The Effects of Injectable Platelet-Rich Fibrin on Implant Stability

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Purpose: To investigate the effects of injectable platelet-rich fibrin (i-PRF) on implant stability. Materials and Methods: A total of 40 implants (BEGO Semados RS/RSX implants, BEGO Implant System) were surgically placed in 15 patients between the ages of 25 and 67 years who had mandibular edentulous areas. After the implant sockets were prepared with the appropriate protocol, i-PRF was applied to the implant surface and socket with the help of a 5-cc sterile syringe in the study group, and implants were placed without i-PRF in the control group. In the research process, the resonance frequency analysis (RFA) method was used to measure implant stability. The implant stability quotient (ISQ) values were determined during the time of the operation and at the first, second, and fourth weeks. Results: The results obtained after the stability measurement periods showed that the decrease in the mean ISQ values in the control group was statistically significant in the first week. Evaluations made in the following weeks were not statistically significant. The study group showed an increase in ISQ values during the measurement periods, and the increases in the second and fourth weeks were statistically significant. Conclusion: i-PRF had positive effects on early implant stability, and i-PRF can be safely used in dental implant surgery and promotes bone healing around dental implants. Int J Oral Maxillofac Implants 2022;37:1145–1150. doi: 10.11607/jomi.9629

Keywords: injectable platelet-rich fibrin, primary implant stability, resonance frequency analysis

Tooth extraction is a common procedure that may occur as a result of disease or trauma and directly affects facial esthetics and chewing function. For these reasons, dental implants are used in treatments for the edentulous part of the arch. Dental implants have been used in dentistry practices for a long time and have achieved a 95% success rate.1 For successful osseointegration, a series of events occur in the wound healing process, and it takes an average of 3 to 6 months for a healthy patient to start and complete the prosthetic stage. The osseointegration process varies depending on many factors, and researchers have conducted various studies to accelerate the osseointegration process and provide early prosthetic loading.2

Osseointegration can be achieved by improving primary stability, which determines the mechanical retention of implants. Although there are various methods for evaluating implant stability, resonance frequency analysis (RFA), which is noninvasive, is frequently used. The advantages of the RFA method are its easy applicability, repeatable measurements, reliable results, and quantitative measurements.3 The RFA method was defined by Meredith et al,4 and in this method, the measurement results are scored according to the implant stability quotient (ISQ), which ranges from 1 to 100.5 Factors affecting ISQ measurements are macro-micro design (surface properties) of the implant surface, implant socket preparation, vertical level of the implant in the alveolar crest, bone quality, and bone density.3

During implant surgery osteotomy, the gap between the implant and bone is filled with blood clots, followed by the attachment of serum proteins—cellular components in the blood—to the implant surface in a thin layer. Platelets then adhere to this layer and activate, releasing growth factors and cytokines, which have important roles in wound healing.6 Alpha granules are a major part of the granule structure of platelets and provide the release of platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF).7 These growth factors have a regulatory effect on cellular migration, adhesion, proliferation, and differentiation. Growth factors and cytokines in the blood play an active role in angiogenesis and tissue regeneration.6–8 Platelet concentrates contain a high number of growth factors, leading to their use in various techniques in maxillofacial surgery. Thrombocyte

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Platelet concentrates have been identified in different works throughout their historical development. In 2009, Do-han Ehrenfest et al\(^9\) classified this subject with their compilation according to the leukocyte and fibrin contents of the platelet concentrates and divided into four categories: pure platelet-rich plasma (P-PRP), leukocyte and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF), and leukocyte and platelet-rich fibrin (L-PRF). Characterized by leukocytes and a dense fibrin network, Choukroun’s L-PRF has taken its place in this classification.

