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Contemporary views on dry socket (alveolar osteitis): a clinical appraisal of standardization, aetiopathogenesis and management: a critical review

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Abstract. The objective of this article is to harmonize descriptive definitions for the condition known as alveolar osteitis and to critically review and discuss the aetiology and pathogenesis of alveolar osteitis. In addition, the need for the identification and elimination of risk factors as well as the preventive and symptomatic management of the condition are discussed. The aim of this critical review is to provide a better basis for clinical management of the condition. A meta-analysis of data was not done.

Key words: alveolar osteitis; fibrinolysis; prophylactic management; symptomatic management.

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Introduction

One of the most common postoperative complications following the extraction of permanent teeth is a condition known as dry socket. This term has been used in the literature since 1896, when it was first described by CRAWFORD[22]. Since then, several other terms have been used in referring to this condition, such as alveolar osteitis (AO), localized osteitis, postoperative alveolitis, alveolalgia, alveolitis sicca dolorosa, septic socket, necrotic socket, localized osteomyelitis, and fibrinolytic alveolitis.

So far, authors do not agree on terminology for this condition. In his seminal articles, Birn labelled the complication 'fibrinolytic alveolitis'[5,7,11] which is probably the most accurate of all the terms, but is also the least used in the literature. In most cases, the more generic lay term 'dry socket' tends to be used. In this article, the condition will be referred to as alveolar osteitis, AO.

Search strategy and literature selection criteria

A computerized literature search using MEDLINE was conducted searching for articles published from 1968–2001. Mesh phrases used in the search were: dry socket, alveolar osteitis, localized osteitis, fibrinolytic alveolitis, prevention and dry socket, management and dry socket. The search was completed by manual searches of selected internationally reviewed journals. Only papers in English and those which stated the diagnostic criteria were reviewed. For the management section randomized controlled and controlled trials were identified to provide the most powerful evidence followed in decreasing order of strength by cohort studies, case-control studies, surveys and case-series.

Standardization of AO

Unfortunately, the literature is replete with varying descriptive definitions for

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Table 1. The variety of definitions used in the literature for the clinical assessment of alveolar osteitis

Author(s) and Year	Definition
Akota et al.[1] (1998)	The presence of a disintegrated blood clot, and/or increased pain in the socket region, and/or foul odour, and/or exudate or pus in the socket
Berwick & Lessin[4] (1990)	Evidence of a denuded socket with or without necrotic debris or foetid breath
Birn[11] (1972)	Partial or complete loss of the blood clot, exaggerated pain radiating to the ear and temporal region, and a putrid odour
Bloomer[12] (2000)	Complain of pain in the extraction site and the presence of exposed bone or necrotic debris
Crawford[22] (1896)	Severe, neuralgiform, irradiating pain and partial or total disintegration of the blood clot in the socket have to be present simultaneously
Davis et al.[23] (1981)	Loss of an adequate clot and development of delayed pain, 2 to 5 days after surgery, that was suffice to require active medical intervention
Fridrich & Olson[26] (1990)	Absence of a demonstrable clot and symptomatic pain in or around the surgical site 36 h after surgery that was suffice to require active medical intervention
Hermesch et al.[46] (1998)	Loss of blood clot and/or necrosis of blood clot and persistent or increasing postoperative pain after the surgery, with throbbing pain at the surgical site that is not relieved with mild analgesics
Laird et al.[34] (1972)	Evidence of breakdown of clot together with the characteristic foul odour
Larsen[35] (1991)	Persistent or increasing postoperative pain beginning after the second day, which is associated with necrotic tissue in the socket, exposed bone, or loss of the clot on clinical examination
Meechan et al.[41] (1987)	Pain from the extraction site and empty or necrotic material containing socket
Ritzau et al.[50] (1992)	The simultaneous presence of a severe irradiating pain originating from the empty socket and the disintegration (partial or total) of the socket coagulum
Rood & Murgatroyd[51] (1979)	A painful socket which is increasing in severity 24 h after the extraction
Sorensen & Preisch[61] (1987)	Return of patient 2 or more days postoperatively complaining of pain in the extraction area and the presence of a denuded socket on clinical examination
Sweet & Butler[64] (1977)	Severe pain, foul, greyish exudate, and necrotic odour and debris at the extraction site
Tjernberg[67] (1979)	Disintegrated blood clot in combination with pain that is not adequately relieved by analgesics
Vedtofte et al.[71] (1974)	Complete or partial loss of the blood clot with denuded bone in the alveolus and severe irradiating pain

AO, usually owing to an inconsistency in diagnostic criteria (Table 1). There is a lack of absolute and objective clinical criteria and varying study designs as well as efficacy variables between studies, conflicting data (including intermingled data from 'cases', 'teeth', and 'surgical sites'), anecdotal reports, poorly designed studies, statistical biases or lack of analysis, and individual opinions camouflaged as scientific evidence make a scientifically sound comparison very difficult. Hence, a systematic review was not done as there is insufficient evidence available. The variety of subjective diagnostic definitions for AO appeared to be so great that this author was tempted to come up with a descriptive definition that could be used universally as a standardized definition for AO: *postoperative pain in and around the extraction site, which increases in severity at any time between 1 and 3 days after the extraction accompanied by a partially or totally disintegrated blood clot within the alveolar socket with or without halitosis.* It is necessary to exclude any other cause of pain on the same side of the face. Occasionally, patients may also complain of a very unpleasant taste.

The denuded alveolar bone may be painful and tender. Some patients may also complain of intense continuous pain irradiating from the empty socket, normally to the ipsilateral ear, temporal region or the eye. Regional lymphadenopathy is also noted occasionally. Trismus is a rare occurrence, but in cases of mandibular third molar extractions it is sometimes seen and is probably due to lengthy and traumatic surgery. True AO, in which premature partial or total loss of a formed extraction socket coagulum occurs, must be distinguished from conditions in which pre-existing alveolar bone hypovascularity, such as generalized vascular or haematological disorders, radiotherapy-induced osteonecrosis, osteopetrosis, Paget's disease and cemento-osseous dysplasia[73] prevent initial formation of a coagulum.

