The closure of oroantral communications with resorbable PLGA-coated β-TCP root analogs, hemostatic gauze, or buccal flaps: A prospective study

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Objective. The aim of this study was to compare the treatment of oroantral communications (OACs) with bioresorbable root analogs made of poly(lactide-co-glycolide) (PLGA)–coated β-tricalcium phosphate (β-TCP), hemostatic gauze or a buccal flap technique.

Study design. In this prospective clinical study, 30 patients with oroantral communications were randomly assigned to a treatment. Clinical success, vestibular depth at the defect site, pain, and swelling were monitored.

Results. The OAC closure was successful in all cases. The vestibular depth stayed constant in the groups treated with the PLGA–β-TCP composite or hemostatic gauze. In contrast, a vestibular depth reduction of 1.2 ± 0.2 mm was observed in the buccal flap group, indicating atrophy of the alveolar ridge in these patients. Furthermore, pain and swelling were more pronounced in this group.

Conclusion. Closures of OACs with PLGA–β-TCP composite or hemostatic gauze are reliable minimally invasive methods that minimize atrophy of the alveolar ridge, swelling, and pain compared with a buccal flap technique. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:844-850)

Communications between the oral cavity and the maxillary sinus occur with frequencies between 0.31% and 4.7% after the extraction of upper teeth.1-4 If untreated, oroantral fistulas may form, which can result in chronic infection of the maxillary sinus. Smaller oroantral communications (OACs), with a diameter of <2 mm, are often closed by a coagulum and heal spontaneously.5,6 However, in the case of larger defect sizes or disturbed blood coagulation, iatrogenic closure of the defect becomes indispensable. Mucoperiosteal flaps of different designs are widely used to seal off the sinus cavity.7-10 To stabilize the coagulum in the extraction socket, hemostatic materials such as hemostatic gauze of lyophilized fibrin glue have been applied with or without flaps.11-13 Flap-based methods have several disadvantages, e.g., flap mobilization may leave a denuded area and lead to scarring and changes in the mucosal topography. Furthermore, preparation, adaptation, and fixation of flaps take a significant amount of practice and time.1

The closure of OACs with synthetic bone graft substitutes constitutes an alternative to flap-based techniques.1,14-16 Besides closure of the opening, these materials may positively affect the surrounding hard tissue, because the insertion of biomaterials into extraction sockets has been reported to reduce alveolar ridge resorption.17 However, this potential benefit of perforation closure with biomaterials has not been assessed yet. The use of synthetic bone graft materials is limited owing to the dislocation of grafting material into the sinus cavity. Thoma et al.1 solved this problem by inserting thermally molded poly(lactide-co-glycolic) acid (PLGA)–coated porous β-tricalcium phosphate (β-TCP) granulate into oroantral perforations in 14 patients. The inherently stable fully degradable root analog successfully closed off the communication.

Here, we present a prospective clinical study where this method was compared with the closure of OACs using hemostatic gauze and with a standard flap-based approach. In addition to the clinical results, the impact of the 3 methods on the vestibular depth was compared and short-term postoperative effects, such as pain and swelling, were assessed. A histologic analysis of a patient who was treated with a β-TCP root analog is also presented.
MATERIAL AND METHODS

All procedures and materials described in this prospective clinical study were approved by the Ethics Committee at the Faculty of Dentistry, University of Belgrade. Treatment strategy of our clinic is that OACs should not be left to heal spontaneously, owing to ethical reasons. Accordingly, 30 patients, with OACs created after tooth extraction, were randomly selected into 3 groups. Closure of perforations was achieved either with PLGA-coated β-TCP granulate, with hemostatic degradable gauze, or by application of a buccal flap. Only patients that were in good general health were included. Smokers and pregnant or lactating woman and patients under any medication were excluded. An informed consent was obtained from each of the patients. The patients’ ages ranged from 17 to 70 years, with an average of 36.9 years (Table I).

For extraction of multirooted teeth, the dental crown was separated from the roots and the roots were extracted one at a time. Second premolars and single-rooted teeth were extracted in 1 step. After tooth extraction, the nose blowing test was performed, and when positive, an OAC was diagnosed. The minimal diameter of the communication was determined using specially devised blunt probes with diameters of 1, 3, and 5 mm† (Table II).

