Biodegradable polyurethane for closure of oroantral communications
Visscher, Susan Henrieke

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Chapter 6

Is biodegradable PU foam as effective as surgery for closure of oroantral communications? A prospective clinical trial.

Susan H Visscher, Baucke van Minnen, Wim J Sluiter, Rudolf RM Bos

Submitted
Abstract

To analyze the effectiveness of biodegradable polyurethane (PU) foam for closure of oroantral communications (OACs) in terms of recurrences, in a large number of patients.

In this prospective trial consecutive patients with OACs existing less than 24 hours were treated with PU foam at the Oral and Maxillofacial Surgery Department of University Medical Center Groningen (Groningen, the Netherlands). The outcome variable was permanent closure of the OAC. The treatment outcome was compared to results of surgical closure of OACs which were obtained in a retrospective study, using a non inferiority design.

36 patients were included in the study (mean age 42 years). In 19 patients the OAC was closed successfully without any complication. In 16.7% of the patients the OAC recurred and required additional surgical closure. A fully sequential statistical analysis proved that the results of PU treatment of OACs are significantly inferior to conventional surgical closure (P < .05). Failure could not be related to the size of the OAC, the location, smoking habits or the time between occurrence and treatment.

Closure of OACs with biodegradable PU foam is not a suitable alternative for conventional surgical closure.

Introduction

Surgical closure of oroantral communications (OACs), preferably within 24 hours either with a buccal or palatal flap, still is the treatment of choice to minimize the chance of fistula formation and chronic sinus disease (1). Application of this common surgical treatment was successful, meaning that the OAC did not recur, in about 9 out of 10 cases in a retrospective study in 308 patients (2). However, as with any surgical procedure, the use of a buccal or palatal flap results in postoperative pain and swelling. The use of a buccal flap also has the risk of permanently decreasing the buccal sulcus depth which could hinder the fitting of a dental prosthesis in the future (3). Lastly, in most cases the patient has to be referred to a maxillofacial surgeon for closure of the OAC. A new treatment strategy for OACs should ideally overcome these drawbacks of surgical closure. It should also be quick and easy to perform, and result in an equal or better treatment outcome to be considered a suitable alternative.

Closure of OACs with biodegradable polyurethane (PU) foam has already been studied extensively both in animal experiments and human studies (4-7). However, no clinical study in a large number of patients has been conducted until now. The purpose of the present study is therefore to analyze the effectiveness of biodegradable PU foam for closure of OACs in a large number of patients. It was hypothesized that closure with PU foam was at least as effective as surgical closure in terms of the percentage of recurrences.

Patients, material and methods

Study design and sample
This study was a prospective clinical trial. All patients included in the trial were treated with PU foam. Historical data from al large group of surgically treated patients served as control.

All consecutive patients with fresh OACs (i.e. existing less than 24 hours) who presented to the Department of Oral and Maxillofacial Surgery at the University Medical Center Groningen in a period of 2 years were included. Patients with pre-existent or chronic maxillary sinusitis were excluded using a case report form containing questions regarding clinical symptoms, and additional consultation of the medical history. When necessary, an X-Waters view was obtained. Patients on antibiotic prophylaxis were also excluded.

All participating patients were informed and written consent was obtained. The procedures, including the material, were approved by the medical ethical committee of the University Medical Center Groningen (UMCG).

Before treatment age, sex, medical history, smoking habits and duration of the
OAC were recorded. The local intraoral situation was described using the following data: (estimated) size of the OAC, location and possible presence of radices relictae.

Experimental treatment

The biodegradable polyurethane foam (Polyganics B.V., Groningen, the Netherlands) used in both this study and the preceding studies (4,5), consists of hard urethane segments synthesized with 1,4-butanediisocyanate and butanediol and soft segments made of (50/50) D/L lactide and ε-caprolactone. Five percent polyethylene glycol (PEG) was added to the polyester soft segment to make the PU foam more hydrophilic and more rapidly degradable. The foam retains its mechanical properties for a period of 2 weeks.