AO remains a common postoperative problem resulting in pain, lost days at work, loss of productivity, and return surgical practice/hospital visits. This is also costly to the surgeon, as 45% of patients who develop AO typically require at least four additional postoperative visits in the process of managing this condition[47].

Incidence

The incidence of AO has been reported as 3–4% following routine dental extractions[51] and ranges from 1% to 45% after the removal of mandibular third molars[3,26,54,58]. This great variability in the reported incidence of AO 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 intraoperative and postoperative management of extraction sites; in patient populations with respect to age or to surgical techniques or surgical skill. Also, 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[26,37] and this review concludes that AO occurs approximately 10 times more frequently following the removal of these teeth than from all other locations.

Onset and duration

Early and recent studies have reported that AO onsets 1–3 days after tooth extraction[26,45,51] and within a week between 95% and 100% of all cases of AO have been registered[24]. It is highly

unlikely for AO to occur before the first postoperative day, because the blood clot contains anti-plasmin that must be consumed by plasmin before clot disintegration can take place. The duration of AO varies to some degree, depending on the severity of the disease, but it usually ranges from 5–10 days.

Aetiology

Myriad aetiological and precipitating factors for AO have been suggested in the literature. Although AO is generally believed to be of multifactorial origin, the following have been implicated most commonly as aetiological, aggravating and precipitating factors:

1. Oral micro-organisms and AO

The role of bacteria in AO has long been postulated[39,51]. This concept was supported by various reports of the increased frequency of AO in patients with poor oral hygiene[48], pre-existing local infection such as pericoronitis and advanced periodontal disease[55]. A causative relationship with bacteria has further been strengthened by the reduced incidence of AO in conjunction with antibacterial measures[19,42,51,62].

There have been numerous attempts to isolate a specific causative organism. The possible association of *Actinomyces viscosus* and *Streptococcus mutans* in AO was highlighted by Rozanis et al.[54] where they demonstrated delayed healing of the extraction socket following the inoculation of these organisms in animal models.

Nitzan et al.[44] showed a possible significance of anaerobic organisms (which are also the predominant organisms in pericoronitis) in relation to the aetiology of AO.

Nitzan et al.[44] observed high plasmin-like fibrinolytic activities from cultures of the anaerobe *Treponema denticola*, which is also known to be a putative micro-organism in the development of periodontal disease. In addition, AO virtually never occurs during childhood, a period when this organism has not yet colonized the mouth.

As bacteria increase in number in AO, and because certain species constantly secrete pyrogens at the basal level, it has been postulated that bacterial pyrogens are indirect activators of fibrinolysis *in vivo*[17]. Catellani[17] studied the efficacy of bacterial pyrogens for treating thromboembolic disease where pyrogens injected intravenously produced a sustained increase in fibrinolysis.

2. Difficulty and trauma during surgery and AO

Most authors agree that trauma and difficulty of surgery play an important role in the development of AO[2,11,13,21]. Surgical extractions that involve the reflection of a flap and sectioning of the tooth with some degree of bone removal have also been reported to be more likely to cause AO[37]. One interesting study indicates that less experienced surgeons caused a significantly higher incidence of complications after the removal of impacted third molars; the most common complication being AO[60].

Excessive trauma has been known to result in delayed wound healing[11]. This has been attributed to the compression of the bone lining the socket, which impairs its vascular penetration. Alternatively, excessive trauma may result in thrombosis in the underlying vessels. Several authors have associated trauma with a reduction in tissue resistance and consequent wound infection[36,70].

Birn[11] proposed that trauma during extraction damages the alveolar bone cells, causing inflammation of the alveolar bone marrow and the subsequent release of direct tissue activators into the alveolus, where they may precipitate fibrinolytic activity, thus playing a major role in the pathogenesis of AO.

3. Roots or bone fragments remaining in the wound and AO

Birn[11] suggested this complication as a possible cause of AO. Simpson[59] has shown that such fragments are commonly present after normal extraction or surgical removal of teeth, and that small bone and tooth remnants do not necessarily cause complications during healing as they are often externalized by the oral epithelium. The results were derived after histological examination of healing extraction wounds in monkeys.

Despite a lack of scientific evidence for these remnants to be the causative factor for AO, it seems logical that fragment and debris remnants could lead to disturbed wound healing, and thereby possibly contribute to the development of AO.

4. Excessive irrigation or curettage of the alveolus after extraction and AO

It has been postulated that energetic repeated irrigation of the alveolus might interfere with clot formation and give rise to infection, and that violent curettage might injure the alveolar bone[11]. However, scientifically sound investigations confirming these contributions in the development of AO are lacking. Furthermore, since energetic excessive irrigation is not easily measurable, it is difficult for it to be assessed.

5. Physical dislodgement of the clot and AO

It has not been substantiated that the physical dislodgement of the blood clot either by manipulation or negative pressure, such as sucking on a straw, would be a major contributory factor to AO.

6. Local blood perfusion, anaesthesia and AO

Three aspects of blood supply have been confused in the literature; the vascular architecture, the circulation, and the integrity of the blood clot. Kruger[33] associated poor local blood supply with an increased incidence of AO in mandibular molar extractions. The presence of thick cortical bone, it was suggested, resulted in the poor perfusion of blood and it was suggested that minor perforations into the alveolar marrow cavity would allow blood vessels to grow in more easily. This was disputed by Birn[11] who demonstrated that the mandibular molar region is one of the most richly vascularized regions of the mandible, its blood supply being far better than that of the incisal region.

The vasoconstrictors in local anaesthetic solutions have been suggested as alternative factors in the pathogenesis of AO[41]. On the other hand, AO also follows tooth extractions carried out under general anaesthesia where no vasoconstrictor was used.

