Review

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Injectable platelet-rich fibrin: a new material in medicine and dentistry

Enjekte edilebilen trombositten zengin fibrin: Tıpta ve diş hekimliğinde yeni bir materyal

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Abstract

Blood concentrates have been used in medicine and dentistry for many years as a wide variety of products. However, injectable platelet-rich fibrin (i-PRF), an autogenous blood concentrate found three years ago, is noteworthy. It is not difficult to predict that this completely autogenous blood concentrate, which can be used with minimally invasive methods and has many indications, will be used very widely in the future.

Key words: *platelet rich fibrin, injectable platelet rich fibrin, platelet rich plasma, PRF, i-PRF, PRP*

Özet

Kan konsantreleri tıpta ve diş hekimliğinde uzun yıllardır çok çeşitli ürünler olarak kullanılmaktadır. Buna rağmen, üç yıl önce bulunan bir otojen kan konsantresi olan enjekte edilebilen trombositten zengin fibrin (i-PRF) dikkati çekmektedir. Minimal invazif yöntemlerle kullanılabilen ve şimdiden birçok endikasyonu olan bu tamamen otojen kan konsantresinin gelecekte çok yaygın kullanılacağını tahmin etmek güç değil.

Anahtar kelimeler: *trombositten zengin fibrin, enjekte edilebilir trombositten zengin fibrin, trombositten zengin plazma, TZF, E-TZF, TZP*

Introduction

Platelet-rich plasma (PRP) was developed in 1954 by Kingsley as a platelet concentrate and used in the treatment of patients with severe thrombocytopenia.[1] The first attempts to use concentrated platelet growth factors were made to support healing process of wounds during and after surgery.[2,3] The growth factors involved in PRP and its concentration were first demonstrated in Marx and colleagues' publications in 1998 which describes the effects of platelet-rich preparation used in maxillo-facial reconstruction applications.[4] Preparation of PRP varies

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according to the protocols used and takes between 30-60 minutes. Two centrifugation methods are applied in PRP and during the first centrifuge, natural coagulation is prevented by tubes coated with ethylenediamine tetraacetic acid (EDTA) and citric acid (CA). After the erythrocytes are settled by the first centrifuge, in the second and rapid centrifugation process, bovine thrombin and calcium chloride or another artificial coagulant are added into the received plasma to form artificial coagulation.[5] PRP is a first-generation platelet concentrate that can be used in liquid or gel form, which appears as a weak fibrin network after activation of centrifuged blood with thrombin and calcium. They are not completely autogenous products because there is an artificial addition of bovine thrombin and calcium chloride from the outside during the obtaining process.

PRP has been shown to contain more than 95% platelets in its content. Platelets are cells that have a direct effect on osteoblasts, connective tissue cells, periodontal ligament cells and epithelial cells.[6,7] Although PRP developers have been shown to play an important role in the release of growth factor and at different stages of wound healing, they aimed to remove leukocytes from blood concentrates.[8]

Disadvantages associated with the additional use of anti-coagulants which is found in PRP have been demonstrated to inhibit the wound healing process.

Disadvantages of PRP;

1. Since the resulting product is not completely autogenous, it can prevent natural inflammation by creating a foreign substance reaction in the first period of wound healing.[9,10]
2. The fibrin matrix structure formed by artificial coagulation is more rigid, unlike the fibrin matrix structure formed by natural coagulation. This hard structure causes the growth factors in its content to be released quickly and in a short time rather than with a controlled slow release.[10,11]
3. It causes a loss of time due to its high cost and the preparation process which consists of many steps.[12]

