

# Interventions for the prevention of dry socket: an evidence-based update

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## VERIFIABLE CPD PAPER

### IN BRIEF

- Provides an update on the clinical and histological stages of normal healing of an extraction socket.
- Highlights the causes and management of dry socket.
- Supplies current evidence for measures available to prevent dry socket.
- Stresses implications for current clinical practice and future research.

This paper reviews the latest evidence for local and systemic interventions for the prevention of alveolar osteitis (dry socket). Dry socket is a painful and common post-operative complication following exodontia. Any interventions for the prevention of dry socket could reduce both its incidence and help avoid this painful complication. Prophylactic measures proposed in the literature are discussed. Furthermore, this article discusses both the clinical and histological stages of a normal healing socket.

## INTRODUCTION

Alveolar osteitis (AO) or 'dry socket' is a relatively common post-operative complication that is reported to be associated with up to 37% of dental extractions.<sup>1</sup> The condition develops when a blood clot fails to form or becomes dislodged from the socket of an extracted tooth. Symptoms typically include increased pain occurring 1–3 days post-operatively around the extraction site and this is commonly unresponsive to analgesics.<sup>1</sup> In addition, some patients may also complain of oral malodour.<sup>2</sup>

Diagnosis is based on the history, symptoms and clinical presentation. Typically AO presents as an exposed socket devoid of blood clot (Fig. 1). In contrast, a normally healing socket consists of a blood clot that is subsequently replaced by granulation and connective tissue with gingival healing typically over a 1–2 week period. Healing by secondary intention eventually leads to tissue consolidation and the socket becomes remodeled with bone.<sup>3</sup>

Although the exact aetiology of AO remains unclear, several risk factors have been found to be implicated in the loss of the blood clot, including:

- Non-compliance with post-operative care instructions<sup>4,5</sup>

- Bacterial breakdown and fibrinolysis<sup>1,6</sup>
- Impaired clot formation secondary to: smoking,<sup>7</sup> oral contraceptive use,<sup>8</sup> surgical trauma during extraction<sup>2,5</sup> and infection around the tooth to be extracted such as pericoronitis<sup>9</sup>
- Women and those with a previous history of dry socket are also thought to be at a higher risk of developing AO.<sup>10</sup>

The site of extraction has been shown to be significant with greater than 30% of mandibular molar extractions, including impacted third molar extractions, resulting in AO; this is in comparison to a much lower prevalence at other sites, which may only account for up to 5% of routine extractions.<sup>1,11</sup>

The development of AO is not only associated with patient morbidity, but is also associated with other significant implications, which are multifaceted and include both societal<sup>12</sup> and healthcare costs. The post-operative care associated with AO is costly to the health service, employers and patients alike. Furthermore, the painful and often distressing experience associated with AO could serve to reinforce a negative stigma associated with the dental profession and extractions in particular. Therefore, effective modalities for the prevention and management of AO are crucial for dentists carrying out extractions both in a practice and hospital setting.

Two recently published Cochrane Systematic Reviews<sup>10,13</sup> evaluated the available evidence for such local and systemic interventions used in the prevention and treatment of dry sockets. This paper presents a summary of the current evidence alongside recommendations and implications for clinical practice.



Fig. 1 Clinical presentation of alveolar osteitis (dry socket)

## SUMMARY OF THE EVIDENCE BASE

### Prevention

#### Local modalities

Following a comprehensive literature search, 18 out of 21 randomised controlled trials (RCTs) meeting the inclusion criteria were included in the analysis of local interventions for the prevention of AO.<sup>10</sup> The RCTs evaluated the effectiveness of antiseptic mouthrinses or intrasocket interventions in preventing dry socket occurrence. Sixteen of the trials were concerned with sockets of mandibular third molar teeth, while the remainder reported on AO associated with other teeth.

From four of the trials there was some evidence that rinsing with chlorhexidine mouthwash, either 0.12% or 0.2% concentration, both pre- and post-operatively was beneficial in reducing the occurrence of dry sockets (RR 0.58, 95% CI 0.43–0.78;  $p < 0.001$ ), compared with a placebo. However, three of these trials were considered to be at high risk of bias, so the level of evidence was deemed to be moderate. The number of people that need to be treated with a chlorhexidine mouthrinse to prevent one dry socket also varied considerably depending on