In addition, patients who require repeated injections of local anaesthetic solution may have a reduced pain threshold, which may account for complaints of pain originating from the extraction socket.

Some investigators claimed an increase in the incidence of AO when periodontal intraligamental (PDL) injections were used rather than block or infiltration injections[41]. These findings have been attributed to the spread of bacteria, especially with multiple injections to the affected site. This was however, disputed by Tsirlis et al.[69] who have shown that PDL anaesthesia did

not result in a higher frequency of AO than when block anaesthesia was used.

7. Oral contraceptives and AO

Contrary to studies conducted prior to 1960, studies from the 1970s and later showed a significantly higher incidence of AO occurring in females[20,58,64]. This was attributed to the increased use of oral contraceptives from the 1960s onwards as these were shown to have a definite positive correlation to the incidence of AO[65].

It has been proposed that oestrogens, like pyrogens and certain drugs, will activate the fibrinolytic system indirectly, and thus are believed to contribute to the occurrence of AO by increasing lysis of the blood clot[74]. Catellani et al.[18] concluded that the probability of AO increases with increased oestrogen dose in the oral contraceptive and that fibrinolytic activity appears to be lowest on days 23 through 28 of the menstrual cycle. Others studied the effect of oral contraceptives on the coagulation and fibrinolytic system and demonstrated an increase in the number of many factors such as factor II, VII, VIII, X, and in particular plasminogen[74].

Interestingly, a recent prospective randomized controlled study reported that females have a higher incidence of AO compared to males regardless of whether they are on oral contraceptives[19]. However, the conclusions drawn from this study, owing to the small sample size of male participants, are tentative.

In the case of females not using oral contraceptives, there is little published evidence on the effects of the various points in the menstrual cycle on the incidence of AO.

8. Smoking and AO

Sweet & Butler[66] have reported that among patients with a total of 400 surgically removed mandibular third molars, those who smoked a half-pack of cigarettes per day had a four- to five-fold increase in AO (12% *vs* 2.6%) compared to non-smoking patients. The incidence of AO increased to more than 20% among patients smoking more than a pack per day, and to 40% among patients who smoked on the day of surgery, or on the first postoperative day.

This phenomenon could be due to the introduction of a foreign substance that could act as a contaminant in the surgical site, and/or the suction applied to the cigarette which might dislodge the clot from the socket and interrupt healing. No references exist in the literature correlating the effects of heat from burning tobacco, contaminants in the smoke, or the systemic effects of the ingredients in cigarettes with AO.

Pathogenesis

Clinical and laboratory studies have shown the significance of locally increased fibrinolytic activity in the pathogenesis of AO[5,7,8,11].

Birn[11] claimed that partial or complete lysis and destruction of the blood clot was caused by tissue kinases liberated during inflammation by a direct or indirect activation of plasminogen in the blood. When direct tissue activators are released after trauma to the alveolar bone cells, plasminogen (which is laid down in the fibrin network as it is formed) is converted to plasmin, resulting in the break up of the clot by disintegrating the fibrin. This conversion is accomplished in the presence of tissue or plasma pro-activators and activators. These activators have been recently classified as direct (physiologic) and indirect (nonphysiologic) and further subclassified according to their origin as intrinsic and extrinsic activators[73]. Intrinsic activators originate from plasma components whereas extrinsic activators originate outside of the plasma/blood *per se*. Direct intrinsic activators include Factor XII (Hageman factor)-dependent activator and urokinase, which are mediated by leukocytes. Direct extrinsic activators include tissue plasminogen activators and endothelial plasminogen activators. Tissue plasminogen activators are found in most tissue types, including alveolar bone[6]. Indirect activators include substances such as streptokinase and staphylokinase, which are produced by bacteria and bind to plasminogen to form an activator complex that then cleaves other plasminogen molecules to plasmin. This strengthens the theory of the involvement of micro-organisms in the development of AO.

Birn[9] attributed the cause of pain to the presence and formation of kinin locally in the socket. It has been shown that kinins activate the primary afferent nerves, which may have already been presensitized by other inflammatory mediators and algogenic substances, and in concentrations as low as 1 ng/ml they are able to produce intense pain[9,46].

Plasmin is also involved in the conversion of kallikreins to kinins in the alveolar bone marrow[9]. Thus, the presence of plasmin may give a possible explanation for the two most characteristic features of AO, namely neuralgic pain and disintegrated blood clot. This is in accordance with Birn's observations[11] who noted an increased fibrinolytic activity in extraction sockets with AO when compared to normal healing sockets. He stated that: 'fibrinolytic alveolitis resulted when fibrinolysis or another proteolytic activity in and around the alveolus was capable of destroying the blood clot'.

Birn & Myhre-Jensen[8] have investigated the role of alveolar bone in increasing the local fibrinolytic activity. They concluded that the surrounding bone of the alveolus contains, among other components, stable tissue activators that may explain the local fibrinolytic activity in AO, and these stable activators are linked up with the osteoblasts of the endosteum. These results agreed with other findings that demonstrated a high fibrinolytic activity in the endosteal layer in rats[40].

Prophylactic management

In an era of evidence-based care, few areas of clinical controversy pose as substantial a dilemma to clinicians, as the topic of the alleged factors that are targets for the various preventive regiments, and the topic of what prophylactic medicaments and materials, if any, should be placed in an alveolar socket following exodontia.

References in the literature correlating to the prevention of AO can be divided into non-pharmacological and pharmacological preventive measures. Effective non-pharmacological preventive measures include a comprehensive history of the patient with identification, and if possible, elimination of risk factors associated with an increased risk to develop AO. These risk factors are summarized in Table 2. Moreover, besides the possible elimination of risk factors, it is imperative for active non-pharmacological preventive measures to be implemented. These preventive measures are summarized in Table 3.

