# Do Penicillin-Allergic Patients Present a Higher Rate of Implant Failure?

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***Purpose:*** *The aim of this clinical study was to determinate if patients allergic to penicillin present a higher incidence of dental implant failure compared with nonallergic patients.* ***Materials and Methods:*** *This cross-sectional clinical study analyzed patients rehabilitated with endosseous dental implants between September 2011 and July 2015, at the University Dental Clinic, School of Dentistry, International University of Catalonia (UIC). Prophylactic antibiotic therapy was prescribed for all patients: a single dose of 2 g of amoxicillin taken orally 1 hour before implant surgery for non–penicillin-allergic patients, and 600 mg of clindamycin taken orally 1 hour before the implant surgery for penicillin-allergic patients. Postsurgical antibiotics were prescribed to prevent early implant failures and postoperative infections: amoxicillin 750 mg three times a day for 7 days for nonallergic patients, and in patients with penicillin allergy, 300 mg clindamycin every 6 hours for 7 days. Implant failure was defined as the removal of the implant for any reason and was classified as early or late failure.* ***Results:*** *A total of 1,210 patients' files were analyzed; 8.03% of nonallergic patients and 24.68% of penicillin-allergic patients presented at least one implant failure. In penicillin-allergic patients, 21.05% were classified as late implant failure and 78.95% as early implant failure, with a lack of osseointegration (80%) being the mean reason for an early implant failure. Penicillin-allergic patients demonstrated a higher risk of implant failure with a risk ratio of 3.84 (95% CI) compared with nonallergic patients.* ***Conclusion:*** *Penicillin-allergic patients treated with clindamycin presented almost four times the risk of suffering dental implant failure, although other variables such as implant brand, location, and the surgeon's skill might have influenced these results.* Int J Oral Maxillofac Implants 2018;33:1390–1395. doi: 10.11607/jomi.7018

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Dental implants are a highly effective, safe, and predictable means of rehabilitation in partially or fully edentulous patients and enjoy a high long-term survival rate. The fifth International Team for Implantology (ITI) consensus conference reported a 5-year survival rate of 97.1% of implant-supported restorations.[1] However, despite this excellent survival rate, implant restorations are not exempt from esthetic, technical, or biologic complications that may cause early or late implant failure. Technical complications may compromise implants or prostheses, the most frequent being veneer or reconstructive material fracture, followed by screw or abutment loosening, component fracture (for example, abutments or screws), and—although rare—fracture of the implant itself.[2,3]

Possible biologic complications include soft tissue complications (fistula, hyperplasia, infections, and/or inflammation), sensory disturbances, and peri-implant disease (mucositis and peri-implantitis), which can result in early or late implant failure.[1,4] The most common complication leading to early dental implant failure is postoperative infection occurring during the osseointegration process, which may be due to bacterial contamination during the implant surgical

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procedure or during postsurgical healing. A variety of prophylactic and postoperative systemic antibiotic regimes have been proposed to minimize the possibility of infection.[5–7]

To prevent infective endocarditis in high-risk patients undergoing dental implant surgery, the American Dental Association (ADA) and American Heart Association (AHA) have recommended intravenous penicillin and oral amoxicillin as the traditional first-line treatment, due to their superior absorption and prolonged serum levels.[8] However, recently, these guidelines have been updated, only recommending prophylactic amoxicillin for high-risk patients.[9] Nevertheless, because of the fear of implant failure, many surgeons use them routinely in healthy patients,[10] even though no consensus has been reached as to whether prophylactic and/or postoperative antibiotics reduce postoperative infections and prevent early implant failure.[11,12] This situation often leads to the overmedication of patients. Consequently, contemporary populations present increasing levels of allergy to penicillin. Penicillin allergy has become the most frequently reported drug allergy, with a prevalence of 8% to 12%, depending on the racial population evaluated.[13] The ADA and AHA recommend clindamycin or azithromycin as the antibiotics of choice for penicillin-allergic patients.[8]

Clindamycin has high oral absorption, significant bone tissue penetration, stimulatory effects on the immune system, and is highly effective against anaerobic gram-positive and gram-negative organisms: *Streptococcus viridans, Peptococcus, Peptostreptococcus, Veillonella, Clostridium, Fusobacterium,* and *Bacteroides*, including the *fragilis* species.[14,15] Given that dental and implant infections have anaerobic or mixed polymicrobial microflora, clindamycin is also effective against maxillofacial infections.

