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Review

Treatment of oroantral communication with Platelet-Rich Fibrin: A systematic review

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ABSTRACT

Background: Oroantral communication (OAC) is the opening between the maxillary sinus and the oral cavity, which constitutes a gate for the mucosal infection in the maxillary sinus. On the other hand, an OAF develops when the OAC does not close spontaneously, remains manifest and is epithelialized. Several methods have been proposed to solve these situations, however, they are associated with increased postoperative morbidity and/or higher associated costs and require some experience of the surgeon to perform them. To overcome these disadvantages, the use of Platelet-Rich Fibrin (PRF) is proposed. The present study aims to perform a systematic review of the literature, collecting cases in which PRF was used in the treatment of OACs/OAFs.
Materials and methods: An electronic search of the MEDLINE database (via PubMed) and Web of Science was performed using the following MeSH terms (*Medical Subjects Headings*): (oroantral communication OR oroantral fistula OR buccosinusal communication) AND (platelet-rich fibrin OR prf OR fibrin mesh). The criteria used were those described by the PRISMA® Statement. The search was not time-restricted and was updated to April 2021.
Results: After searching, 11 articles were included that met the established criteria. In these, PRF was used alone or in combination with bi- or trilaminar techniques achieving complete resolution in 100% of cases (n = 116).
Conclusions: With the limitations of this study, it can be established that PRF can be used alone for the treatment of OACs/OAFs up to 5 mm and, in larger defects, it is advisable to combine it with bi- or trilaminar techniques. PRF is an effective therapeutic option, with minimal associated postoperative morbidity compared to other techniques and allows the position of the mucogingival junction to be preserved. Its combination with bone grafting improves the starting point before the replacement of the missing tooth with a dental implant.

1. Introduction

Oroantral communications (OACs) and oroantral fistulas (OAFs) are complications frequently encountered by oral and maxillofacial surgeons. OAC is an unnatural communication between the maxillary sinus and oral cavity [1,2] which constitutes a gate for the mucosal infection in the maxillary sinus [3]. The frequency of such complication is between 0.5 and 13% and it depends on numerous factors, such as the anatomical structure of the maxillary sinus and its relationship with maxillary molar and premolar roots [3,4]; bone resorption secondary to tooth loss due to periodontitis [4]; the presence of the maxillary cysts and tumours; as a result of osteomyelitis and trauma; implant surgery and/or sinus augmentation procedures; radiation treatment; orthognathic surgeries or pathologic entities; the enucleation of these cysts and tumours may lead to OAC [1].

The primary factor for the treatment of acute OAC is closing the communication because it is essential to prevent food and saliva contamination that could cause bacterial infection, chronic sinusitis, and impaired healing [1,4]. In the absence of sinus infection, OACs can close spontaneously if the defect is up to 3–5 mm in diameter [1,2,5] and if the blood clot remains stable in the post-extraction alveolus during initial healing as it acts as a scaffold for epithelial cells to grow from the mucosal margins towards the centre of the defect [6]. Larger OACs require surgical intervention [1]. Clinically, it is complicated to determine the size of an OAC. Therefore, it is difficult to predict whether an OAC will heal without intervention [5]. Another

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prognostic factor is the timing of treatment to tooth extraction. Considering current opinions, OAC should be closed in 24 h. In this regard, the success rate associated with primary closure of an OAC is up to 48 h after its occurrence is 90–95%, after which time the risk of chronic sinusitis increases as does the risk of oroantral fistula (OAF). On the other hand, an OAF develops when the OAC does not close spontaneously, remains manifest and is epithelialized. Therefore, an OAF is a pathological unnatural canal lined by epithelium that may be filled by granulation tissue or by polyposis of the sinus membrane [5,7–10]. This epithelialization usually occurs when the perforation persists for at least 48–72 h. After this period, in approximately half of the patients intensified inflammatory changes make it impossible to effectively conduct the treatment [7,11]. The success rate for secondary closure of OAFs has been reported to be as low as 67% [1,7].

There are several therapeutic options in the treatment of OACs/OAFs, such as buccal advancement flap (BAF) [2], rotation of the buccal fat pad (BFP), placement of a gingival or connective tissue graft, free or pedicled, as well as autogenous distant flaps - tongue flap, auricular/ septal cartilage, or temporalis muscle flap. They can be combined with regenerative techniques, such as monocortical bone grafts [12], hydroxyapatite blocks [13], or collagen membrane placement. Tooth transplantation, interseptal alveolotomy or biostimulation with laser light, among others, have also been described [14]. Furthermore, the approach can be intraoral or combined with an endoscopic approach. However, these techniques have several disadvantages, and several authors have described the use of Platelet-Rich Fibrin (PRF) as an alternative to these techniques.

PRF was discovered in 2001 by Choukroun et al. [15] and constitutes the second generation of platelet concentrates, which do not require the addition of any platelet-activating substances (such as bovine thrombin or calcium chloride), like another previously described platelet-concentrates – such as Platelet-Rich Plasma (PRP) or Plasma Rich in Growth Factors (PRGF) [16]. In other words, glass tubes are used without any additives. After centrifugation, the blood is separated into three fractions: an upper fraction or platelet-poor plasma; an intermediate fraction consisting of a fibrin clot; and a final fraction, located at the base of the tube, consisting of erythrocytes [17]. The part used is the PRF clot which, once partially dehydrated, allows the obtention of membranes or plugs, as well as the released exudate, rich in growth factors.

The present study aims to perform a systematic review of studies describing the use of PRF in the treatment of OACs/OAFs.