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the prevalence of dry socket; for instance, for a dry socket prevalence of 1%, 232 patients would need to be treated, whereas for a dry socket prevalence of 5%, 47 patients need to be treated. Adverse reactions relating to the use of chlorhexidine mouthwash were reported in four trials and included teeth staining, gastrointestinal symptoms, paraesthesia and bad taste.<sup>14–17</sup> There were no serious adverse effects reported in any of the trials, but serious events have recently been reported in the literature and this should be borne in mind when prescribing chlorhexidine to patients.<sup>10</sup>

Twelve RCTs evaluated the preventative effects of intrasocket interventions, however, ten trials assessed different interventions and it was therefore not possible to produce reliable evidence or indeed a consensus regarding their effectiveness from these single studies. There was, however, a demonstrative benefit in placing 0.2% chlorhexidine gel in third molar extraction sockets compared to a placebo or no treatment in preventing dry sockets from two included trials with low and high risk of bias (RR 0.42, 95% CI 0.21–0.87;  $p = 0.02$ ).<sup>18,19</sup> Nevertheless, the number of patients that need to be treated with chlorhexidine gel to prevent one patient developing a dry socket is still high at 173, for a control dry socket risk of 1%.<sup>10</sup> Interestingly, no adverse reactions were reported in the trials evaluating the effectiveness of chlorhexidine gel placed immediately following extraction.<sup>18–20</sup>

### Systemic modalities

There was a body of evidence of moderate quality from nine trials that indicated prophylactic antibiotics used pre- and post-operatively may reduce the risk of dry socket development following impacted mandibular third molar extractions (RR 0.62, 95% CI 0.41–0.95;  $p = 0.03$ ).<sup>13</sup> Thirty-eight patients would need to be treated with antibiotics to prevent one dry socket development, but this is at the expense of mild adverse effects. Consequently, their benefits are best reserved for those patients presenting with a clear risk<sup>13</sup> and prophylactic use of systemic antibiotics is not regularly advocated. Evidence regarding the preventative effects of systemic antibiotics for extractions of teeth other than third molars is still lacking.

### Treatment

Three of the studies evaluated interventions for treating dry sockets that had occurred post-operatively, however, these were unable to provide strong and reliable evidence to support the use of any of the treatment interventions. None of these treatment trials reported any adverse outcomes.<sup>10</sup>

### Local modalities

Two RCTs reported on different local medicaments to treat AO.<sup>21,22</sup> One was deemed to be at high risk of bias and thus data could not be used to ascertain the effectiveness of the various interventions investigated.<sup>10</sup> The remaining trial by Burgoyne<sup>22</sup> showed no difference in pain levels occurring after 48 hours of treatment using two different interventions, topical anaesthetic gel compared with eugenol.

### Systemic modalities

Evidence from one RCT that evaluated the use of metronidazole compared to a placebo indicated that the duration of treatment can be reduced with the use of systemic antibiotics ( $p = 0.004$ ).<sup>23</sup> However, the risk of bias within in this trial was unclear.

## DISCUSSION

Alveolar osteitis is a relatively common complication following dental extractions. General dental practitioners (GDPs)<sup>24</sup> should therefore be aware of the effectiveness of available local and systemic interventions for the prevention and treatment this painful and often distressing complication. As outlined in this report, the evidence available in the form of two Cochrane systematic reviews suggests that in terms of prevention: the use of chlorhexidine gel (0.2%) placed into extraction sockets immediately post treatment could help to prevent approximately 60% AO.<sup>10</sup> Furthermore, the authors concluded that there is some evidence that rinsing with chlorhexidine (0.12% and 0.2%) also provides some benefit in preventing dry socket. In terms of treatment for AO: the use of systemic therapy showed that antibiotics might reduce the risk of AO by 38%.<sup>13</sup>

### Normal healing socket

It is prudent for the clinician to identify what the appearance of a normal healing socket is in order to realise when healing has become impaired. A significant clinical and histological change occurs following an extraction. Distinctive stages occur between the healing stages, which can be observed both clinically and histologically. It is important to remember that the speed of healing is variable between individuals with significant factors impairing the speed regeneration such as older age,<sup>25</sup> compromised medical status (such as diabetes, anaemia)<sup>25</sup> or in smokers.<sup>26</sup>

Figures 2–8 show the clinical stages of a healing socket. The procedure of extraction inadvertently damages local blood capillaries surrounding the tooth, following which blood fills the socket.<sup>27</sup> Furthermore the



Fig. 2 46 site pre-extraction



Fig. 3 Extraction socket immediately post-extraction. Blood has filled the extraction site completely. Activated platelets have now slowed the initial blood hemorrhage



Fig. 4 Extraction socket at day 3. The blood clot has been lysed by macrophages and migration of fibroblasts into the clot lay down granulation tissue providing a framework for further healing



