Bone defects in revision knee arthroplasty: filling with bone allograft plus platelet-derived growth factors. A prospective, randomized study

ABSTRACT

Background: One of the most challenging aspects of revision knee arthroplasty is the management of bone loss. The objective of the study is to show the capability to augment bone mineral density in areas with bone loss with platelet-derived growth factors.

Methods: Patients who underwent total knee replacement revision with tibial-damaged metaphyseal bone were randomly allocated to have a revision total knee arthroplasty and to fill the bone defects with lyophilized bone allograft mixed with platelet growth factors (experimental group, \( n = 9 \)) or with lyophilized bone allograft alone (control group, \( n = 7 \)). To evaluate bone mineral density between groups, dual-energy X-ray absorptiometry (DEXA) was performed preoperatively, at 1 month, 6 months and 1 year after surgery.

Results: The study was comprised of a total of 16 patients. We found no significant differences during the follow-up between groups in bone mineral density.


Key words: Bone defects, total knee replacement, platelet-derived growth factors, bone allograft.

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BACKGROUND

One of the most challenging aspects of knee arthroplasty revision is bone loss control, which affects the fixation and stability of the implant. There are various treatment options, depending on the type of defect: metallic augmentation, bone autograft or allograft, demineralized bone matrix, materials based on calcium and cement, among others. Cavitary defects, depending on the size and surgeon preference, tend to be filled with one type of graft with good results.

There are various presentations of bone allografts: demineralized bone matrix, morselized or chips of cancellous bone, cortical grafts or corticocancellous, and complete bone segments. Some have osteoinductive and osteoconductive properties. The cancellous bone graft is an osteoconductive matrix that supports new bone growth; however, its osteogenic potential is low.

Use of plasma-rich platelets (PRP) has demonstrated its osteoinductive ability, emits molecular signals in a variety of growth factors, and perhaps as cell matrix support in the form of a fibrin matrix. Recently, a combination of osteoconductive with osteoinductive materials was studied and the results are encouraging. Some studies have demonstrated that the incorporation of platelet-derived growth factors increases the biological and biomechanical properties of the bone grafts. However, the greater number of these studies have been done in the realm of experimental animal surgeries or in oral or spinal surgeries.

The objective of our study was to compare the ability of increasing bone mineral density in areas of bone loss, between lyophilized bone allograft (our standard procedure) and lyophilized bone allograft plus PRP in patients subjected to knee revision arthroplasty with cavitary bone defects.

METHODS

We performed a prospective, randomized, blind study approved by the Ethics Committee of our institution. All patients signed informed consent for their participation. Patients had aseptic loosening of the primary knee arthroplasty and required revision knee surgery, with proximal tibial bone defect, type IIA or IIB. Bone defects were classified according to the guidelines of the classification of bone defects of the Anderson Orthopedics Research Institute (AORI). Patients were randomly assigned to two groups. The defects of the experimental group were filled with lyophilized bone allograft and PRP, and the control group was treated with only lyophilized bone allograft. Patients were recruited during a 5-year period. All surgeries were performed in the Hospital Clinic of Barcelona.

Preoperative evaluation

Radiographs. Patients had plain x-rays of the knees taken in two projections: antero-posterior and lateral. Bone defects were grouped according to the AORL classification and an area of bone loss in the tibia out of its center was used as a reference during the study to avoid the tibial stem.

Dual-energy absorptiometry (DEXA). In the previously selected area on the radiographs, DEXA was done. Bone mineral density in this area was expressed in g/cm². During the study, the results were used as a reference value for each patient.

Preparation of the PRP

From each patient, 120 ml of blood was taken and immediately sent to the Hematology Department for preparation. For preparation of the PRP, 100 ml of blood was used and the remaining 20 ml was kept for serological studies and in vitro evaluation of the platelets. For preparation of the
PRP, the indications by Anitua were followed. During the surgical procedure, the gel formed by the PRP was combined with the cryodessicated bone allograft and impacted into the tibial bone defect.

**Surgical Technique**

The surgery was done by the same surgical team (FMB, JSV). The prosthesis placed was the revision model Profix (Smith & Nephew®, Memphis, TN. USA) proximal and distal modular type, cemented, without patellar replacement. After removing the primary prosthesis, all defects were evaluated according to the AORI classification. Bone defects were filled as has already been explained.

**Follow-up**

To see the integration of the graft, lines of radiolucency and the alignment of the prosthesis, plain radiographs of the knees were taken of all patients in two projections antero-posterior and lateral. The films were evaluated blindly by two observers. Also, to evaluate the bone mineral density in the tibial area previously selected during the preoperative study, DEXA studies were done at 1 month, 6 months and at 1 year postsurgery. At 1 year postoperatively, a two-phase bone scan was also performed. Films were taken immediately after injecting 740 mBq of $^{99m}$Tc methylene diphosphonate ($^{99m}$Tc-MCP) (vascular phase) and 2 h after administration of the isotope (bone phase) in anterior, posterior and lateral projections. The results were evaluated by only one radiologist who searched for areas of increased uptake and tried to localize the areas of bone loss.