2. Methods

2.1. Search strategy

An electronic search of the MEDLINE/PubMed database and Web of Science was performed using the following MeSH terms (*Medical Subjects Headings*): (oroantral communication OR oroantral fistula OR buccosinusal communication) AND (platelet-rich fibrin OR prf OR fibrin mesh). At the same time, a Google Scholar search was conducted for articles that met the criteria described above. The bibliographic references of the selected articles were analysed for publications that did not appear in the initial search and might be of interest. The search was not time-restricted and was updated to April 2021.

The criteria used were those described in the PRISMA® Statement [18] (*Preferred Reporting Items for Systematic Reviews and Meta-analysis).* The present systematic review aimed to answer the following "PICO" question (P=patient/population/problem; I=intervention; C=comparison; O=outcome):

In patients with OACs/OAFs (P), does PRF treatment (I) in comparison to other therapeutic options (C) produce better results and/or fewer postoperative complications (O)?

2.2. Clinical relevance

The present study is the first systematic review of the literature that attempts to evaluate the effect of PRF in the treatment of OACs/OAFs.

2.3. Eligibility criteria

Before starting, inclusion and exclusion criteria were defined for the resulting articles:

2.3.1. Inclusion criteria

Included articles were: (a) studies conducted in humans; (b) articles published in English or Spanish; (c) articles analysing the effect of PRF in the treatment of OACs/OAFs; (d) meta-analyses; (e) systematic reviews; (f) randomized clinical trials (RCTs); (g) cohort studies; (h) observational studies; (i) comparative studies; and (j) multi-centric studies.

2.3.2. Exclusion criteria

The exclusion criteria determined the exclusion of the following: (a) experimental laboratory studies; (b) animal studies; (c) articles whose main topic was not the treatment of OACs/OAFs employing PRF; (d) literature reviews; (e) duplicate articles; (f) books or book chapters; (g) letters to the Editor; and (h) commentaries.

2.4. Study records

Two researchers (A.-O.S.-P. and J.-F.P.-C.) independently compared the results to ensure completeness and removed duplicates. Then, the full title and abstracts of the remaining papers were screened individually. Finally, full-text articles to be included in this systematic review were selected according to the criteria described above. Disagreements over eligible studies to be included were discussed with a third author and a consensus was reached (N.K.).

2.5. Risk of bias

Data collection was conducted using a predetermined table designed in advance of the assessment of the resulting articles. Two independent reviewers (A.-O.S.-P. and A.U.) evaluated the methodological quality of eligible studies following the Joanna Briggs Institute (JBI) Critical Appraisal Tool for Case Reports [19], which incorporates 8 domains. The studies were classified as low-quality assessment studies (0–4 domains), or as high-quality assessment studies (5–8 domains). Moreover, NIH Quality Assessment Tool for Case-Control Studies [20] was also used. In both data extraction and risk of bias assessment, disagreements between the two were resolved through the intervention of a third author (J.-F.P.-C.).

3. Results

3.1. Study selection

After the initial search in MEDLINE/PubMed, 15 articles were found. After reading the titles and abstracts, 5 articles were excluded because they did not relate to the purpose of the study. Therefore, 10 full-text articles were considered. Finally, 9 articles were included through the MEDLINE/PubMed search [1–5,21–24]. Through Web of Science, after analyzing the 12 titles and abstracts and eliminating duplicate articles, one full-text article was evaluated and included [25]. Furthermore, one more article was included after analysing the references of the selected articles and through Google Scholar [26]. Therefore, 11 studies were included in the present systematic review (Fig. 1 and Table 1).

3.2. Study characteristics

All included studies were case reports (n = 4) [4,22,24,25] or case series (n = 6) [2,3,5,21,23,26], only one was a comparative study between PRF and BAF [1]. For this reason, and given the heterogeneity between the different studies, only a comparison between the two techniques could be established. The number of patients treated with PRF among the included studies was 116. In 100% of the cases, there was a complete resolution of the OACs/OAFs during the evaluated follow-up periods (7 days to 18 months). The protocols used to obtain the PRF were very diverse. The most commonly used was the "revolutions per minute (rpm) protocol", specifically, centrifugation of blood tubes at 3000 rpm, 10 min [1,5,21,24,26] or 15 min [25], although other authors used other parameters such as 1500 rpm, 8 min [2] or 14 min [4] and 2700 rpm, 12 min [3]. Only Gülşen et al. [23] referred to a "relative centrifugal force protocol", specifically, 400 g 10 min.

Five authors treated OACs immediately after tooth extraction [1,2,5,23,24], two studies did not specify [21,26] and the rest (n = 4) did so at variable times, which meant that there was an associated development of OAF, which were treated with PRF [4,21,22,26]. In the case of placing PRF directly on the OAC, most authors recommend suturing it to the gingiva surrounding the alveolus, to prevent migration of the PRF clot/membrane into the sinus and to favour the stabilisation of the blood clot [1,2,4,5,23–25].

Of the 5 authors who treated OAC immediately after tooth extraction [1,2,5,23,24], in three cases the diameter of the OAC was larger than 3 mm [1,5] or 5 mm [23], in one case it was up to 5 mm [2] and in another, the diameter was not specified [24]. In addition to the above, two other authors treated OACs larger than 5 mm [4,22]. The authors who used them in defects up to 5 mm claim that they can be used in larger defects, however, they were unable to demonstrate this as all cases included were 3–5 mm in diameter [2]. The method of calculating the size of the OACs varied from using a modified ball burnisher instrument of 3 mm in diameter [1,5] or measuring the diameter of the roots of the extracted teeth [2].

PRF in the treatment of OACs/OAFs was used alone, or as a part of bi- or trilaminar techniques:

3.2.1. PRF as a sole grafting material

Assad et al. [26] extracted a single tube of blood from which they obtained a PRF clot. One-third of this clot was introduced into the alveolus to seal the OAC and the remaining two-thirds were compressed to obtain a membrane that was used to seal the surgical site coronally. Bilginaylar [1,5] and Gülşen et al. [23] sealed OACs using two PRF clots in a single approach, while Demetoglu et al. [2] introduced 3–4 overlapping membranes.