The urethane segments were synthesized with 1,4-butanediisocyanate and 1,4-butandiol. Chain extension was performed, resulting in a PU with urethane segments with a uniform length of 5 urethane moieties. The overall PEG content was 5 wt%. The polyurethane was dissolved in 1,4-dioxane, resulting in a concentration of 4 wt% polyurethane. Water (7.5 wt%) was then added to obtain an interconnected pore structure after which the solution was poured in a conically shaped mould. After cooling down the solution to -18 °C, it was freeze dried to remove the dioxane and water crystals. The porosity of the resulting foam was 94%. Three sizes of PU foam were synthesized, i.e. 8 x 10 x 5 mm (size 1), 11 x 10 x 7 mm (size 2) and a cube measuring 10 x 10 x 10 mm (size 3). Prior to the study the foams were sterilized using ethylene oxide.

All patients were treated by, or under the supervision of, the same 2 maxillofacial surgeons. The OAC was confirmed by inspection, and by both nose and mouth blowing. The size of the perforation was estimated and documented as either ≤ 5 mm, 5-7 mm or > 7 mm. Based on size of the OAC, a PU foam was selected that resulted in a tight fit. Next, a safety suture (4.0 Vicryl® Rapid, Ethicon, Amersfoort, the Netherlands) was attached to the PU foam to facilitate removal of the foam in case it had been malpositioned. The PU was then fitted in the perforation. Gingival margins were approximated with 4.0 Vicryl® Rapid without attempting to accomplish complete mucosal coverage. The procedure was carried out under local anaesthesia with 4% articain and 1:100,000 epinephrine (Aventis Pharma BV, Hoevelaken, the Netherlands).

All patients were instructed to avoid putting pressure on the OAC such as nose blowing. Postoperative analgesics (ibuprophen and/or paracetamol) and 2 % chlorhexidine mouth rinses 2-3 times daily were prescribed. As in accordance with the guidelines of the Dutch Society of OMF Surgeons, antibiotics or decongestants were not prescribed beforehand. Patients were evaluated 2 weeks and 8 weeks after the procedure. Remaining sutures were removed after 2 weeks. Intraoral photographs were taken to document the tissue healing.

Success was considered as permanent closure of the OAC. A conventional surgical flap procedure (buccal or palatal flap) was used to close the OAC in case it recurred.

Results

Fourteen women and 22 men, aged between 24 and 71 years (mean 42 yrs) were included in this study. Most of the patients were in their fourth decade of life at the time (Figure 1). Nine of them were smokers.

The locations of the OACs were almost equally distributed; 11 times at the first molar, 13 times at the second molar and 12 times at the third molar. Reason for extraction was caries in most cases (19 x), followed by non functionality (8 x), endodontic reasons (4 x), periodontal problems (3 x) and crown fracture (2 x). The size of the OAC was estimated as being ≤ 5 mm in 19 cases and as 5-7 mm in 18 cases. In 1 patient, extraction of the left third molar resulted in an OAC both at the palatal and distobuccal root. In the latter patient both OACs were subsequently closed with PU.
foams (size 1 and size 2). In 17 cases, size 1 PU foam was used. In 20 patients the medium sized PU foam was used. In 1 patient a size 3 PU foam was used in addition to a size 2 PU foam, and in 1 patient only a size 3 PU foam was used.

The durations of the OACs (representing the time passed between extraction and closure of the OAC) are presented in Figure 2. Most OACs were closed immediately after diagnosing. The 2 second large groups were referred from the dental practice and subsequently treated within 1-5 hours.

In 19 patients closure with PU foam was successful and no further treatments like antibiotics, drainage of the sinus or surgical retreatment were necessary. In Figure 3 the healing course of 1 of these 19 patients is shown.

Maxillary sinusitis was diagnosed clinically in 9 patients. In 2 patients the sinusitis resolved conservatively with decongestants. Six patients responded well to antibiotics. In 1 patient the sinusitis persisted and drainage was carried out followed by surgical closure of the OAC.

In 1 patient abscess formation was noticed in the buccal fold which drained spontaneously. Additional antibiotics were prescribed for this patient. Discomfort persisted in 1 patient and an additional x-ray revealed a radix relicta. For this reason the OAC was reopened and surgically closed with a buccal flap.

