Sinus Augmentation Failure and Postoperative Infections Associated with Prophylactic Clindamycin Therapy: An Observational Case Series

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Purpose: This observational study was based on a series of clinical cases in which failure of sinus augmentations occurred in patients who received prophylactic clindamycin therapy. Materials and Methods: Between the years 2006 and 2010, a retrospective observational study was performed. The study consisted of 1,874 patients (723 males and 1,151 females) in whom sinus augmentations were performed prior to placement of dental implants. Results: In nine (0.48%) patients (four males and five females), infection of the graft material inside the sinus floor occurred, and six patients developed an abscess in the site of surgery, 4 to 6 weeks postoperatively. In three patients, a buccal fistula with pus draining was observed 5 to 8 weeks postoperatively. In all patients, the source of infection was from the grafted material within the sinus. A common manifestation in all nine patients was that they had self-reported penicillin allergy and had been prescribed clindamycin (300 mg every 6 hours for 10 days). Conclusion: Prophylactic clindamycin therapy following sinus augmentation procedures seems to be a risk factor for infections and loss of grafting material following these surgical techniques. INT J ORAL MAXILLOFAC IMPLANTS 2018;33:1136–1139. doi: 10.11607/jomi.6517

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It has been reported that the risk of dental implant failure is two to three times higher if preoperative prophylactic antibiotics are not given.1 Penicillin is the most commonly used antibiotic in dental implant surgery prophylaxis.2,3 This is primarily because antibiotics in the penicillin group are nontoxic and have a bactericidal effect against most oral microbiota.4,5 However, adverse reactions to antibiotics including penicillin prescribed or administered in a dental setting can be perturbing. According to the Joint Task Force on Practice Parameters, every 10% of patients report a history of allergy to antibiotics belonging to the penicillin group.6 In a recent retrospective study, French et al7 investigated whether or not self-reported penicillin allergy contributes to a higher rate of postoperative infection and implant failure. The results showed that implant failure rates were 10 times higher among patients with penicillin allergy compared with those without penicillin allergy.7

Among patients with penicillin allergy, lincosamides, such as clindamycin, are considered the drug of choice.8 Clindamycin inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits. Despite the fact that clindamycin exhibits bactericidal and/or bacteriostatic properties (depending on the targeted microbes and/or drug concentration),9 in the present observational study, the authors report a series of cases in which failure of sinus augmentation procedures occurred prior to implant placement among patients who had received prophylactic clindamycin therapy. It is therefore hypothesized that prophylactic...
clindamycin therapy is associated with failure of surgical interventions such as sinus augmentation. The present study is based on a series of clinical cases in which sinus augmentation failure occurred in patients who received prophylactic clindamycin therapy.

MATERIALS AND METHODS

This study included all the infections that occurred idiopathically after the grafting of the posterior maxilla. These infections were encountered in the time between the years 2006 and 2010. All patients received sinus floor elevation with or without simultaneous implant placement following the layer technique. The criteria for simultaneous implant placement were minimal bone height of 5 mm of the alveolar crest and primary stabilization of the implant. The layer technique consists of grafting the cranial part of the elevated space with the biomaterial (Algipore, Dentsply Sirona Implants) and the crestal part with pure autogenous bone chips, allowing early placement and loading of the implants. In addition, some patients received lateral or vertical bone block grafting following the split bone block technique. This technique consisted of longitudinal splitting of the bone block harvested from the mandibular retromolar area into two thin blocks. These blocks were stabilized with microscrews on distance to the local bone in the form of a shell for lateral augmentation or in the form of a box for vertical augmentation. The space between the thin block and the alveolar crest was filled with autogenous bone chips. The implants were placed 3 months after the grafting procedure. All the grafting procedures in the posterior maxilla were performed after preoperative oral antibiotic prophylaxis with amoxicillin 2 g per day continuing for 10 days, postoperatively. Clindamycin, with a daily oral dose of 1.2 g per day for 10 days, was prescribed to patients who reported a history of penicillin allergy.

