

New paradigm in explaining Dry Socket : Case studies

ABSTRACT

Dry socket is considered as the most common complication after tooth extraction. It is mainly manifested by severe irradiating pain that start 2 to 4 days after dental extraction with a denuded socket. Although many risk factors are associated with it, no clear and direct cause has been described to explain its etiopathogenesis. Here, we suggest new pathogenesis and new management of Dry Socket based on new microbiological findings from three cases.

We present a series of three dry socket cases from which alveolar swabs were taken for microbial exploration. Material from the 3 cases were subjected to bacterial culture and susceptibility testing.

Microbiological results showed the presence of *Pseudomonas aeruginosa* in all samples. Furthermore, the antibiogram showed sensitivity to Ciprofloxacin. These results suggest a new approach in preventing and treating Dry Socket based on an infectious process .

Keywords: Dry Socket, localized alveolitis, alveolar osteitis, *Pseudomonas aeruginosa*, bacterial biofilm

1. INTRODUCTION

The Dry Socket is considered as the most common complication following dental extraction , it begins two to four days after the extraction when the blood clot partially or totally disintegrates,the alveolus becomes denuded ,exposed (Fig.1) , tender to touch,, and sometimes covered by necrotic gray tissue. Mainly manifested by with severe ,irradiating and resistant pain,and may be associated with bad odour and taste and lymphadenitis (1).The aim of the paper is to suggest a new paradigm in explaining and treating Dry Socket by presenting 3 different cases in which bacterial cultures was performed in order to explore a new microbiological aspect of Dry Socket.

2. CASE REPORTS

We present three cases of Dry Socket in 3 different patients, aged 23 to 60 years.

The first case involved a 60-year-old woman with acute periapical periodontitis on first lower right molar. The persistent and severe pain after extraction, made her physician son worried and concerned about the complicated pain and suggested doing a bacterial culture to explore any possible microbial source behind this pain. For this purpose a swab of the alveolus was done for bacterial culture. The result showed the presence of *Pseudomonas aeruginosa*, which was sensitive to Ciprofloxacin. This drug was therefore prescribed at a dose of 500 mg, three times a day, according to the anti-pseudomonal protocol. Twenty-four hours after taking it, the patient was completely relieved.

The second case was associated with the surgical extraction of the mandibular third molar with anterior pericoronitis. The third case was a simple extraction of an infected lower second premolar with a periapical abscess.

The details are summarized in (Table 1).

All patient's medical history was noncontributory. Alveolar swab was performed for all and showed positive culture to *Pseudomonas aeruginosa*, topical treatment of Dry Socket, that rely on the use of topical eugenol as alveolar dressing was inefficient for all patients, therefore they were treated by Ciprofloxacin tablet with a dose of 500 mg for three times per day, all patients were completely relieved from symptoms within 24 to 36 hours.

The diagnosis of Dry Sockets was based on clinical signs and symptoms including three main criteria : 1)onset of symptoms between two and four days,2)the clinical appearance of denuded socket (Fig.1)(Fig.2)(Fig,3) and 3)the rebellion aspect of pain to conventional analgesics such as pure analgesics and nonsteroidal anti-inflammatory drugs.

Table 1. Details of the three studied cases of Dry Socket

Tooth number	Age	Gender	Simple extraction	Surgical Extraction	Presence of preexisting Infection
46	60	female	+		+
48	23	male		+	+



Figure.1. Clinical appearance of Dry Socket of Case 1



Figure. 2. Clinical appearance of Dry Socket of Case 2



Figure. 3. Clinical appearance of Dry Socket of Case 3

3. DISCUSSION

According to previous literature, a specific cause of Dry Socket has not yet been identified, but several local or systemic risk factors play a role in its mediation. Local predisposing factors

include difficult or traumatic extractions, use of vasoconstrictors such as epinephrine, amount of anesthesia, pre-existing infection like pericoronitis and periodontitis, and poor oral hygiene (2). Systemic predisposing factors include age, the use of oral contraceptives and anti-inflammatory drugs, the presence of comorbidities such as diabetes and chemotherapy(2)(3). Women are at higher risk. Dental extraction during the first three weeks of the menstrual cycle may increase the incidence of Dry Socket (4).

To date, all theories that tried to explain the pathophysiology of Dry Sockets are based on the role of blood clots either by lack of formation, abnormal formation, or early disintegration (1).