Because AO is probably the most common local post-extraction complication that exists, a successful method of pharmacological prevention has long been sought. The literature reports a variety of materials and techniques that have been and still are being investigated

Table 2. Risk factors associated with true AO

- Previous experience of AO
- Deeply impacted mandibular third molar (risk factor is directly proportional to increasing severity of impaction)
- Poor oral hygiene of patient
- Active or recent history of acute ulcerative gingivitis or pericoronitis associated with the tooth to be extracted
- Smoking (especially >20 cigarettes per day)
- Use of oral contraceptives
- Immunocompromised individuals

Table 3. A summary of non-pharmacological measures to prevent AO

- Use of good quality current preoperative radiographs
- Careful planning of the surgery
- Use of good surgical principles
- Extractions should be performed with minimum amount of trauma and maximum amount of care
- Confirm presence of blood clot subsequent to extraction (if absent, scrape alveolar walls gently)
- Wherever possible preoperative oral hygiene measures to reduce plaque levels to a minimum should be instituted
- Encourage the patient (again) to stop or limit smoking in the immediate postoperative period
- Advise patient to avoid vigorous mouth rinsing for the first 24 h post extraction and to use gentle toothbrushing in the immediate postoperative period
- For patients taking oral contraceptives extractions should ideally be performed during days 23 through 28 of the menstrual cycle
- Comprehensive pre- and postoperative verbal instructions should be supplemented with written advice to ensure maximum compliance

for their success. These pharmacological prophylactic interventions are related to one or more of the following groups:

1. Antibacterial agents
2. Antiseptic agents and lavage
3. Antifibrinolytic agents
4. Steroid anti-inflammatory agents
5. Obtundent dressings
6. Clot support agents

1. Antibacterial agents

Prophylactic antibacterials, either given systemically or used locally, are considered to reduce the incidence of AO. Systemic antibacterials reported to be effective in the prevention of AO include the penicillins[32,34], clindamycin[15,34], erythromycin[15], and metronidazole[3,51]. In addition, it has been reported that the preoperative administration of antibacterial agents is more effective in reducing the incidence of AO than when given postoperatively[34,53]. However, of all systemic antibacterials referred to in the literature for the prevention of AO, the only that stood trial successfully in randomized double-blind studies was metronidazole[3,51]. Owing to its narrow antibacterial spectrum (anaerobicidal), metronidazole is associated with fewer and more infrequent side-effects than the high resistance developing penicillins and erythromycin, and the pseudomembranous colitis inducing clindamycin. Caution should however be taken with metronidazole in patients taking warfarin, disulfiram, phenytoin and possibly antihypertensives because of possible drug interactions. Concurrent alcohol should be avoided.

Nowadays, the routine use of systemic pre- and/or postoperative antibacterials given prophylactically is highly disputed and by many considered to be controversial because of the development of resistant bacterial strains and possible systemic side effects, such as hypersensitivity and unnecessary destruction of host commensals.

Myriad studies have been carried out to evaluate the effectiveness of topical (intra-alveolar) medicaments in preventing AO including various types of antibacterials used alone or in combination in varying formulations and dosages. However, very few studies are in agreement. The cited incidence in some studies is higher with antibiotics than in other studies without antibiotic use. In some cases, the antibacterial or base material used to carry the antibiotic has caused more significant complications than the AO[2].

Chapnick & Diamond[19] investigated in a double-blind study the effectiveness of topical clindamycin and they reported a significantly reduced incidence of AO in mandibular third molar sockets following light socket irrigation with Betadine® and the topical application of clindamycin in Gelfoam. They attributed their findings to the effectiveness of clindamycin but the irrigant used by them prior to wound closure is an iodophore with its own antibacterial properties. Furthermore, the subjects of their study also received multiple oral doses of systemic antibiotics postoperatively; thus making it impossible to attribute their findings to either of the antibacterials alone used in their study.

Trieger & Schlagel[68] examined in a double-blind crossover study involving 86 patients with 172 bony impacted mandibular third molars, the effect of the topical placement of clindamycin saturated gel sponge inserted into randomized unilateral extraction sites immediately following surgery. Each patient received a placebo in the contralateral site and served as his or her own control. The authors reported 7 cases of AO in the control group and none in the test group. Based on the significant difference in AO rates at a significance level of $P<0.5$ they concluded that the aetiology of AO is related to an infection with anaerobic bacteria and that clindamycin applied topically can be effective in the prevention of AO.

Many studies with topical tetracycline powder, aqueous suspensions of tetracycline, tetracycline on gauze drain or tetracycline-soaked Gelfoam sponges have been reported to be effective in significantly reducing the incidence of AO[1,23,61,62]. The latter mixture is thought to provide a firm clot in addition to preventing infection. However, side-effects including foreign body giant-cell reactions have been reported in association with topically applied tetracycline[43,75].

The topical application of a petroleum-based combination of tetracycline and hydrocortisone has also been reported in several studies to significantly reduce the incidence of AO[26,56]. Lynch et al.[38] reported however, the occurrence of the chronic problem of myospherulosis in extraction sites that received this combination and they suggested that this may arise as a result of the action of the lipid substances of the petrolatum carrier vehicle on the extravasated erythrocytes.

Nevertheless, no adverse reactions to the topical application of aqueous tetracycline suspensions or to impregnated tetracycline gauze drains in the socket have been described, and besides their claimed effectiveness in decreasing the incidence of AO, they are also considered to be an economical preventive modality[73].

2. Antiseptic agents and lavage

Chlorhexidine (CHX) is a bisdiguanide antiseptic with antimicrobial properties. The use of CHX as both a mouthrinse and as a preoperative irrigant of the gingival crevice has been shown to significantly reduce the quantity of oral microbial populations[72]. Several studies have reported that the pre- or perioperative use of CHX mouthrinse significantly

reduces the incidence of AO after the surgical removal of mandibular third molars[4,29,35,67]. Ragno & Szkutnik[49] noted nearly a 50% reduction in the incidence of AO in patients who pre-rinsed for 30 s with a 0.12% CHX solution.

