Acta Biomaterialia 7 (2011) 3595–3600

Contents lists available at ScienceDirect

Acta Biomaterialia

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

Bone bonding ability and handling properties of a titania–polymethylmethacrylate (PMMA) composite bioactive bone cement modified with a unique PMMA powder

C. Fukuda [a,*], K. Goto [a], M. Imamura [a,b], M. Neo [a], T. Nakamura [a]

[a] Department of Orthopaedic Surgery, Faculty of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin Sakyo, Kyoto 606-8507, Japan
[b] Ishihara Sangyo Kaisha Ltd., 2-3-1 Nishi-shibukawa, Kusatsu, Shiga 525-0025, Japan

ARTICLE INFO

Article history:
Received 30 March 2011
Received in revised form 4 June 2011
Accepted 7 June 2011
Available online 13 June 2011

Keywords:
Titanium oxide
Titania particle
Bioactivity
Osteoconduction
In vivo

ABSTRACT

One of the challenges of using bioactive bone cements is adjusting their handling properties for clinical application. To resolve the poorer handling properties of bioactive bone cements we developed a novel bioactive bone cement containing a unique polymethylmethacrylate (PMMA) powder, termed SPD-PMMA (40 μm in diameter), composed of cohered minute particles of PMMA (0.5 μm). The present study aimed to examine the mechanical and handling properties and the in vivo bone bonding strength of this cement. The titania content of the cement varied from 10 to 30 wt.% (Ts10, Ts20, and Ts30). The mechanical and thermal properties of Ts10 and Ts20 exceeded those of commercially available PMMA cements (PMMAc). The setting properties of Ts20, including a shorter dough time and a working time that was comparable with that of PMMAc, were adequate for clinical application. Hardened cylindrical cement specimens were inserted into rabbit femurs and the interfacial shear strengths were measured by a push-out test at 6, 12, and 26 weeks after the operation. The interfacial shear strength values (in Newtons per square millimeter) of Ts10, Ts20, and Ts30 at 12 weeks and those of Ts20 and Ts30 at 26 weeks were significantly higher than that of PMMAc ($P < 0.05$). These results show that a bioactive titania–PMMA composite bone cement modified by SPD-PMMA particles possesses adequate mechanical and handling properties, as well as osteoconductivity and in vivo bone bonding ability, and can be used for prosthesis fixation.

1. Introduction

Since Charnley developed the first bone cement in the 1960s using polymethylmethacrylate (PMMA) [1] PMMA bone cements have been widely used for prosthesis fixation. However, it has been shown that PMMA bone cement cannot bond directly to the bone. Experiments with cement–bone interface specimens have shown that an intervening soft tissue layer usually exists between the cement and the bone [2], and the interface degrades over time by fatigue loading [3,4]. In the clinical setting a lack of direct bonding at the cement–bone interface may cause loosening of the prosthesis over a long period, which is a critical complication requiring total joint replacement revision surgery.

Many types of bioactive bone cements have been developed to avoid this problem [5–8]. We have focused on composite cements in which bioactive titania fillers are blended with polymers of a PMMA cement [9–11]. Titania has been reported to form hydroxyapatite on its surface in simulated body fluid [12] and is generally considered a non-biodegradable and bioactive material in vitro and in vivo [13,14]. In addition, bioactive titania fillers exposed on the surface of PMMA cements are considered to act as a bioactive layer, which leads to direct bonding of the cement–bone interface [11].

One of the challenges of using bioactive bone cements is adjusting their handling properties for clinical application. The working time of bioactive PMMA-based composite cements in our previous study was much shorter than that of commercial PMMA cements, rendering them undesirable for use in prosthesis fixation. To resolve this problem we aimed to shorten the dough time, which leads to a longer working time when the setting time is maintained. In addition, a shorter dough time is beneficial for clinical use. To shorten the dough time we considered ways to accelerate the speed of the polymerization reaction between PMMA particles and a monomer at an early stage. The smaller a PMMA particle is the more quickly the polymerization reaction will proceed. First, in preliminary tests, we added micron sized PMMA particles at a low content ratio to large sized PMMA particles. However, the polymerization reaction proceeded too quickly, and the working time was not increased (data not shown). Next, we hypothesized that coherent minute PMMA particles, which divide into minute particles, could gradually accelerate the polymerization reaction.

* Corresponding author. Tel.: +81 75 751 3365; fax: +81 75 751 8409.
E-mail address: mediswim@gmail.com (C. Fukuda).

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doi:10.1016/j.actbio.2011.06.006

In this study we developed a novel bioactive bone cement containing an original coherent PMMA powder (termed SPD-PMMA, with an average particle size of 40 μm), which was composed of coherent minute PMMA particles with an average particle size of 0.5 μm. To the best of our knowledge this is the first time that the use of coherent PMMA particles to control the handling properties of PMMA-based bone cements has been reported.

This study aimed to evaluate the mechanical and handling properties of this SPD-PMMA-modified bioactive titania cement. Furthermore, we investigated the in vivo bone bonding strength of the cement and the changes in the bone–cement interface occurring for up to 26 weeks after implantation.