Platelet-rich plasma (PRP) was defined as a platelet concentrate toward the end of the 1990s, and it is more complex compared to other platelet concentrates used today. When preparing PRP, bovine-derived thrombin or calcium chloride (CaCl\(_2\)) is used to prevent clotting. The disadvantage of this method is that thrombin use is accompanied by a risk of cross-infection and inhibits wound healing.\(^10\) A second-generation platelet concentrate, termed platelet-rich fibrin (PRF), that does not use anticoagulants and has shorter preparation times was therefore developed, as defined by Choukroun et al.\(^9,11\) This method provides plasma, white blood cells, and platelets in a 3D fibrin scaffold by separating blood from red blood cells using tubes with no anticoagulant. PRF contains a high-density fibrin scaffold with 97% more platelets and 50% more leukocytes than normal blood samples.\(^8\)

Ghanaati et al\(^12\) developed a new PRF protocol. The low-speed centrifugation concept (LSCC) reduces the relevant centrifugation force (RCF) to provide a looser fibrin scaffold, thereby facilitating cell penetration and increasing the number of inflammatory cells and platelets. This new PRF protocol was named advanced platelet-rich fibrin (A-PRF).\(^12\) The idea of LSCC has led to the development of injectable PRF (i-PRF) as a liquid platelet concentrate that uses plastic tubes with no anticoagulant. The advantages of i-PRF are that it provides longer-term release of growth factors such as TFF-β, PDGF, and VEGF; stimulates local angiogenesis; increases the adhesion of stem cells; modulates the immune system; and increases epithelial mitogenesis.\(^13\) These studies have found that i-PRF affects the migration, proliferation, and differentiation of human osteoblasts and osteoblast behavior more clearly than PRP.\(^14\) In another study, a comparative analysis of the total number of cells in i-PRF with other liquid blood concentrates, such as PRGF and PRP, showed a significantly higher number of platelets, leukocytes, monocytes, and granulocytes in i-PRF.\(^15\)

Various applications have been done to implant surfaces to accelerate the osseointegration process of implants, and the use of platelet concentrates for this purpose has been included in the literature.\(^16,17\) As such, this study aims to investigate the effects of i-PRF on the early period of implant stability.

**MATERIALS AND METHODS**

The study was carried out by the Zonguldak Bülent Ecevit University Clinical Research Ethics Committee with permission number 2018-32-30 / 01, and all stages of this study were performed in the Zonguldak Bülent Ecevit University Oral and Maxillofacial Surgery clinic.

In the clinical study, a total of 40 implants (BEGO Semados RS/RSX implants, BEGO Implant System) were Surgically placed in 15 patients between the ages of 25 and 67 years who had edentulous areas in their mandible. Criteria for inclusion in the study were patients with deficiencies in two or more teeth in the same area or symmetrically in the mandible and no tooth extraction history within the 6-month period preceding inclusion in the study. Patients who have sufficient bone volume and quantity during implant operations and did not require additional augmentation processes were included. Patients with any systemic conditions that may contraindicate implant operations, patients with poor oral hygiene, and smoking patients were excluded from the study.

The patients were evaluated with panoramic radiographs taken during routine examinations. To standardize this study, patients with type 2 bone quality and density according to the Lekholm and Zarb classification\(^18\) were included. During the operation, the bone type was determined by hand by the surgeon. Radiographic and clinical examinations were used to determine the fit of each patient for the study according to the inclusion criteria. The patients included in the study were randomly divided into two groups: study (i-PRF) and control groups.

Before the operations, the patients were informed in detail about the implant treatment and all stages of this study, and informed voluntary consent forms were read and signed. This study was completed in accordance with the principles of the Declaration of Helsinki.