OAC closure using PLGA-coated β-TCP

Root analogs were made according to the manufacturer’s instructions with PLGA-coated synthetic, phase-pure, porous β-TCP granules (Degradable Solutions, Schlieren, Switzerland). In brief, the root above which the OAC was located was cleaned of granulation tissue with curette, incubated in 96% H₂O₂ for 1 minute, and rinsed with sterile physiologic saline solution. The cleaned root was pressed into impression material (Degradable Solutions) in the chamber of a heating device. After the impression material had set, the mold was cut and the tooth removed. The mold was replaced in the heating device and was filled with PLGA-coated β-TCP granules. After 1 minute of heating, the granules condensed to form a solid but porous copy of the extracted root. Polylactide powder (Degradable Solutions) was applied onto the coronal end of the root analog and sealed using a heated condenser (Degradable Solutions), thus forming an integrated membrane. The mold was removed from the heater and the root analog was removed from the mould after a short cooling period (Fig. 1, A). Fresh bleeding was induced by curettage of the extraction site. The root analog was placed in the extraction socket and carefully pushed up until proper seating was achieved (Fig. 1, B). The wound edges were approximated by a single endless suture (Fig. 1, C).

OAC closure with hemostatic gauze

Resorbable hemostatic gauze composed of reconstituted oxidized cellulose (Surgicel; Johnson and Johnson, Somerville, NJ) was used for closure of the OAC. The gauze was cut into small pieces (Fig. 1, D), which were inserted one at a time into the extraction socket (Fig. 1, E). Care was taken not to compress the gauze, because the material quells by taking up blood. The wound edges were approximated digitally and secured with a single endless suture (Fig. 1, F).

OAC closure with buccal flaps

Buccal sliding flaps were applied as described by Rehrmann9 (Fig. 1, G and H).

All patients were advised to restrain from blowing their nose, blowing up balloons, playing brass instruments, drinking through a straw, or taking antibiotics or analgesics that contain acetylsalicylic acid. Any sutures were removed after 7 days.

Postoperative follow-up

Control appointments were made 1, 2, and 7 days and 1, 3, and 6 months after the intervention. All patients received 4 mg dexamethasone intramuscularly, nonsteroidal antiinflammatory drugs for pain relief, and detailed instructions concerning oral hygiene. During the first week, the vestibular depth, swelling, and pain intensity were assessed. The vestibular depth was measured with a compass as the distance between the

### Table I. Basic characteristics of patients included in the study

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (mean ± SD)</th>
<th>Teeth*</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 (53%) female</td>
<td>36 ± 16 years</td>
<td>4 (13%) second premolar</td>
</tr>
<tr>
<td>14 (47%) male</td>
<td>4 (13%)</td>
<td>21 (70%) first molar</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 (13%) second molar</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 (3%) third molar</td>
</tr>
</tbody>
</table>

*Oroantral communication created following the removal of corresponding tooth.

### Table II. Diameters of oroantral communications (OACs)

<table>
<thead>
<tr>
<th>Method</th>
<th>OAC diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLGA-coated β-TCP</td>
<td>1-3 mm: 1</td>
</tr>
<tr>
<td></td>
<td>3-5 mm: 7</td>
</tr>
<tr>
<td></td>
<td>≥5 mm: 2</td>
</tr>
<tr>
<td>Hemostatic gauze</td>
<td>1-3 mm: 3</td>
</tr>
<tr>
<td></td>
<td>3-5 mm: 5</td>
</tr>
<tr>
<td></td>
<td>≥5 mm: 1</td>
</tr>
<tr>
<td>Buccal flap</td>
<td>1-3 mm: 1</td>
</tr>
<tr>
<td></td>
<td>3-5 mm: 6</td>
</tr>
<tr>
<td></td>
<td>≥5 mm: 3</td>
</tr>
</tbody>
</table>
marginal gingiva of the extraction site to the highest point in the vestibule in the same frontal plane (Fig. 2, A and B). Swelling was measured extraorally by assessing the distance between the intertragic notch and the corner of the mouth (Fig. 2, C). The pain intensity was quantified using a visual analog scale \(^8\) that ranged from 0 to 100 arbitrary units. Whereas vestibular depth measurements were continued during the 6 month observation period, swelling and pain were assessed only during the first week. Furthermore, the patients were advised to perform the nose blowing test at each follow-up appointment.