Recent systematic reviews suggest that a single dose or short course of prophylactic antibiotic before surgery could significantly reduce dental implant failure, when implants are placed under ordinary conditions.[16–18] However, it is not clear whether postoperative antibiotics prevent the risk of postoperative infections, nor which antibiotic protocol is the most effective.[16–18] These studies did not provide any evidence relating to penicillin-allergic patients, as the randomized controlled clinical trials included for meta-analysis only assessed the antibiotic amoxicillin, and did not investigate other types of antibiotics, such as clindamycin.

Clindamycin has been recommended by the ADA and AHA as the antibiotic of choice for penicillin-allergic patients. However, few studies have assessed implant failure rates in penicillin-allergic patients prescribed clindamycin pre- or postoperatively. Thus, the possible benefits of pre- and/or postoperative clindamycin in the prevention of implant failure and postoperative infection in patients treated with dental implants remain unknown. The aim of this retrospective clinical study was to determinate if patients allergic to penicillin have a higher incidence of dental implant failure compared with nonallergic patients.

## MATERIALS AND METHODS

### Study Design

This cross-sectional clinical study analyzed patients treated by means of endosseous dental implants between September 2011 and July 2015, at the University Dental Clinic, School of Dentistry, International University of Catalonia (UIC, Barcelona, Spain). The University Ethical Committee for Clinical Research approved the study protocol (CIR-ECL-2015-01). Data analysis was designed to ensure the anonymity of the participants.

The clinical guidelines for dental implant surgery established by the UIC were fulfilled throughout the procedure. Prior to implant placement surgery, all patients underwent periodontal examination; in cases of a Plaque Index > 20%, the patient received root scale and polishing. If periodontal disease persisted, implant surgery was postponed until achieving periodontal health. Prophylactic antibiotic therapy was prescribed (established in the UIC guidelines), a single dose of 2 g of amoxicillin taken orally 1 hour before surgery for non–penicillin-allergic patients and 600 mg of clindamycin taken orally 1 hour before implant surgery for penicillin-allergic patients. Dental implant placement was performed by postgraduate students, overseen by experienced oral surgeons, and following the implant manufacturers' guidelines. Antibiotics were prescribed to prevent early implant failure and postoperative infection: amoxicillin 750 mg three times a day for 7 days. In the cases of penicillin allergy, 300 mg clindamycin were administered every 6 hours for 7 days. In addition, postoperative chlorhexidine mouthwash 0.12% was prescribed twice a day for 1 week.

Implant location was based on each individual patient's needs and prosthetic requirements. The surgical protocols applied included implant placement with and without bone grafting, sinus elevation procedures, and immediate implant placement. All types of loading protocols were included in the study (immediate, early, and late).

### Inclusion Criteria

The inclusion criteria were as follows: patients aged over 18 years, of either sex, requiring at least one dental implant surgery; follow-up period of at least 1 year; and patients' files containing the following data:

**Table 1 Summary of Cases Studied**

| | Patients | |
|---|---|---|
| | n | % |
| No penicillin allergy | 1,133 | 94 |
| Penicillin allergy | 77 | 6 |
| Implant survival | 1,100 | 91 |
| Implant failure | 110 | 9 |

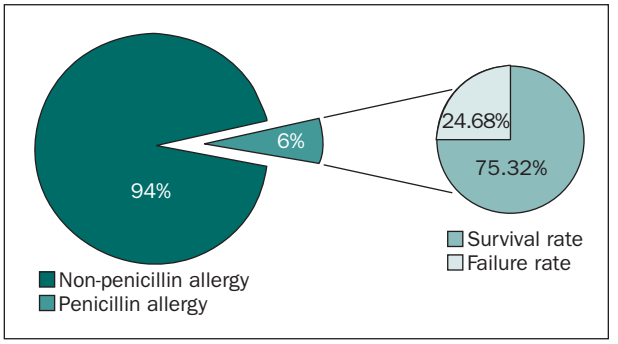


**Fig 1** Percentages of non–penicillin-allergic and penicillin-allergic patients. Percentages of implant survival and failure rate in penicillin-allergic patients at the patient level.