Fotos et al.[25] examined in a randomized double-blind placebo-controlled study involving 70 patients with 140 uncomplicated non-infected third molars, the effect of the topical insertion of an intra-alveolar chlorhexidine gluconate solution-soaked Gelfoam into an extraction site and compared it to an intra-alveolar saline-soaked Gelfoam inserted on the contralateral side. They reported that the use of the former significantly reduced postoperative discomfort, but the incidence of AO was not specifically documented. They also reported that the 0.1% chlorhexidine solution did not significantly reduce postoperative discomfort whereas the use of the higher 0.2% concentration was significantly efficacious in reducing these symptoms. The authors acknowledged that Gelfoam exhibits a degree of hydrophobicity that precludes efficient absorption of chlorhexidine before intra-alveolar placement. Also, pre-shaped Gelfoam morphology does not allow its placement to the full depth of the socket. No reference was found in the literature correlating the local applications of the biodegradable chlorhexidine Periochip® nor that of chlorhexidine Corsodyl® gel with AO.

In a crossover study[31] the antiseptic agent, 9-aminoacridine, saturated in Gelfoam was placed in mandibular third molar extraction sites, and was compared with the use of Gelfoam alone placed in the contralateral mandibular third molar extraction sites. The authors concluded that 9-aminoacridine was ineffective in reducing the incidence of AO.

Hellem & Nordenram[28] studied the prophylactic effectiveness of antiseptic dressings by suturing a gauze sponge saturated with Whitehead's varnish (a combination of iodoform, balsam tolutan, and Styrax liquid in a base liquid) over mandibular third molar extraction sites. The authors claimed to record a significant decrease in the incidence of postoperative pain, haemorrhage and swelling when compared to a control group, but the incidence of specifically diagnosed AO was not addressed.

Following a lavage study[63] it was reported that the incidence of AO after the removal of mandibular third molars was significantly reduced from 10.9% using 25 ml normal saline solution for lavage to 5.9% with the use of 175 ml lavage. In another lavage study[14], no significant differences were found in the incidence of AO following the removal of mandibular third molars between volumes of 175 ml and 350 ml of normal saline solution, but both these volumes were more effective than a volume of 25 ml. The reason for this may be that sufficient lavage mechanically removes more of the root remnants and/or bone fragments (and other debris) possibly still left in the extraction socket and which might contribute to the development of AO.

3. Antifibrinolytic agents

Earlier investigations[10,57] into the fibrinolytic nature of AO indicated that the topical use of para-hydroxybenzoic acid (PHBA), in extraction wounds significantly decreased the incidence of AO in a dose-dependent fashion. However, as PHBA is available on the market as a component of Apernyl® (Bayer AG, Germany)—an alveolar cone with a formulation of 32 mg acetylsalicylic acid, 3 mg propyl ester of PHBA and 20 mg unknown tablet mass, it is not possible to attribute the reported findings to PHBA alone or perhaps to the anti-inflammatory properties of acetylsalicylic acid. In addition, PHBA has also been reported to have some antibacterial properties which may also have contributed to the reported findings[73]. Subsequent histological studies[16] however, showed that acetylsalicylic acid in contact with bone causes a local irritating effect accompanied by serious inflammation of the extraction socket, possibly resulting in AO.

The antifibrinolytic agent Tranexamic acid (TEA) has been reputed to prevent AO when applied topically in the extraction socket following exodontia, but controlled investigations with special reference to impacted mandibular third molar extraction wounds have not shown a significant reduction in the incidence of AO when compared to a placebo group[27].

Given the lack of a scientifically confirmed advantage, and many possible problems, there seems to be no rationale for the use of these agents.

4. Steroid anti-inflammatory agents

Only one reference was found in the literature regarding the individual use of topical corticosteroids in the prevention of AO. Even though the corticosteroid has been reported to decrease immediate post-operative complications, it failed to reduce the occurrence of AO after extraction[36]. The topical application of a hydrocortisone and oxytetracycline mixture however, has been shown to significantly decrease the incidence of AO after the removal of impacted mandibular third molars[26,56]. Unfortunately, the contribution of the antibiotic cannot be separated from that caused by the steroid.

Given the lack of scientific evidence substantiating any benefit to this regimen its use as a preventive measure for AO is inappropriate.

5. Obtundent dressings

A recent crossover study[12] on the prevention of AO following the bilateral removal of 200 mandibular molars claimed a significant decrease in the incidence of AO, following the immediate placement of an eugenol containing dressing into randomly selected unilateral extraction sockets. The contralateral sockets were not packed and served as the patients own controls. However, the irritant local effect of eugenol and the delay in wound healing due to elective prophylactic packing is well documented in the literature[2,19,57].

6. Clot support agents

In the 1980s, a biodegradeable ester polymer, polylactic acid (PLA) was widely promoted as the ultimate solution for preventing AO, and it is still available today under the brand name of DriLac (Osmed, Inc, Costa Mesa, CA, USA). It was suggested that PLA would provide a biological stable support for the blood clot and for the future granulation and osteoid tissue. A study by Brekke & associates[13] in 1986 reported an incidence of AO of 2.2% with PLA, placed in mandibular third molar extraction sites, as compared with 18.1% incidence without the use of PLA. This was however followed in 1990 by an article by Moore & Brekke[43] that highlighted 18 cases of complications with tetracycline-treated PLA, and in 1995, Hooley & Golden[30] reported a higher incidence of AO when PLA was used in the control group (23.6% with PLA, 13.6% without). The latter prospective study suggests that the use of PLA might actually increase the incidence of AO.

Table 4. Summary of non-dressing interventions to manage AO

- Remove any sutures to allow adequate exposure of the extraction site. As the socket may be exquisitely tender local anaesthesia may be required
- Irrigate the socket gently with warm sterile isotonic saline or local anaesthetic solution, which is followed by careful suctioning of all excess irrigation solution
- Do not attempt to curette the socket, as this will increase the level of pain
- Prescription of potent oral analgesics
- The patient is given a plastic syringe with a curved tip for home irrigation with chlorhexidine solution or saline and instructed to keep the socket clean. Once the socket no longer collects any debris, home irrigation can be discontinued.