2. Materials and methods

2.1. Preparation of cements

Spherical titania powder particles (Ishihara Sangyo Kaisha, Osaka, Japan) with an average size of 3.0 μm and a specific surface area of 2.8 $m^2 g^{-1}$ was used as supplied. Micron sized titania particles were synthesized by spray drying a titanic acid slurry and then washing with hydrochloric acid and heating at 850 °C for 6 h. The main phase of titania particles was rutile. The morphology, powder X-ray diffraction, and particle distribution of the titania powder have been discussed in detail in a previous article [11]. The PMMA particles were spherical, with an average molecular weight of 141 kDa and an average diameter of 34 μm. The PMMA powder was synthesized by suspension polymerization. The SPD-PMMA particles were spherical, with an average molecular weight of 330 kDa and average particle size of approximately 40 μm. The particle morphology was examined using scanning electron microscopy (SEM) (S-4800; Hitachi, Tokyo, Japan), and the average particle size was calculated using SEM images (Fig. 1). The SPD-PMMA particles were composed of minute coherent particles of PMMA with an average particle size of 0.5 μm. These 0.5 μm minute particles of PMMA were synthesized by emulsion polymerization; this suspension was spray dried and then the minute PMMA particles aggregated into particles of about 40 μm in size. The SPD-PMMA powder was added at 13.5 wt.% of PMMA powder. The titania particles were mixed with PMMA and SPD-PMMA powder to yield three cements with dispersions of 10, 20, and 30 wt.% TiO_2, which were designated Ts10, Ts20, and Ts30, respectively. To prepare the cements liquid methyl methacrylate (MMA) monomer (Wako Pure Chemical Industries, Osaka, Japan) was used. Benzoyl peroxide (Nacalai Tesque, Kyoto, Japan) at 5.4 wt.% of the monomer was added to the PMMA powder containing titania particles as an initiator, and *N*,*N*-dimethyl-*p*-toluidine (Wako Pure Chemical Industries) was dissolved in the liquid to 0.95 wt.% of the monomer as an accelerator. Each cement type was prepared by mixing the powder with the liquid for 1.5 min. The cement compositions are shown in Table 1. The commercially available PMMA-based bone cement (PMMAc) (Simplex® P, Stryker Howmedica Osteonics, Limerick, Ireland) was used as the control material.

2.2. Mechanical evaluation

The flexural strength, flexural modulus, and compressive strength of Ts10, Ts20, Ts30, and PMMAc were measured using five pre-hardened cement specimens for each mechanical test. For mechanical flexural analysis a 4-point bending test was performed with rectangular specimens of size 70 × 10 × 3.3 mm. For compressive mechanical analysis pre-hardened cylindrical specimens of 6 mm diameter and 12 mm length were prepared. Measurements were performed using a Model EZ Graph testing machine (Shimadzu Corporation, Kyoto, Japan) with a cross-head speed of 20 mm min^{-1} according to the ISO 5833 standard.

2.3. Setting of cements

The setting properties were measured according to the ISO 5833 standard. Cement pastes were mixed for 1.5 min and poured into a cylindrical mold made of Teflon (inner diameter 68 mm, inner depth 20 mm). Onset of dough time was indicated by failure of the material to stick to the surface of a surgically gloved probing finger. The temperature change during the setting reaction was measured using a thermocouple in the mold under ambient conditions of 23 °C and 55–65% humidity. By plotting the time and temperature the setting times of Ts20 and PMMAc were determined according to the ISO 5833 standard.

2.4. Animal experiments

The animals were reared and experiments on them were carried out at the Institute of Laboratory Animals, Graduate School of Medicine, Kyoto University, Japan. All procedures were performed according to the Principles of Laboratory Animal Care advocated by the Kyoto University Animal Experiment Committee. Japanese white rabbits, weighing 2.5–3.5 kg, were operated under general anesthesia induced by intravenous injection of sodium 5-ethyl-5-(1-methylbutyl) barbiturate (Nembutal (pentobarbital), Dainippon Pharmaceutical Company, Osaka, Japan) at 70 mg kg body $weight^{-1}$. The bilateral femoral shafts were exposed using a lateral

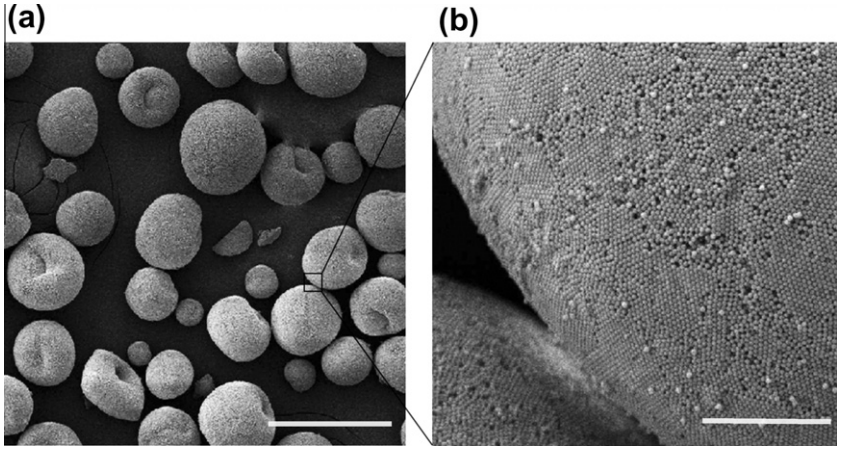

Fig. 1. (a) Scanning electron micrograph of SPD-PMMA particles. Bar = 100 μm. (b) High magnification view of the image in (a). Bar = 10 μm.