The only comparative study was by Bilginaylar [1], who compared PRF (n = 21) versus BAFs (n = 15), both in a stand-alone approach. At 7 days postoperatively, they observed healthy granulation tissue

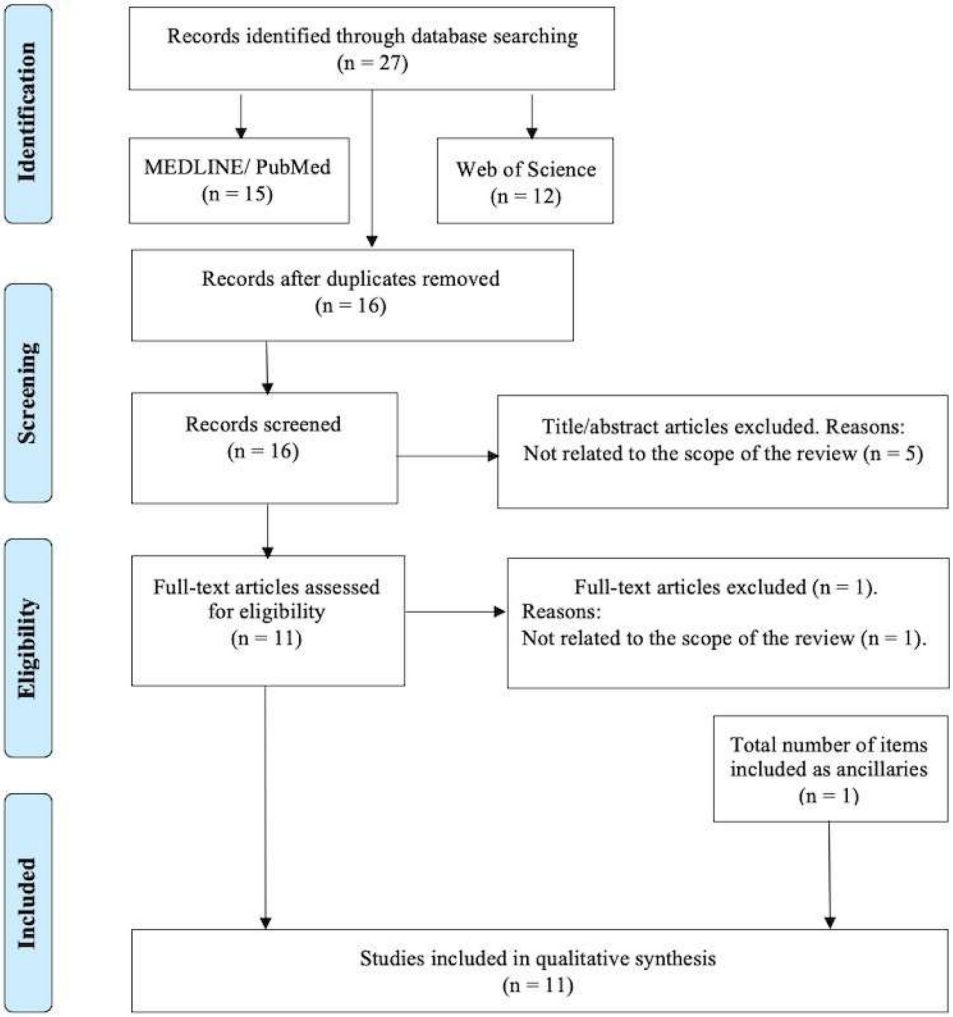

Fig. 1. PRISMA® flow diagram of the search processes and results.

Table 1
Results of included studies (BAF., buccal advancement flap; BFP., buccal fat pad; vs., versus; OAC., oroantral communication; OAF., oroantral fistula; 1M., first permanent molar; 2M., second permanent molar; 3M., third molar; 1PM., first premolar; 2dM., second deciduous molar; UNS., unspecified by authors; MRONJ., medication-related osteonecrosis of jaws; y., years; m., months; d., days; mins., minutes; rpm., revolutions per minute).