Due to the disadvantages of first-generation PRP, platelet-rich fibrin (PRF) from the second-generation blood product has emerged. PRF is obtained by centrifuging the blood which is taken into the glass coated tube without any anticoagulant additions. PRF consists of a fibrin structure in a complex three-dimensional architecture where platelets, leukocytes and cytokines are concentrated. It has been asserted that 97% of platelets and 50% of leukocytes in the blood samples taken are found in the PRF clot. After centrifugation, three layers are formed; red blood cells (erythrocytes) are in the lower layer of the tube, the upper layer consists of platelet-poor plasma, and the middle layer of the tube includes platelet-rich fibrin clot. If the blood which is taken into the glass tube is put into the centrifuge late, the desired result cannot be obtained since these three natural coagulation layers will be formed without separation.[13] Obtaining a completely autogenous fibrin structure has made researchers looking for better blood products rich in cytokines, growth factors and leukocytes. Various PRF materials have been developed by changing the type of the tube, the centrifuge cycle and the centrifuge time (Table 1). Due to the glass-activated fibrin network structure, it resorbs in human tissues in 7-11 days.[14] However, this resorption period is sufficient only for soft tissue healing. Titanium platelet-rich fibrin (T-PRF) has been developed to eliminate the possibility of silica particles hanging in the fibrin structure in glass tube and passing to the patient.[15,16] It has been shown that T-PRF can remain in the tissue for more than 30 days without resorption. It has been reported to give good results in soft tissue and bone healing because of its long resorption time and richness in growth factors.[17] Advanced platelet rich fibrin types which are produced according to the low speed centrifugation concept have been shown to significantly increase the number of inflammatory cells and growth factor release. Therefore, regenerative potential has been reported to increase.[18-20]

Coagulation in the PRF begins with the contact of blood and the silica in the glass tube.[11,21] In T-PRF, a tighter fibrin network structure is formed when the blood comes

Table 1. Platelet-rich fibrin types

	Centrifugal speed	Centrifuge minute	Tube type	The nature of the obtained PRF
Platelet-rich fibrin (L-PRF)	2700 rpm	12 minutes	Glass tubes	Solid
Titanyum platelet-rich fibrin (T-PRF)	2700 rpm	12 minutes	Titanyum tubes	Solid
Advanced platelet-rich fibrin (A-PRF)	1300 rpm	14 minutes	Glass tubes	Solid
Advanced platelet-rich fibrin + (A-PRF +)	1300 rpm	8 minutes	Glass tubes	Solid
Injectable platelet-rich fibrin (i-PRF)	700 rpm	3 minutes	Plastic tubes	Liquid

into contact with the titanium surface instead of silica.[22] Compared to PRP, the only factor which restricted the usage areas of PRF is that PRF could only be produced in solid form. With the low-speed centrifugation concept, i-PRF can be obtained in liquid form without forming a PRF membrane.[23] The advantages of i-PRF, the second-generation blood products, are shown in Table 2. In addition, the preparation of i-PRF can be seen in Fig. 1.

There are very few clinical studies in which i-PRF used. Albilia et al.[30] stated that their study in which they used i-PRF in the temporomandibular joint showed