Fig. 5 One week post-extraction the superficial layers of the socket contain a dense layer of inflammatory cells; the regenerated gingival tissue appears erythematous. Early epithelial migration leads to slight contact between the regenerated gingival tissues across the socket

normal clotting mechanisms of the intrinsic and extrinsic clotting pathways as part of the coagulation cascade<sup>28</sup> produces a loose clot (Fig. 3) that fills the socket. Initially platelets are activated and adhere to the site of insult forming a platelet plug; this aims to reduce the blood loss.<sup>28</sup> The platelets then retract the clot so that it gradually becomes harder and subsequently shrinks below the level of the



**Fig. 6** Two weeks post-extraction. The socket is now filled with granulation tissue and osteoid (pre-ossified bone matrix). The gingival tissue overlying the socket still appears erythematous and swollen as the lingual and buccal portions almost approximate



**Fig. 7** One month post-extraction. The regenerated gingival tissues almost approximate and appear less swollen appearing pinker in colour rather than erythematous red. New bone formation commences at the apical and lateral aspects of the socket<sup>32</sup>



**Fig. 8** Six weeks post-extraction. The site has healed almost entirely on the surface. The regenerated gingival tissue now approximates over the majority of the socket. Histologically bone deposition dominates the healing process

soft tissues; this contraction pulls the soft tissue inwards reducing the socket size. This is usually complete within 4 hours and the clot stabilises by fibrin crosslinking.<sup>29</sup> This is why avoiding rinsing is essential within the first 24 hours post-extraction as this could destabilise the clot and ultimately expose the socket and impair healing.

Two days later lysis of the clot begins by activation of the fibrinolytic enzyme plasmin. This is done by the conversion of plasminogen to plasmin via the plasminogen activator (PA) system.<sup>30</sup> Plasminogen is found primarily within the plasma and is synthesised within the liver.<sup>30</sup> This pro-enzyme is activated by the release of tissue-type PA (t-PA), which is found within the walls of the endothelium that lines the blood

vessels. This then cleaves a specific peptide bond located within plasminogen pro-enzyme, converting it to the active plasmin.

Within 4 days' time, fibroblasts begin migrating into the blood clot from the socket wall.<sup>29</sup> The growth of new capillaries with the migration of fibroblasts into the socket begins the synthesis of granulation tissue depicted in Figure 4. Granulation tissue is a connective tissue matrix comprising mesenchymal cells and infiltrates of leucocytes (macrophages, lymphocytes and neutrophils).<sup>3</sup> Phagocytosis of the remnants of the clot by leucocytes (predominantly by macrophages) allows for replacement by granulation tissue. As is seen in Figure 4 the superficial layer of the clot appears white and is in fact porous histologically. This surface layer contains high levels of bacteria such as *Staphylococcus aureus*, which act like t-PA and activate plasmin, leading to further clot destruction and degradation of the surface fibrin.<sup>31</sup>

A week post-extraction the socket now almost entirely filled with granulation tissue synthesised by fibroblasts as shown in Figure 5. This tissue is soft and has a swollen appearance to it as it contains little collagen. The superficial layers also contain a dense layer of inflammatory cells; as shown in by the slight erythema of the regenerated gingival tissue seen clinically.<sup>29</sup> Furthermore early resorption is taking place at the lamina dura by osteoclasts. Between 7 and 10 days early epithelial migration occurs, as can be seen in Figure 5, there is slight contact between the regenerated gingival tissues across the socket.

Figure 6 shows the socket 2 weeks post-operatively. At this stage the socket is now entirely filled with granulation tissue and osteoid, a pre-ossified bone matrix.<sup>3</sup> The earliest woven bone trabeculae form on the periphery of the socket<sup>27,32</sup> and also at the apical portion of the socket.<sup>3</sup> This can be seen clinically (Fig. 7), with the base of the socket appearing less hollow as these early depositions form much of the contents. However, at this early stage the majority of healing involves the rejection of the original socket wall and the exfoliation of bony fragments.<sup>27,32</sup>

Figure 7 shows healing at 1 month as the extraction site enters the early intermediate phase. The majority of the socket is now filled with early woven bone,<sup>29</sup> however, there is still some fibrous connective tissue with some, albeit very few, inflammatory cells.<sup>33</sup> As can be seen clinically, the regenerated gingival tissue overlying the socket appears far less erythematous than before.

