Materials Science and Engineering C 33 (2013) 1894–1899

Contents lists available at SciVerse ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Clinical evaluation of β-TCP in the treatment of lacunar bone defects: A prospective, randomized controlled study

Zhen Wang [a,1], Zheng Guo [a,1], Hua Bai [b], Jing Li [a], Xiangdong Li [a], Guojing Chen [a,*,1], Jianxi Lu [c,*,1]

[a] Department of Orthopaedics, Xijing hospital, Fourth Military Medical University, Xi'an 710032, PR China
[b] Department of Toxicology, Faculty of Preventive Medicine, Fourth Military Medical University, Xi'an 710032, PR China
[c] Department of Orthopaedics, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 710048, PR China

A R T I C L E I N F O

Article history:
Received 31 July 2012
Received in revised form 31 October 2012
Accepted 5 December 2012
Available online 13 December 2012

Keywords:
β-TCP
Lacunar bone defects
Clinical application

A B S T R A C T

The aim of this study was to investigate the potential wide application of beta tricalcium phosphate (β-TCP) only for bone defects as compared to allograft. 95 patients with a solitary bone cyst were randomly assigned to the treatment. A new radiographic scoring system was employed to calculate the biodegradation of bone graft and to evaluate the influence of multiple factors. At an average of 28.43 months after surgery, a radiographic semi-quantitative analysis revealed that the degradation rates of β-TCP and the allograft were comparable ($p > 0.05$). Age, complication, packing methods and granule diameters have a significant influence on β-TCP degradation. The loose packing method and 3–5 mm granule size should be employed in clinical practice. A histological analysis of biopsy showed that β-TCP supported the growth of fibrous tissue, vascular tissue, as well as bone tissue into the implants. The results proved that single β-TCP is an advantageous alternative to allografts for lacunar bone defect repair and would well guide the design and clinical application of the β-TCP.

1. Introduction

Orthopedists are often faced with large bony defects during surgical procedures. Treatment of delayed union, malunion and nonunion is a challenge to the orthopedic surgeons and adjunctive measures such as bone-graft or substitutes of bone-graft are of paramount importance [1]. More than 2.2 million bone graft operation are performed each year worldwide [2]. Either autograft or allograft tissue is used in 90% of procedures. Autograft is ideal to serve as a bone graft because it possesses all the necessary characteristics for a new bone growth. However, donor–site morbidity and issues of limited supply created the problems of autograft. Allograft is an alternative to autograft but it still has the risk of disease transmission from donor to recipient [3,4]. Therefore, despite the benefits of autografts and allografts, the limitations of each have necessitated the pursuit of alternatives. With the progress of biomaterials and tissue engineering techniques, investigators have developed several alternatives, some of which are available for clinical use and others of which are still in the developmental stage. Beta-tricalcium phosphate (β-TCP) is a very promising osteoconductive, ceramic bone substitute. In animal studies tricalcium phosphates have shown favorable biocompatibility, osteoconduction and resorption properties. It appeared that the β-TCP gradually resorbs and in the end is completely replaced by a remodeled bone [5–14]. Beta-TCP alone or in combination with other materials such as chemicals or biological growth factors or allograft together has been used for the repair of bony defects resulting from osteotomy [15], bone resection [16] and spinal surgery [17] in clinical studies. The macro-porosity of the material facilitates bone ingrowth. The resorption characteristics depend on the mineral composition and the degree of sintering as well as the porous structure. In 2002, a new type of β-TCP with high porosity and purity has been manufactured in our department by using a mechanochemical method, and is available as a potent bone-grafting substitute for clinical use [18,19]. Our previous study showed that the macro-porosity of the material facilitates bone ingrowth. The absorptive characteristics of the material depend on the mineral composition and the degree of sintering as well as the porous structure [20–22]. In animal studies, β-TCP had shown favorable biocompatibility, osteoconduction and resorption properties. It appeared that the β-TCP is gradually resorbed and in the end completely replaced by a remodeled bone [23–25]. However, further studies to optimize clinical outcomes using this porous β-TCP particle are warranted.

This study concerns a radiographic and histological follow-up examination of 95 patients with a solitary bone cyst treated with curettage. The bone defect was filled with allograft or β-TCP granules. Three questions were expected to be answered: (1) The clinical outcomes and efficacy of β-TCP in lacunar bone defect repair compared with those of allograft. (2) The influence of various factors on biodegradation of β-TCP and allograft. (3) The incorporation process of β-TCP in humans revealed by histological and radiographic observations.

* Corresponding authors. Tel./fax: +86 29 84775281.
E-mail address: guojing_chen@sohu.com (G. Chen).
[1] These authors contributed equally to this paper.

0928-4931/$ – see front matter
http://dx.doi.org/10.1016/j.msec.2012.12.041

2. Materials and methods

2.1. Patients

Between January 2003 and December 2008, 95 patients scheduled for bone cyst curettage were enrolled in this prospective randomized controlled clinical trial. The series comprised males and females, with a mean age of 19.7 years (4 to 48). The histological and radiographic diagnoses were simple bone cysts. A total of 40 patients were randomized to allograft implantation and 55 patients were randomized to β-TCP implantation. The mean follow-up was 28.43 month (7 to 48). The patients' data are listed in Supplementary Tables 1 and 2. All patients were fully informed about the procedures, including the surgery and bone substitute materials. They were asked for their cooperation during treatment and research. All gave their informed consent. Local ethical committee provided ethics approval.

