



COMPARISON OF THE USE OF FIBRIN ENRICHED WITH PLATELETS ALONE AND WITH B-TRICALCIUM PHOSPHATE IN IMPLANTOLOGY

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Filling existing cavities has an important role in implantology. Therefore, numerous studies have examined different types of replacement materials and their influence on wound healing. In this study, with a total of 5 cases, we examined the use of standard PRF (platelet rich fibrin) alone or in combination with synthetic beta-tri-calcium phosphate (β -TCP) and their effect on the healing process at the extraction site and in immediate implantation. The following success criteria were used: absence of signs of inflammation, clinical healing of the wound, and filling of the cavity determined by X-ray. The results of our research determined that the X-ray cavity filled over 4 months, with good healing of the soft tissue and without clinical and radiological signs of inflammation. The combination of PRF and β -TCP also showed good signs of healing with osseointegrative and osseoconductive properties. However, further monitoring of progress will show whether there is a complete conversion to new bone or not. Additional research, as well as improvement of the material, will certainly affect the range of indications and give more precise answers to this topic.

Keywords: PRF, β -TCP, IMPLANTOLOGY, WOUND HEALING, IMMEDIATE IMPLANTOLOGY

INTRODUCTION

Since implantation has become a standard method in dentistry for replacing a missing tooth, there are many implant systems on the market, which, if used correctly, have a high probability of success. However, problems often occur in the healing phase, where various causes can lead to early implant loss. This explains why fulfilling of the existing cavities plays an important role in implantology. So, it is no wonder that the application of different bioactive substitute materials and their influence on inflammation-regulation and wound healing has been the subject of many investigations and studies.

PRP (platelet-rich plasma) has been used in surgery since the early 1990s, showing good clinical results because of its effect on osseoprogenitor cells. However, because of its need for non-

autologous anticoagulants and more complex centrifugation process, it is no longer applicable in clinical procedures.

In 2001, Choukroun and colleagues developed an entirely new method called platelet-rich fibrin-PRF that does not require any additional anticoagulants or biochemical manipulation. The fact that it is the body's material makes it strictly an autologous preparation and at the same time increases patient acceptance. This biomaterial offers an additional barrier, which explains why it is being used to regulate inflammation, speed up the healing process, as well as to improve implant osseointegration, and preserve the surrounding bone. It consists of platelets, white blood cells, stem cells, growth factors, and cytokines entrapped in a fibrin matrix, which makes an ideal environment for wound healing and regeneration of tissue. Besides showing several advantages over PRP, in the last few years, the centrifugation protocol has also been adapted to get a higher concentration of neutrophils in the PRF membrane (1).

Except for being used as a single graft material, PRF can also be used in combination with other bone substitute materials, like beta-tri-calcium phosphate (β -TCP) -synthetic, animal-free graft material. These materials theoretically should improve its regenerative potential and ensure a more favourable environment for bone formation.

MATERIALS AND METHODS

This report, with total of 5 cases was carried out in Dental Clinic Burrow in Split, Croatia from January 2021 to January 2022. In 3 of the cases, we followed the healing process of the wound or immediate implantation wound with PRF only, while in two of them we followed it in combination with β -TCP. ICX implant system was used in all of the cases and all the procedures were carried out following the ethical standards of commissions of competent institutions and Helsinki Declaration.

Two different types of PRF were produced in two different types of tubes. Standard PRF is being produced at a speed of 2700 rpm for 8 minutes, while

advanced PRF, also known as A-PRF is being produced at a speed of 1300 rpm and an increase in the centrifugation time to 14 minutes, which results in a lower number of platelets and higher number of white blood cells in the transition layer on the back wall of the glass tube. The protocol for each included blood sampling from the median cubital vein that was put into 8 tubes that did not contain any additional anticoagulants. Collected blood samples were put into the fixed-angle centrifuge as soon as possible. Depending on, what kind of PRF we wanted, centrifuges were set at 2700 rpm for 8 minutes or 1400 rpm for 14 minutes. After the centrifugation process, we removed the cap from the tube and let it stand for 10 minutes, after which we removed the membrane. Further manipulation of the membrane included pressing the membrane in the PRF box.

