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Review Article

Platelet-Rich Fibrin Concentrate use and Alveolar Osteitis Incidence: A Systematic Review of Literature

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Abstract

Aim: This article features a systematic literature review analyzing the relationship between the use of platelet-rich fibrin concentrate (PRF) in post-extraction sockets and alveolar osteitis occurrence risk.

Materials and Methods: The review was performed through Web of Science database using the following terms: "(alveolar osteitis OR dry socket) AND (prf OR platelet rich fibrin)." Five articles were chosen after careful selection and application of inclusion and exclusion criteria. The risk of study bias was assessed using the Cochrane Risk of Bias (RoB) tool.

Results: The analyzed articles evaluated an average reduction in the occurrence of dry alveolitis following PRF application in post-extraction sockets. The articles have also defined that platelet-rich fibrin concentrate, administered either in combination with other substances or in isolation, may be able to promote both the wound healing process and the patient's postoperative course.

Conclusions: PRF use may represent an excellent option for the clinician to reduce post-extraction alveolitis occurrence. PRF application should always be evalated taking in consideration all the pros and cons of its specific use and all the patient's characteristics.

Introduction

Alveolar osteitis, also called " dry alveolitis" or "post-extraction alveolitis", is one of the most severe pathological events that may happen after dental extraction [1]. This postoperative complication is defined as an infectious-inflammatory phenomenon of dental socket. Dry alveolitis causes the development of a strong pain, which increases between the first and third day following dental extraction [2]. Post-extraction alveolitis is a pathological disorder induced by clot formation failure, or clot removal, and thus a faulty wound healing process. This leads to the infection of the socket and to the development of local tissue necrosis, halitosis, severe diffuse pain, potential alveolar bone exposure, possible lymph node enlargement and fever. Many conditions favor dry alveolitis occurrence, such as smoking habits, poor oral hygiene, different systemic diseases, corticosteroids consumption, intra-oral infections, oral contraceptives intake and local trauma [3]. Moreover, post-extraction alveolitis probability ranges from 0.5 to 5 % and may even exceed 30 % in relation to the lower third molar [4]. The reason for the increased dry alveolitis occurrence following lower third molar extraction is not completely clear. This, however, may be related to an increased intraoperative trauma during extraction procedures and increased bony vascularization of mandibular posterior areas. Although the higher vascularization could certainly lead to clot formation, it could also bring blood factors responsible for incorrect clot development [5]. Treatment of this condition includes socket revising to remove necrotic residues and using antiseptic solutions to both reduce infectious component and achieve better socket clearance. It's also necessary to ensure the presence of bleeding in socket to allow clot formation. Gauze soaked with antibacterial and analgesic material may also be positioned within the socket to promote healing. Analgesic, anti-inflammatory and, when necessary, antibiotics are also prescribed to favour patient's postoperative course and to reduce microbial component [6].

The best current weapon against alveolar osteitis is its prevention and many possible solutions to reduce its occurrence have been described in literature. One of the most common methods is the use of gels or chlorhexidine solutions within the post-extraction socket. This substance, due to its antiseptic and disinfectant properties, is active against the microbial component that, according to Nitzan, represents the primary etiologic agent of clot degradation [7]. The use of chlorhexidine is the most evidence-based method in literature regarding its preventive action against post-extraction alveolitis occurrence. The review of Blánaid Jm Daly et al. showed that the use of chlorhexidine (0.12% and 0.2%) both as pre- and post-operative rinse and as gel placed in post-extraction sockets is able to reduce the occurrence of dry alveolitis [8]. Other substances have been proposed as potential preventive solutions and platelet-rich fibrin (PRF) is one of them. PRF is a platelet-rich fibrin concentrate obtained from patient's blood. A patient's venous blood is drawn and a centrifugation of the sample is carried out. This procedure allows the patient's blood components to be separated and a fibrin-based compound is then obtained. PRF is rich in platelets and contains a high amount of growth factors that can promote new vessel formation and bio-stimulation of bone growth [9].