**Statistical analysis**

Statistical analysis was done with the Student $t$ test for continuous variables and with the computer program SPSS (v.22, SPSS, Chicago, IL). The level of significance was $p < 0.05$.

**RESULTS**

During a 2-year period there were 16 patients included in the study. The majority were females with a primary degenerative etiology (Table 1). All patients completed the follow-up period.

With regard to the results during the follow-up examinations there were no objective differences seen in the integration of the bone graft on the plain radiographs. Imaging studies reported postoperative changes without noting whether there was an increase or decrease in bone uptake. During the year of evolution, the patient's densitometry demonstrated changes in bone mineral density. In the first postoperative month there was a discrete increase of bone mineral density compared with the preoperative results. The increase was most pronounced at 6 months of evolution (Table 2). At 1-year follow-up a reduction of the levels was seen. The same behavior was observed in both groups, but when it was compared with the densitometry there were no significant differences appreciated in the follow-ups, neither for an increase or decrease of bone mass with respect to the previous situation.

**DISCUSSION**

The number of knee revision surgeries continues to be higher, in part because primary replacements are being done in younger, more active patients. Revision surgery is a complex procedure that requires careful preoperative planning: deciding the appropriate approach, removing the components and cement, avoiding increasing bone loss, reconstructing the bone defects, placing the new components and degree of joint constriction required. One of the most important aspects
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is the reconstruction of bone defects. At present, one of the treatments for large cavitary defects is bone allograft, which has shown acceptable results.

The bone allograft has variable osteoinductive and osteoconductive properties; however, it lacks osteogenic properties and there are no living cells. The biggest advantage of cadaveric bone allograft is the great availability of shapes and sizes; moreover, there are no problems with morbidity of the donor site, transmission of infectious agents is virtually eliminated with the processing and sterilization of the tissue and mechanically speaking are stable. Frozen bone grafts have less immunological response, mechanical and osteoinductive properties. They have a greater index of delay in incorporation or incomplete incorporation compared with autografts.

Plain x-rays do not demonstrate if bone density increases or not because the information they provide is subjective; in addition, evaluation of bone quality around the prosthesis is easy. In a preoperative study, bone scan is useful for diagnosing prosthetic loosening, but not for the follow-up because there is a tendency to be reported as postoperative changes, without identifying whether or not bone regeneration has increased. Some authors have been able to quantify the results via bone scan, but it has only been useful during the first postoperative year.

Bone densitometry is a quantifiable method, useful for evaluating bone quality around the prosthetic stems and is superior to conventional radiographs. We did not observe significant differences between groups according to our results according to either bone increase or decrease. In our patients, PRP together with the cryodessicate did not increase bone mass during the study period.

In experimental animal studies PRP has been used with positive results that increase the osteogenic potential of bone grafts and help its integration. Incorporation of PRP enhances

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<th>Table 1. Demographic data of both patient groups</th>
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<td><strong>Lyophilized bone allograft + PRP</strong> (Group A)</td>
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<td><strong>Lyophilized bone allograft</strong> (Group B)</td>
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<td>Total patients</td>
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<td>Average age (years)</td>
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<td>Female/Male</td>
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<td>Etiology of primary revision (arthritis-trauma)</td>
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Group A: experimental, Group B: control.

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<th>Table 2. Results of DEXA*</th>
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<td><strong>Group</strong></td>
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Note: Group A: experimental, Group B: control (p < 0.05). DEXA: dual-energy absorptiometry.
the biological and biomechanical properties of the auto- and allografts. In those studies an increase in the levels of consolidation, greater integration of the allograft, behavior similar to autograft, and less bone resorption was reported; however, the postoperative time is short.4-40

In the evaluation in humans there are contradictory reports. Bieleck et al.41 did not report favorable results with PRP in filling cystic lesions. Other authors such as Wei et al.42 obtained results similar to the autograft when they applied it to calcaneal fractures, which is considered to be the treatment of choice in patients with these fractures. Some studies dispute these advantages and others require prudence, based on the lack of scientific evidence.18 Our studies support this finding because we were not able to demonstrate any advantage in our patients with the use of PRP, in addition to the fact that this extraordinary procedure increases costs and risks of infection or anaphylactic reaction.

The first reports of the placement of a bone allograft with PRP to patients who had revision arthroplasty of the knee showed no advantages in the repair of the bone defects; however, more studies with longer follow-up time are required, quantification of the use of platelets used to ensure the correct concentrations due to the adequate quantity and concentration of the platelets, tend to be decisive for this therapy.14,14

In conclusion, PRP administered to patients who had revision arthroplasty because of aseptic loosening showed no increase in bone mineral density.

REFERENCES