The role of bacteria in the pathogenesis of Dry Sockets has been described as a contributing factor. Bacteria, mainly present in the oral cavity as *Treponema denticola* (4), can release enzymes, like streptokinase and staphylokinase, to activate fibrinolysis. Other bacteria, such as *Capnocytophaga ochracea*, *Fusobacterium nucleatum*, *Prevotella melaninogenica*, *Treptococcus anginosus*, *Treponema socranskii*, or *Streptococcus sanguis*, can also affect the alveolar repair process by producing higher levels of C-reactive proteins (5).

Bacteria forming biofilms such as *Pseudomonas aeruginosa* has never been mentioned as the principal cause of Dry Socket. Biofilm is a collection of complex microbial communities that can attach to a surface or form aggregates without adhering to the surface, as in the cases of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and other types of bacteria (6).

Pseudomonas aeruginosa by forming a biofilm lead a bacterial resistance and systemic antimicrobial would be in most cases inefficient (6) . This bacteria can disseminate bone and could be associated with mandibular osteomyelitis (7).

According to our findings, which are based on bacterial culture and based also on the positive response to a specific antimicrobial agents on 3 different cases(targeting *Pseudomonas aeruginosa*), we concluded that pathogenesis exclusively premised on disorder in blood clot cannot alone explain the pathophysiological and clinical aspects behind the Dry Socket therefore we hypothesized that the Dry Socket is a complication that might be caused by a specific bacteria, disorder in blood clot is considered as a stage in the pathophysiological infectious process. Infection due *Pseudomonas aeruginosa* could better explain the pathophysiology of Dry Socket and in particular the four clinical hallmarks of this complication as detailed below.

1-The onset: clinical symptoms culminate in up to 4 days, and mainly manifest through severe pain, this period is equivalent and just refer to the incubation period of *Pseudomonas aeruginosa* (8).

2-Exposed and denuded alveolus (mainly caused by fibrinolysis): *Pseudomonas aeruginosa* could manifest intrinsic fibrinolytic properties, in order to enhance invasiveness, it can bind to plasminogen and convert it to plasmin and as consequence could have fibrinolytic effect (9). In addition, *Pseudomonas aeruginosa* by inducing p38MAP kinase also can affect coagulation and fibrinolysis (10), This fibrinolysis effect would eventually lead to a denuded and exposed alveolus or socket.

3-Inflammation process and severity of pain.

Inflammation in the presence of *Pseudomonas aeruginosa* could be explained by the fact that bacteria's presence induces p38MAP kinase-dependent IL-6 and CXCL8 by the bacteria and via a Syk kinase pathway, IL-6 and CXCL8 are proinflammatory cytokine/chemokine, the cytokine IL-6 is responsible for triggering the acute phase proteins and immune cell differentiation and CXCL8 is associate to neutrophil migration to the site of infection (11), this proinflammatory chemicals related to infection in addition to others related to trauma (during extraction) could explain the associated severe pain.

4-Lymphadenitis.

The infection process can best explain lymphadenitis present in Dry Socket.

Pseudomonas aeruginosa can be present in the tissue surrounding the tooth before extraction in a chronic or acute form of infection (pericoronitis, periapical infection, periodontitis) or could also contaminate the socket during extraction from other sources (saliva, irrigating water from handpiece) ...

Hence, according to our observations and findings, the presence of bacteria might explain the pathogenesis of Dry Socket and specifically the presence of bacteria that could form biofilm and in particular *Pseudomonas aeruginosa* that could be considered as main cause of this complication.

This hypothesis (infectious process) is grounded on the following facts:

1-All predisposing factors, previously mentioned, that would lead to Dry Socket are in fact associated to local and systemic immune decrease and polymorphonuclear(PMN)cells

dysregulation. For example, it has been shown that smoking can have negative effect on oral PMN and local immunity (12). In addition to that, the presence of previous infection at the site before extraction can exhaust the function of PMNs. As for woman taking oral contraceptives, they showed lower phagocytic capacity of their neutrophils compared to control(13). Moreover, traumatism during tooth removal can induce ischemia in the site, moreover, difficult and traumatic procedure can raise the level of patient's stress that might lead to neutrophil dysregulation (14). Conversely lower incidence of Dry socket with the use of oral antiseptic. or systemic antibiotics (15) support more an infectious process.

2-The presence of *Pseudomonas aeruginosa* associated to Dry Socket cases revealed by bacterial culture.