As a matter of fact, Vasilena Ivanova et al. reported an increased amount of vital bone formation four months after extraction of 90 tooth without bone defects [10]. PRF has an antalgic and anti-inflammatory effect due to its polarizing action on macrophages. Moreover, it promotes wound healing due to its high platelets' concentration [11]. Regarding diagnostic and intra-operative management pathway, the clinician must evaluate which are the most favorable conditions and situations according to each specific case. The high occurrence of dry alveolitis in lower third molar extraction, especially in smoking patients, may lead the clinician to use some substances, such as PRF. However, it is necessary to analyze what are the scientific

literature findings in order to define the clinical utility and the advantages that PRF can provide. The use of PRF must be evaluated in relation to its disadvantages, considering what this solution entails for the patient. The aim of this paper is to describe a literature systematic review about preventive PRF use in post-extraction sockets in relation to dry alveolitis occurrence. This review wants to give the clinician a clearer view when choosing the best therapeutic solution for each specific case.

Materials and Methods

This literature review was made using the Prism 2020 work protocol (Preferred Reporting Items for Systematic reviews and Meta-Analyses). Articles were searched through Web of Science platform and studies published from 2011 to 2022 were analyzed. The research was carried out using the following keywords: "(alveolar osteitis OR dry socket) AND (prf OR platelet rich fibrin)." 68 initial articles were identified. The identified studies were then selected by title and abstract. The following inclusion and exclusion criteria were then applied.

INCLUSION CRITERIA	EXCLUSION CRITERIA
English-language articles.	Case reports and Case series.
Articles published from 2011 to the present.	Narrative reviews, systematic reviews and meta-analyses.
Articles comparing preoperative PRF use and alveolar osteitis occurrence.	Articles with text or abstract not available.
	Animal studies.
	A-PRF o L-PRF.

Figure 1: Inclusion and exclusion criteria.

Five articles that satisfied the inclusion and exclusion criteria were selected and these studies were included in our review.

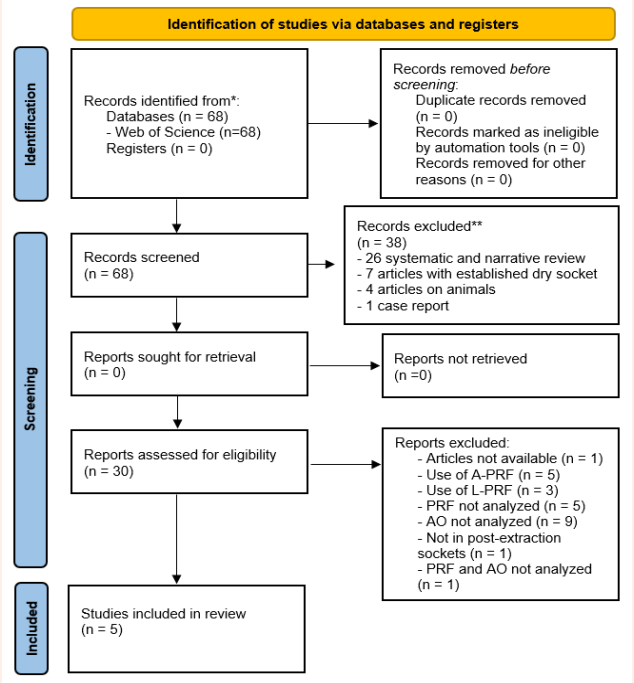

Figure 2: PRISMA 2020 flow diagram for new systematic reviews, which included searches of databases and registers only

	RANDOM SEQUENCE GENERATION (SELECTION BIAS)	ALLOCATION CONCEALMENT (SELECTION	BLINDING OF PARTECIPANTS AND PERSONNEL (PERFORMANCE BIAS)	BLINDING OF OUTCOME ASSESSMENT	INCOMPLETE OUTCOME DATA (ATTRITION	SELECTIVE REPORTING (REPORTING BIAS)	OTHER BIAS
Majid Eshghpour et al. (2014)	+	?	+	+	?	?	+
H. Unsal et al. (2018)	+	?	+	+	+	?	+
Majid Eshghpour et al. (2018)	+	?	+	+	-	?	+
F Asutay et al. (2016)	?	?	+	?	+	?	+
Huda Moutaz Asmael et al. (2018)	?	-	?	+	+	?	+

Figure 3: Risk of bias assessed through Cochrane Risk of Bias (RoB). Results for each study (+ = low; - = high; ? = unclear).

