YIJOM-3763; No of Pages 8

ARTICLE IN PRESS

Int. J. Oral Maxillofac. Surg. 2017; xxx: xxx-xxx http://dx.doi.org/10.1016/j.ijom.2017.02.1279, available online at http://www.sciencedirect.com



Clinical Paper Dental Implants

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Clinical application of autogenous partially demineralized dentin matrix prepared immediately after extraction for alveolar bone regeneration in implant dentistry: a pilot study

T. Minamizato, T. Koga, Takashi I, Y. Nakatani, M. Umebayashi, Y. Sumita, T. Ikeda, I. Asahina: Clinical application of autogenous partially demineralized dentin matrix prepared immediately after extraction for alveolar bone regeneration in implant dentistry: a pilot study. Int. J. Oral Maxillofac. Surg. 2017; xxx: xxx–xxx. © 2017 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. The aim of this study was to examine the efficacy and safety of autogenous partially demineralized dentin matrix (APDDM) prepared onsite, for clinical application in bone regeneration procedures related to implant dentistry, including socket preservation, alveolar ridge augmentation, and maxillary sinus floor augmentation. In this study, 16 patients underwent dental implant placement using APDDM transplantation. There were no systemic or local complications (including surgical site infection) in any of the cases, and oral rehabilitation using dental implants was successful in all cases for at least 2 years after attachment of the suprastructure. This report describes the clinical application of APDDM prepared immediately after tooth extraction to bone augmentation, taking advantage of the relatively short preparation time due to partial demineralization. APDDM, as introduced in this study, is an efficient, safe, and reasonable bone substitute. Consequently, this material has the potential to become one of the options as a bone substitute in implant dentistry.

Key words: demineralized dentin matrix; alveolar bone augmentation; implant dentistry.

Accepted for publication 14 February 2017

^a Tokutaro Minamizato and Takamitsu Koga contributed equally to this study.

0901-5027/000001+08

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Please cite this article in press as: Minamizato T, et al. Clinical application of autogenous partially demineralized dentin matrix prepared immediately after extraction for alveolar bone regeneration in implant dentistry: a pilot study, *Int J Oral Maxillofac Surg*

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Oral rehabilitation using dental implants has become a highly predictable treatment option. Accordingly, the demand for alveolar bone augmentation is rising with the increase in indications. Autogenous bone grafting remains the gold standard for bone augmentation because it shows excellent bone formation^{1,2}. However, it has drawbacks, including limited availability and donor site morbidity. Furthermore, the autogenous bone graft shows high resorption rates of up to 50%. Alternative graft materials including allografts, xenografts, and alloplastic bone grafts are utilized in the clinical setting³, but these also have their respective disadvantages, such as potential disease transmission, high cost, and limited osteoinduction capability. Hence, an alternative material that overcomes these shortcomings would be of benefit.

It is well known that the structure and composition of dentin is similar to that of bone, consisting of collagen 20%, hvdroxyapatite 70%, and body fluid 10% by weight⁴. Dentin is thought to have a high osteoconductivity since it is a natural mineralized tissue consisting of hydroxyapatite. Furthermore, dentin matrix is expected to exhibit osteoinductivity because it contains bone morphogenetic proteins (BMPs)⁵. In some patients, tooth extraction is required before dental implant treatment, and these teeth are usually discarded. It would be beneficial if they could be utilized as autogenous grafting material and thereby avoid the risk of disease transmission.

Several previous studies have examined the potential of dentin or dentin matrix as a bone substitute. Some studies using mineralized dentin matrix have shown that the material possesses excellent biocompatibility but is less effective than bone-derived products in bone formation^{6,7}. On the other hand, several basic animal studies have shown demineralized dentin matrix (DDM) to be not only biocompatible, but also osteoinductive, similar to demineralized bone matrix $^{8-10}$. In terms of clinical studies, Gomes et al. first reported the application of autogenous DDM to the extraction sockets of mandibular third molars, along with a membrane for guided bone regeneration; they showed superior healing of the dental sockets with autogenous DDM¹¹. Kim et al. applied both mineralized dentin and DDM particles in dental implant surgery and obtained successful bone regeneration results^{12,13}. However, most of these studies utilized completely demineralized dentin matrix, which was difficult to apply at the operation site since the preparation of materials takes a long time.