- Sociodemographic data: patient file number, sex, and age
- Penicillin allergy data: absence or presence specified
- Antibiotic therapy prescribed: prophylactic and postoperative antibiotic regime
- Dental implants and dimensions: The brand, length, diameter, and location of the implants. Five brands of dental implant systems were recorded: Astra Tech (Astra Tech), Biomet 3i, MIS (MIS Implants Technologies), Nobel Biocare, Straumann (Institut Straumann)
- Location of implant: anterior maxilla, posterior maxilla, anterior mandible, and posterior mandible

Failures were classified as: *(1)* early failures, occurring before abutment connection; or *(2)* late failure, after abutment connection. Implant failure was defined as the removal of the implant for any reason. The reason for implant failure was registered as: *(1)* pain on function; *(2)* lack of osseointegration; *(3)* radiographic bone loss of > 50% of the length of the implant; *(4)* uncontrolled infection; and/or *(5)* no longer in mouth.

### Exclusion Criteria

The exclusion criteria were as follows:

- Patient file with incomplete data
- Patients who failed to follow or who modified the antibiotic regime
- Patients who failed to attend follow-up visits

### Statistical Analysis

Data were collected and collated in a Microsoft Excel Office 2011 (Microsoft) spreadsheet. To avoid possible risk of bias, patients were considered as sample, making samples independent; also, implants were considered as sample. Statistical analysis was performed using SPSS 21.0 statistical software (SPSS, IBM). The percentages of patients with failed implants and with penicillin allergy were calculated. Pearson's chi-squared test was used to determine the relationship between categorical variables—penicillin allergy and implant failure (yes/no)— to test the hypothesis that penicillin-allergic patients were more likely to experience implant failures than nonallergic patients. The estimates of relative effect were expressed as risk ratio (RR) with a 95% confidence interval (CI).

## RESULTS

A total of 1,210 patient files were analyzed. The study population consisted of 665 (55%) men and 545 (45%) women, with no significant differences ($P > .05$). The mean age was 61.53 ± 9.88 years for men and 58.64 ± 11.74 years for women. In the whole sample, 1,133 (94%) patients did not report any history of penicillin allergy, and 77 (6%) patients were allergic to penicillin. In 1,100 (91%) patients, no implants failed, while 110 (9%) suffered at least one implant failure (Table 1).

Patients in both groups were comparable regarding age, sex, general health status, periodontal health, number of implants, implant brand, surgical approach, type of restoration, and distribution of implants in the jaws, so there was no need to take these variables into consideration.

In the statistical analysis at the patient level, of the 1,133 patients not allergic to penicillin, 91 (8.03%) presented at least one implant failure; of the 77 penicillin-allergic patients, 19 patients presented at least one implant failure (24.68%) (Fig 1). Analyzing the relationship between variables, this means that 1 out of 12 (8%) of nonallergic patients and 1 out of 4 (25%) of penicillin-allergic patients presented an implant failure (Table 2). Thus, the implant failure rate was significantly higher in the penicillin-allergic group ($P = .032$). Penicillin-allergic patients demonstrated a greater risk of implant failure with an RR of 3.84 (95% CI) compared with patients not allergic to penicillin. In penicillin-allergic patients (at the patient level), 21.05% of the failures were classified as late implant failure and 78.95% as early implant failure. The reasons for early implant failure were: lack of osseointegration (80%) > uncontrolled infection (20%). The reasons for late implant failure were: radiographic bone loss of > 50%

**Table 2 Cross Tabulation of Penicilin Allergy and Implant Failure at Patient Level**

| | Patients (n) | Failure (n) | Failure rate (%) |
|---|---|---|---|
| Non-penicillin allergy | 1,133 | 91 | 8.03 |
| Penicillin allergy | 77 | 19 | 24.68 |
| Total | 1,210 | 110 | 9.09 |

**Table 3 Cross Tabulation of Penicillin Allergy and Implant Failure at Implant Level**

| | Implants (n) | Failure (n) | Failure rate (%) |
|---|---|---|---|
| Non-penicillin allergy | 2,572 | 133 | 5.17 |
| Penicillin allergy | 175 | 33 | 18.86 |
| Total | 2,747 | 166 | 6.04 |

of the length of the implant (75%) > implant mobility (25%).

A total of 2,747 implants were included in the study; 133 failed in non–penicillin-allergic patients (5.17%), and 33 failed in penicillin-allergic patients (18.86%) (Table 3). The implant failure rate was significantly higher in the penicillin-allergic group ($P = .046$). At the implant level, the penicillin-allergic patients demonstrated a greater risk of implant failure with an RR of 3.64 (95% CI) compared with patients not allergic to penicillin. In penicillin-allergic patients (at the implant level), 27.27% of the failures were classified as late implant failure and 72.72% as early implant failure. The reasons for early implant failure were: lack of osseointegration (87.5%) > uncontrolled infection (12.5%). The reasons for late implant failure were: radiographic bone loss of > 50% of the length of the implant (55.55%) > implant mobility (33.33%) > implant fracture (11.11%).