Two different types of red cap tubes were used in each case, Choukron A-PRF- glass tubes without additives (10 ml) and VACUETTE® TUBES (9 ml) - plastic silica-coated tubes- serum clot activator tubes are coated with micronized silica particles that activate clotting when the tubes are gently turned.

The comparison between the two centrifugation protocols shows that a larger clot volume is obtained with glass tubes containing 1 ml more (A-PRF- glass tubes without additives) and the standard protocol (2700 rpm and 8 minutes), which is more than would have been expected with just 1 ml larger tube volume. With the A-PRF protocol (1300 rpm for 14 minutes), the clots are smaller, but centrifugation is gentler with more white cells in the transition zone. Talking about the costs, although they are significantly lower with plastic tubes, we decided to use glass tubes to get the best results, as well as avoid the influence of substances that are related to the usage of the plastic tubes.

No signs of inflammation, clinical wound healing, and x-ray cavity fulfillment was taken as a criterion of success. On the other side, any signs of inflammation occurring, poor wound healing, and incomplete cavity x-ray fulfillment were considered as a criterion of failure.

RESULTS

PRF for extraction site management

Results from our use of standard PRF only for extraction site management of the former tooth 24. Cavity fulfillment can be seen on the control x-ray, which was taken 5 months after extraction, compared to the one taken initially after extraction (Figure 1). No inflammation signs occurred.

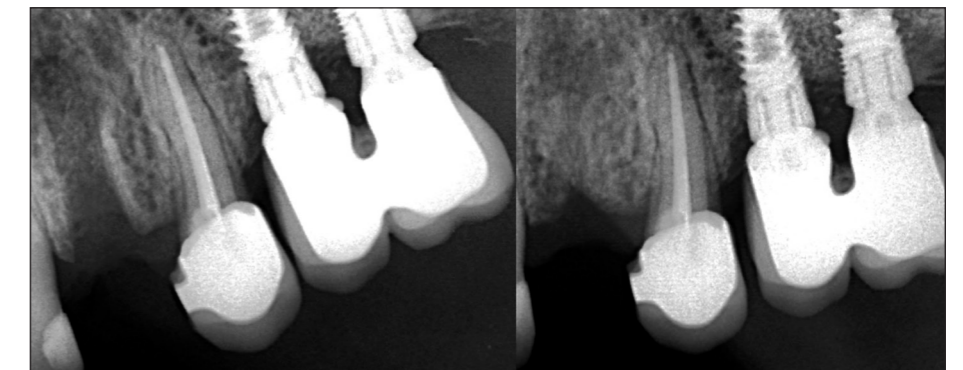


Figure 1. Healing observed 5 months after extraction.

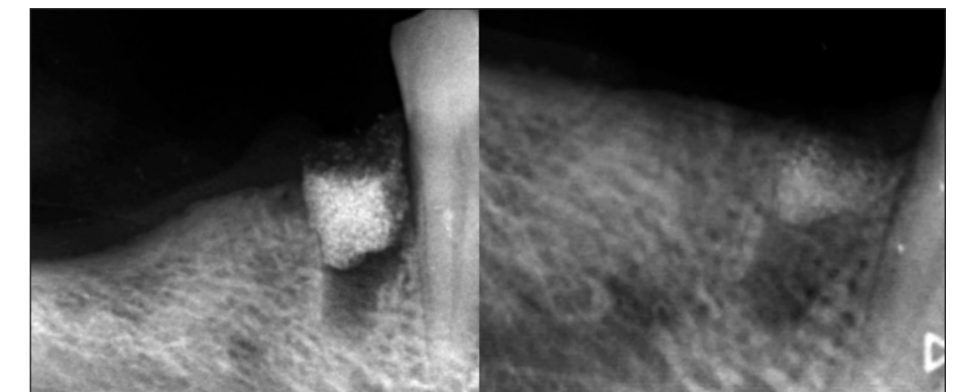


Figure 2. Cavity fulfilling over a 5 months period.