Autor(s)/ year	Technique and PRF product	PRF protocol	Position of OAC/ OAF	Defect type	Sample size	Age (years)	Time since tooth extraction	Success rate (%)	Follow-up	PostOp evolution
Al-Noori [25]	1 PRF clot over the OAC + BAF	3000 rpm, 15 min	2M	UNS	1	35	UNS. History of 2 surgical interventions using BAFs	100	1 m	10 d: OAF was epithelialised
Pandikanda et al. [24]	1 PRF membrane over the OAC + PRF clot mixed with collagen sponge and composite + PRF membrane	3000 rpm, 10 min	UNS	UNS	1	UNS	Immediate	100	2 m	2 m: The patient did not develop any sign of sinusitis.
Bilginaylar [1]	Only 2 PRF clots over the OAF	3000 rpm, 10 min	PRF: 1M ($n = 18$), 2M ($n = 3$) / BAF: 1M ($n = 11$), 2M ($n = 4$)	> 3 mm	21 PRF/ 15 BAF	UNS	Immediate	100	7 d	1 w: PRF., healthy granulation tissue; BAF., primary wound closure.
Esen & Akkulah [21]	2 PRF membranes + BFP + BAF	3000 rpm, 10 min	UNS	Stage III MRONJ	7	64.7 (± 8.6)	UNS	100	18 m	2 w: 2-3 mm of wound dehiscence persisted. 4 w: Mucosa completely re-epithelialised without dehiscence, infection, or necrosis. 18 m: No recurrence of OAC.
George [22]	PRF + BFP + BAF	UNS	1M	14 × 10 mm	1	77	Delayed. The aetiological factor was a dental implant.	100	9 d	9 d: Complete epithelialisation and no postoperative complications.
Demetoglu et al. [2]	Only 3–4 PRF membranes.	1500 rpm, 8 min	1M ($n = 14$), 2M ($n = 4$), 3M ($n = 2$), 2dM ($n = 1$)	≤ 5 mm	21	UNS	Immediate	100	2 m	3–5 w: Full epithelisation.
Al-Juboori et al. [4]	Slow-resorption collagen membrane + 1 PRF membrane + BAF	1500 rpm, 14 min	1PM	> 5 mm	1	32	> 3 m	100	6 w	1 w: The patient reported no pain or disconfort. 2 w: The wound matured, without signs of inflammation. 6 w: gingival hypertrophy.
Bilginaylar [5]	2 PRF clots	3000 rpm, 10 min	UNS	> 3 mm	21	UNS	Immediate	100	3 w	1 w: Healthy granulation tissue. 3 w: Full epithelialisation.
Assad et al. [26]	1/3 of the PRF clot was placed over OAC + 2/3 of the clot was pressed for forming a membrane	3000 rpm, 10 min	1M	UNS	2	36.5 (± 7.5)	UNS, but the socket was fresh	100	8 w	8 w: No signs of discontinuing on the lamina of the sinus were seen in radiograph examination.
Kapustecki et al. [3]	Mandibular bone blocks + 3–5 PRF membranes + BAF	2700 rpm, 12 min	1M	UNS	20	UNS	< 2 weeks	100	6 m	2 w: Complete healing ($n = 18$). Uncovering of the graft stabilizing screw ($n = 2$). 3 m: Mobility of aggregating elements ($n = 3$). 6 m: No graft

(*continued on next page*)

Table 1 (*Continued*)

Autor(s)/ year	Technique and PRF product	PRF protocol	Position of OAC/ OAF	Defect type	Sample size	Age (years)	Time since tooth extraction	Success rate (%)	Follow-up	PostOp evolution
Gülşen et al. [23]	Only 2 PRF clots	400 g, 10 min	UNS	> 5 mm	20	UNS	Immediate	100	3 w	resoption or inflammatory symptoms. 1 w: Healthy granulation tissue. 3 w: Full epithelisation.

formation in the PRF group, while primary wound closure was achieved in the BAF group in the same period. The oral mucosa had epithelialised by the third week in both groups. The Visual Analogue Scale (VAS) was used for pain assessment on postoperative days 1, 2, 3 and 7. The mean value in the PRF group was significantly lower, specifically 31.2 ± 15.9 (8.0–81.5), while in the BAF group it was 59.0 ± 19.5 (25.0–90.0) (p = 0.0001). When specifically analysing the values obtained per day reviewed, significant differences were obtained on the first and second day, but not on the third and seventh day, indicating that the use of PRF is especially useful in reducing pain during the 48 h postoperative period. This pain resulted in a significantly lower number of analgesic doses during the first 7 days (PRF, 3.7 ± 1.8 [1.0–8.0] vs. BAF, 5.5 ± 1.7 [3.0–9.0]; p = 0.003). When analysing these values per day, significant differences were observed only on the first and second days. Facial swelling was also assessed using the modified method by Gabka and Matsamura [27], converting each value into a percentage using the following formula: ([Maximum postoperative value - Preoperative value]/ Preoperative value) x 100. In the PRF group, no patient experienced facial swelling, however, in the BAF group, a mean of 0.94% ± 0.26 (p = 0.0001) was obtained.

3.2.2. PRF in bilaminar techniques

PRF was also used in bilaminar techniques. In this regard, Al-Juboori et al. [4] after the use of PRF performed a BAF because the radiograph showed that the bone defect was anterior to the fistula opening in the soft tissue. Thus, a wide area needed to be exposed to include the bone and soft-tissue defect, which could be achieved only with a BAF. This same technique was performed by Al-Noori [25], placing a single PRF clot. Also, a sandwich technique was described [24], i.e., one PRF membrane was placed directly over the OAC in the socket, a mix of PRF clot with collagen sponge and composite was placed over the stabilized PRF membrane and, finally, a second PRF membrane was placed over the mesh layer and was secured under the buccal and palatal mucoperiosteal flap by horizontal mattress suture.

3.2.3. PRF in trilaminar techniques

Some authors carried out trilaminar techniques, placing a collagen membrane over the OAC, on which they placed a folded PRF membrane (double layer) and, on top of this, a BAF [4]. Other authors placed PRF under or on top of a BFP, depending on the size of the defect (in small defects, the PRF was placed under the BFP and, in large defects, the other way round) [21].

One study evaluated the effect of the PRF in the treatment of OAFs and oronasal fistulas secondary to stage III medication-related osteonecrosis of the jaws (MRONJ), presented with maxillary sinusitis, swelling, mucosal ulceration, infection, and bone exposure. Previously, they administered amoxicillin/ clavulanic acid 2 g per day and ornidazole 1 g per day, for two weeks, and mouthwashes with gluconate chlorhexidine were also prescribed. Then, sequestrectomy and bone debridement were performed, and the maxillary sinus was abundantly irrigated with saline solution. Then, the PRF was placed under the BFP in patients who had small OAF and adequate bone cavity. On the other hand, the PRF was placed in the form of membranes over the BFP in patients who had large OAF and unfavourable bone cavities. The oral mucosa was sutured to achieve primary healing and without tension using a BAF. Antibiotic treatment was continued for the 5 days following surgery [21]. George [22] performed the same approach to treat an OAF secondary to implant failure. Covering the BFP graft with PRF creates an environment beneficial for healing. This allowed the suture line to close early, preventing inflammation and infection from bacteria [22].