**I-PRF Preparation**

In the process of obtaining i-PRF, 10 mL of venous blood was taken with a sterile syringe set to plastic tubes with no anticoagulant (BD Vacutainer, Z [No Additive]). The tubes were centrifuged in a centrifuge device (Process for PRF) for 3 minutes (60 g) at 700 rpm. After centrifugation, the red blood cell layer at the bottom of the tube and the yellow-orange i-PRF layer at the top were obtained. Liquid i-PRF was aspirated with disposable 5 cc injectors and applied to the implant surface and prepared implant socket (Fig 1).
Surgical Procedure
All stages of this study were carried out by the same surgeons (S.G. and M.C.D.) and team in the Zonguldak Bülent Ecevit University Faculty of Dentistry Oral and Maxillofacial Surgery Department clinic. Clinical and radiographic examinations of the patients were performed in order to plan the positions of the implants before the operations. All surgical operations were performed under local anesthesia (maxicaine fort). The full-thickness flap (mucoperiosteal) was elevated after the horizontal crestal incision, and if necessary, a vertical incision was made in the edentulous area. While preparing the implant sockets in the bone, the operations were continued by following the appropriate protocol set by the BEGO implant system (BEGO Implant System). According to the clinical and radiologic examination results, implants with diameters of 3.75 and 4.1 mm and lengths of 8.5, 10.0, and 11.5 mm were preferred. After the implant sockets were prepared with the appropriate protocol, i-PRF was applied to the implant surface with the help of a 5-cc sterile syringe. Control group implants were inserted without i-PRF application. One-stage implant surgery was performed to acquire RFA measurements, and the implants were healed with gingival formers.

After the operations, patients were prescribed antibiotics (amoxicillin and clavulanic acid, 2 × 1), analgesic (dexketoprofen, 2 × 1), and mouthwash (0.2% chlorhexidine gluconate, 3 × 1). The patients were informed in detail about possible complications that could be encountered after the operation and were called for the determined follow-up periods. Sutures were removed after an average of 7 to 10 days.

Implant Stability Measurement
In the research process, the RFA method was used to measure implant stability. The Penguin RFA device and Multipeg (Integration Diagnostics Sweden) transducer were used for RFA measurements (Fig 3). The ISQ values were determined at the operation time and at the first, second, and fourth weeks (Figs 4 and 5). During the measurements, the Multipeg part was fixed in the implant, and the arithmetic mean of the ISQ values was calculated after measurements on the four surfaces of the Multipeg part (buccal, lingual, mesial, and distal).

Statistical Analysis
Shapiro-Wilk test was used to evaluate the normality of the data. Mann-Whitney U test was used to compare the numerical data on ISQ variables between groups. Friedman and Wilcoxon signed-rank tests were used to compare numerical data of the ISQ values within the group at specified times. \( P < .05 \) was considered statistically significant. The Statistical Package for Social Sciences (SPSS) 19.0 was used to evaluate the data.
RESULTS

All operations to place implants in the 40 patients included in this study were successfully completed, and no complications were encountered in the subsequent control periods. Measurements in the periods determined by the RFA method were performed successfully (Table 1).

The average ISQ values of the groups according to the determined periods are shown in Table 2. Comparative analysis of both groups according to the determined periods showed high values in the control group during the operation, and the study group showed high values in the subsequent measurements, but there was no statistically significant difference in any period ($P > .05$).

When the ISQ average values of the groups according to the measurement periods were examined (Table 2), operation time and first week measurements were compared in the control group. The mean ISQ values decreased, and this decrease was statistically significant ($P = .021$). The mean ISQ changes of the control group at the second and fourth weeks were not statistically significant (Table 2 and Fig 6).

The ISQ averages of the i-PRF group between the periods were analyzed. ISQ average values increased in the periods after the operation; this increase was statistically significant in the periods between the second week ($P = .048$) and the fourth week ($P = .004$; Tables 1 and 2, Fig 6).

DISCUSSION

At the end of the study, 40 implants had been successfully surgically placed, and no complications were encountered in any of the groups during the follow-up periods. According to the consensus decision published in 2007 by Misch et al, ensuring complete osseointegration results in the initial mechanical connection being replaced by a biologic connection. It is critical to provide primary stability during this process, as it determines the mechanical connection of the implants. In this study, the effect of i-PRF on implant stability in the early healing period was studied, and the results showed that i-PRF had positive effects.