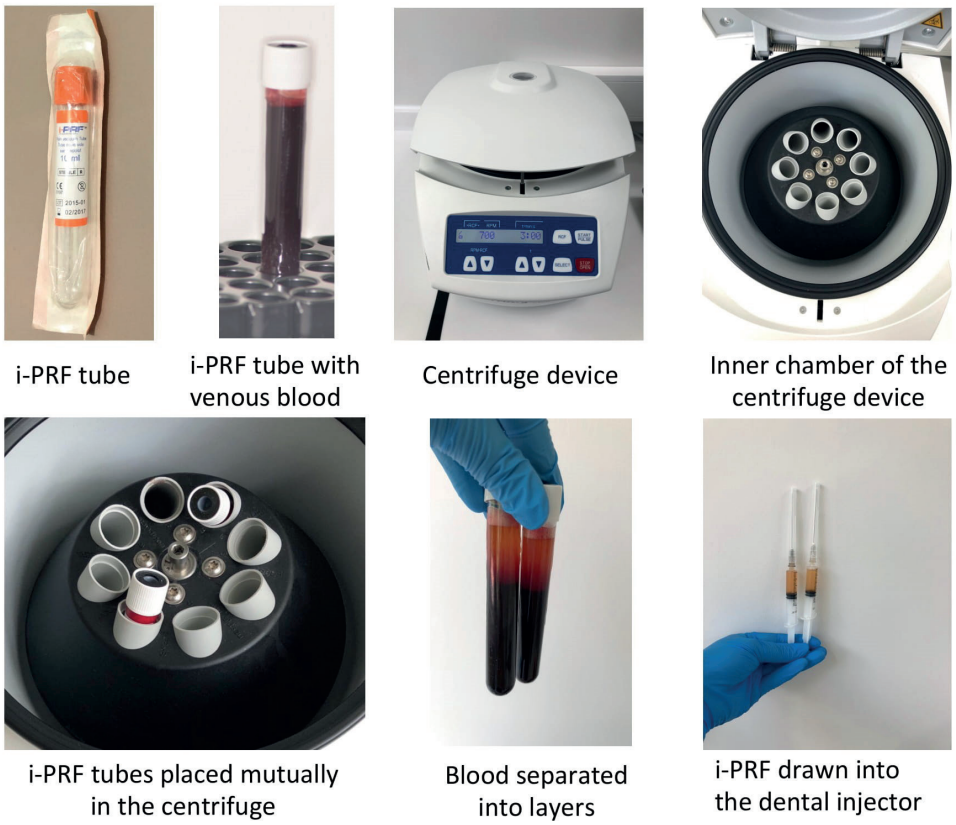

Fig. 1. The preparation of i-PRF

Table 2. i-PRF in medicine and dentistry

Article	Year	Aim	Conclusion
Miron et al.[24]	2017	Comparing PRP with i-PRF	Although the growth factor release was higher in the PRP at the beginning, the total release was found higher in the i-PRF at the end of the tenth day. They showed similar tissue compatibility. While PRP was associated with higher cellular proliferation, i-PRF showed higher cellular migration. In cell culture, i-PRF induced m-RNA expression of TGF-ß and collagen-1 at 7th day.
Wang et al.[25]	2017	Comparison of i-PRF and PRP on fibroblasts cultured on titanium implant surfaces	More cell migration, higher levels of PDGF, TGF-ß, collagen-1 and fibronectin messenger RNA levels were detected in i-PRF. In addition, collagen-1 synthesis has been found in the highest i-PRF group.
Abd El Raouf et al.[26]	2017	Experimental rabbit study to examine cartilage regeneration in knee joint	Compared to PRP and the control group, it was found that in the i-PRF group, chondrocyte proliferation significantly increased collagen type II and aggrecan mRNA levels.
Karde et al.[27]	2017	To compare the antimicrobial property and platelet count of i-PRF with other blood products	The inhibitory effect of PRP on the growth of oral bacteria is not statistically significant. i-PRF has maximum antimicrobial efficacy and higher platelet count compared to other PRF and PRP. Therefore, it can be said that it has a better regenerative potential.
Choukroun et al.[20]	2018	To investigate leukocyte, platelet and growth factor release in liquid PRF products	Low-speed centrifugation enriches leukocytes, platelets and growth factors in liquid PRF-based matrices.
Wang et al.[28]	2018	Comparison of PRP and i-PRF in osteoblast culture	According to the control tissue culture, PRP increased osteoblast migration 2-fold and i-PRF 3-fold. i-PRF showed higher osteoblast proliferation and differentiation.
Varela et al.[29]	2018	To evaluate cell content, morphological aspects, gene expression of type I collagen and release of growth factors in i-PRF	They stated that i-PRF, which includes platelets, leukocytes, type I collagen, osteocalcin and growth factors, can be a good approach for soft and mineralized tissue healing.
Albilia et al.[30]	2018	Using i-PRF in the temporomandibular joint	Pain and dysfunction in the tempromandibular joints in which i-PRF is used showed a continuous decrease for up to 12 months.
Kour et al.[31]	2018	To evaluate the antimicrobial efficacy of PRP, PRF and i-PRF in *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* strains	They reported that PRP, PRF and i-PRF had antibacterial activity, but PRP and i-PRF are more active compared to PRF.

