagnostic criteria and in the methods of assessment; in intermingled and conflicting data from non-impacted, partially impacted, and fully erupted mandibular third molars extractions; in dry socket prevention and postoperative management of extraction sites; and in patient populations with respect to age or to surgical techniques or surgical skill. Furthermore, there is a large variation of pain thresholds within the population. Studies claiming 1% incidence lack clinical credibility, whereas those with unusually high incidence rates (>30%) suggest that other unaddressed variables were introduced or the sample size was insufficient. The better-controlled studies have reported the incidence as 25–30% after the removal of impacted mandibular third molars, and this review concludes that dry socket occurs approximately 10 times more frequently following the removal of these teeth than from all other locations. \(^2\)\(^7\)

**TREATMENT**

**Antimicrobial Photodynamic Therapy (APDT)**

APDT seems to be a new and promising possibility for the prevention of alveolar osteitis. Certain studies showed the low occurrence of dry socket when APDT was used. With APDT dry socket occurred at one extraction site and in the control group without APDT, it occurred in 13 cases. \(^3\)

**Low-Level Laser Therapy (LLLT)**

Laser irradiation will significantly decrease pain, swelling, bruising, and inflammation after an extraction, thus requiring a decreased need for postoperative analgesics. The speed of healing of the extraction site will also be increased, and there will be a reduced occurrence of a dry socket. In cases of a dry socket use, LLLT will dramatically decrease the pain and increase the growth of fibroblast.

On comparing the efficacy of LLLT, SaliCept, and Alvogyl in the management of alveolar osteitis, it was found that LLLT increases the speed of wound healing and reduces inflammation when compared to Alvogyl and SaliCept. LLLT is applied after irrigation of socket with continuous-mode diode laser irradiation (808 nm, 100 mW, 60 s, 7.64 J/cm\(^2\)). \(^1\)\(^1\)\(^3\)\(^4\)

**Biodegradable Polymers**

Polylactic acid, a biodegradable ester, acts as a clot supporting agent by providing a stable support for blood clot. The use of polylactic acid granules decreases the incidence of dry socket. \(^12\)

**Oxidized Cellulose Foam (OCF)**

Oxidized cellulose form is a potent hemostatic, the use of which reduces the incidence of dry socket. The incidence of alveolar osteitis in patients treated with OCF was found to be 5% which was found to be significantly lower than in patients who were not treated with OCF. \(^12\)

**Platelet-rich Fibrin (PRF)**

PRF can be successfully used for the treatment of dry socket. According to use, the advantages of this method are that it is easy to perform, can be performed by every dentist, and has a rapid influence on pain levels, followed by a quick epithelization of the socket. Certain studies showed around the 8th day after the operation complete epithelization was observed. \(^15\)\(^16\)
Chlorhexidine
There are mixed opinions regarding chlorhexidine as an effective preventative measure, but there is a greater quantity of stronger evidence demonstrating its efficacy. There is some evidence to show that the effect is greater with 1% chlorhexidine in comparison with 0.2% in addition, it appears to have no impact whether chlorhexidine application is pre-, intra-, or post-operative, or if in liquid or gel form, although a significant reduction in dry socket incidence has been observed when using the gel. Multiple perioperative rinses (continued for several days post-extraction) with chlorhexidine have been shown to be more effective than a single rinse on the day of surgery. Nevertheless, the risk of hypersensitivity is present no matter what the application and should be considered in the dental setting whenever chlorhexidine may be indicated. This could be more important if considering intra-alveolar irrigation as opposed to oral rinses alone due to the increased direct contact with the bloodstream. However, clinicians should not be deterred from using chlorhexidine where it is indicated, as long as the allergy status of the patient is negative. With such widespread use within medicine and surgery, rare cases of anaphylaxis will occur, but with such a long history of being a safe and effective antimicrobial, it should not be avoided unnecessarily. According to a recent study, there was a significant association between the frequency of dry socket and application of chlorhexidine gel. The relative risk of developing dry socket in sockets received chlorhexidine gel was 0.22 of the control sockets.

Chlorhexidine gel was effective in reducing the risk of dry socket development. Hence, it could be applied as a prophylactic approach, especially in patients with high risk of developing dry socket.[2,3,8,17]

SaliCept
SaliCept is a patch that can be applied directly to the extracted socket. SaliCept is shown to be an effective treatment for dry socket and comparable with Alvogyl. However, despite praise in the literature, it is unclear as to whether this product is still available on the market, even though it has other applications within oral medicine. It may be beneficial to explore the potential of Aloe vera derivatives in the management of dry socket on the basis of salient’s success, as very little research around this area is available.[14]

Pastille GECB
In some study, the use of pastille GECB has more effect in treating dry socket and reduces pain when compared to zinc oxide eugenol.[13,14]

Plasma Rich in Growth Factors (PRGF)
In comparison with normal healing sockets, dry sockets with a bacterial presence have been shown to have lower levels of growth factors present within 14 days post-extraction and a lower density of blood vessels, bone formation, and connective tissue within 7 days post-extraction. PRGF also includes plasma proteins, coagulative factors, signaling proteins, and platelet granules, and these factors help in pain relief and increase the healing rate. These factors also trigger differentiation, increase collagen synthesis, increase chemotaxis, which leads to increases angiogenesis, and induce fibroblast.

