ORIGINAL ARTICLE

Studies of the Clinical Usefulness of Porous Hydroxyapatite in the Field of Dental and Oral Surgery

Souichiro Asanami, Osamu Koike, Masamichi Chikata, Hideyuki Shiba, Shinobu Ikeuchi, Yutaka Okada, Fumihiro Ohsaka and Tanekuni Nomoto

Department of Dentistry and Oral Surgery, School of Medicine, Keio University
Tokyo, Japan

(Received for publication on February 2, 1988)

Abstract

Porous and granular hydroxyapatite (HAP) was implanted in bone defects resulting from oral surgery in 21 patients and from periodontal disease in 14 patients. Excellent results were obtained, the overall clinical usefulness being 91.4%. HAP leakage after implantation was observed in a small number of cases; however, there was almost no wound infection or failure to heal. A series of x-rays confirmed its good adaptation to the bone.

Key words: hydroxyapatite, bone defect

Introduction

In order to correct bone defects in the oral and maxillary fields, bone transplantation has long been performed, especially autogenous bone grafting, which has consistently yielded the most favorable results. However, some problems, such as the necessity for additional surgical intervention to harvest a bone, remain unsolved. Preserved bones are usually difficult to obtain and are also considered inappropriate for clinical use, mainly because clinical results have shown them to be inferior to auto-
genous bones. Attempts have therefore been made to develop biomaterials which may be substituted for natural bone. Special attention has been focused on ceramic materials because of their high affinity for body tissues.1

The present communication reports on the use of hydroxylapatite (HAP), which has superior biocompatibility in the oral and maxillary fields; its safety and usefulness were also studied.

**Materials and Methods**

Materials: We studied 21 patients with bone defects, such as cavities which developed after either the removal of jaw bone cysts or after the extraction of impacted teeth; 14 patients with vertical bone resorption were also studied. All of these 35 pa-

Fig. 1 Scanning electron microscopic photographs of HAP.

Fig. 2 X-ray diffraction patterns of HAP.
tients had visited the Department of Dentistry and Oral Surgery at Keio University Hospital. The following patients were excluded from the study: those who did not exhibit adequate wound closure at the time of implant insertion, those with serious underlying diseases, pregnant women or those likely to be pregnant, those with strong inflammatory reaction around the lesion, and those who were judged, for some other reason, to be unsuitable for the study by the doctor in charge.

Implant Preparation: Pure HAP, crystalline cellulose, and polyvinyl alcohol are mixed in a certain ratio to create a granular material, which is then sintered at 1350°C to produce porous granules. This biomaterial is prepared by the TKD Co. Crystalline cellulose determines the pore size and the volume. Polyvinyl alcohol is used as a bonding agent. These two substances are sufficiently pure to be decomposed by sintering without leaving any traces. The substance thus prepared is kept in a vial, sterilized by ethylene oxide gas at low pressure to facilitate bubble breaking.

Particle Morphology: The supplied material are irregular granules (two kinds, either 0.5 or 1.0 mm in diameter) with perforated pores ranging from 20 to 50 μm (Fig. 1).

X-ray Analysis: X-ray diffraction patterns of α-tricalcium phosphate (α-TCP) or β-TCP (Fig. 2).

Chemical Analysis: The material used is prepared from highly selected substances so pure that lead and arsenic could not be detected within their detectable limits; 10 ppm and 1.0 ppm respectively.

Infrared spectrophotometry: The absorption spectra for the hydroxyl radical (3573, 635 cm⁻¹) were clearly detected by infrared analysis; therefore, the chemical properties of the material were not shown to be altered by heating.

Implant Procedure: A sterile syringe was used to inject saline into the vial to facilitate the loss of bubbles and to moisten the material. The bone defects were filled by implantation of proper quantities of the experimental material. The wound was then closed completely.

Follow-up Methods

Clinical Observation: Mucosal redness, swelling, tenderness, implant leakage, and wound dehiscence were basically observed preoperatively, on postoperative days 1, 7 and 14, and 1 month and 3 months after the operations. Additionally, in patients with periodontal disease, the depth of the cavity and the place of attachment were also checked. Clinical observation was extended as needed.

Radiological Assessment: X-rays were taken on each regularly scheduled visit and on any additional days needed thereafter.

Clinical Laboratory: CBC, liver-function test, renal-function test, CRP, and ESR
were all performed as needed, before and after surgery.
Criteria for Evaluation of Response during Follow-up Period Regarding Oral-surgical cases:

Very Useful: Complete absence of reactive inflammation, very early appearance of bone formation, and excellent apposition to the bone.

Fair Useful: Slight reactive inflammation and delayed bone formation, but some apposition to the bone. No discernible effect: HAP failed to facilitate bone formation.