**Histologic analysis**

A Straumann wide neck implant (Straumann, Basel, Switzerland) was placed 6 months after closure of the OAC with PLGA-coated \(\beta\)-TCP granulates. During this process, tissue samples were taken with a trephine drill from the site where the alloplastic material had been inserted. The sample was fixed in 10% formalin for 48 hours, decalcified in 10% formic acid (pH 5) for 2-3 weeks, and embedded in Paraplast. Histologic sections (8 \(\mu\)m; McCormic Scientific, LLC, Maryland Heights, MO, USA) were cut with a microtome (Leica; SM 2000), stained with hematoxylin and eosin, and observed by light microscopy (Leica DM1000).

**RESULTS**

**Clinical outcome**

In 70% of all cases, the OAC had occurred after extraction of first maxillary molars, the other cases occurred after extraction of second premolars and second and third molars (Table I). The average minimum diameter of the OAC did not differ among the 3 groups that were assigned to the 3 methods (Kruskal-Wallis test: \(P = .320\); Table II). Healing of
the OAC was controlled at every appointment by pressurizing the nasal and the oral cavity. Closure was successful in all 30 patients and took place without complications. An implant was set in 1 patient at the site where the communication had occurred (Fig. 3). The implant showed a good primary stability. The stability quotient (ISQ) measured with an Osstell mentor device (Osstell, Gothenburg, Sweden) was 64 immediately after implant insertion. Within 6 weeks, the ISQ increased to 80.

Vestibular depth is preserved in patients treated with a β-TCP root analog or hemostatic gauze

Vestibular depth was measured before, immediately after, and after 7 days, and after 6 months. During the 6 months’ observation period, vestibular depth did not change in the group treated with PLGA-coated β-TCP (Table III) (analysis of variance [ANOVA]: P < 1.00). In patients treated with surgical gauze, vestibular depth was slightly decreased on day 7 and did not change any more thereafter. However, these slight variations were not significant (ANOVA: P < .98). In contrast, application of a buccal flap led to a pronounced change in vestibular depth (ANOVA: P < .02). A decrease of vestibular depth immediately after the intervention was observed. The patients treated with a buccal flap had a significantly reduced vestibular depth after 6 months (paired t test; P < .01). The average depth loss was 1.2 ± 0.2 mm (mean ± SEM), varying between 0 and 2.5.

Subjective pain intensity was the lowest for the group treated with a β-TCP root analog

The subjective pain intensity was the highest for the first day after the intervention independent of the method that was used for OAC closure. However, pain intensities differed among the 3 groups. Patients with buccal flaps reported the highest pain, and pain was lower in the groups treated with hemostatic gauze or β-TCP, with the latter showing the lowest value (Table IV). On the second day after the intervention, pain intensities were reduced. Again, the patients treated with a buccal flap suffered the most and the patients treated with β-TCP the least pain. The differences between the treatments were significant (Mann-Whitney U tests: P < .01 for each comparison). After 7 days, the groups treated with a β-TCP root analog or hemostatic gauze were painless whereas pain was still reported by patients with buccal flaps.

Swelling was negligible in patients treated with a β-TCP root analog

Swelling was assessed by measuring the distances between the mandibular angle and the chin tip (MC) and from the intertragus notch to the angle of the mouth (IC). Distances did not change over time in patients who were treated with PLGA-coated β-TCP (ANOVA: P < 1.00 [MC]; P < .42 [IC]), indicating that the treatment did not induce swelling. A slight but significant increase in the IC distance was observed in the hemostatic gauze group (ANOVA: P < .01), indicating that swelling was triggered by the treatment. The patients with the buccal flap showed the most pronounced swelling (ANOVA; P < .01).

