Anitua, Eduardo
DDS, PhD, Eduardo Anitua Foundation, Vitoria, Spain.

Original article

Use of Endoret® (PRGF®) (Platelet Rich Growth Factor) in the post-extraction socket: a new regenerative approach

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ABSTRACT

Objective. There are numerous techniques on preserving or regenerating the post-extraction socket described in the international literature that employ different materials alone or in combination.

Materials and methods. A randomized double-blind clinical trial was conducted in which post-extraction sockets in mandibular molars were regenerated over a period of 12 weeks. A total of 60 patients were recruited and randomized either to the Endoret® (PRGF®) group (36 patients) or the control group (24 patients).

Results. Dental CT analysis (cone beam computed tomography: CBCT) at 12 weeks after extraction revealed that the group treated with Endoret® (PRGF®) achieved a socket regeneration volume greater than or equal to 75% in 96.67% of cases, while ony 45.45% of the control group, with statistically significant differences (p=0.005). The percentage of newly formed bone measured by histopathologic examination was 63.08% for Endoret® (PRGF®) compared with 35.56% for the control group. Better epithelialization was also observed at 3, 7 and 15 days in the experimental group as well as lesser pain.

Conclusions. The technique evaluated in this clinical trial can be considered safe, no negative adverse effects occurred, and it was more effective in improving different aspects of post-extraction socket regeneration (patient quality of life and post-extraction socket regeneration).

KEYWORDS

Post-extraction socket; Regeneration; Endoret-PRGF®.

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Correspondence address:
Dr. Eduardo Anitua
C/ Jose Maria Cagigal,19
10005 Vitoria, Spain
lapica77@yahoo.es
Phone no: 608 037 486

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INTRODUCTION

There are numerous techniques on preserving or regenerating the post-extraction socket described in the international literature that employ different materials alone or in combination[1-3]. Endoret® Platelet Rich Growth Factor (PRGF®) and autologous fibrin are 100% autologous products that are simple and inexpensive to obtain. It is also important to highlight that the use of this biological socket regeneration technique does not have side effects or dangerous effects for the patient. It is recommended as a preventive therapy for alveolitis by significantly reducing its incidence as demonstrated in the studies carried out by Mancuso et al., 2003[4] (on 117 patients) y Rutkowski et al., 2007[5] (on 506 patients), in addition to our experience over the years[6-9].

One of the first studies published on the potential of Endoret® (PRGF®) as a regenerator of post-extraction areas for future placement of dental implants was reported in 1999[7]. In this study, epithelialization of 10 patients treated with Endoret® (PRGF®) was excellent. In three patients, split-mouth extractions were carried out with Endoret® (PRGF®) and a control, and in these patients differences in epithelialization could be compared under the same circumstances.

In 2009, an animal model study was published in which the regenerative power of Endoret (PRGF®) was determined[8]. The study was carried out on goats in which 5mm diameter cavities in the tibias were prepared to simulate artificial sockets that were then refilled with Endoret® (PRGF®). Evaluation of the regeneration of the defects was done at 8 weeks after surgery using histological preparations where the newly formed bone was studied and tissue histomorphometric analysis was performed.

Newly formed trabecular bone surrounded by a densely vascularized connective tissue could be histologically identified in the Endoret® (PRGF®) group. The pathologic specimens in the control group consisted of highly cellular connective tissue with some small areas of intramembranous bone tissue.

Finally, in 2010, a new study revealed the regenerative potential of Endoret® (PRGF®) in humans[9]. The study was performed on 14 patients who underwent tooth extractions and were treated using the Endoret® (PRGF®) technology compared to patients in whom teeth were extracted without the use of Endoret® (PRGF®) by conventional treatment (filling the socket with blood clot). After the waiting period for placement of the implants (between 11 and 14 weeks), Cone Beam Computed Tomography (CBCT) was performed to measure the volume of regenerated bone inside the socket as well as the density of the new bone in Hounsfield units in the interior and exterior portion of the future site of the implant and inside the socket defect.

Densitometry of the interior and exterior of the measuring cylinder for the implant on CBTC and the center of the regenerated socket revealed differences between both groups, being statistically significant in the areas corresponding to the implant's measuring cylinder.

The objective of this study is to evaluate the efficacy of Endoret® (PRGF®) as regenerative material for the post-extraction socket in humans via a randomized double-blind clinical trial .

MATERIALS AND METHODS

A randomized double-blind clinical trial was carried out in which post-extraction sockets in mandibular molars were regenerated over a period of 12 weeks. A total of 60 patients were recruited who were then randomized to either the Endoret® (PRGF®) group (36 patients) or the control group (24 patients).

