Morphologie (2017) 101, 164—172

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GENERAL REVIEW

Basic research and clinical application of beta-tricalcium phosphate (β-TCP)

Recherche fondamentale et application clinique du bêta-tricalcium phosphate (β-TCP)

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Available online 24 April 2017

KEYWORDS
Bone substitute;
β-TCP;
Bone formation;
Osteoclasts;
Coupling

Summary The mechanism of bone substitute resorption involves two processes: solution-mediated and cell-mediated disintegration. In our previous animal studies, the main resorption process of beta-tricalcium phosphate (β-TCP) was considered to be cell-mediated disintegration by TRAP-positive cells. Thus, osteoclast-mediated resorption of β-TCP is important for enabling bone formation. We also report the results of treatment with β-TCP graft in patients since 1989. Two to three weeks after implantation, resorption of β-TCP occurred from the periphery, and then continued toward the center over time. Complete or nearly complete bone healing was achieved in most cases within a few years and was dependent upon the amount of implanted material, the patient's age, and the type of bone (cortical or cancellous). We have previously reported that an injectable complex of β-TCP granules and collagen supplemented with rhFGF-2 enabled cortical bone regeneration of rabbit tibiae. Based on the experimental results, we applied this technique to the patients with femoral and humeral fractures in elderly patients, and obtained bone union.

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http://dx.doi.org/10.1016/j.morpho.2017.03.002
1286-0115/

MOTS CLÉS
Substituts osseux ;
β-TCP ;
Formation osseuse ;
Ostéoclastes ;
Couplage

Résumé Le mécanisme de résorption des matériaux de substitution osseux implique deux processus : une destruction en solution et une médiée par les cellules. Dans nos études précédentes chez l'animal, le principal processus de résorption du phosphate bêta-tricalcique (β-TCP) était considéré comme une résorption cellulaire par des cellules TRAP-positives. Ainsi, la résorption du β-TCP due aux ostéoclastes est importante pour permettre la formation osseuse (couplage). Nous rapportons également les résultats du traitement par greffe avec du β-TCP chez des patients depuis 1989. Deux à trois semaines après l'implantation, la résorption de β-TCP est survenue à partir de la périphérie, puis a continué au cours du temps de façon centripète. La cicatrisation osseuse complète (ou presque complète) a été obtenue dans la plupart des cas en quelques années et dépendait de la quantité de matériel implanté, de l'âge du patient et du type d'os (cortical ou trabéculaire). Nous avons déjà rapporté qu'un complexe injectable de granules de β-TCP et de collagène supplémenté avec du rhFGF-2 a permis la régénération osseuse corticale des tibias de lapin. Sur la base des résultats expérimentaux, nous avons appliqué cette technique aux patients âgés atteints de fractures fémorale et humérale et obtenu une union osseuse.

Introduction

Autologous bone is the preferred graft material for treating bone defects. However, disadvantages of autografting are significant and include procurement morbidities, increased operative time, and limited availability. In addition, autologous bone is difficult to obtain when the patient is a child. Allografts have commonly been used as substitutes for autogenous bone grafts in Europe and the United States but not in Japan. Significant problems associated with allograft introduction include a low bone-fusion rate and disease transmission [1,2]. Recently, bone substitute materials have been advocated as alternatives to autografts and allografts. Hydroxyapatite (HAP) is widely used as a bone substitute because of its excellent biocompatibility and osteoconductive properties [3]. However, HAP has several disadvantages, such as slow biodegradation during the repair of bone defects [4]. Calcium phosphate cement (CPC) has good biocompatibility, bioactivity, low setting temperature, adequate stiffness, and easy shaping into complicated geometrics [5]. However, the resorption rate is slow. β-TCP has recently received considerable attention as a bone graft substitute because of its biocompatibility and biodegradability [6—10]. In animal experiments, β-TCP is gradually degraded during bone remodeling and is finally replaced by mature new bone [11—13]. In this study, we report experimental animal results and the representative clinical results of β-TCP implantation in patients with bone defects.

Materials and methods

The β-TCP products used in this study was synthesized with a mechanochemical method and provided by Olympus Terumo Biomaterials Co. (Tokyo, Japan). Briefly, $CaHPO_4/H_2O$ and $CaCO_3$ at a molar ratio of 2:1 were mixed into slurry with pure water and zirconia ball in a pot mill for 24 hours and dried at 80 °C. The calcium-deficient HAP was converted to β-TCP by calcinations at 750—900 °C. Following the preparation of forming slurry of β-TCP with forming agent and drying process, the preforming porous body of β-TCP was obtained. After the preforming body was sintered at 1050 °C for 1 hour, a porous β-TCP block with 75% porosity was obtained. A bimodal pore size distribution in the β-TCP block with 75% porosity was observed on the evaluation by porosimeter, where one peak existed in a region of more than 100 μm and the other peak existed in a region of less than 5 μm. The β-TCP block with 60% porosity was synthesized by the same method as 75% porosity except that the amount of forming agent was changed.

Animal experiments

Cylindrical cancellous bone defects were created by drilling of the rabbit distal femur. Bone defects were filled with cylindrical β-TCP blocks. Rabbits were sacrificed after surgery, and the distal part of the femur was removed. Decalcified sections were obtained for HE and tartrate-resistant acid phosphatase (TRAP) staining.

Clinical application

From 1989 to 2004, we have used β-TCP with 75% porosity. Since 2005 we have used β-TCP with both 75 and 60% porosity. Patients ranged in age from 2 to 91 years at the time of surgery. In several cases, β-TCP was placed on the periosteum after fibula harvest.

A new evaluation system of new bone formation and β-TCP resorption

We have recently established a new evaluation system to measure bone formation and β-TCP resorption in opening high tibial osteotomy. All patients underwent CT examination at 2 weeks and 6 years. The CT image data were divided into 3 areas by tracing manually on the screen of the computer. CT attenuation values (in Hounsfield units [HU]) of the area implanted with β-TCP of 60% porosity, the area