The only study that evaluated the treatment of OACs using PRF and bone grafts was Kapustecki et al. [3] Specifically, they used monocortical bone blocks from mental protuberance or mandibular

Table 2
JBI critical appraisal checklist for case reports [19] (+ Yes; - No).

	Al-Noori [25] (2019)	**Pandikanda et al.** [24] (2019)	**Esen and Akkulah** [21] (2019)	**George** [22] (2018)	**Demetoglu et al.** [2] (2018)	**Al-Juboori et al.** [4] (2018)	**Bilginaylar** [5] (2018)	**Assad et al.** [26] (2017)	**Kapustecki et al.** [3] (2016)	**Gülsen et al.** [23] (2015)
1. Were patient's demographic characteristics clearly described?	+	+	+	+	+	+	+	+	+	-
2. Was the patient's history clearly described and presented as a timeline?	-	+	+	+	+	+	+	+	+	+
3. Was the current clinical condition of the patient on presentation clearly described?	+	+	+	+	+	+	+	-	+	+
4. Were diagnostic tests or assessment methods and the results clearly described?	+	-	-	+	-	-	+	+	-	-
5. Was the intervention(s) or treatment procedure(s) clearly described?	+	+	+	+	+	-	+	+	+	-
6. Was the post-intervention clinical condition clearly described?	-	+	+	-	+	+	+	+	+	+
7. Were the adverse events (harms) or unanticipated events identified and described?	+	+	+	+	+	+	+	-	+	-
8. Does the case report provide takeaway lessons?	-	+	+	+	-	-	+	+	+	-

Table 3
NIH Quality Assessment Tool for Case-Control Studies [20] (CD., cannot determine; NA., not applicable; NR., not reported).

	Bilginaylar [1] (2019)		
Criteria	**Yes**	**No**	**Other(CD/ NR/ NA)**
	X		
1. Was the research question or objective in this paper clearly stated and appropriate?	X		
2. Was the study population clearly specified and defined?		X	
3. Did the authors include a sample size justification?	X		
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?		X	
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	X		
6. Were the cases clearly defined and differentiated from controls?		X	
7. Is less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?	X		
8. Was there use of concurrent controls?	X		
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?		X	
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?		X	
11. Were the assessors of exposure/risk blinded to the case or control status of participants?		X	
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?			

oblique line. The bone blocks were shaped in a way that made it possible to wedge them in the cavity and tightly wardrobe the defect. The graft was stabilized using bicortical screws or titanium mini plates. The graft and the surrounding bone were covered with a PRF membrane. Subsequently, the surgical site was covered with BAF. This technique not only compensates for the crestal bone changes after tooth extraction in the horizontal direction, with an average loss of 0.5 mm but in the vertical direction, an average gain of 0.5 mm is observed at 3–6 months post-surgery.

3.3. Risk of bias within studies

Risk of bias and study quality analyses were performed independently by two review authors (A.-O.S.-P. and A.U.). Using the predetermined 8 domains for the methodological quality assessment according to the JBI Prevalence Critical Appraisal Tool for Case Reports [19], it was determined that all the papers have a high-quality assessment (5–8 domains) [2–5,21,22,24–26], except Gülsen et al. [23] that had a low-quality assessment (0–4 domains) (Table 2). shows a more detailed description of the articles included. On the other hand, NIH Quality Assessment Tool for Case-Control Studies [20] was used to analyse the Bilginaylar [1] study. After its analysis, it was determined that it was a “fair” quality study (Table 3).

4. Discussion

Typically, when intraoperative OAC occurs, the reasons for not treating it immediately are that it is not diagnosed by the surgeon or that the surgeon lacks the experience and/or expertise to address it [4]. There are a multitude of therapeutic options and the choice of the most appropriate technique will depend on the idiosyncratic factors of each patient, such as the amount of keratinized tissue present, the presence/absence of teeth, and the size and position of the OAC/OAF [28]. Bone grafts used in these cases may fail due to infection by native sinus bacteria or secondary to their exposure. The current treatments available have several drawbacks. In particular, BAF is the most commonly used, however, this procedure results in increased postoperative pain and oedema and a coronal displacement of the mucogingival line (MGJ), which in many cases will require a second surgery to increase the width of the attached gingiva (vestibuloplasty) [2]. The BFP technique also requires surgical intervention and has disadvantages, such as partial or total necrosis of adipose tissue, changes in facial contour, postoperative facial oedema and sometimes facial fistulas [29]. Other alternatives, such as monocortical bone grafts [12], provide an advantage regarding the future replacement of the lost tooth with a dental implant, however, they entail morbidity of the donor area and greater postoperative discomfort. Another option is the use of hydroxyapatite blocks, which do not require a donor site, cause less morbidity and can be left exposed to the oral environment [13]. Other alternatives, such as the use of a collagen membrane, have also been described. Its advantage is that it can be left partially exposed to the oral environment and, within 14 days, will be covered by epithelium, however, it is associated with a higher cost.

Some of these described drawbacks could be avoided by using PRF. PRF is a polymerised mesh or matrix with a tetramolecular structure [15] that contains a large number of leukocytes and platelets (approximately 70% and 95% of the initial clot, respectively) [30], as well as monocytes [31] and circulating stem cells [30]. It is a natural polymer that replicates the normal healing process, optimising and accelerating the healing of both hard and soft tissues [6], which is why it is used in the treatment of OACs/OAFs.

The first allusion to its use for these purposes was in 2015. In it, Agarwal et al. [6] proposed the de-epithelialisation of the mucosal edges of the OAC/OAF and washing of the area with sterile saline and gentamicin. They then elevated a buccal and palatal mucoperiosteal flap, but without displacing it coronally. They drew 4 tubes of blood to obtain 4 PRF membranes, three of which they linked together to form a plug that is sutured to the buccal and palatal flaps and condensed apically to seal the OAC/OAF, holding it in place with the suture (still unknotted). This prevents its migration into the sinus. Finally, a PRF membrane is placed over the surgical site, extending the edges of the membrane under the buccal and palatal flap, and the suture is tied at this point.