Given the lack of scientific evidence, there seems to be no benefit in its use.

Symptomatic management

Although numerous authors[21,42,52] often refer to the 'treatment' of AO, this appears to be rather misleading, as the condition cannot be treated as long as the underlying aetiology has not been firmly established. Meanwhile, AO can only be managed and as management is directed primarily towards the prompt relief of the patient's pain during the healing stages, it takes place primarily by palliative means.

References in the literature relating to the management of AO can be divided into non-dressing and dressing interventions. The non-dressing interventions are summarized in Table 4.

Several authors[42,62,68] advocate, with or without prior non-dressing interventions, the use of intra-alveolar medicated dressings. The active components of the dressings reported in the literature for managing the condition can be broadly classified as follows:

1. Antibacterial dressings
2. Obtundent dressings
3. Topical anaesthetic dressings, and
4. Combinations of 1–3.

The use of dressings is empirical and their reported effectiveness in reducing patient discomfort is largely based on circumstantial personal clinical experience and ample anecdotal reports. Although the placement of dressings is controversial in the literature and concrete evidence regarding their placement is lacking, it has been suggested[73] that in cases of diagnosed AO, dressings might be an effective malady that could be used as an adjunct to non-dressing interventions. Arguments in the literature supporting the use of intra-alveolar dressings include the achievement of greater local concentration of the substance(s) than can normally be expected from systemic administration, the minimizing of possible side effects and sensitization that may accompany systemic administration, the localized obtundent effect, and the closing of the socket so that food debris can be kept out. The exact incidence of complications secondary to dressings placed in extraction sockets is unknown.

To date, no scientific studies have been carried out that specifically investigate the incidence of potential side effects and tissue damage arising from the placement of intra-alveolar dressings. Although a theoretical potential for the development of resistant bacterial strains with intra-alveolar antibiotic use has been reported[2], there have not been any reliable data in the literature to substantiate this theoretical complication. However, case reports regarding the occurrence of other local complications have been described in the literature[38,43,56,75] and it is generally acknowledged that dressings delay the healing of the extraction socket.

Discussion

All the clinical and histological evidence supports that AO results from disturbed healing of the extraction wound. The introduction of a standardized descriptive criterion for AO may provide a sound basis for more objective and reliable comparisons in future investigations related to AO.

Although the full aetiology of AO has yet to be firmly established and despite the plethora of theories available for its aetiopathogenesis, substantial evidence suggests that it is most particularly related to a complex interaction between excessive localized trauma, bacterial invasion and their association to plasmin and subsequently, the fibrinolytic system. Another factor that should merit attention and has not been investigated earlier is the possibility of a genetic factor. If there is a genetic predisposition to AO, it is likely to arise from polymorphisms of one or more genes. This possibility could be investigated by undertaking large association studies or transdisequilibrium testing. The possibility of a genetic association with AO is worthy of further investigation.

Prevention of AO entails reducing the number of possible risk factors, meticulous attention to procedural details and surgical skills. Despite a plethora of published articles, relatively little reliable data are available for formulating a scientifically sound philosophy regarding the pharmacological prevention and symptomatic management of AO. To date, no single method has gained universal success or acceptance, although a large number of practitioners continue to use 'their method', probably because it was passed from one generation to another, often without controlled studies to support its use.

Dressings should not be placed into extraction sockets for merely prophylactic reasons as the possible side effects and unnecessary additional costs to the patient contraindicate this. Based on the first dictum of medicine as stated by Hippocrates (421 B.C.): 'At first do no harm', it seems prudent to limit the pharmacological preventive interventions to measures which are supported by sufficient evidence to be effective, and equally, show a minimum of side-effects. Besides ample surgical lavage, the reported prophylactic effectiveness, economy and lack of adverse side effects of chlorhexidine solution justify its use as a preoperative irrigant or mouthrinse in the prevention of AO[29,35,49].

The review of the literature with reference to dressings provides a cautionary note, that even though severe reactions from the use of antibacterials, gelfoam, or other preparations placed in sockets are uncommon, all are accompanied by risks for reactions, complications, and delayed healing. Should adverse reactions develop in a patient, the practitioner may find medicolegal defence of the use of the material difficult, based on the documented problems reported in the literature, rare as they might be. To date, insufficient scientific evidence exists for the amelioration of pain following the application of dressings.

Despite many years of research there has been little progress over the years to address this very painful condition for patients. However, further investigations and well controlled studies are necessary to draw firm conclusions which can lead to increased clarity regarding the most beneficial management of the patient presenting with AO.

