David French

Clinical retrospective study of self-reported penicillin allergy on dental implant failures and infections

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Objective: The aim of this retrospective study was to investigate whether self-reported allergy to penicillin may contribute to a higher rate of postsurgical infection and implant failure. **Method and Materials:** This retrospective, non-interventional, open cohort study reports on implant survival and infection complications of 5,576 implants placed in private practice by one periodontist, and includes 4,132 implants that were followed for at least 1 year. Logistic regression was applied to examine the relationship between self-reported allergy to penicillin and implant survival, while controlling for potential confounders such as smoking, implant site, bone augmentation, loading protocol, immediate implantation, and bone level at baseline. The cumulative survival rate (CSR) was calculated according to the life table method and the Cox proportional hazard model was fitted to data. **Results:** Out of 5,106 implants placed in patients taking penicillin it was found that 0.8% failed, while 2.1% failed of the 470 implants placed for patients with self-reported allergy to penicillin ($P = .002$). Odds of failure for implants placed in penicillin-allergic patients were 3.1 times higher than in non-allergic patients. For immediate implant placement, penicillin-allergic patients had a failure rate 10-times higher than the non-allergic cohort. Timing of implant failure occurring within 6 months following implantation was 80% in the penicillin-allergic group versus 54% in the non-allergic group. From the 48 implant sites showing postoperative infection: penicillin-allergic patients had an infection rate of 3.4% (n = 16/470) versus 0.6% in the non-allergic group (n = 32/5,106) ($P < .05$). **Conclusion:** Self-reported penicillin allergy was associated with a higher rate of infection, and primarily affected early implant failure. *(doi: 10.3290/j.qi.a36887)*

Key words: dental implants, failure, immediate, infection, penicillin allergy, socket, survival

Early implant loss may relate to impaired healing of the host bone site, disruption of a weak bone-to-implant interface after abutment connection, or infection in situations with complicated surgery.[1] Early dental implant failures may be due to bacterial contamination at implant insertion or soon after, and practitioners often take precautions regarding infection based on early guidelines.[2,3] A variety of prophylactic systemic antibiotic regimens have been suggested to minimize infections after dental implant placement, with recent protocols recommending short-term antibiotic prophylaxis, if used.[4,5]

Though various types of antibiotics have been empirically tested for dental implant surgery, penicillin

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has a long history of use in dental implant surgery prophylaxis, is effective against most human oral microbiota, is bacteriocidal and non-toxic, and is therefore commonly the first choice in antimicrobial prophylaxis for dental implant surgery.[6,7] Clindamycin is a commonly used alternate for amoxicillin as part of the American Heart Association (AHA) guidelines on prophlyaxis.[8] In an overview of 5,000 patients in 1997, Dent et al[9] reported that the risk for implant failure of osseointegration during healing (stage I) and uncovering (stage II) was two to three times higher if no prophylactic antibiotics were given preoperatively. Nonetheless, the use of prophylactic antibiotics in dental implant surgery remains controversial due to the conflicting data on their efficacy, as reported in various studies, as well as the adverse side-effects of antibiotic use and increased risk of antibiotic-resistant bacteria.[10-13]

Although the benefits of prophylactic and postoperative antibiotics remain contentious, they continue to be prescribed postoperatively, especially following complex implant surgeries such as bone grafts, immediate implant placement, or long procedures with placement of a high number of implants.[6,14] Certain surgical procedures may be more at risk, as Wagenberg and Froum[15] demonstrated in immediate socket placement patients wherein those with an allergy to penicillin were 3.3-times more likely to experience implant failure than patients who received amoxicillin, and 5.7-times more likely to experience implant failure due to infection than patients without allergy to penicillin.[15]

The purpose of this retrospective, non-interventional, open cohort study is to investigate the potential impact of self-reported allergy to penicillin on infection and implant failure. This study is unique in that all implant case types were included, for example conventional and immediate placement, sinus lift procedures, non-grafted sites, and sites with simultaneous implant and bone grafting. The data were analyzed to recognize statistical relationships between explanatory variables and early implant failure.

METHOD AND MATERIALS

This retrospective observational study consisted of 5,576 dental implants (985 Nobel Biocare and 4,591 Straumann). The inclusion criterion was the presentation of a micro-rough surface (TiUnite, sand-blasted, large-grit, acid-etched [SLA]) dental implant in retrospective review, and the only exclusion criterion was medically compromised patients (American Society of Anesthesiologists [ASA] class 3 or higher).[16,17]

The cohort selection was based on technical adoption of digital radiographs, which enabled systematic retrospective retrieval of all implants placed between 1999 and 2005; in 2005 a digital patient record that allowed field search of multiple parameters was adopted. All paper records were retained in addition to the digital record so no case was excluded due to missing information. In 2012, data compilation and analysis was performed for all micro-rough surface implants placed between 1999 and 2012 (TiUnite and SLA). The few machined titanium implants placed between 1998 and 2000 were excluded since these behave differently in peri-implant infection compared to the micro-rough surfaces in use today.[18] There were no other exclusion criteria other than patient unfit for dental implant surgery such that all patient and site risk factors were included to better represent private practice experience.