RESULTS

Between the years 2006 and 2010, a total of 1,874 patients (723 males and 1,151 females) received grafting of the sinus floor following the described technique. Lateral and/or vertical bone block grafting were performed in 1,398 patients additionally. Antibiotic prophylaxis was performed in 1,725 patients with amoxicillin and in the remaining 149 patients (7.95%) with clindamycin due to penicillin allergy. In nine (0.48% of the total patients, 6% of the clindamycin group) patients (four men and five women), infection of the graft material inside the sinus floor occurred, and six patients developed an abscess in the site of surgery, 4 to 6 weeks postoperatively. In three patients, a buccal fistula with pus draining was observed 5 to 8 weeks postoperatively. After the treatment of the acute infection (abscess incision and drainage), a surgical revision of the site was performed. In all patients, the infection and granulation tissue had their source from the grafted material within the sinus floor and not from the additional block grafting. None of the nine patients reported a history of sinus infection, and there were no complications (such as perforation of the sinus mucosa, wound dehiscence, graft exposure, and/or tissue necrosis) encountered during the surgical phase. A common manifestation in these nine patients was that they had self-reported a history of penicillin allergy and were prescribed clindamycin as an alternative prophylactic antibiotic. Therapeutically, the grafted material was removed from the floor of the sinus after taking a probe for microbiology and antibiogram, and the empty cavity was washed with 3% hydrogen peroxide for 3 minutes and with metronidazole for another 3 minutes. The decontamination of the whole area was performed using antimicrobial photodynamic therapy (Helbo laser, Bredent) after minimal reducing of the grafted bone blocks. The elevated sinus cavity was then filled with platelet-rich fibrin (PRF), and the wound was closed using interrupted 6-0 mono file sutures (Glycolone, Resorba). All patients were prescribed metronidazole (250 mg 3 times daily for 7 days). With this protocol, it was possible to control the infection and to continue the treatment as planned.

Implants were placed after 3 months and remained functionally stable up to 8 years of follow-up (Table 1).

DISCUSSION

Antibiotics are routinely administered in clinical settings for the prevention of infections during oral surgical interventions. One of the major goals of providing prophylactic antibiotic coverage is to limit potential pathogens from colonizing the vicinity of the surgical sites. In the present clinical observational study, all patients (n = 149) who had self-reported penicillin allergy were prescribed clindamycin as an alternate antibiotic. Although clindamycin continues to be a commonly used antibiotic among patients with penicillin allergy, in the present case series, all infection of the grafted sinus (n = 9) occurred within a few weeks of placement in this group (6.04%). To the authors’ knowledge from indexed literature, this is the first report that associated failure of sinus grafting following prophylactic clindamycin therapy. Two factors can be discussed as a possible reason for the complications.
The authors of the present observational case series support the results of an in vitro study that showed that clindamycin, at high concentrations, reduces alkaline phosphatase activity and decreases extracellular matrix calcification.\textsuperscript{16} The authors applaud the study by Rashid et al\textsuperscript{17} in which clindamycin administration was shown to increase the proportions of clindamycin-resistant \textit{Prevotella} species in the saliva at various time points. It is pertinent to mention here that \textit{Prevotella} species, predominantly \textit{Prevotella intermedia} and \textit{Prevotella aeruginosa}, often colonize peri-implantitis sites.\textsuperscript{18,19} It is therefore hypothesized that individuals in the present study developed resistance to clindamycin, which in turn augmented oral colonization of pathogenic microbes (such as \textit{Prevotella} species) associated with the etiology of peri-implant diseases. It is hypothesized that among patients with recent exposure to clindamycin, continuation of the same antibiotic for 10 days postoperatively may contribute to colonization of the sinus with clindamycin-resistant organisms. In the present observational study, the nine patients who reported having a history of penicillin allergy were prescribed clindamycin pre- and postoperatively. It is likely that this factor may have contributed toward colonization of the sinus sites with clindamycin-resistant organisms.