The importance of objectively and quantitatively evaluating implant stability to decide the functional loading time has been emphasized in past studies. RFA, described by Meredith et al, has been preferred as a method for stability measurements in many studies because of its easy applicability, repeatable measurements, reliable results, and quantitative ISQ values. The RFA method takes

<table>
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<th>Table 1</th>
<th>Comparison of ISQ Average values of Control and Study Groups According to Measurement Periods</th>
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<tbody>
<tr>
<td></td>
<td>Operation</td>
</tr>
<tr>
<td>Control</td>
<td>74.67 ± 8.92</td>
</tr>
<tr>
<td>i-PRF</td>
<td>72.48 ± 8.52</td>
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<tr>
<td>$P$</td>
<td>.330</td>
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$P < .05$ was considered statistically significant.

<table>
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<th>Table 2</th>
<th>Analysis of ISQ Values of Groups Between Periods</th>
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<tr>
<td></td>
<td>Operation–1 wk</td>
</tr>
<tr>
<td>Control</td>
<td>0.021*</td>
</tr>
<tr>
<td>i-PRF</td>
<td>0.125</td>
</tr>
</tbody>
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$P < .05$ was considered statistically significant. *Statistically significant values.

Fig 6 Distribution of ISQ mean values by measurement periods. * = Significant difference was observed in i-PRF group compared with measurements during operation.

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measurements according to the ISQ values ranging from 1 to 100, and studies have reported mean ISQ values between 52 and 90.15,26

Furthermore, previous studies have reported that the mean ISQ values decreased in the first month of implant placement, and they associated this with resorption and remodeling during the healing period between bone and implant contact.22,27,28 Han et al29 reported that the decrease in ISQ mean values was highest in the third week, and stability values approached the operation measurements at the end of 8 weeks. Monov et al18 reported that the decrease in ISQ values in the 0- to 4-day measurement period was statistically significant. According to the data, it was reported that the first-week ISQ mean values of the control group decreased and were statistically significant. In the i-PRF group, the average ISQ values increased during the measurement periods. This increase is thought to be due to the growth factors released by i-PRF.

In the i-PRF group, the second and fourth weeks showed the highest average ISQ values, and it was statistically significant. In a study that had similar results to those of the present study, Miron et al13 reported that the growth factor present (PDGF, VEGF, and IGF) of i-PRF was high in the 10-day period. Researchers have also reported the positive effects of i-PRF on cell migration.13 In another study, Wang et al14 investigated the effects of i-PRF on human osteoblast cell behaviors and reported more osteogenic potential than PRP and the control tissue culture plastic group. The authors additionally emphasized the advantages of i-PRF—containing leukocytes and fibrin proteins.14

At the end of this study, the i-PRF group results showed a similar increase in mean ISQ values compared to those reported by Öncü et al29 in a study with PRF. In this study, the effects of PRF on implant stability were measured using the RFA method in the first and fourth weeks and showed that early stability had been increased.30 In another clinical study, Pirpir et al31 used concentrated growth factor (CGF) from platelet concentrates and reported the positive effects of CGF on the early healing period of osseointegration with the RFA method.31 A literature review also showed that some studies have advocated for the opposite results. Monov et al18 and Ergün et al32 analyzed the effects of PRP using the RFA method and reported that it had no effect on stability. These studies emphasized the effect of the type of bone on implant stability.

When the results of the i-PRF and control groups were compared, there were no significant differences according to the measurement periods. The reason for this is that the ISQ mean values obtained in both groups showed high implant stability, meaning sufficient bone quality and density were provided. Makary et al13 also pointed to the effects of bone type on implant stability. This study was completed on type 2 bone in the mandible with sufficient bone support. As such, it is possible that i-PRF would be more effective in implants applied to bone types with low stability.

CONCLUSIONS

This study demonstrated that i-PRF promotes bone healing around dental implants. However, further randomized controlled trials with standardized methods and long follow-ups are required to gain a deeper understanding of the role of i-PRF in the healing process.

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