Thus, the aim of the present study was to examine the efficacy and safety of autogenous partially demineralized dentin matrix (APDDM), prepared onsite, for clinical application in alveolar bone regeneration procedures related to implant dentistry, including socket preservation, alveolar ridge augmentation, and maxillary sinus floor augmentation.

Patients and methods

Patient selection and study design

The Ethics Committee for Clinical Study at Nagasaki University Hospital approved the protocol of this prospective single cohort study. The study was conducted between 2011 and 2014 at Nagasaki University Hospital. All participants were informed about the surgical treatment procedure and provided their written informed consent to participate in the study. A total of 16 patients, 10 female and six male, aged 25-73 years (mean age 50.0 vears), were included in this study. The total number of teeth used for APDDM preparation was 25, with an average 1.6 per patient. All patients were treated with dental implants.

The subjects were patients who required bone augmentation for dental implant treatment, including (1) socket preservation, (2) maxillary sinus floor augmentation, and (3) alveolar ridge augmentation, and dental implant placement simultaneous with tooth extraction. A tooth or teeth that required extraction as part of the dental implant treatment was used in all patients except one, for whom a third molar was utilized. Patients who had undergone radiation therapy in the oral and maxillofacial region, who had undergone other bone grafting in the surgical area, or who had a history of maxillary sinus disease or symptoms were excluded. Patients with any uncontrolled systemic disease were also excluded.

Preparation of autogenous partially demineralized dentin matrix (APDDM)

Both vital and non-vital extracted teeth were used. Following extraction, the soft tissues, calculus, crown restorations, and root fillings were removed, and the teeth rinsed twice in phosphate buffered saline. Next, the teeth were crushed with ice cubes in a ceramic cup using a specific machine with a high-speed rotation ceramic blade (Takigen, Japan; international patent application No. PCT/ JP2007/053321, international published No. WO2007/099861 A1). The resulting particles, ranging from 400 μ m to 800 μ m in size, were washed in 1.0 M sodium chloride and partially demineralized in 2% HNO₃ (pH 1.0) for 10 min. The APDDM particles were rinsed extensively twice in 0.1 M Tris–HCl (pH 7.4) for 10 min. This process took approximately 40 min^{14,15}.

Transplantation of APDDM and dental implant placement

APDDM was transplanted into the defect during the same session as the tooth extraction. The average defect size was estimated by computer simulation using Simplant software (Dentsply Implant, Tokyo, Japan): 0.5-0.6 ml (mean 0.53 ml) for ridge augmentation, 0.7-1.5 ml (mean 1.1 ml) for socket preservation, and 2.6-4.0 ml (mean 3.3 ml) for sinus floor augmentation. A sufficient volume of APDDM was achieved for the defects in all cases, and this was transplanted with platelet-rich plasma (PRP). The use of PRP allows easier handling of the APDDM, as the particles are bound with the fibrin. Furthermore, PRP is also expected to accelerate bone healing. Primary closure was achieved after transplantation in most of the cases, except in two cases of socket preservation, in which the wound was covered with a collagen membrane to prevent the material from scattering.

Histological analysis

A bone biopsy sample was collected using a 2.0-mm trephine bur at 4 to 6 months postoperative from the transplanted sites of the patients who underwent socket preservation. The specimen was demineralized with 10% formic acid after fixation in 10% neutral-buffered formalin. Paraffin sections 6 μ m thick were stained with haematoxylin and eosin (HE) for histological evaluation. A polarizing microscope was used to observe the collagen fibre structure¹⁶.

Radiological analysis

Bone formation was assessed radiographically at the extraction socket and maxillary sinus floor using dental and panoramic X-rays obtained immediately after the operation, and at 4 weeks, 12 weeks, and >24 weeks after the implantation of APDDM for all patients included in this study. Bone formation was also assessed by computed tomography (CT) (3D Accuitomo F17D; J. Morita

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