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References

1. Akota I, Alvsaker B, Bjornland T. The effect of locally applied gauze drain impregnated with chlortetracycline ointment in mandibular third molar surgery. Acta Odontolol Scand 1998: **56**: 25–29.
2. Alexander RE. Dental extraction wound management: A case against medicating postextraction sockets. J Oral Maxillofac Surg 2000: **58**: 538–551.
3. Barclay JK. Metronidazole and dry socket: prophylactic use in mandibular third molar removal complicated by non-acute pericoronitis. New Zealand Dent J 1987: **7**: 71–75.
4. Berwick MJE, Lessin ME. Effects of a chlorhexidine gluconate oral rinse in mandibular third molar surgery. J Oral Maxillofac Surg 1990: **48**: 440–448.
5. Birn H. Bacterial and fibrinolytic activity in 'dry socket'. Acta Odontolol Scand 1970: **28**: 773–783.
6. Birn H. Fibrinolytic activity of normal alveolar bone. Acta Odontolol Scand 1971: **29**: 141–153.
7. Birn H. Fibrinolytic activity of alveolar bone in 'dry socket'. Acta Odontolol Scand 1972: **30**: 23–32.
8. Birn H, Myhre-Jensen, G. Cellular fibrinolytic activity of human alveolar bone. Int J Oral Surg 1972: **1**: 121–125.
9. Birn H. Kinins and pain in dry socket. Int J Oral Surg 1972a: **1**: 34–42.
10. Birn H. Antifibrinolytic effect of Apernyl in dry socket. Int J Oral Surg 1972b: **1**: 190–194.
11. Birn H. Etiology and pathogenesis of fibrinolytic alveolitis ('dry socket'). Int J Oral Surg 1973: **2**: 215–263.
12. Bloomer CR. Alveolar osteitis prevention by immediate placement of medicated packing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000: **90**: 282–284.
13. Brekke JH, Bresner M, Reitman MJ. Effect of surgical trauma and polylactate cubes and granules on the incidence of alveolar osteitis in mandibular third molar extraction wounds. J Can Dent Assoc 1986: **52**: 315–320.
14. Butler DP, Sweet JB. Effect of lavage on the incidence of localized osteitis in mandibular third molar extraction sites. Oral Surg Oral Med Oral Pathol 1977: **44**: 14–20.
15. Bystedt H, Nord CE, Nordenram A. Effect of azidocillin, erythromycin, clindamycin and doxycyclie on postoperative complications after surgical removal of impacted mandibular third molars. Int J Oral Surg 1980: **9**: 157–165.
16. Carroll PB, Melfi RC. The histologic effect of topically applied acetylsalicylic acid on bone healing in rats. Oral Surg Oral Med Oral Pathol 1982: **33**: 728–735.
17. Catellani JE. Review of factors contributing to dry socket through enhanced fibrinolysis. J Oral Surg 1979: **37**: 42–46.
18. Catellani JE, Harvey S, Erickson SH, Cherkink D. Effect of oral contraceptive cycle on dry socket (localized alveolar osteitis). J Am Dent Assoc 1980: **101**: 777–780.
19. Chapnick P, Diamond L. A review of dry socket: A double-blind study on the effectiveness of clindamycin in reducing the incidence of dry socket. J Can Dent Assoc 1992: **58**: 43–52.
20. Cohen ME, Simecek JW. Effects of gender-related factors on the incidence of localized alveolar osteitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995: **79**: 16–22.
21. Colby RC. The general practitioner's perspective of the etiology, prevention, and treatment of dry socket. Gen Dent 1997: **9**: 461–467.
22. Crawford JY. Dry socket. Dent Cosmos 1896: **38**: 929.
23. Davies W Jr, Buchs AU, Davies W. The use of granular gelatin-tetracycline compound after third molar removal. J Oral Surg 1981: **39**: 466–467.
24. Field EA, Speechley JA, Rotter E, Scott J. Dry socket incidence compared after a 12 year interval. Br J Oral Maxillofac Surg 1988: **23**: 419–427.
25. Fotos PG, Koorbusch GF, Sarasin DS, Kist RJ. Evaluation of intra-alveolar chlorhexidine dressing after removal of impacted mandibular third molars. Oral Surg Oral Med Oral Pathol 1992: **73**: 383–388.
26. Fridrich KL, Olson RAJ. Alveolar osteitis following removal of mandibular third molars. Anaesth Prog 1990: **37**: 32–41.
27. Gersel-Pedersen N. Tranexamic acid in alveolar sockets in the prevention of alveolitis sicca dolorosa. Int J Oral Surg 1979: **8**: 421–429.
28. Hellem S, Nordenram A. Prevention of postoperative symptoms by general antibiotic treatment and local bandage in removal of mandibular third molars. Int J Oral Surg 1973: **2**: 273–278.
29. Hermesch CB, Hilton TJ, Biesbrock AR, Baker RA, Gerlach RW, McClanahan SF. Perioperative use of 0.12% chlorhexidine gluconate for the prevention of alveolar osteitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998: **85**: 381–387.
30. Hooley JR, Golden DP. The effect of polylactic acid granules on the incidence of alveolar osteitis after mandibular third molar surgery. A prospective randomized study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995: **80**: 279–283.
31. Johnson WS, Blanton EE. An evaluation of 9-aminoacridine/Gelfoam to reduce dry socket formation. Oral Surg Oral Med Oral Pathol 1988: **66**: 167–170.
32. Krekmanov L, Nordenram A. Postoperative complications after surgical removal of mandibular third molars. Int J Oral Maxillofac Surg 1986: **15**: 25–29.
33. Kruger GO. Textbook of Oral and Maxillofacial Surgery. St Louis: Mosby 1973: 226.
34. Laird WRE, Stenhouse D, MacFarlane TW. Control of postoperative infection. Br Dent J 1972: **133**: 106–109.
35. Laresen PE. The effect of a chlorhexidine rinse on the incidence of alveolar osteitis following the surgical removal of impacted mandibular third molars. J Oral Maxillofac Surg 1991: **49**: 932–937.
36. Lele MV. Alveolar osteitis. J Indian Dent Assoc 1969: **41**: 69–72.
37. Lilly GE, Osborn DB, Rael EM. Alveolar osteitis associated with mandibular third molar extractions. J Am Dent Assoc 1974: **88**: 802–806.
38. Lynch DP, Newland JR, McClendon J. Myospherulosis of oral hard and soft tissues. J Oral Maxillofac Surg 1984: **42**: 349–355.
39. MacGregor AJ. Aetiology of dry socket: A clinical investigation. Br J Oral Surg 1968: **6**: 49–58.
40. Magnusson B, Gustafsson GT. Localisation of fibrinolytic activity during tooth eruption in rats. Scand J Dent Res 1973: **81**: 315–318.
41. Meechan JG, Venchard GR, Rogers SN. Local anesthesia and dry socket: A clinical investigation of single extractions in male patients. Int J Oral Maxillofac Surg 1987: **16**: 279–284.
42. Mitchell L. Topical metronidazole in the treatment of 'dry socket'. Br Dent J 1984: **156**: 132–134.
43. Moore JW, Brekke JH. Foreign body giant cell reaction related to placement of tetracycline-treated polylactic acid: Report of 18 cases. J Oral Maxillofac Surg 1990: **48**: 808–812.
44. Nitzan D, Sperry JF, Wilkins D. Fibrinolytic activity of oral anaerobic bacteria. Arch Oral Biol 1978: **23**: 465–470.
45. Nitzan DW. On the genesis of 'dry socket'. J Oral Maxillofac Surg 1983: **41**: 706–710.
46. Nørholt SE. Treatment of acute pain following removal of mandibular third molars. PhD thesis. Int J Oral Maxillfac Surg 1998: **27**: 1–41.
47. Osborn TP, Frederickson G, Small I, Torgerson TS. A prospective study of complications related to mandibular third molar surgery. J Oral Maxillofac Surg 1985: **43**: 767–769.
48. Penarrocha M, Sanchis JM, Sáez, U, Bagán JV. Oral hygiene and postoperative pain after mandibular third molar surgery. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001: **92**: 260–264.
49. Ragno JR, Szkutnik AJ. Evaluation of 0.12% chlorhexidine rinse on the prevention of alveolar osteitis. Oral Surg Oral Med Oral Pathol 1991: **72**: 524–526.
50. Ritzau M, Hillerub S, Branebjerg PE, Ersbol BK. Does metronidazole prevent alveolitis sicca dolorsa? Int J Oral Maxillofac Surg 1992: **21**: 299–302.