3-The total efficacy of antibiotic protocol based on antibiogram and designed against *Pseudomonas aeruginosa*(Ciprofloxacin 20mg / kg/day). Conversely, other antibiotic with broad spectrum but not designed or not targeting *Pseudomonas aeruginosa* such as Penicillin A plus Clavulanic acid were inefficient in treating Dry Socket(2).

4-In previous studies, the only molecule that showed systemic prophylactic efficacy in reducing the onset of Dry Socket was the azithromycin (2) ,and it is the only molecule, among that were used, that had demonstrated therapeutical effect against *Pseudomonas aeruginosa*(16).

5- Theories based on blood clot cannot explain the occurrence of Dry Socket as a complication of coronectomy, the procedure in which only a part of the tooth is removed (the crown) leaving the root in the socket that means neither a real socket nor a blood clot is present in this procedure (17)

6- The efficient use of topical eugenol in the socket described by many authors (2), support the theory of bacterial biofilm causality rather than theory based on blood clot, because eugenol has beside it sedative effect, an antibacterial effect and mainly as biofilm disruptor related to *Pseudomonas aeruginosa* (18).

7- Disorder in blood clot cannot explain the pathophysiology and in particular lymphadenitis and the severity of pain manifested in Dry Socket,while infection process due to pseudomonas can explain lymphadenitis and the severity of inflammatory pain.

8- The isolation of *Pseudomonas aeruginosa* in dental infection by many authors support our hypothesis (19)(20).

Based on our hypothesis, we propose some measures for Dry Socket management. Preoperatively we should:

- 1-Improve oral hygiene before any dental extraction to reduce the bacterial load.
- 2-Mouth washing with 2% Chlorhexidine for 30 seconds before extraction.
- 3-Prescribe prophylactic antibiotics particularly for risky patients, during invasive procedures, and in cases of pre-existing surgical site infection. The best prophylactic molecule against *Pseudomonas aeruginosa* is Azithromycin or Ciprofloxacin.
- 4- Irrigate the socket copiously after extraction, using 2% Chlorhexidine and 5% Iodine.

Postoperatively, a pharmacological treatment should be applied:

- 1-Antimicrobial protocol designed against *Pseudomonas aeruginosa* in rebellion cases to topical treatment ,this mainly consist of Ciprofloxacin (20mg/kg): If azithromycin was not prescribed preoperatively or was not effective.
- 2-Painkillers if necessary.

4. CONCLUSION

Dry Socket is one of the most morbid complications associated with tooth extraction. The management of Dry Socket is a challenge, especially when conventional treatment is ineffective. Knowing the exact etiopathogenesis of Dry Socket would help the dental surgeon to apply an effective and targeted treatment and would help him to reduce its incidence by applying appropriate measures based on an antimicrobial approach.

LIMITATIONS

The limitations of our results lie in the fact that they are based on a limited number of patients. Further investigations are needed on a larger number of patients, with microbiological and immunological explorations, in order to find stronger evidence and to explore the infectious process more deeply. The study of the possible involvement of other bacteria in the pathogenesis of dry sockets is also necessary.

CONSENT

Written consent has been signed by patients before performing bacterial culture and using results by author.