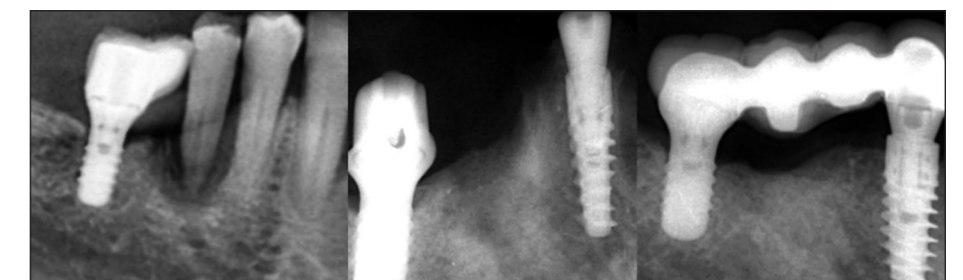


Figure 3. Healing observed 6 months post-implantation.

Combination of PRF and TCP for extraction site management

The next case shows us the results of apical use of PRF in combination with synthetic beta-tri-calcium phosphate (TCP) in the upper part of the wound in extraction site management of a former tooth 44. On the control x-ray, which was taken 5 months later, we can see fulfillment of the cavity compared to the initial postextraction photo (Figure 2). In the meantime, neither clinical, nor radiographical signs of inflammation occurred during this period.

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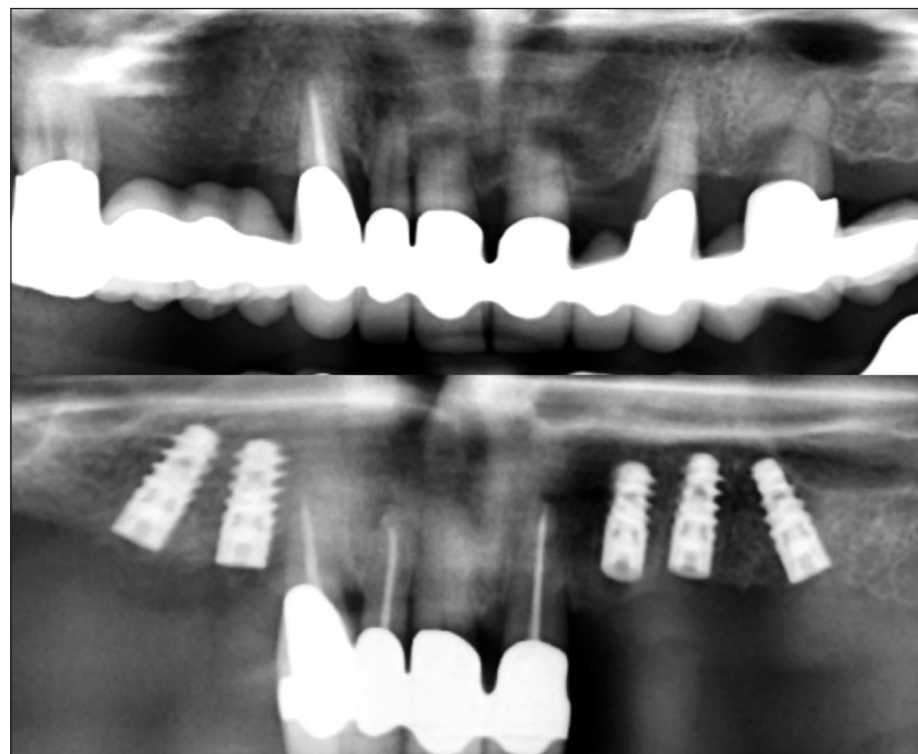


Figure 4. Healing progress at 13 weeks post-implantation.



Figure 5. Healing observed over a four-month period.