Several authors recommended using sterile saline to clean the surgical site before sealing the OAC/OAF with PRF [1,4,5,21,23,24,26], however, it is advisable to use the exudate obtained from the dehydration of PRF membranes, as it contains a large number of growth factors and has a high proliferative effect on medullary bone stem cells, osteoblasts and osteoarthritic chondrocytes [32]. The reason why they did not use this "enriched serum" is that in several studies they compressed the PRF clots between sterile gauzes, wasting it [1,5,26,33].

In this sense, it is advisable to use specific surgical boxes (PRF Box) to make use of this exudate. Currently, several commercial firms offer kits with the specific material necessary to perform the PRF technique. On the other hand, it is possible to perform "free protocols", i.e., to obtain products compatible with the technique separately without depending on a commercial firm. In this respect, the included articles employed very heterogeneous protocols. When commercially supplied kits are used, "protocols per revolutions per minute" are often employed. Depending on the manufacturer, the most widespread protocols are 3000 rpm for 10 min [15] (Process, Nice, France) or 2700 rpm for 12 min [34] (Intra-Lock, Boca Raton, FL, USA). However, when "free protocols" are carried out, "relative centrifugal force" (RCF) protocols, measured in g-force, must be applied, which depends among others on the rotor radius of the centrifuge used, describing values of 400 g for 10–12 min [35,36] or 300 g for 10 min [37]. To calculate it, the following equation must be used: RCF = $1.118 \bullet 10^{-5} \bullet r \bullet N^2$, where $1.118 \bullet 10^{-5}$ is a constant, "r" is the radius of rotation or horizontal distance from the axis of rotation to the bottom of the sample tube (measured in centimetres) and "N" is the speed of rotation expressed in rpm [38]. Therefore, the disparity in the protocols used by the different authors may indicate that they used "free protocols" to obtain PRF.

The use of PRF in the treatment of OACs/OAFs has several advantages, such as maintaining the position of the MGJ as it does not require the coronal displacement of mucoperiosteal flaps [1,5,6], thus preventing associated bone loss [4] and reducing postoperative morbidity, in particular, there is less pain during the following 48 h, which reduces analgesic intake, compared to other techniques such as BAF [1] and no second surgery site or donor site is needed to close the communication or there is no need for re-entry surgery to remove the membrane or fixation tools [4]. In addition, there is less bleeding, not only because it avoids elevating flaps, but also because of its haemostatic properties [1], which makes it very interesting in patients with haemostasis disorders or patients being treated with antiplatelet/anticoagulant drugs, as well as in patients with wound healing disorders, such as diabetics or patients being treated with medication-related osteonecrosis of the jaw (MRONJ) [21], as PRF favours accelerated revascularization and neoangiogenesis [39].

It is a versatile biomaterial that has proven effective in sealing small and large OACs (> 5 mm) as well as chronic OAFs (> 3 weeks of evolution) [4], due to its adhesive properties, the binding of PRF to Schneider's membrane is easier, which enables its reparation [2]. However, the authors recommend that in OACs/OAFs larger than 5 mm, PRF should be used in combination with bi- or trilaminar techniques, as PRF takes 15 days to resorb [40], which is the insufficient time considering that Schneider's membrane requires 6–8 weeks to self-regenerate [41]. In defects up to 5 mm, PRF could be used alone as the sole biomaterial.

PRF also has a local modulating action on the immune system, which controls inflammation and reduces the rate of postoperative infections [34]. Neutrophils trapped in the fibrin clot eliminate bacteria, necrotic tissues and pathogens from the surgical site by phagocytosis and by producing free radicals and digestive enzymes, preventing secondary infections [42]. In addition, it contains macrophages involved in the healing and repair process, playing a key role in the transition between inflammation and wound repair during osteogenesis [31,42], decreasing healing time by observing complete wound closure within two weeks [4], as well as surgical time [1]. Due to the ease with which the technique is performed, it eliminates the need for special surgical expertise [5], it is also inexpensive [4,5], compared to the use of commercial biomaterials, and quick (it requires 15–20 min). The result after its use is soft tissue hypertrophy and an increase in tissue thickness, providing more support for wound sealing [4]. It eliminates the risk of cross-disease or autoimmune rejection reactions, as it is autologous and does not require the use of additives, lacking any ethical limitations to its use [43].

However, every technique has certain disadvantages. In this regard, the use of needles may be a limitation in apprehensive patients [1] and venipuncture may be difficult in those whose veins are not visible. It cannot be performed in patients with certain ideological constraints, such as Jehovah's Witnesses, because their religion advocates that blood leaving the body should be discarded. A major disadvantage is that, during healing, if there is not enough residual bone, a fusion between the sinus membrane and the oral mucosa may occur. Such fusion will prevent future treatments, such as sinus lift and implant placement. The placement of a resorbable collagen membrane prevents this fusion. Moreover, the sinus mucosa will have the chance to regenerate and return to its normal morphology and prevents the proliferation of soft tissue into the osseous defect, which would enhance bone formation and closure of the bony defect [4].

4.1. Strengths and limitations

This systematic review presents several strengths, such as the searching process for the different studies, data extraction and risk of bias assessment performed in duplicate.

Nonetheless, some limitations may be related to this systematic review. First, the limited evidence of the included articles. Second, the heterogeneity of the protocols used to obtain the PRF among the different studies. For these reasons, the data provided by this systematic review should be interpreted with caution.