It is imperative to understand that failure of osseointegration is a multifactorial phenomenon,\textsuperscript{20,21} and solely drug allergy (such as penicillin allergy) cannot be credited in this regard. However, it is hypothesized that antibiotic prophylaxis using clindamycin is a potential risk factor for failure of sinus augmentation, as well as osseointegration for the reasons stated earlier. In the study by French et al,\textsuperscript{7} 2.1% of the 140 implants failed that had been placed among patients with self-reported penicillin allergy. The authors predicted that penicillin allergy is associated with “early” implant failure.\textsuperscript{7} It is, however, noteworthy that in this study,\textsuperscript{7} all patients with self-reported penicillin allergy were administered clindamycin pre- and postoperatively. Although French et al\textsuperscript{7} reproached penicillin allergy as a potential risk factor for failure of osseointegration, the backstage role of clindamycin (that could have jeopardized the function of osteoblasts) seems to have been overlooked.

A limitation of the present study is that the results were based on a series of clinical observations. Further long-term clinical trials are needed to assess the effect of clindamycin prophylactic therapy in sinus grafting and oral implantology. In addition, it is recommended that clinicians and researchers should be elucidated about the side effects of prophylactic antibiotics that are routinely prescribed in dental settings, such as clindamycin.

**CONCLUSIONS**

Prophylactic clindamycin therapy following sinus augmentation seems to be a risk factor for loss of grafted material following sinus grafting.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (sex)</th>
<th>Surgical procedure</th>
<th>Postoperative complication</th>
<th>Treatment</th>
<th>No. of implants placed</th>
<th>Follow-up of implant after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56 y (male)</td>
<td>Right SE and VBA</td>
<td>Abscess at 4 wk</td>
<td>Incision and drainage, PRF and PDT</td>
<td>1</td>
<td>8 y</td>
</tr>
<tr>
<td>2</td>
<td>58 y (female)</td>
<td>Left SE and LBA</td>
<td>Abscess at 4 wk</td>
<td>Incision and drainage, PRF and PDT</td>
<td>3</td>
<td>7 y</td>
</tr>
<tr>
<td>3</td>
<td>47 y (male)</td>
<td>Left SE</td>
<td>Fistula formation at 8 wk</td>
<td>Revision, PRF and PDT</td>
<td>3</td>
<td>7 y</td>
</tr>
<tr>
<td>4</td>
<td>59 y (female)</td>
<td>Right SE, implant placement, and LBA</td>
<td>Fistula formation at 5 wk</td>
<td>Revision, PRF and PDT</td>
<td>2</td>
<td>7 y</td>
</tr>
<tr>
<td>5</td>
<td>62 y (male)</td>
<td>Left SE and LBA</td>
<td>Fistula formation at 8 wk</td>
<td>Revision, PRF and PDT</td>
<td>3</td>
<td>6 y</td>
</tr>
<tr>
<td>6</td>
<td>58 y (female)</td>
<td>Right SE, implant placement, and LBA</td>
<td>Abscess at 5 wk</td>
<td>Incision and drainage, PRF and PDT</td>
<td>2</td>
<td>6 y</td>
</tr>
<tr>
<td>7</td>
<td>51 y (male)</td>
<td>Right SE and VBA</td>
<td>Abscess at 5 wk</td>
<td>Incision and drainage, PRF and PDT</td>
<td>2</td>
<td>5 y</td>
</tr>
<tr>
<td>8</td>
<td>53 y (female)</td>
<td>Left SE</td>
<td>Abscess at 4 wk</td>
<td>Incision and drainage, PRF and PDT</td>
<td>3</td>
<td>4 y</td>
</tr>
<tr>
<td>9</td>
<td>64 y (female)</td>
<td>Left SE and LBA</td>
<td>Abscess at 5 wk</td>
<td>Incision and drainage, PRF and PDT</td>
<td>2</td>
<td>4 y</td>
</tr>
</tbody>
</table>

SE = sinus elevation; VBA = vertical block augmentation; LBA = lateral block augmentation; PDT = photodynamic therapy; PRF = platelet-rich fibrin.

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The authors reported no conflicts of interest related to this study.

REFERENCES