Histologic analysis

Histologic analysis of the samples taken during the implant placement procedure did not show signs of necrosis or inflammation, which is in accordance with the reported biocompatibility of PLGA-coated β-TCP granulate. Mature lamellar bone was observed (Fig. 4, A), and numerous osteocytes were present in lacunae (Fig. 4, B). Osteoblasts and newly formed bone matrix could be observed, indicating an ongoing osteogenesis (Fig. 4, C).

DISCUSSION

Oroantral communications should be treated by establishing a physical barrier to prevent infection of the maxillary sinus and fistula formation. Despite the possibility for small-sized OAC to heal spontaneously, von Wowern20 reported that only 2 out of 9 OACs heal on their own in a study on 116 patients with OAC. Based on the results from that study, it was concluded that every OAC should be treated irrespective of its size.
In most cases, OACs are covered with mucoperiostal flaps of different designs. However, these methods have inherent disadvantages like postoperative pain and swelling. Long-term effects may include scar formation and alveolar ridge resorption, which may impede implant placement and prosthetic treatments.

In the present study, 3 different methods for the closure of OAC were compared by assessment of posttreatment pain, swelling, and loss of alveolar ridge depth. Oroantral perforations were closed with either a porous custom-fit root analog made of phase-pure PLGA-coated β-TCP granules, hemostatic gauze, or a buccal flap.

The closure of oroantral perforations was successful in all of the patients, and fistula formation was prevented. For buccal flaps following Rehrmann, success rates between 84% and 94% are reported, which is in agreement with our findings. Solid custom-made hydroxyapatite blocks have been reported for the closure of oroantral fistulas, which was successful in all 6 patients enrolled in the present study. However, hydroxyapatite blocks became loose and were eventually lost as the fistulas closed. In contrast, all root analogs were maintained. This positive outcome may be due to the osteoconductive properties and the biodegradability of porous β-TCP, which is resorbed slowly by solution in body fluids and by cellular

### Table III: The effects of methods of closure of oroantral communication on the values of the vestibular depth

<table>
<thead>
<tr>
<th>Method of closure</th>
<th>Baseline</th>
<th>Postop 7 days</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x ± SD</td>
<td>Median</td>
<td>Min.</td>
</tr>
<tr>
<td>Root analog</td>
<td>12.65 ± 1.49</td>
<td>12.75</td>
<td>15</td>
</tr>
<tr>
<td>Hemostatic gauze</td>
<td>13.55 ± 1.23</td>
<td>13.75</td>
<td>11</td>
</tr>
<tr>
<td>Buccal flap</td>
<td>13.4 ± 1.61</td>
<td>13.75</td>
<td>10</td>
</tr>
</tbody>
</table>

NOTE: Analysis of variance test: P < .02 for buccal flap.

### Table IV: Pain intensity after closure of oroantral communication in the postoperative period

<table>
<thead>
<tr>
<th>Method of closure</th>
<th>1st day</th>
<th>2nd day</th>
<th>7th day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x ± SD</td>
<td>Median</td>
<td>Min.</td>
</tr>
<tr>
<td>Root analog</td>
<td>6.4 ± 4.3</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Hemostatic gauze</td>
<td>8.6 ± 3.66</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Buccal flap</td>
<td>19.3 ± 3.4</td>
<td>19.5</td>
<td>15</td>
</tr>
</tbody>
</table>

NOTE: Mann-Whitney U test: P < .01.

Fig. 3. Implant placement at the site of the oroantral communication. Radiographs before and 3, 6, and 7.5 months after tooth extraction and treatment with poly(lactide-co-glycolide)–coated β-tricalcium phosphate. The last image shows the tooth after completion of the prosthetic treatment (6 weeks after implant placement).
uptake as bone ingrowth closes the defect. If left untreated, small OACs may close spontaneously. Healing depends on the maintenance of a coagulum in the perforation, which was the rationale for closure of the OACs with hemostatic gauze. To our knowledge, the success rate of this method never has been assessed. The present results suggest that the clinical outcome of the closure with hemostatic gauze is similar to the other treatments, although estimation of the success rate requires a larger study.