Haraji et al. compared between the zinc oxide eugenol dressing and PRGF with gelatin sponge in the treatment of dry socket and reported that patient’s healing was better in patients treated by PRGF with gelatin sponge than the patients who were treated by zinc oxide eugenol, but symptomatic pain relief was faster in the second group. This is certainly an intriguing concept which has seemingly promising results, but with such complex preparation and specialized equipment, this is unlikely to become a realistic treatment modality for dry socket.[18]

Simvastatin
Simvastatin belongs to a group of drugs called as statins. These simvastatin simulates the bone anabolic factor such as vascular endothelial growth factors and bone morphogenic protein, which helps in osteoblast differentiation and mineralization. Local application of simvastatin induces bone formation in extraction sockets. Application is very simple and provides a very cost-effective way of faster bone regeneration following tooth extraction. However, the study with larger sample size and longer follow-up is needed before drawing any definitive conclusion. Further research is also needed to make out the difference in bone formation on different anatomic sites on local application of simvastatin.[19]

Alveolar Socket Preservation with Demineralized Bovine Bone Mineral and A Collagen Matrix
The application of DBBM particles covered with a collagen matrix to the extraction sockets allowed the preservation of an adequate hard and soft tissue volume to place implants, without the need for further augmentation procedures 6 months after tooth extraction. From a histological point, the xenograft particles were partially resorbed and surrounded by newly formed bone, supporting the effectiveness of this material in promoting socket preservation. The collagen matrix demonstrated clinical efficacy for creating sufficient width and thickness of newly formed keratinized tissue, even if left exposed.[20]

Topical Antibiotics
Topical applications such as clindamycin, tetracycline, and metronidazole all have evidence to show effectiveness in reducing dry socket incidence, but
it is tetracycline which appears to have the strongest position as a topical agent typically, studies have involved placement of a resorbable gelatin sponge into the socket, impregnated with a solution of the antibiotic. Alternatively, antibiotics can be available in gel form, notably metronidazole gel which is more commonly used in the treatment of periodontal disease and available in preparations such as elyzol. While topical antibiotics are certainly proven to be effective in dry socket prevention, a clinician must also consider cost-efficiency, as more readily available agents with better shelf-life may produce a similar result.[2,3,14,15]

**Antifibrinolytic Agents**

Tranexamic acid and para-hydroxybenzoic acid (PHBA) are both antifibrinolytic agents, which inhibit both plasmin and plasminogen, both have been investigated as preventative measures for treating dry socket. Tranexamic has only been shown to have a marginal reduction in dry socket incidence, with no significant effect demonstrated. PHBA was previously available in Apernyl cones - a resorbable medicament originally contains 3 mg PHBA and 32 mg acetylsalicylic acid. Many studies into its effect on dry socket prevention produced favorable results. However, it has been speculated that there may be some element of confusing due to the presence of acetylsalicylic acid, with it having a local anti-inflammatory effect that reduces the inflammatory component of dry socket. The literature surrounding antifibrinolytic agents in regard to the management of dry socket seems to reflect a passing trend. Though antifibrinolytic agents are still available on the market, Apernyl no longer contains PHBA.[2,3,7]

**Surgical Intervention**

Curettage can be used as a method of treatment for dry socket. However, it is not recommended due to the induction of more pain. Curettage involves administration of anesthesia, surgical debridement of socket, and primary closure by advancement flap. Turner stated that curettage and removal of granulation tissue resulted in fewer visits than zinc oxide eugenol or iodoform gauze with eugenol technique.[13]

**Future Scope**

From many survey, it is observed that there is no proper dosage form for the prevention and management of dry socket. If a dosage form was developed for treating dry socket, it should provide a decrease bacterial infection, increase wound healing, act as hemostatic, and provide an analgesic effect.

**CONCLUSION**

The occurrence of dry socket is unavoidable. It can be prevented by copious use of irrigation, antibiotics, and maintenance of oral hygiene. Although there is no specific treatment for dry socket, eugenol dressings and curettage reduce the incidence of it. Despite many years of study about the most commonly encountered and unpleasant post-operative condition in patients, treatment and many prevention techniques were formulated. Studies have varying designs and statistical biases, lack analysis, or consist of individual opinions. The full etiology of alveolar osteitis has not been established, and varying descriptive definitions and diagnostic criteria exist to explain alveolar osteitis. Research attempting to prevent this complication yields no single universally acceptable method or success. However, a multitude of intra-alveolar medicaments is suggested in the literature and is available on the market. Even though complications/severe reactions from preparations placed in the socket are rare, almost all have reported some negative reactions. If adverse reactions do occur, the current body of literature does not provide enough support for the treating practitioner. The formula to the management of this complication should begin with patient education and patients with identifiable risk factors should be informed in detail about this anticipated complication. Further investigations and well-designed studies are necessary to draw firm conclusions and to clarify this complication.

**REFERENCES**


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