PRF for immediate implantation

When talking about immediate implantation, the following results show us PRF supported the healing process of the implant on the position of the former tooth 44 with the previous extraction of teeth 43, 44 and 45. On Figure 3 we can see the initial condition with a bone loss on position 43, 44, 45 and the healing process right after immediate implantation compared to the one made simultaneously with final restoration 6 months later. No signs of inflammation were noticed.

The next case is also presenting the use of PRF only for immediate implantation. In Figure 4 we can see the initial condition where teeth 17, 23, and 25 could no longer be preserved and a result of PRF supported immediate implantation with previously extracted mentioned teeth, taken 13 weeks after the surgery.

Combination of PRF and TCP for immediate implantation

The following case presents the results of extraction of the destroyed tooth 36 with its bone loss at the bifurcation

and immediate implantation. After the extraction, the gap at 36 was covered with multilayer PRF membranes apically and filled with TCP in the upper part of the alveolus supporting the shape of gum formation. We can see the x-ray osseointegration process followed during 4 months (Figure 5).

DISCUSSION

Results from cases showed positive signs of healing, both, clinical and radiographical when using PRF membranes for extraction site management and immediate implantation.

Following the results from our research, Borie et al. in their studies have demonstrated safe and promising results related to the use of PRF alone or in combination with other biomaterials. They claim that it has several advantages and possible indications not only in dentistry but in medicine, generally. At the moment, PRF seems to be an accepted minimally invasive technique with low risks and excellent clinical results (1).

Research led by Strauss et al. also supports the use of PRF, claiming that it has shown positive effects on ridge preservation and in the early phase of osseointegration, although its impact on pain reduction and soft tissue healing remains unclear (2).

Furthermore, results of the systematic review and meta-analysis lead by Guan et al. also suggest that PRF can not only speed up bone healing and help in new bone formation, but it also increases implant stability (3).

Another in a series of studies that confirms our results is the study led by cf. Hauser F. et al. and Canellas J. et al. where they have shown that wound healing with PRF leads to improved bone structure and wound healing, due to the growth factors present in the PRF. Pain after extraction has also shown to be less (4, 5)

Except for being used as a single graft material, in our research, PRF has also shown positive healing signs in combination with β -TCP.

In accordance with previous statement, Mendoza-Azpur et al. in their research showed less resorption of the buccolingual volume, when PRF is being used in combination with synthetic β -TCP (6).

In the recent studies of the GBR conducted by Moussa et al. and Hartlev et al. block augmentations were covered with PRF membrane. While reduced resorption compared to the control group was demonstrated in Moussa et al., Hartlev et al. on the other hand, could not determine any difference (7, 8)

Marelli M. and Tatullo M. have found good preservation of the crestal bone and good soft tissue healing with preservation of the papilla by filling the gap with PRF and covering the wound with a PRF membrane, which goes along with the results of our study (9).

R. J. Miron et al. also support the use of PRF for periodontal and soft tissue repair. Despite this, they consider that future clinical studies evaluating the impact of the PRF on hard tissue regeneration are necessary (10).

On the other side, S. Al-Maawi et al. consider that PRF is most effective only in the early healing period of 2-3 months after extraction (11).

Furthermore, K. Zwitter et al. reported on beneficial effects of PRF application in intrabony defects, especially when talking about third molar extractions, socket preservation, and guided bone regeneration (12).

However, Pasarelli et al. showed no statistically significant difference comparing the results of periodontal healing of the distal sites of the mandibular second molars, after extraction therapy of the third molar with and without PRF (13).

As opposed to the results of our research, when talking about PRF and its effect on the immediate implantation, it was investigated by C. Diana et al. and no higher primary stability was found during the three-month healing phase compared to the control group. Conversely, Öncü E et al. found a significant

increase in implant stability with immediate implantation after coating the implants with PRF membrane (14, 15).

A. S. Baghel et al. have also found that the use of PRF presents an innovative, safe, and efficient method for controlling the healing process around immediate implant placement (16).