The vestibular depth was taken as a measure for the vertical dimension of the alveolar process. It is obvious that the vestibular depth is reduced immediately after application of a buccal flap. In the course of 6 months, the vestibular depth gradually increased in these patients but did not reach pretreatment dimensions, which strongly suggests that the application of a buccal flap resulted in a decreased vestibular depth. In contrast, the vestibular depth of the patients treated with PLGA-coated β-TCP or hemostatic gauze was unchanged after 6 months; therefore, these methods should be preferred if preservation of the alveolar process is necessary. Indeed, the filling of extraction sockets with various bone graft substitutes has been reported to prevent postextraction alveolar atrophy and may thus render augmentative measures that would be required to treat the atrophied alveolar ridges unnecessary. Using β-TCP for the treatment of an OAC thus may fulfill 2 clinical needs: to close the OACs efficiently and to preserve the alveolar ridge.

Pain was most intense for patients that were treated with a buccal flap. Patients that had received a degradable root analog reported the least pain, whereas pain intensities were intermediate for the group treated with hemostatic gauze. Also, the patients treated with coated β-TCP or hemostatic gauze were free of pain after 7 days, whereas patients with a buccal flap were still suffering from pain. Similarly, swelling, which was measured extraorally, was intense for the patient group treated with buccal flaps and moderate for the hemostatic gauze group. Remarkably, swelling was absent in patients treated with PLGA-coated β-TCP. These findings agree with Thoma et al., who reported that postoperative pain and swelling were markedly reduced if OACs were closed with PLGA-coated β-TCP compared with buccal sliding flaps. The closure of an oroantral opening with PLGA-coated β-TCP or hemostatic gauze is less invasive than procedures requiring flap mobilization, which explains the low pain.

Table V. Amount of swelling after closure of oroantral communication according to applied methods, using metric measurement from the inter-tragic notch to the angle of the mouth

<table>
<thead>
<tr>
<th>Method of closure</th>
<th>Baseline</th>
<th>Postop</th>
<th>1st day</th>
<th>7th day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X ± SD</td>
<td>Median</td>
<td>Min.</td>
<td>Max.</td>
</tr>
<tr>
<td>Root analog</td>
<td>15.05 ± 0.8</td>
<td>15</td>
<td>13.5</td>
<td>16</td>
</tr>
<tr>
<td>Hemostatic gauze</td>
<td>14.55 ± 1.23</td>
<td>15</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Buccal flap</td>
<td>15.25 ± 1.01</td>
<td>15</td>
<td>14</td>
<td>17</td>
</tr>
</tbody>
</table>

NOTE. Analysis of variance test: *P* < .01 for buccal flap and hemostatic gauze at first postoperative day.

Fig. 4. Histologic analysis. Hematoxylin-eosin–stained thin sections of tissue samples taken at the site 6 months after poly(lactide-co-glycolide)–coated β-tricalcium phosphate had been applied. A, Major lamellar bone is observed. B, Numerous osteocytes (oc) are present. C, Woven bone (wb) with associated osteoblast-like cells. Magnifications: ×40 for A, ×400 for B, and ×200 for C.
Porous β-TCP has osteoregenerative properties. Because a solid bony support is a prerequisite for stable placement of an implant, treatment of an oroantral perforation with β-TCP may be advantageous if a prosthetic treatment is planned. Histologic analysis after 6 months showed that bone had formed at the site where the β-TCP had been inserted and that remaining β-TCP granules were in close contact with bone tissue, underscoring the biocompatibility of this biocomposite. The implant during whose placement the tissue sample for the histology was collected was stably integrated. In this study, no comparisons of bone quality and quantity at the former defect sites were made. However, the observation that the vestibular depth was reduced in the patients who were treated with buccal flaps suggests that bone loss may have occurred in these cases.

In conclusion, we found that closure of OACs with hemostatic gauze or PLGA-coated β-TCP was as effective as the well established buccal flap approach. However, in contrast to buccal flaps, pain intensities were lower for these 2 minimally invasive methods, and swelling was virtually absent in patients treated with PLGA-coated β-TCP granules. Together with the osteoconductive properties of porous β-TCP, the latter, therefore, may form a valuable alternative for the closure of oroantral openings with flaps, especially if prosthetic treatments are anticipated.

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REFERENCES


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