The inclusion criteria were: adult patients of both sexes, with indication for single exodontia of mandibular molars that could be followed during the treatment period.

The exclusion criteria were: included third molars or those with horizontal inclination, severe inflam-

mation prior to the intervention in the areas of exodontia, severe hematological alteration or disease, having received radiation therapy, chemotherapy or immunosuppressant therapy in the previous 30 days, as well as systemic corticosteroids and/or anticoagulants, on regular nonsteroidal anti-inflammatory treatment, history of chronic hepatitis or liver cirrhosis, diabetes mellitus or poor metabolic control (glycosylated hemoglobin greater than 9%), dialysis patients, presence of malignant tumors, hemangiomas or angiomas in the area of the extraction, history of ischemic heart disease in the previous year, pregnancy, metabolic bone disease, and patients on oral or intravenous bisphosphonate treatment.

The main variable studied was the percentage of sockets that achieved 75% of regenerated bone volume at the end of follow-up in each treatment group. Secondary variables were also evaluated: final bone density (measured in Hounsfield units on CBCT, soft tissue epithelialization index (scale 1 to 5), keratinized thickness of the gums, postoperative pain (measured on a visual analogue scale) and inflammation (scale of 0 to 3). Bone and soft tissue biopsies were also performed at the time patients received dental implants, after the follow-up period.

The clinical trial was approved by the Ethics Committee. Patients signed informed consent. The clinical trial reference number was: ClinicalTrials.gov (NCT01465399).

The pain scale from 0 to 10 and the percentage of socket closure, the percentage of newly formed bone and the final bone density of the socket were evaluated as quantitative variables and the means were compared between the control and treatment groups using Student's t test, with a statistically significant p-value of $p \leq 0.05$. To evaluate the soft tissues and degree of inflammation, as well as the type of bone obtained in the regenerated zone, the Mann-Whitney test was used with a statistically significant value of $p \leq 0.05$.

RESULTS

Inspection of the socket after extraction of the lower molars indicated the presence of radicular septum in 54.16% of the control group, while the septum was only preserved in 38.9% of the defects in the treatment group. Because of this difference, the defects in the Endoret® (PRGF®) group were of greater volume than those treated in the control group, as shown in Figure 1.

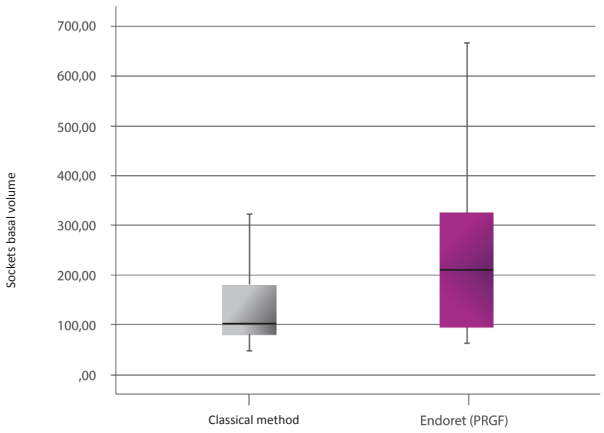

Figure 1. Comparison of defects treated by the classical method (blood clot-control group) and the Endoret® (PRGF®) group.

The group treated with Endoret® (PRGF®) achieved a socket regeneration volume greater than or equal to 75% in 96.67% of cases, while ony 45.45% in the control group, differences being statistically significant (p=0.005) (Figure 2).

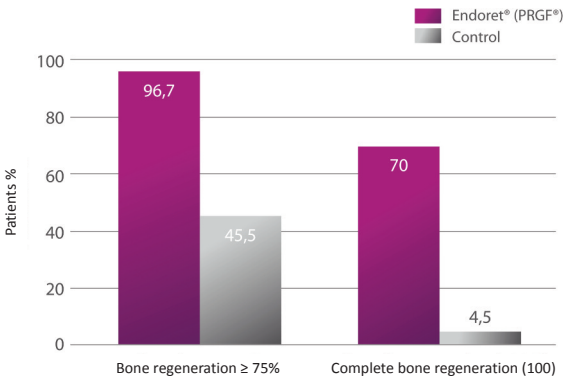

Figure 2. Bone regeneration in the Endoret® (PRGF®) group (purple) compared with the control group (gray) of 75% and 100% of the socket volume.