## DISCUSSION

Dental implants enjoy a high success rate, although occasionally complications and implant failures do occur. Postoperative infection has been reported to be a common cause of implant failure, and thus, the use of antibiotics could provide a means of preventing early failure. Nevertheless, the current literature remains inconclusive, and no consensus has been reached as to whether prophylactic and/or postoperative antibiotics reduce early failure and postoperative infections. However, many surgeons continue to use them to minimize the risk of postoperative infection and to eliminate this cause of implant failure.

The present study confirmed that penicillin-allergic patients were more likely to suffer dental implant failure than patients who received pre- and postoperative penicillin prescription. Penicillin-allergic patients were found to have a 3.8-times higher risk of implant failure compared with nonallergic patients. No intraoperative complications occurred.

This result concurs with Wagenberg and Froum,[19] who conducted a retrospective study of immediate implants placed between 1988 and 2004, with follow-up periods of 1 to 16 years; patients unable to take postsurgical penicillin were 3.34 times more likely to suffer implant failure than patients administered postsurgical penicillin (with a statistically significant difference). In a study by French et al (2015),[20] the long-term survival of 4,591 Straumann dental implants was analyzed, identifying the following variable risk factors for implant failure: implant location, length, immediate implantation, bone grafting procedures, male sex, autoimmune diseases, heavy smokers, and penicillin allergy. Later, the same authors (with an extended sample) found that the risk of implant failure was 3.1 times higher among penicillin-allergic patients who were administered clindamycin, compared with nonallergic patients, who received penicillin; moreover, the risk increased to 10 times for implants placed immediately after tooth extraction.[21]

Nevertheless, several articles have failed to find any difference in failure rates in patients not prescribed antibiotics.[8,22,23] However, the present study and others agree that penicillin-allergic patients are approximately three times more likely to suffer implant failure compared with nonallergic patients. Moreover, a study by Camps-Font et al (2015)[24] observed that clindamycin alone or in combination with surgical therapy was slightly more effective than amoxicillin for treating postoperative infections. However, Diz Dios et al (2006)[25] observed that prophylactic clindamycin before dental extractions was ineffective for avoiding the bacteremia of *Streptococcus viridans*, *Neisseria*, and *Prevotella*; amoxicillin was found to be the most effective antibiotic.

The main reason for implant failure in penicillin-allergic patients was lack of osseointegration, so it might be that clindamycin has a harmful effect on osseointegration. Curiously, clindamycin has been reported to be cytotoxic or cytostatic in high concentrations for bone cells in vivo after local administration[26]; amoxicillin also has been associated with a negative effect on osseointegration, leading to lower bone-to-implant contact values.[27]

The survival rate obtained in the present study was significantly lower than rates generally reported in the literature,[28,29] although it was high compared with literature on the success of implant procedures conducted by postgraduate students.[24] This could be explained by the fact that the surgeons were master's degree students guided by experienced oral surgeons.

The results should be treated with caution for several reasons: first, this was a retrospective study; second, dental implant surgeries were performed by inexperienced surgeons; and finally, there was considerable heterogeneity of implant locations, surgical procedures, and loading protocols, all of which could have affected the results. Different implant brands were used in the study; however, implant survival rates were not reported at brand level to avoid possible conflicts, due to the high risk of bias caused by the heterogeneity of the studied variables. Further investigation is needed to determine an optimal antibiotic protocol for healthy patients undergoing dental implant treatment.

Unfortunately, there is insufficient evidence to confirm the cause of higher implant failure rates in penicillin-allergic patients. More, better-designed studies are needed to validate the hypothesis that penicillin-allergic patients suffer a higher risk of implant failure. Future research should take the form of randomized controlled clinical trials to assess dental implant failure rates in nonallergic patients treated with and without clindamycin, and penicillin-allergic patients treated with and without clindamycin, to explain the higher implant failure rate among penicillin-allergic patients. In vivo studies are needed to evaluate the influence of antibiotics on the osseointegration of dental implants and on bone healing.

## CONCLUSIONS

Within the limitations of this retrospective study, penicillin-allergic patients treated with clindamycin were almost four times more likely to suffer dental implant failure, compared with non–penicillin-allergic patients. However, other variables such as implant brand, implant location, and the surgeon's skills should be taken into consideration. Future studies should focus on clarifying antibiotic guidelines to improve implant success rates.

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