Table 2. Continued

Tunali et al.[32]	2018	To compare the effect of i-PRF and corticosteroid in erosive lesions of oral lichen planus	It has been found that i-PRF is similar to corticosteroid injection in the treatment of erosive lesions of oral lichen planus
Gode et al.[33]	2019	To assess the effect of i-PRF on the diced cartilage	It has been indicated that i-PRF increased the survival rate of post-operatively diced cartilage.
Xie et al.[34]	2019	To investigate the regeneration power of i-PRF in lateral sinus operations	It has been reported that i-PRF improved the effect of osteogenesis
Turer et al.[35]	2020	To assess the additional contribution of i-PRF to surgical operations for gingival recession	It has been stated that gingival recession decreased more in the group applied i-PRF in operations with coronally advanced flap with connective tissue graft.
Ozsagir et al.[36]	2020	To evaluate the effect of i-PRF and i-PRF + micro-needling in individuals with thin gingival phenotype	It has been indicated that i-PRF and i-PRF + microneedling application can increase gingival thickness without surgical procedures in individuals with thin gingival phenotype.

the constant reduction of pain and dysfunction in the temporomandibular joint up to 12 months. It might be due to the possibility of i-PRF having the ability to repair joint homeostasis.

Tunali et al.[32] in split-mouth studies evaluated the effect of i-PRF on erosive lesions of oral lichen planus. They applied i-PRF on one side of the bilateral erosive lichen planus lesions of 13 patients and intralesional corticosteroid injection on the other side. In both i-PRF and corticosteroid groups, it was reported that pain and lesion size decreased in the control session, compared the beginning. In addition, significant statistical difference was not observed between the i-PRF and corticosteroid groups regarding the changes in pain and lesion size. It has been reported that i-PRF injection can be used instead of depot-corticosteroid injection, which has systemic and local side effects.

Gode et al.[33] evaluated the effect on diced cartilage survival utilized for dorsum camouflage in rhinoplasty. They applied diced cartilage and i-PRF in the study group, and only diced cartilage in control group. It was mentioned that in cartilage measurement on ultrasound, more loss of cartilage graft thickness was observed in the control group compared to the study group. They reported that i-PRF was successful in reducing the post-operative resorption rate by increasing the viability of the diced cartilage or maintaining its form.

Xie et al.[34] investigated whether the i-PRF has an additional contribution to the graft in the lateral maxillary sinus lift operation. They pointed out that i-PRF effectively reduces healing time, increases osteogenesis and it is a reliable material that can be used in maxillary sinus lift operations.

Turer et al.[35] evaluated the additional contribution of i-PRF application in patients who received coronally advanced flap with connective tissue graft. They reported that i-PRF had an additional supplement to keratinized tissue width and covering the root surface.

Ozsagir et al.[36] used i-PRF alone and in combination with micro-needling for gingival augmentation in individuals with thin gingival phenotype. It was reported that the increase in gingival thickness was statistically significant in both groups. In the 6th month control session, the group using i-PRF combined with micro-needling showed a statistically significant increase in gingival thickness compared to the group using only i-PRF. It is mentioned that i-PRF can be

applied before the treatments to increase the success of periodontal plastic surgery operations and reduce the complications of orthodontic treatments.

PRP is used as an injection in areas such as knee arthroplasty, face lift surgeries, reducing the incidence of infections after heart surgeries, sports injuries, tendon/ligament injuries, osteoarthritis, meniscus healing, alopecia, musculoskeletal regenerative procedures, and acne.[37,38] Since i-PRF is completely autogenous, it does not prevent natural inflammation.

In conclusion, i-PRF can be used in all areas where PRP is used and will provide a positive benefit in regeneration compared to PRP, since platelet, leukocyte and growth factors in its content are higher than PRP.

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