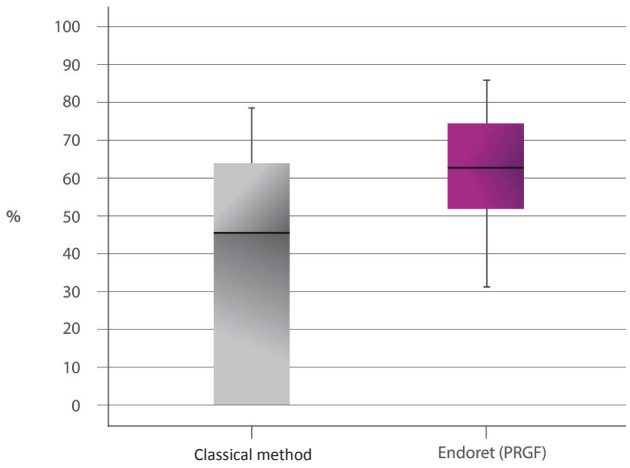

Figure 3. Newly formed bone in the Endoret® (PRGF®) group and the control group.

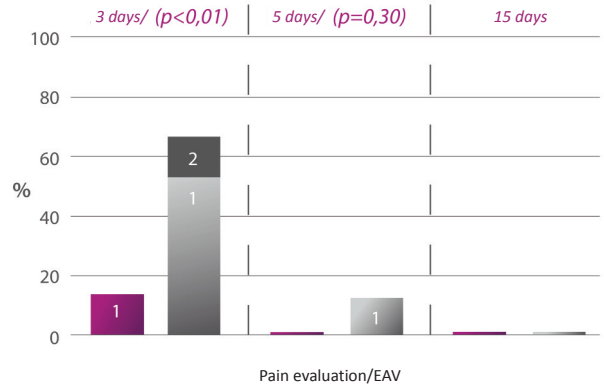

Figure 4. Postoperative pain evaluation at days 3rd, 7th and 15th in both groups.

The percentage of newly formed bone measured by hystopathologic examination was 63.08 for the Endoret® (PRGF®) group compared to 35.56% for the control group, as shown in Figure 3. Bone density of the newly formed bone as measured on CBCT was greater in the treatment group (mean 450 HU) compared to the control group (mean 318 HU), statistically significant (p=0.04).

In this trial, we also evaluated the effect of Endoret® (PRGF®) in extractions on the patient quality of life by evaluating postoperative pain, inflammation and epithelialization, since despite the impression provided by patients treated with Endoret® (PRGF®) following tooth extraction, there were no studies to confirm this.

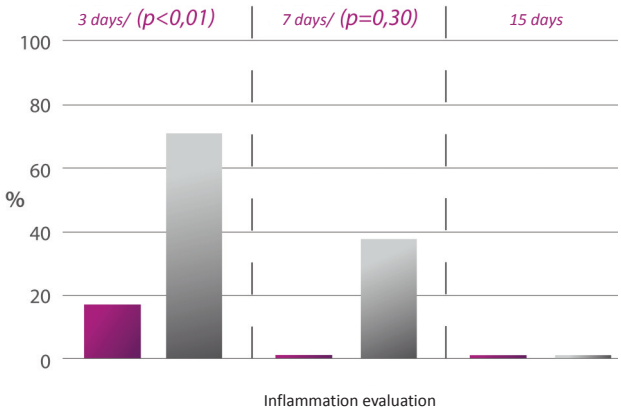

Figure 5. Postoperative inflammation evaluation at days 3rd, 7th and 15th in both groups.

On pain evaluation at day 3rd, there was pain in 18% of patients in the treatment group, while we found pain in 62% of patients in the control group, statistically significant (p=0.003). The pain had disappeared at day 7th in the Endoret® (PRGF®) group while it was still present in 15% of the control group. Pain was absent at day 15th in both groups (Figure 4).

On evaluation of the inflammation index at day 3rd, inflammation was found in 18% of patients in the Endoret® (PRGF®) and 65% of the control group, differences being statistically significant (p=0.03). Inflammation persisted at day 7th in 39% of the control group, while it had disappeared completely in the treatment group, differences statistically significant (p=0.038). The inflammation disappeared in both groups at day 15th (Figure 5). Figure 6 shows one of the cases included in the control group compared to another case included in the Endoret® (PRGF®) group.

DISCUSSION

All of the studies published in the international literature that have tested the potential of Endoret® (PRGF®) as a post-extraction socket regenerator have demonstrated its good performance in obtaining bone and soft tissue regeneration outcomes.[5-9] The results of our study reinforce these data both in hard tissue and

soft tissue, in addition to adding other variables such as pain, inflammation and therefore indirectly evaluating patient quality of life following tooth extraction and its regeneration with Endoret® (PRGF®).