2.2. Graft preparation

The β-TCP porous bioceramics, obtained from Bio-Lu Bioceramics (Shanghai, China), was whitish granules, 1–3 mm or 3–5 mm in diameter with a $75 \pm 10\%$ porosity of 500 ± 200 μm and interconnection pore size of 150 ± 50 μm. The surface morphology of β-TCP has been reported in our previous studies [17]. Allograft granules were from the bone bank at Xijing hospital.

2.3. Surgery implantation

The cyst was exposed through an appropriately sized bone window. Careful and thorough curettage was performed to excise the cyst completely. Then the cavity was irrigated with sterile water and four to six swabs soaked in 50% zinc chloride solution were used to cauterize the walls for 5 min [26]. This process was repeated three times after which the cavity was irrigated with sterile water again. Finally, reconstruction was performed by packing the cavity with granules of the sterilized allograft or β-TCP.

2.4. Radiographic evaluation

X-ray evaluations were performed every three months for one year, bi-annually for a further three years for all the patients. The X-rays were reviewed in a blinded fashion and the last X-ray was used for the radiographic evaluation. In order to quantitatively assess the degradation of bone substitutes in a bone defect with standard radiographic examination, a more refined radiographic classification system was proposed based on a three-stage evaluation system of filling materials reported by Matsumine [27]. The degradation of implanted biomaterials (allograft or β-TCP) was classified into five radiographic stages (Fig. 1(A)): stage 1 (−): clear margin and internal structure, stage 2 (+): hazy margin and clear internal structure, stage 3 (++): hazy margin and internal structure, stage 4 (+++): fusion of granules to each other, and stage 5 (++++): complete absorption of materials. A degradation percentage of materials was calculated by use of a partitioned allocation strategy (16 grids) (Fig. 1(B)). The percentage of stage 5 (++++) was used as an indicator of the degradation efficiency.

2.5. Histological analysis

There were two local recurrences of bone cyst from the β-TCP group of patients. The biopsies were obtained at the second operations. The samples were fixed in a 10% buffered formaldehyde solution (pH = 7.2) for 14 days and then were rinsed under tap water for 12 h. After being dehydrated through gradient alcohols (80–100%), they were embedded in methylmethacrylate without decalcification. The cross sections were cut to about 200 μm thick with a Microtome (SP1600, Leica, Germany). Then they were ground and polished to about 50 μm thick with an Exakt Grinder (Leica, Germany). All the sections were colored with van Gieson's picro-fuchsine stain, Masson's trichrome stain or special bone stain fixed by our own lab (Fast green:Orange G: Gzure II:Basic fuchsin = 0.3:0.75:0.3:1).

2.6. Statistics

A statistical analysis was performed by using statistical software SPSS 10.0 (Chicago, USA). Stepwise regression was used to estimate the correlation between degradation efficiency and various factors. Results were expressed as mean ± standard deviation (SD). The $p < 0.05$ was considered as a statistical significance.

3. Results

3.1. Clinical findings

Ninety-five patients underwent the implantation of allografts or β-TCP in bone defects. The application of allografts or TCP granules did not generate the amount of clinical complications in this study. The patient's general conditions were well, but one patient from the β-TCP group and five patients from the allograft group experienced wound exudate at graft site. One patient from the allograft group experienced the infection of the graft site that was treated with suture removal and debridement. One patient from the allograft group suffered a post-operative fracture within two weeks of the initial operation and this fracture was united without deformity after the immobilization in a cast. Besides, there were three local recurrences of a bone cyst. Two were from the β-TCP group and one from the allograft group. The three patients required repeat curettage and implantation after the initial surgery.

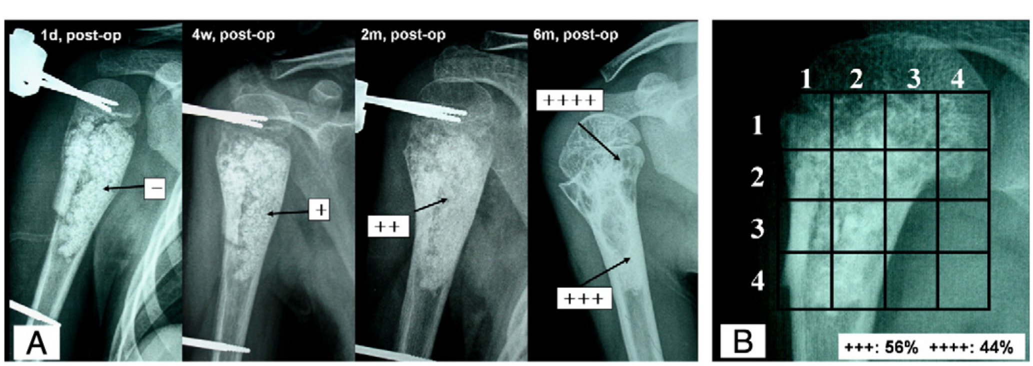

Fig. 1. (A) Classification of the radiographic stages by X ray photography. (B) A partitioned allocation strategy of 16 grids used to qualify the degradation efficiency of the implanted material.