Unusable: Systemic and local side effects with severe reactive inflammation which necessitated the removal of all the HAP.

Regarding Periodontal disease:

Very Useful: Significant improvement in the pocket depth, the attachment level, and tooth mobility, with obvious bone formation.

Fairly Useful: Slight improvement in the pocket depth, the attachment level, and tooth mobility, with some bone formation.

No discernible effect: No significant improvement in the pocket depth, the attachment level, or tooth mobility, nor any bone formation.

Unusable: Systemic and local side effects with severe reactive inflammation, which necessitated the removal of all the test substances.

As has been described above, usefulness was evaluated in four grades over an observation period of more than three months.

Results

All of the cases were designated as either oral surgical or exhibiting periodontal disease, and were then evaluated.

Oral surgical cases: As is shown in Table 1, “very useful” describes 8 cases (38%),

<table>
<thead>
<tr>
<th>Table 1 Clinical Effect of HAP in the Field of Oral Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Cysts</td>
</tr>
<tr>
<td>Sockets following extraction of impacted teeth</td>
</tr>
<tr>
<td>Bone defects due to alveolar fracture</td>
</tr>
<tr>
<td>Maxillo-palatal clefts</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
Fig. 3 Orthopantomogram (before implantation).

Fig. 4 Orthopantomogram (9 months after implantation).
"fairly useful" describes 12 cases (57%), and "no discernible effect" was found in 1 instance (5%); therefore, the overall usefulness was 95%. No effect was observed in a 4-year-old patient with a maxillo-palatal cleft. He underwent a second attempt to close the tract into the nasal cavity when HAP was implanted into the bone defect. The wound developed dehiscence, and gradual leakage of HAP resulted in only a little of the material remaining. No adverse effect was observed.

Report of Case: Case A 13-year-old male was referred from a dentist for further workups of an impacted tooth $\overline{4}$ and bone resorption around it. Diagnosis of an impacted tooth $\overline{4}$ accompanied by a follicular cyst was established by means of
Fig. 6 Implantation of HAP.

X-ray and other examinations (Fig. 3). Under general anesthesia, the impacted tooth was extracted and the cyst removed. The cyst was almost spherical, measuring about 3 cm in diameter. 2.0 grams of HAP was implanted in the bone defect after the removal. No leakage of HAP was noted after surgery, and the wound healed well. Orthopantomography, 9 months after surgery, revealed that the margins between the HAP and the surrounding bone were slightly obscured (Fig. 4). This suggested new bone formation. During the study period, no adverse effect, either systemic or local, was observed.

Case A 28-year-old male visited our department complaining of swelling of the gingiva on the labial surface. X-ray examination revealed a well-demarcated, small finger-tip-sized radiolucent bone lesion at the root apex (Fig. 5). After the inflammation had been brought under control by root-canal treatment and the administration of antibiotics, we undertook to remove the cyst, diagnosed as a radicular cyst, using local anesthesia. Complete hemostasis was obtained, and 1.0 gram of HAP was implanted into the bone defect (Fig. 6). The course after surgery was uneventful. Three months after surgery, dental radiography revealed that the margins between the HAP and the surrounding bone were obscured. This also suggested new bone formation.
Fig. 7 Dental radiogram (3 months after implantation).

Table 2 Clinical Effect of HAP in Peridontal Disease

<table>
<thead>
<tr>
<th></th>
<th>Very useful</th>
<th>Fairly useful</th>
<th>No effect</th>
<th>Unusable</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontal disease</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Juvenile periodontitis</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>14</td>
</tr>
</tbody>
</table>
Case A 47-year-old male visited our department complaining of fistula formation and swelling of the 1\ and 2\ gingivae on the labial surface. A diagnosis of a 1\ radicular cyst was established by dental X-rays (Fig. 8). The diseased tooth 1\ was extracted and a thumb-tip-sized cyst removed. 2.0 grams of HAP was implanted in the bone cavity, and a complete closure was secured (Fig. 9). The course thereafter was uneventful, and a bridge was put into place after the stitches had been taken out. Good adaptation to the bone was observed by dental X-rays one month after surgery (Fig. 10).

Periodontal diseases: As is shown in Fig. 2, “very useful” was indicated in 5
cases (36%), “fairly useful” in 7 (50%), and “no effect” in 2 (14%); no adverse effects were evident. The overall usefulness was, therefore, 86%. In the cases showing no effect, almost all of the HAP leaked out because of wound dehiscence after surgery.

The following case was selected at random for presentation from all the cases with periodontal diseases.