Figure 8 shows healing stage at 6 weeks. Amler's study on clinical and histological stages of the healing socket states that it normally takes 24 to 35 days for total epithelial

coverage of the socket.<sup>34</sup> The majority of healing now takes place beneath the epithelial surface; with histological samples at this stage showing that the number of osteoblasts reach a peak at this stage.<sup>3</sup> The emphasis shifts from bone resorption and epithelial regeneration to bone deposition; usually reaching a peak of bone deposition by 3 months.<sup>35</sup>

### Implications for current practice

The Cochrane reviews reporting on local measures to prevent AO found that 232 patients would have to be treated with a preventive intervention to stop one patient developing AO.<sup>10</sup> Furthermore the Cochrane review on systemic measures (antibiotics) indicated that to prevent one case of AO, between 24 and 250 people would need to receive prophylactic antibiotics.<sup>13</sup> In addition, the review concluded, 'the size of the benefit is not enough to recommend a routine use of this practice'.<sup>13</sup>

There are measures GDPs can take as an alternative to anti-bacterial prophylaxis to reduce the risk of AO. These include reducing the amount of vaso-constrictive local anaesthetic used, carrying out the extraction with minimal trauma as possible, or advising on smoking cessation.<sup>29</sup> Furthermore, identifying patients that are at high risk of developing AO is important. Risk factors include:<sup>29,36-38</sup>

- Oral contraceptives
- Radiotherapy
- Previous history of AO
- Lower molar extractions
- Smokers
- Female gender
- Osteosclerotic disease (Paget's disease)
- Older age group (above 26)
- Experience of surgeon.

It would be wise for the GDP to take precautions to reduce the risk of AO in this cohort of high-risk patients. As outlined above, simple clinical measures to reduce the risk can be taken, and in those patients who have osteosclerotic disease or are undergoing radiotherapy it is advised these patients are referred to secondary care for treatment under the supervision of a specialist. It is important to remember that if there is any doubt with regards to a patients' medical/dental/drug/social background, then liaising with either the patients' general medical practitioner (GP) or a specialist in secondary care would be a useful source of guidance.

Another consideration when deciding on how to manage AO should be that of antibiotic resistance. Due to the increasing prevalence of bacterial resistance to many common antibiotics, including those

used routinely in dentistry, clinicians should think carefully as to whether the risk outweighs the potential benefit. Additionally, thought should be given to the potential for hypersensitivity reactions that can be associated with chlorhexidine and antibiotic prophylaxis. Recent reports have highlighted two cases of death due to anaphylaxis following the use of chlorhexidine in post-extraction tooth sockets.<sup>39</sup> The case report concluded that there needs to be an increased awareness of the possibility of anaphylaxis to chlorhexidine-based products; with dentists playing an active role in reporting adverse drug reactions to the British National Formulary (BNF). Furthermore following their analysis of the case reports it was postulated that 'open wounds'<sup>39</sup> might increase the likelihood of allergic reactions occurring. Nevertheless, chlorhexidine-based products are widely used in routine dentistry. In fact chlorhexidine gluconate 0.2% accounts for 10.2% of all prescribed drugs by the GDP.<sup>40</sup> However, considering how routinely chlorhexidine is used in both primary and secondary care, the incidences of hypersensitivity are contextually still very low. Although mounting evidence of hypersensitivity reactions to chlorhexidine will place its routine use into question.

### Implications for future research

Currently the majority of studies focus on the development of AO following the removal of third molars, therefore, there is a need for future research into prophylactic interventions for other high risk patients. In addition, all of the studies identified by the Cochrane reviews were conducted in a hospital setting and this is in contrast to the fact that the majority of extractions in the UK are performed in primary and specialist settings. The robustness and applicability of future research would be improved if large studies (prospective randomised controlled trials) were conducted in primary/specialist practice settings. Furthermore, in order to ascertain the most recent trials on the effectiveness of antibiotics or chlorhexidine (CHX) prophylaxis to alveolar osteitis, the search terms used in the Cochrane reviews were re-run. This enabled any recent studies to be highlighted and also analysed. The results showed that no new studies had been published examining the benefits of systemic antibiotic prophylaxis to AO, while only one study had been published on the effectiveness of CHX. This was a double blind split mouth randomised controlled clinical trial, which concluded that 0.2% CHX gel postoperatively can significantly reduce the incidence of AO following third molar extraction.<sup>41</sup>

### CONCLUSION

There is potential for the use of local and systemic prophylactic interventions for the prevention of AO, however, further well conducted research in primary/specialist care is required for conclusive guidance. Trials should concentrate on high-risk individuals and highlight ways of reducing likelihood of developing AO.

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