4.2. Recommendations for further research

Future studies should include the design of RCTs to specifically analyse the influence of using PRF alone or in combination with bi- or trilaminar techniques in the treatment of OACs/OAFs. It would also be interesting to compare PRF vs. other therapeutic options mentioned in the manuscript as the only comparison currently available is the PRF vs. BAF.

5. Conclusions

With the limitations of this study, it can be established that PRF can be used alone for the treatment of OACs/OAFs up to 5 mm and, in larger defects, it is advisable to combine it with bi- or trilaminar techniques. In clinical circumstances where delayed implant placement is planned and residual bone is insufficient, it is recommended to combine PRF with a collagen membrane to prevent fusion between the oral mucosa and Schneider's membrane, facilitating subsequent rehabilitative reconstructive surgical procedures. Therefore, PRF is an effective therapeutic option, with minimal associated postoperative morbidity compared to other techniques and allows the position of the mucogingival junction to be preserved. Its combination with bone grafting improves the starting point before the replacement of the missing tooth with a dental implant.

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Declaration of Competing Interest

The authors reported no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jormas.2022.03.014.

References

[1] Bilginaylar K. Comparison of the clinical outcomes of buccal advancement flap versus platelet-rich fibrin application for the immediate closure of acute oroantral communications. J Craniofac Surg 2019;30:e45–9. doi: 10.1097/SCS.0000000000004958.

[2] Demetoglu U, Ocak H, Bilge S. Closure of oroantral communication with plasma-rich fibrin membrane. J Craniofac Surg 2018;29:e367–70. doi: 10.1097/SCS.0000000000004360.

[3] Kapustecki M, Niedzielska I, Borgiel-Marek H, Różanowski B. Alternative method to treat oroantral communication and fistula with autogenous bone graft and platelet rich fibrin. Med Oral Patol Oral Cir Bucal 2016;21:e608–13. doi: 10.4317/medoral.21037.

[4] Al-Juboori MJ, Al-Attas MA, Magno Filho LC. Treatment of chronic oroantral fistula with platelet-rich fibrin clot and collagen membrane: a case report. Clin Cosmet Investig Dent 2018;10:245–9. doi: 10.2147/CCIDE.S179751.

[5] Bilginaylar K. The use of platelet-rich fibrin for immediate closure of acute oroantral communications: an alternative approach. J Oral Maxillofac Surg 2018;76:278–86. doi: 10.1016/j.joms.2017.07.168.

[6] Agarwal B, Pandey S, Roychoudhury A. New technique for closure of an oroantral fistula using platelet-rich fibrin. Br J Oral Maxillofac Surg 2016;54:e31–2. doi: 10.1016/j.bjoms.2015.09.039.

[7] Yalçın S, Oncü B, Emes Y, Atalay B, Aktaş I. Surgical treatment of oroantral fistulas: a clinical study of 23 cases. J Oral Maxillofac Surg 2011;69:333–9 Off J Am Assoc Oral Maxillofac Surg. doi: 10.1016/j.joms.2010.02.061.

[8] Procacci P, Alfonsi F, Tonelli P, Selvaggi F, Menchini Fabris GB, Borgia V, et al. Surgical treatment of oroantral communications. J Craniofac Surg 2016;27:1190–6. doi: 10.1097/SCS.0000000000002706.

[9] Pourdanesh F, Mohamadi M, Samieirad S, Banimostafaee H, Sadeghi HMM. Closure of large oroantral communication using coronoid process pedicled on temporalis muscle flap: a new alternative approach. J Craniofac Surg 2013;24:1399–402. doi: 10.1097/SCS.0b013e3182997184.

[10] Borgonovo AE, Berardinelli FV, Favale M, Maiorana C. Surgical options in oroantral fistula treatment. Open Dent J 2012;6:94–8. doi: 10.2174/1874210601206010094.

[11] Anavi Y, Gal G, Silfen R, Calderon S. Palatal rotation-advancement flap for delayed repair of oroantral fistula: a retrospective evaluation of 63 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:527–34. doi: 10.1016/s1079-2104(03)00470-0.

[12] Haas R, Watzak G, Baron M, Tepper G, Mailath G, Watzek G. A preliminary study of monocortical bone grafts for oroantral fistula closure. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:263–6. doi: 10.1016/s1079-2104(03)00375-5.

[13] Zide MF, Karas ND. Hydroxylapatite block closure of oroantral fistulas: report of cases. J Oral Maxillofac Surg 1992;50:71–5 Off J Am Assoc Oral Maxillofac Surg. doi: 10.1016/0278-2391(92)90201-a.

[14] Parvini P, Obreja K, Begic A, Schwarz F, Becker J, Sader R, et al. Decision-making in closure of oroantral communication and fistula. Int J Implant Dent 2019;5:13. doi: 10.1186/s40729-019-0165-7.

[15] Choukroun J, Adda F, Schoeffler C, Vervelle A. Une opportunité en paro-implantologie: Le PRF. Implantodontie 2001;42:55–62.

[16] Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 2009;27:158–67. doi: 10.1016/j.tibtech.2008.11.009.

[17] Salgado-Peralvo AO, Salgado-García A, Arriba-Fuente L. New tendencies in tissue regeneration: leucocyte-rich platelet-rich fibrin. Rev Española Oral Maxilofac 2017;39:91–8. doi: 10.1016/j.maxilo.2016.03.001.

[18] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097. doi: 10.1371/journal.pmed.1000097.

[19] Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Systematic reviews of etiology and risk Joanna Briggs Inst.. Reviewers' Manual. The Joanna Briggs Institute; 2017.

[20] NHLBI. Quality Assessment of Case-Control Studies; 2021.

[21] Esen A, Akkulah S. Management of large oroantral fistulas caused by medication-related osteonecrosis with the combined sequestrectomy, buccal fat pad flap and platelet-rich fibrin. J Maxillofac Oral Surg 2021;20:76–82. doi: 10.1007/s12663-019-01278-x.