The validity of the studies was analyzed and assessed by means of Cochrane Risk of Bias (RoB) tool. The comparison parameters were: randomization technique, allocation concealment, patient blindness, staff blindness, outcome examiner blindness, completeness of outcome data, outcome selection and other bias. Results were classified as follows:

Low risk of bias: all domains judged to be at "low risk of bias."

Unclear risk of bias: "unclear risk of bias" in at least one domain and no domains with "high risk of error."

High risk of bias: at least one domain with "high risk of bias".

Results

Table 1: Study table of articles.

AUTHOR	TYPE OF STUDY	PATIENTS NUMBER AND POST-EXTRACTION SOCKETS NUMBER	POST-EXTRACTION SOCKETS WITH AND WITHOUT PRF	AO FREQUENCE
Majid Eshghpour et al. (2014)	Rtc	- 78 patients (non-smokers) - 156 bilateral impacted lower third molars (2 for each patient)	- 78 with PRF -78 without PRF (one for each patient)	- Frequency of AO in PRF group is 44% compared with control group. - Overall AO frequency was 14.74%.

H. Unsal et al. (2018)	Rtc	- 50 patients (32 smokers) - 100 bilateral, symmetrically oriented, partially erupted lower third molars (two for each patient)	- 50 with PRF - 50 without PRF (one for each patient)	- Frequency of AO in PRF group is 8% and in control group 18%. - Non-smokers had AO and 37.5% of smokers had AO.
Majid Eshghpour et al. (2018)	Rtc	- 241 patients (non-smokers) - 482 bilateral impacted mandibular third molars (two in each patient)	- 118 patients: one socket treated with PRF and the other socket without PRF. -123 patients: one socket treated with PRF-CHX and the other socket without PRF-CHX.	-Overall frequency of AO is 15.14%. - Frequency of AO in PRF is 17.37%. -Frequency of AO in PRF-CHX group is 13%. - Frequency of AO in PRF group is 46% compared with control group. - Frequency of AO in PRF-CHX group is 18% compared with control group. - Frequency of AO in PRF-CHX group is 37% compared with PRF group.
F Asutay et al. (2017)	Rtc	- 30 patients (non-smokers) - 60 bilateral symmetric impacted lower third molars (two in each patient)	- 30 with PRF - 30 without PRF (one for each patient)	-3 cases of AO in control group and 1 case of AO in PRF group.
Huda Moutaz Asmael et al. (2018)	Rtc	- 20 patients (smokers) - 40 dental elements (2 for each patient, same type of tooth: 2 central incisors, two premolars, two molars...)	- 20 with PRF - 20 without PRF (one for each patient)	- The rate of post-extraction osteitis in the control group was 5%, while it was 0% in the study group.

Discussion

Five "Randomized Controlled Trial" were selected and analyzed in this systematic review. This type of article has the highest scientific evidence level after meta-analyses and systematic reviews. The risk of bias assessment identified two articles with a high risk of bias and three articles with an unclear risk of bias. An important factor to take into account is that comparison between post-extractive socket treated with PRF and without PRF was performed on the same patient. This aspect allowed for the elimination of distorting factors determined by inter-individual differences in subjects. Four studies of the review examined alveolar osteitis incidence following lower third molar extraction. It is relevant to notice that dry alveolitis occurrence appeared to be higher for lower third molar extraction than all other dental elements. Moreover, the post-extraction alveolitis incidence featured in this review is increased due to the fact that the articles considered only impacted or partially erupted third molars. The first article evaluated the PRF use in post-extraction sockets of impacted lower third molars in preventing alveolar osteitis occurrence. The patients were non-smokers and variables such as age, gender, complexity of surgery, operator experience and number of anesthetic cartridges used were evaluated. No significant differences were found among the control and treated group in terms of the above variables. On the overall sample, there was a 14.74 % of AO total occurrence. Outcomes related to AO incidence, assessed in the first week after surgery, were lower in the PRF-treated sockets group than in the control group [12].