Alisa et al., (2010) reported a decrease in pain within the first three days in the experimental group versus the control group and better primary intention closure, both variables presenting statistically significant differences ($p<0.05$).[10] Other authors like Gürbuzer et al., (2008), Ogundipe et al., (2011) and Celio-Mariano et al., (2012) focused the results of their studies on bone regeneration without evaluating pain or soft tissues.[11-13] They found improvement in the bone volume achieved in the experimental group compared with the control group, as evaluated by different techniques (subjective gray scale, Scintigraphy, dental cone beam tomography), though none of them found statistically significant differences between groups.

CONCLUSIONS

The decrease in pain and inflammation, and the achievement of a faster primary closure observed in this study confirms that the quality of life of patients treated with Endoret® (PRGF®) is superior to the conventional treatment (blood clot).

The technique evaluated in this clinical trial can also be considered safe as there were no negative or adverse effects. In addition, we were able to predict outcomes like:

- Closure of the socket greater than or equal to 75% with better density and better proportion of newly formed bone.
- Better epithelialization at days 3rd, 7th and 15th with statistically significant differences, obtaining a greater thickness of the keratinized gum.
- Significant differences in pain at day 3rd (early postoperative, where there is a greater pain level), as well as in inflammation at days 3rd and 7th.

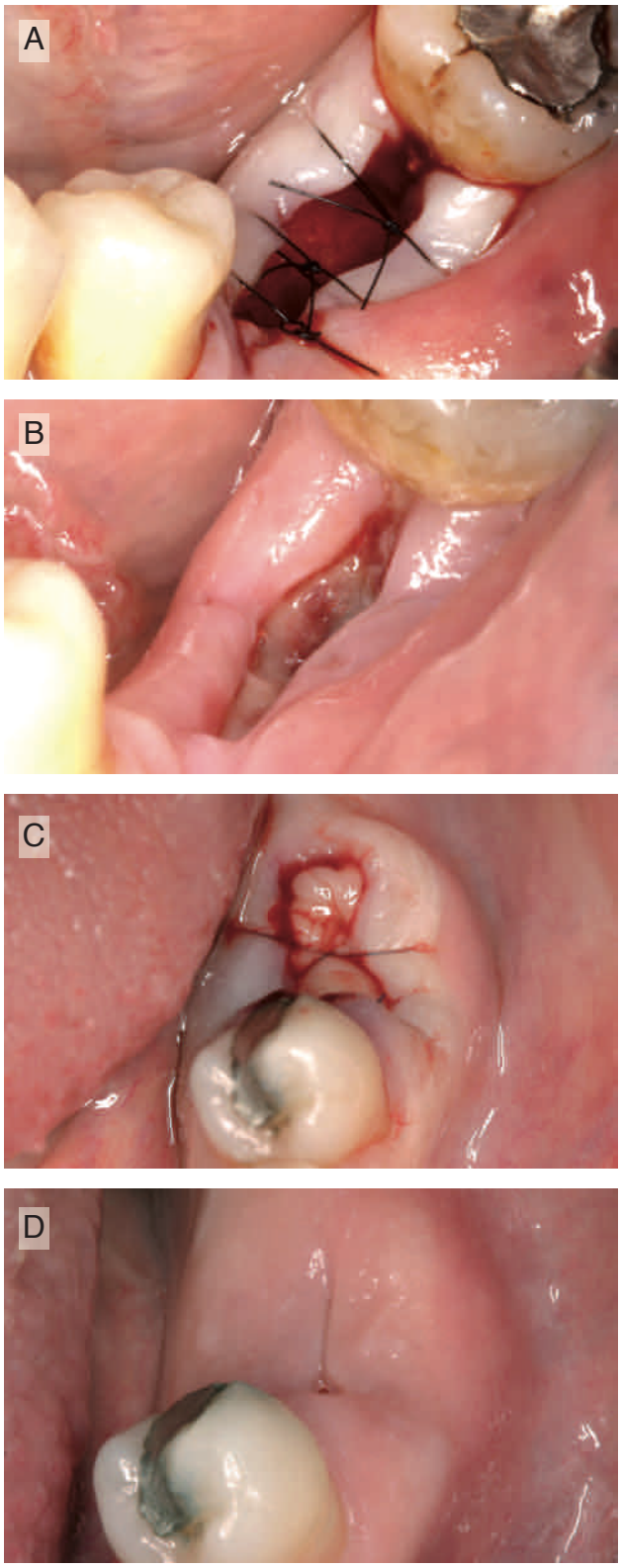

Figure 6. A) Tooth extraction included in the control group. B) Socket regeneration at day 15th. C) Tooth extraction included in the Endoret® (PRGF®) group. D) Socket regeneration at day 15th.

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