[22] George E. Triple-layered closure of an oroantral fistula: a case report. Int J Oral Maxillofac Implant 2018;33:e33–6. doi: 10.11607/jomi.5725.

[23] Gülşen U, Şentürk MF, Mehdiyev İ. Flap-free treatment of an oroantral communication with platelet-rich fibrin. Br J Oral Maxillofac Surg 2016;54:702–3. doi: 10.1016/j.bjoms.2015.09.037.

[24] Pandikanda R, Singh R, Patil V, Sharma M, Shankar K. Flapless closure of oroantral communication with PRF membrane and composite of PRF and collagen - a technical note. J Stomatol Oral Maxillofac Surg 2019;120:471–3. doi: 10.1016/j.jormas.2018.12.012.

[25] Al-Noori N. Platelet rich fibrin (PRF) for treatment of oroantral fistula: a case report. J Res Med Dent Sci 2019;7:17–20.

[26] Assad M, Bitar W, Alhajj MN. Closure of oroantral communication using platelet-rich fibrin: a report of two cases. Ann Maxillofac Surg 2017;7:117–9. doi: 10.4103/ams.ams_77_17.

[27] Gabka J, Matsumura T. [Measuring techniques and clinical testing of an anti-inflammatory agent (tantum)]. Munch Med Wochenschr 1971;113:198–203.

[28] Batra H, Jindal G, Kaur S. Evaluation of different treatment modalities for closure of oro-antral communications and formulation of a rational approach. J Maxillofac Oral Surg 2010;9:13–8. doi: 10.1007/s12663-010-0006-y.

[29] Alcântara MT, Ribeiro NR, Abreu DF. Complications associated with bichectomy surgery: a literature review. Minerva Dent Oral Sci 2021;70:155–60. doi: 10.23736/S0026-4970.20.04415-5.

[30] Kang YH, Jeon SH, Park JY, Chung JH, Choung YH, Choung HW, et al. Platelet-rich fibrin is a Bioscaffold and reservoir of growth factors for tissue regeneration. Tissue Eng Part A 2011;17:349–59. doi: 10.1089/ten.TEA.2010.0327.

[31] Dohan Ehrenfest DM, Del Corso M, Diss A, Mouhyi J, Charrier JB. Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. J Periodontol 2010;81:546–55. doi: 10.1902/jop.2009.090531.

[32] Kardos D, Hornyák I, Simon M, Hinsenkamp A, Marschall B, Várdai R, et al. Biological and mechanical properties of Platelet-Rich Fibrin membranes after thermal manipulation and preparation in a single-syringe closed system. Int J Mol Sci 2018;19. doi: 10.3390/ijms19113433.

[33] Saleh EA, Issa IA. Closure of large oroantral fistulas using septal cartilage. Otolaryngol Neck Surg Off J Am Acad Otolaryngol Neck Surg 2013;148:1048–50. doi: 10.1177/0194599813482091.

[34] Dohan Ehrenfest DM, Bielecki T, Mishra A, Borzini P, Inchingolo F, Sammartino G, et al. search of a consensus terminology in the field of platelet concentrates for surgical use: platelet-rich plasma (PRP), platelet-rich fibrin (PRF), fibrin gel polymerization and leukocytes. Curr Pharm Biotechnol 2012;13:1131–7. doi: 10.2174/138920112800624328.

[35] Mazor Z, Horowitz RA, Del Corso M, Prasad HS, Rohrer MD, Dohan Ehrenfest DM. Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. J Periodontol 2009;80:2056–64. doi: 10.1902/jop.2009.090252.

[36] Castro AB, Meschi N, Temmerman A, Pinto N, Lambrechts P, Teughels W, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part B: sinus floor elevation, alveolar ridge preservation and implant therapy. A systematic review. J Clin Periodontol 2017;44:225–34. doi: 10.1111/jcpe.12658.

[37] Zhang Y, Tangl S, Huber CD, Lin Y, Qiu L, Rausch-Fan X. Effects of Choukroun's platelet-rich fibrin on bone regeneration in combination with deproteinized bovine bone mineral in maxillary sinus augmentation: a histological and histomorphometric study. J Cranio Maxillo Fac Surg 2012;40:321–8 Off Publ Eur Assoc Cranio-Maxillo-Facial Surg. doi: 10.1016/j.jcms.2011.04.020.

[38] Vite-Casanova J. El fraccionamiento de la sangre. Gac Médica Mex 2004;140:S157–9.

[39] Suttapreyasri S, Leepong N. Influence of platelet-rich fibrin on alveolar ridge preservation. J Craniofac Surg 2013;24:1088–94. doi: 10.1097/SCS.0b013e31828b6dc3.

[40] Kawase T, Kamiya M, Kobayashi M, Tanaka T, Okuda K, Wolff LF, et al. The heat-compression technique for the conversion of platelet-rich fibrin preparation to a barrier membrane with a reduced rate of biodegradation. J Biomed Mater Res B Appl Biomater 2015;103:825–31. doi: 10.1002/jbm.b.33262.

[41] Chanavaz M. Maxillary sinus: anatomy, physiology, surgery, and bone grafting related to implantology–eleven years of surgical experience (1979-1990). J Oral Implantol 1990;16:199–209.

[42] Clark RA. Fibrin and wound healing. Ann N Y Acad Sci 2001;936:355–67. doi: 10.1111/j.1749-6632.2001.tb03522.x.

[43] Miron RJ, Fujioka-Kobayashi M, Hernandez M, Kandalam U, Zhang Y, Ghanaati S, et al. Injectable platelet rich fibrin (i-PRF): opportunities in regenerative dentistry? Clin Oral Investig 2017;21:2619–27. doi: 10.1007/s00784-017-2063-9.