In a total of 6 patients treatment of the OAC with PU foam proved insufficient, meaning that the OAC recurred spontaneously. The characteristics of the 6 patients with a recurrence are shown in Table 1 and Table 2. Five of these recurrences were recorded in the statistical analysis. One recurrence was diagnosed after completion of the follow-up period. Therefore, this recurrence was documented and taken up in Table 1 and 2 but could not be included in the statistical analysis. All recurrences were successfully closed with a buccal flap procedure according to the protocol. With the 5th diagnosed recurrence the stopping rule was activated because the upper boundary had been passed. The study was therefore ended prematurely. H₀ was not accepted and the failure rate was declared inferior to P₀.

Lastly, it was noticed that in 11 of 36 patients the PU foam was extruded from the extraction socket spontaneously within 1-2 weeks after treatment. The extrusion of the PU foam was observed in only 1 of the patients with a recurrent OAC. However, this recurrence of the OAC took place later in time (after 5 weeks). Figure 4 shows the extrusion of the PU foam in 1 patient.
Table 1 Overview of the clinical data of patients with a recurrent OAC.

<table>
<thead>
<tr>
<th>Gender (m/f)</th>
<th>Age (yr)</th>
<th>Smoker</th>
<th>OAC Location</th>
<th>Affected root</th>
<th>Indication for Extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>39</td>
<td>No</td>
<td>28</td>
<td>P, DB</td>
<td>Caries</td>
</tr>
<tr>
<td>M</td>
<td>37</td>
<td>No</td>
<td>26</td>
<td>MB</td>
<td>Caries</td>
</tr>
<tr>
<td>M</td>
<td>39</td>
<td>No</td>
<td>18</td>
<td>Fused</td>
<td>Non-functional</td>
</tr>
<tr>
<td>M</td>
<td>52</td>
<td>No</td>
<td>27</td>
<td>Dorsal wall</td>
<td>Caries</td>
</tr>
<tr>
<td>M</td>
<td>31</td>
<td>No</td>
<td>18</td>
<td>Fused</td>
<td>Non-functional</td>
</tr>
<tr>
<td>F</td>
<td>70</td>
<td>No</td>
<td>27</td>
<td>P</td>
<td>Caries</td>
</tr>
</tbody>
</table>

Abbreviations: M; male, F; female, yr; years, OAC; oroantral communication, P; palatal, DB; disto-buccal, MB; mesiobuccal.

Table 2 Characteristics of the treatment results of patients with a recurrent OAC

<table>
<thead>
<tr>
<th>Size OAC</th>
<th>Size PU (1, 2, 3)</th>
<th>Duration OAC</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5 mm</td>
<td>1</td>
<td>13 hrs</td>
<td>After 14 weeks</td>
</tr>
<tr>
<td>5-7 mm</td>
<td>2</td>
<td>16 hrs</td>
<td>After 38 days</td>
</tr>
<tr>
<td>5-7 mm</td>
<td>3</td>
<td>5 min</td>
<td>After 24 days</td>
</tr>
<tr>
<td>≤ 5 mm</td>
<td>2</td>
<td>5 min</td>
<td>After 21 days</td>
</tr>
<tr>
<td>5-7 mm</td>
<td>2</td>
<td>30 min</td>
<td>After 4 days</td>
</tr>
<tr>
<td>5-7 mm</td>
<td>2</td>
<td>10 min</td>
<td>After 25 days</td>
</tr>
</tbody>
</table>

Abbreviations: OAC; oroantral communication, PU; polyurethane, Min; minutes, Hrs; hours

Figure 3 pre-, per- and postoperative views. Figure 3a preoperative view of an OAC located at the left first molar. Figure 3b a safety suture was attached to the PU foam, and the PU foam is placed in the extraction socket. Sutures are placed after verification of proper placement, without attempting to accomplish complete mucosal coverage (figure 3c). Figure 3d postoperative view taken 2 weeks after treatment. A small part of the PU foam is still visible at this stage (arrow). The size of the defect has clearly decreased. Eight weeks after treatment the OAC has fully healed (figure 3e).

Figure 4 figure 4a is a preoperative view of the PU foam in an OAC located at the left second molar (arrow) with sutures placed underneath. Figure 4b shows the OAC 11 days after treatment. Note the extrusion of the PU foam with the suture still attached. A few days after this photo was taken the PU came out spontaneously. In figure 4c the OAC shows complete healing 8 weeks after treatment.
Discussion

The overall purpose of the research on biodegradable polyurethane foam for closure of OACs was to develop a new, easy and straightforward treatment strategy which would also enable the general dental practitioner to close an OAC.