51. Rood JP, Murgatroyd J. Metronidazole in the prevention of 'dry socket'. Br J Oral Surg 1979: **17**: 62–70.
52. Rood JP, Danford M. Metronidazole in the treatment of 'dry socket'. Int J Oral Surg 1981: **10**: 345–347.
53. Rood JP, Collier J. Metronidazole levels in alveolar bone. Royal Society of Medicine International Congress and Symposium Series. London: Academic Press 1979: **18**: 45–47.
54. Rozanis J, Schofield IDF, Warren BA. Is dry socket preventable? J Can Dent Assoc 1977: **43**: 233–236.
55. Rud J. Removal of impacted lower third molars with acute pericoronitis and necrotising gingivitis. Br J Oral Surg 1970: **7**: 153–160.
56. Rutledge JL, Marcoot RM. Terra-Cotril for the reduction of the incidence of localized osteitis following mandibular third molar removal. J Oral Med 1984: **39**: 51–53.
57. Schatz JP, Fiore-Donna G, Henning G. Fibrinolytic alveolitis and its prevention. Int J Oral Maxillofac Surg 1987: **16**: 175–183.
58. Schow SR. Evaluation of postoperative localized osteitis in mandibular third molar surgery. Oral Surg Oral Med Oral Pathol 1974: **38**: 352–358.
59. Simpson HE. The healing of extraction wounds. Br Dent J 1969: **126**: 550–557.
60. Sisk AL, Hammer WB, Shelton DW, Joy ED. Complications following removal of impacted third molars: the role of the experience of the surgeon. J Oral Maxillofac Surg 1986: **44**: 855–859.
61. Sorensen DC, Preisch JW. The effect of tetracycline on the incidence of postextraction alveolar osteitis. J Oral Maxillofac Surg 1987: **45**: 1029–1033.
62. Swanson AE. A double-blind study in the effectiveness of tetracycline in reducing the incidence of fibrinolytic alveolitis. J Oral Maxillofac Surg 1989: **47**: 165–167.
63. Sweet JB, Butler DP, Drager JL. Effects of lavage techniques with third molar surgery. Oral Surg Oral Med Oral Pathol 1976: **41**: 152–168.
64. Sweet JB, Butler DP. Increased incidence of postoperative localized osteitis in mandibular third molar surgery associated with patients using oral contraceptives. Am J Obstet Gynecol 1977: **127**: 518–519.
65. Sweet JB, Butler DP. Predisposing and operative factors: Effect on the incidence of localized osteitis in mandibular third molar surgery. Oral Surg Oral Med Oral Pathol 1978: **46**: 206–215.
66. Sweet JB, Butler DP. The relationship of smoking to localised osteitis. J Oral Surg 1979: **37**: 732–735.
67. Tjernberg A. Influence of oral hygiene measures on the development of alveolitis sicca dolorosa after surgical removal of mandibular third molars. Int J Oral Maxillofac Surg 1979: **8**: 430–434.
68. Trieger N, Schlagel GD. Preventing dry socket: A simple procedure that works. J Am Dent Assoc 1991: **2**: 67–68.
69. Tsirlis AT, Iakovidis DP, Parissis NA. Dry socket: frequency of occurrence after intraligamentary anesthesia. Quint Int 1992: **23**: 575–577.
70. Turner PS. A clinical study of dry socket. Int J Oral Surg 1982: **11**: 226–231.
71. Vedtofte P, Ritzau M, Donatsky O. Use of propylic ester of p-hydroxybenzoic acid after removal of impacted mandibular third molars. Int J Oral Maxillofac Surg 1974: **3**: 394–399.
72. Veksler AE, Kayrouz GA, Newman MG. Reduction of salivary bacteria by pre-procedural rinses with chlorhexidine 0.12%. J Periodontolol 1991: **62**: 649–651.
73. Vezeau PJ. Dental extraction wound management: Medicating Postextraction Sockets. J Oral Maxillofac Journal 2000: **58**: 531–537.
74. Ygge Y, Brody S, Korsan-Bengtsen K, Nilsson L. Changes in blood coagulation and fibrinolysis in women receiving oral contraceptives. Am J Obstet Gynaecol 1969: **104**: 87–98.
75. Zuniga JR, Leist JC. Topical tetracycline-induced neuritis: A case report. J Oral Maxillofac Surg 1995: **53**: 196–199.

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