Case  A 39-year-old male visited our department with the chief complaint of gingival bleeding from the 3 area. Following a diagnosis of periodontal disease of the whole jaw (Fig. 11), initial treatment by brushing, scaling, and temporary anchorage was performed. Abrasion and curettage of the gingiva were performed under 2% xylo-
Caine local anesthesia. 0.5 gram of HAP was then implanted in the bone defect around the 3| area (Fig. 12). The course after surgery was uneventful, and no leakage of HAP, failure of the wound to heal, nor local or systemic adverse reactions were observed. Fourteen months after surgery, standard dental X-ray revealed that the combination between the HAP and the bone was very good, since the margin of the neighboring bone could not be identified. Indeed, a direct bone combination might have occurred, and the HAP, combined with the bone, appeared partially resorbed (Fig. 13). Improvement was recognized in the periodontal tissue, and a 3 mm attachment gain was obtained; therefore, the results of this case were judged as being “very useful.”
Discussion

Among biomaterials used clinically, ceramics have attracted special attention because of their stability in the human body. HAP, a major inorganic chemical component of tooth and bone, has been studied extensively because of its high affinity for tissue, and its great usefulness has been reported.\textsuperscript{2-9} The HAP we used was a granule ranging from 0.5 to 1.0 mm in size and with a structure featuring micropores ranging from 20 to 50 $\mu$m in diameter. It has been recognized during animal experiments to be biologically active and to have excellent biocompatibility, as well as having good potential to stimulate osteogenesis.\textsuperscript{10} Our experimental studies gave the same results.
with tight contact along HAP surface (Fig. 14).

In our present clinical trial, as observed in the oral surgery cases of relatively large bone defects, requiring implants of more than 2.0 grams of HAP, the implanted HAP remained stable. Immediately after surgery, it appeared relatively distinct for each radiopaque particle that was visible and was also distinct from the neighboring bone. Its radiopaque shadow disappeared gradually. In each of the cases, 6 months after surgery the HAP margin with the neighboring bone became obscured and homogeneous on X-rays, suggesting new bone formation. As for the gross appearance of the wound, local redness and swelling, suggestive of reactive inflammation, were observed
in about one-half of the cases immediately after surgery, but most of these signs disappeared within a week. This may have been partly due to an excess amount of implanted material. In addition, in cases in which HAP was implanted into a cavity after the extraction of an impacted tooth, the clinical outcome was slightly poorer in those implanted on the palatal surface compared with those implanted on the labial surface. This was most likely because the implanted HAP was too movable; it was, therefore, unable to secure itself sufficiently to acquire adequate stability.

In patients with alveolar fracture in which the alveolar bone and teeth are broken by trauma, it is thought that prosthetic treatment is not very successful. However,
Fig. 14 Photomicrograph of 7 days after HAP block implantation in rabbit mandible (Hematoxylin and eosin Magnification ×40).

extremely well-shaped residual ridges, made possible by implanting HAP, yield successful results in denture service.

In the case of a maxillo-palatal cleft, a cavity formed after the extraction of a tooth near the implant area prevented a complete wound closure. In addition, the HAP-implant was in a difficult position for the HAP to stabilize; therefore, HAP leaked from the suture line and cavity. Also, HAP might not be suitable for children, such as the small, 4 year-old child whose jaw was not well-developed and whose wound closure could not be expected.
Regarding bone resorption due to periodontal disease, HAP was tried in cases of vertical resorption. This was because when HAP was implanted, the relatively stable approximation of the wound might promise new bone formation. However, the 86% usefulness was slightly lower than in cases of oral surgery. This may have been because leakage developed; since the suture was too close to the implanted area the gingival condition prevented a complete wound closure outcome may have been further influenced significantly by maintenance treatment, such as brushing. In comparison to conventional surgical procedures in periodontal disease, improved stability and large attachment gain could be easily secured. This was because the HAP implant stayed in the defective area, made a fibrous combination with the neighboring bone, and might have promoted new osteogenesis. There were neither side effects, such as local or systemic allergy reactions caused by HAP, nor any abnormal laboratory data after surgery. Therefore, the safety of this substance has been demonstrated.

Conclusions

Clinical trials of porous and granular HAP were conducted in a total of 35 subjects comprising 21 cases of bone defects due to oral surgery and 14 cases of vertical bone defect due to periodontal disease. The following results were obtained:

1. HAP usefulness was observed in 20 out of 21 cases of oral surgery disease (95.2%), and in 12 out of 14 cases of periodontal disease (85.7%).
2. No adverse reactions were noted after HAP implantation, and its safety has been confirmed.
3. Therefore, HAP seems quite useful as a bone substitute for bone defects resulting from oral surgery and also for vertical bone defects due to periodontal disease.

Acknowledgements: We wish to express our appreciation of all the help which the staff of the Research Center of the TDK Co., Ltd. gave us in conducting the clinical trials.

References