In earlier studies the biocompatibility of the PU foam was evaluated. A proof of concept was also provided in the former clinical studies with a smaller number of patients (4, 5). In the present prospective study a total of 36 patients with fresh OACs were treated with PU foam. The goal was to analyze the quality of this treatment strategy in terms of recurrences in a large group of patients. Statistical analysis of the patient cohort within this study proved that the results of PU treatment of OACs were inferior to conventional surgical treatment. In the preceding retrospective study (2) we found that on average 10 % of surgical closure of OACs failed. In this study however, the OAC recurred and required additional surgical closure in 16.7 % of the patients, which is a significantly higher number.

Based on the presented data no factors could be pointed out that predicted recurrence after closure with PU foam. To be precise, the sizes of the OACs differed among the recurrences, the durations of the OACs that recurred ranged from immediate closure to 13 hrs, and the locations of the OACs did not show any pattern. Moreover, all patients with a recurrent OAC were non-smokers. Consequently it does not seem possible to point out predictor variables to identify patients that may be treated successfully with PU foam.

The time frame of the recurrences draws attention: 5 of 6 recurrences took place a quite long time after closure (21 days - 14 weeks). The cause behind the (late) recurrences might be found in contamination of the PU foam by microbial flora from the oral cavity. This contamination is possible because complete mucosal coverage of the PU foam was not attempted and sutures were placed only to approximate wound edges and to minimize the risk of dropping out of the PU foam. Also, during the follow-up period it became clear that after approximately 2 weeks the mucosal overgrowth had proceeded but PU foam was yet still visible. The mechanism behind the failures might be the following: soft tissue healing takes place uncomplicatedly at first but due to the contamination of the PU foam, an inflammatory process sets in beneath the restored mucosal tissue and finally it “bursts” resulting in a fistula.

As shown in Figure 4, the PU foam was completely extruded from the OAC to the oral cavity in some patients. It might well be that this represents the most favorable situation. In these cases soft tissue healing had most likely proceeded cranially of the PU foam and thus no fistula was found after extrusion of the PU foam. A parallel can be drawn with a study by Zide (8), that reports on closure of OACs using hydroxyapatite blocks which extruded from the extraction sockets in all treated patients. However, the extrusion of the hydroxyapatite blocks did not result in recurrences of the OACs and were considered a natural course because they were not caused by infection.

Wes and co-authors (9) used a folded bioresorbable Biogide® membrane to close an OAC. The Biogide® membrane was secondly covered by Peripac® periodontal wound dressing which was secured by sutures when necessary. The Peripac® was removed at the 2 weeks follow-up appointment. This treatment strategy was successful in all 6 treated patients. It remains an interesting and difficult question to what extent the Peripac® wound dressing contributed to the successful treatment outcome in this study. Perhaps a Peripac® wound dressing alone, secured with sutures, could be sufficient for OAC repair. Further research by Wes and co-authors seems desirable.

Buric et al (10) use another biomaterial (Ethisorb®) to close OACs with a comparable non-surgical procedure. They don’t describe any failures due to infection or extrusion of the biomaterial out of the socket. However, antibiotics are routinely prescribed to every patient. In addition, OACs larger than 7mm were not included in this study. Can the new strategy for OAC repair involving PU foam be further optimized to gain a better treatment outcome? This is probably not the case. The feasibility studies (4, 5) were used to optimize the treatment protocol and the shape of the PU foams. Secondly, the biocompatibility of the PU polymer or its handling does not seem to be the problem. It was already concluded that narrowing of the indication for usage is not possible with the current data. Finally, coverage of the PU foam with another medium, like for example the before mentioned Peripac®, does not seem ideal for this purpose. It would be very difficult to create an adequate level of sealing that prevents infection of the PU foam with oral bacterial flora. The only way to prevent infection of the PU foam with the subsequent risk of a recurrence seems mucosal coverage. The latter implies the need for a buccal or palatal flap to be raised and then this strategy simply offers no advantages to standard surgical closure.

Conclusion

Based on the present data, it can be concluded that closure of OACs with biodegradable PU foam is not a suitable alternative for conventional surgical closure.

Acknowledgement

The polyurethane foams were kindly provided by Polyganics BV, Groningen, The Netherlands.
Reference List