In research conducted by R. S. Medikeri effect of PRF and allograft use on immediate implantation at extraction sockets with periapical infection was examined. They found that a combination of PRF with decalcified freeze-dried bone allografts at periapically infected sites made a significant reduction in bone resorption and accelerated bone healing during the initial post-extraction stage. This somehow goes along with the theory of use PRF in combination with other bone-substitute materials, even though it is not β -TCP (17).

When talking about the use of a combination of PRF and bone substitute material and material of choice, Jordana F et al. concluded that the decision depends on several different factors, such as the required bone volume, the handling (injectability, malleability), and mechanical properties (setting time, viscosity, resorbability among others) of the material (18).

Zhao R et al. in their review of current trends and developments have found that limitations of the available materials exist, just like the areas which require further research and development. They also consider that tissue engineering hybrid constructions with improved bone regeneration ability, such as cell-based or growth factor-based bone substitutes, are discussed as an emerging area of development (19).

There are certain limitations in this study, such as the number of subjects, the difference in the bone missing volume, numerically measurable healing parameter, handling of the materials, insufficient information regarding the patient's smoking habits and oral hygiene, as well as any associated conditions.

CONCLUSIONS

Results from our cases showed that implants covered with PRF membranes showed positive x-ray and clinical healing signs with no inflammation signs in any of the cases.

Except for being used as a single graft material, it can also be used in combination with other bone substitute materials, such as beta-tricalcium-phosphate. This combination also showed good healing signs with osseointegrative and osseoconductive properties.

No difference in clinical nor radiological healing was observed, no matter whether we used PRF only or its combination with TCP. However, further progress control will show whether there is a complete conversion into a newly formed bone.

Further studies, as well as the improvement of the materials will influence the range of indications and give more precise answers to this topic.

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SUKOB INTERESA/CONFLICT OF INTEREST
Autori su popunili the *Unified Competing Interest form* na www.icmje.org/coi_disclosure.pdf (dostupno na zahtjev) obrazac i izjavljuju: nemaju potporu niti jedne organizacije za objavljeni rad; nemaju finansijsku potporu niti jedne organizacije koja bi mogla imati interes za objavu ovog rada u posljednje 3 godine; nemaju drugih veza ili aktivnosti koje bi mogle utjecati na objavljeni rad./ All authors have completed the *Unified Competing Interest form* at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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Sažetak

USPOREDBA KORIŠTENJA FIBRINA OBOGAĆENOG TROMBOCITIMA SAMOG I S B-TRIKALCIJ FOSFATOM U IMPLANTOLOGIJI

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Ispunjavanje postojećih kaviteta ima važnu ulogu u implantologiji. Stoga su različite vrste zamjenskih materijala i njihov utjecaj na zacjeljivanje rana predmet brojnih istraživanja. U ovoj studiji, s ukupno 5 slučajeva, ispitali smo upotrebu standardnog PRF (platelet rich fibrin) -a samog ili u kombinaciji sa sintetskim beta-tri-kalcijevim fosfatom (β -TCP) te učinak istih na proces cijeljenja na mjestu ekstrakcije i kod imedijatne implantacije. Kao kriterij uspješnosti korišten je: izostanak znakova upale, kliničko cijeljenje rane te popunjavanje šupljine utvrđene rendgenskom snimkom. Rezultati našeg istraživanja utvrdili su da se rendgenska šupljina ispunila tijekom razdoblja od 4 mjeseca, uz dobro cijeljenje mekog tkiva i bez kliničkih i radioloških znakova upale. Kombinacija PRF-a i β -TCP također je pokazala dobre znakove zacjeljivanja s osteoinduktivnim i osteokonduktivnim svojstvima. Međutim, daljnja kontrola napredovanja pokazat će postoji li potpuna pretvorba u novostvorenu kost ili ne. Daljnja istraživanja, kao i poboljšanje materijala svakako će utjecati na raspon indikacija i dati preciznije odgovore na ovu temu.

Ključne riječi: PRF, β -TCP, IMPLANTOLOGIJA, CIJELJENJE RANE, IMEDIJATNA IMPLANTACIJA

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