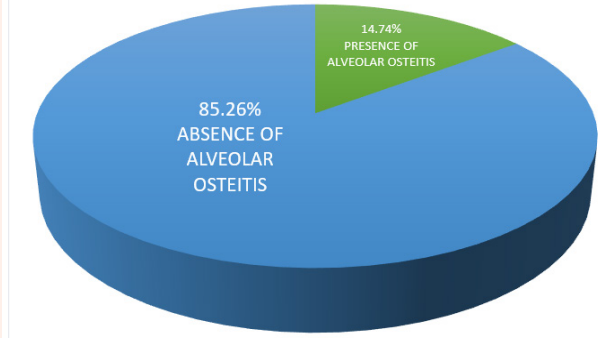

Figure 5: Chart of dry alveolitis onset.

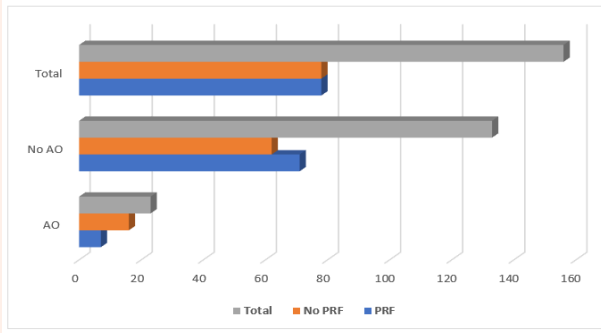

Figure 6: AO frequency in relation to PRF use.

H. Unsal's article examined the relationship between PRF use in post-extraction sockets of 100 partially erupted lower third molars and the occurrence of post-extraction alveolitis in smoking and non-smoking subjects [13]. The incidence of dry alveolitis in the PRF group was 8% while in the control group it was 18%. This difference was not deemed statistically significant by the authors. A clear difference was found between PRF-treated group and control group regarding AO occurrence in smoking patients. In fact, AO was found in 37.5 % of the control group and no cases of dry alveolitis were detected in the PRF-smoking group.

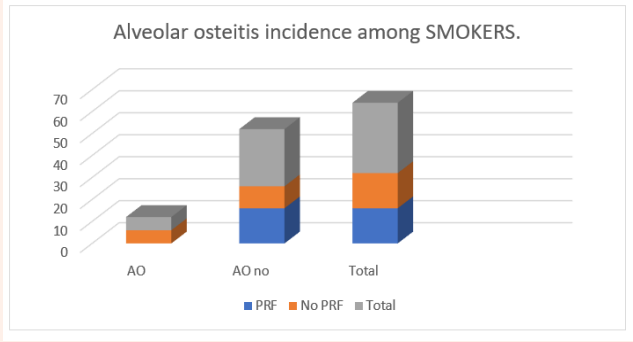

Figure 7: AO frequency among smoking subjects.

Moreover, variables such as mean postoperative pain level and periodontal probing depths were analyzed. Lower values regarding pain after surgery were found in PRF group than in control group and no significant differences were found in periodontal probing depths. The third article analyzed the use of platelet-rich fibrin concentrate in association with 0.2 % chlorhexidine gel in relation to post-extraction alveolitis occurrence [14]. 482 impacted lower third molars in 241 non-smoking patients were extracted. The post extraction sockets were divided in three groups: use of CHX+PRF, use of PRF and control group. The total occurrence frequency of AO was 15.14%. Occurrence of dry alveolitis in PRF-CHX and PRF groups was lower than in the control group and the results were significantly higher for PRF-CHX group than PRF group. This article suggests that the use of PRF and 0.2% chlorhexidine gel may be an excellent tool to prevent post-extraction alveolitis in non-smoking patients, even better than just platelet-rich fibrin concentrate.