REFERENCES

- 1- Cardoso CL, Rodrigues MT, Ferreira Júnior O, Garlet GP, de Carvalho PS. Clinical concepts of dry socket. *J Oral Maxillofac Surg*. 2010;68(8):1922-1932. doi:10.1016/j.joms.2009.09.085
- 2- Tarakji B, Saleh LA, Umair A, Azzeghaiby SN, Hanouneh S. Systemic review of dry socket: aetiology, treatment, and prevention. *J Clin Diagn Res*. 2015;9(4):ZE10-ZE13. doi:10.7860/JCDR/2015/12422.5840
- 3- Almutairi, B, Dry sockets – a systemic review. *Advancements in Life Sciences*. 2019;(7) 48-57.
- 4- Gowda GG, Viswanath D, Kumar M, Umashanker D. Dry socket (alveolar osteitis): Incidence, pathogenesis, prevention and management. *J Indian Acad Oral Med Radiol*. 2013;25(3): 196-9.
- 5- Rodrigues MT, Cardoso CL, Carvalho PS, et al. Experimental alveolitis in rats: microbiological, acute phase response and histometric characterization of delayed alveolar healing. *J Appl Oral Sci*. 2011;19(3):260-268. doi:10.1590/s1678-77572011000300015
- 6- Roy R, Tiwari M, Donelli G, Tiwari V. Strategies for combating bacterial biofilms: A focus on anti-biofilm agents and their mechanisms of action. *Virulence*. 2018;9(1):522-554. doi:10.1080/21505594.2017.1313372
- 7- Coviello V, Stevens MR. Contemporary concepts in the treatment of chronic osteomyelitis. *Oral Maxillofac Surg Clin North Am*. 2007;19(4):523-vi. doi:10.1016/j.coms.2007.07.001
- 8- Al-kafaween, M.A., Hilmi, A.M., Jaffar, N., Al-jamal, H.A., & Zahri, M. Determination of optimum incubation time for formation of *Pseudomonas aeruginosa* and *Streptococcus pyogenes* biofilms in microtiter plate. *Bulletin of the National Research Centre*. 2019;(43):1-5.
- 9- da Silva CM, de Abreu Vidipó L, Nishi R, Cristina Plotkowski M. Binding of plasminogen to *Pseudomonas aeruginosa* results in formation of surface-associated plasmin and enhanced bacterial invasiveness. *Microb Pathog*. 2004;36(2):59-66. doi:10.1016/j.micpath.2003.09.006
- 10- Giri H, Cai X, Panicker SR, Biswas I, Rezaie AR. Thrombomodulin Regulation of Mitogen-Activated Protein Kinases. *Int J Mol Sci*. 2019;20(8):1851. Published 2019 Apr 15. doi:10.3390/ijms20081851
- 11- Coates MS, Alton EFWF, Rapeport GW, Davies JC, Ito K. *Pseudomonas aeruginosa* induces p38MAP kinase-dependent IL-6 and CXCL8 release from bronchial epithelial cells via a Syk kinase pathway. *PLoS One*. 2021;16(2):e0246050. Published 2021 Feb 1. doi:10.1371/journal.pone.0246050

- 12- Kenney EB, Kraal JH, Saxe SR, Jones J. The effect of cigarette smoke on human oral polymorphonuclear leukocytes. *J Periodontal Res.* 1977;12(4):227-234. doi:10.1111/j.1600-0765.1977.tb00126.x
- 13- Giraldo E, Hinchado MD, Garcia JJ, Ortega E. Influence of gender and oral contraceptives intake on innate and inflammatory response. Role of neuroendocrine factors. *Mol Cell Biochem.* 2008;313(1-2):147-153. doi:10.1007/s11010-008-9752-2
- 14- Tsukamoto K, Machida K. Effects of psychological stress on neutrophil phagocytosis and bactericidal activity in humans--a meta-analysis. *Int J Psychophysiol.* 2014;91(2):67-72. doi:10.1016/j.ijpsycho.2013.12.001
- 15- Houston JP, McCollum J, Pietz D, Schneck D. Alveolar osteitis: a review of its etiology, prevention, and treatment modalities. *Gen Dent.* 2002;50(5):457-465.
- 16- Imperi F, Leoni L, Visca P. Antivirulence activity of azithromycin in *Pseudomonas aeruginosa*. *Front Microbiol.* 2014;5:178. Published 2014 Apr 22. doi:10.3389/fmicb.2014.00178
- 17- Pitros P, O'Connor N, Tryfonos A, Lopes V. A systematic review of the complications of high-risk third molar removal and coronectomy: development of a decision tree model and preliminary health economic analysis to assist in treatment planning. *Br J Oral Maxillofac Surg.* 2020;58(9):e16-e24. doi:10.1016/j.bjoms.2020.07.015
- 18- Lou Z, Letsididi KS, Yu F, Pei Z, Wang H, Letsididi R. Inhibitive Effect of Eugenol and Its Nanoemulsion on Quorum Sensing-Mediated Virulence Factors and Biofilm Formation by *Pseudomonas aeruginosa*. *J Food Prot.* 2019;82(3):379-389. doi:10.4315/0362-028X.JFP-18-196
- 19- Vieira Colombo AP, Magalhães CB, Hartenbach FA, Martins do Souto R, Maciel da Silva-Boghossian C. Periodontal-disease-associated biofilm: A reservoir for pathogens of medical importance. *Microb Pathog.* 2016;94:27-34. doi:10.1016/j.micpath.2015.09.009
- 20- Souto R, Silva-Boghossian CM, Colombo AP. Prevalence of *Pseudomonas aeruginosa* and *Acinetobacter* spp. in subgingival biofilm and saliva of subjects with chronic periodontal infection. *Braz J Microbiol.* 2014;45(2):495-501. Published 2014 Aug 29. doi:10.1590/s1517-83822014000200017