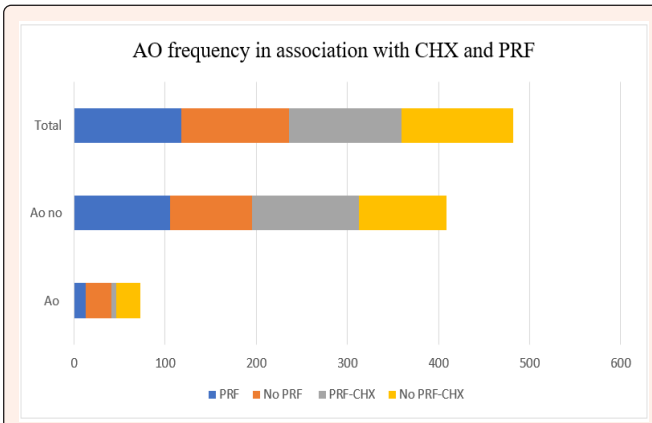

Figure 8: AO frequency in association with CHX and PRF.

F. Asutay's article found no significant differences in postoperative pain, edema and trismus after the extraction of 60 impacted lower third molars in 30 non-smoking patients [15]. One AO case was found in PRF group and only 3 cases of AO were detected in control group. By considering limitations like the small number of specimens and lack of comprehensive evaluation of sample characteristics, this article did not show clinical advantages regarding PRF use in post-extractive sockets. This was particularly evident regarding AO occurrence probability. Huda Moutaz Asmael's study compared PRF use in post-extraction sockets following the removal of different dental types [16]. Patients were all smokers. Soft tissue healing was better and post-operative inflammation was lower in PRF group than in control group. However, no significant differences were found in alveolar osteitis occurrence. The frequency of post-extraction alveolitis were 5 % for control group and 0 % for PRF group. The articles of this review have many limitations, like sample size, specimen characteristics, smoking or non-smoking patients and tooth kind. The analysis performed in this systematic review supports that platelet-rich fibrin, or its combination with substances like hyaluronic acid or chlorhexidine, may be a potential factor in reducing post-extraction alveolar osteitis occurrence. This is due to the biological characteristics of the substance, which is able to promote neo-angiogenesis, bone formation and improve immune system. This review also reveals that PRF seems to have the capability to reduce postoperative pain and promote tissue healing, as reported by J. Zhu et al. regarding mandibular third molar extraction [17]. The study of J. Zhu et al. also showed that the use of PRF following mandibular third molar extraction resulted in a lower incidence of alveolar osteitis compared with the control group [17]. In addition, the article of Ming-Zhe Bao et al. affirmed that the use of PRF in post-extraction sockets of mandibular third molars is also able to reduce both postoperative swelling and degree of trismus following surgery [18]. Moreover, no significant differences were found in demographic variables like sex, gender, intra-oral conditions and systemic features of patients. Except for smoking in two articles, the studies excluded cases with factors that could interfere with the results, such as corticosteroids intake, poor oral hygiene, presence of current pericoronitis, antibiotic consumption before surgery and pregnant patients. However, more studies are needed to obtain as much scientific evidence as possible about all these topics.

Conclusion

Despite the limitations of this review, like small number of studies, differences within the sample groups and various intra-operative characteristics, use of platelet-rich fibrin concentrate, or its combination with other substances, may reduce alveolar osteitis incidence in post-extractive sockets. However, further studies are needed to get more scientific evidence regarding benefits of PRF use in post-extraction sockets. In addition, the clinician must consider not only the advantages but also the disadvantages of using this substance, such as the increased invasiveness and the higher biological cost. This is necessary to provide benefits optimization and postoperative morbidity reduction according to patient's characteristics and conditions.

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