Implants were inserted according to manufacturer guidelines and used according to approved indications. All potential implant locations were used, and the location of each implant was determined based on individual patient and prosthetic requirements; no set location or group of locations were planned or declined.

All patients had a periodontal screening exam, and if active periodontal disease was present then root planing and recall evaluation was performed prior to dental implant surgery. Patient education and consent to implant surgery was obtained, and the study is part of an ongoing long-term evaluation of dental implants associated with the University of British Columbia retrospective clinical study on dental implants approved by the Clinical Research Ethics Board at the University

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of British Columbia, Vancouver, Canada. Data analysis was designed to preserve the anonymity of the patients.

Surgical protocols included implant placement with and without bone grafting and immediate placement in extraction sockets. Implants were placed using flap surgery except for immediate placement in extraction sockets, which was performed flapless. Immediate placement was chosen when a patient was informed of, and preferred, the option; this was limited to single root sites with no apical infection, 3 mm of bone beyond the apex, and the implant size could be selected to have 1 to 1.5 mm buccolingual bone gap such that no bone graft or membrane was used at a residual horizontal defect. When placing implants in a fresh extraction socket, the sockets were thoroughly degranulated with curettes and burs to ensure the remnants of soft tissue fibers had been removed. In sites of an atrophied ridge that required a bone graft, a particulate graft with membrane was performed at the time of implant placement using autogenous bone, bovine xenograft, or combinations with an expanded polytetrafluoroethylene (e-PTFE) or collagen membrane. Defect morphology guided decision on membrane selection, with self-contained defects that had 3 mm or less of exposed implant surface being treated with resorbable membrane while e-PTFE was used in non-self-contained and larger defect sites. Sinus procedures were divided into two groups. In one group, a lateral window (LW) sinus elevation procedure was performed prior to implant placement using a mixture of autogenous and bovine xenograft in combination with a slowly resorbable collagen membrane. In the other group, an indirect osteotome sinus floor elevation (OSFE) procedure was performed simultaneous to implant placement using straight wall osteotomes with no added bone graft.[19] Site selection for indirect osteotome-mediated elevation was > 4 mm if a single site, and 2 to 4 mm if multiple adjacent sites; otherwise a LW was performed prior to implant placement. The reader is referred to French et al[19,20] for details on tri-factorial determinants of sinus procedure selection.

All patients who were not reporting an allergy to penicillin, received preoperative amoxicillin (2 g amoxicillin 1 hour prior, and 500 mg 8 hours as a single postoperative dose), whereas patients with self-reported allergy to penicillin were typically prescribed clindamycin (600 mg 1 hour prior, and no postoperative dose). Postoperative antibiotic use was only prescribed, as per routine, when there was a bone graft, sinus procedure, or immediate socket placement (amoxicillin use continued at 250 mg three times a day for 1 week; or if penicillin-allergic then clindamycin use continued at 150 mg four times a day for 1 week, except if sinus elevation then levaquin 250 mg, twice a day for 1 week was used postoperatively in penicillin-allergic patients). One patient with two implant sites was penicillin allergic but had a prior history of gastrointestinal complications, so clarithromycin was used for premedication; this case had no implant loss or infection data so was pooled with the clindamycin data.

Loading protocols varied based on individual case requirements but were divided into three categories; immediate loading (within 48 hours of placement), conventional loading (2 to 3 months after placement), and delayed loading (6 months after placement if very low-density bone and low insertion stability). When adjacent implants were placed, they were typically splinted together, and when 6-mm implants were used, they were always splinted to adjacent implants. The prescribed schedule of follow-up was postsurgical evaluation at 1 week and 3 weeks. The patients were evaluated at 2 to 3 months post-implant insertion for implant stability via a 35-Ncm torque test and radiographic bone measurements, which provided a baseline for future assessment.

Patients were recalled 1 month after prosthesis to evaluate oral hygiene access, retained cement, and occlusion. Follow-up was then scheduled on 1-, 3-, and 5-year intervals in addition to routine recalls at the general dental referral practice. Longer term cases (5 to 12 years) were seen if there was a complication noted by the general dentist, or a new implant site, or if it was a large complex restorative case.

Case parameters recorded for comparative evaluation were divided into two major categories:

- patient-related factors, such as age at implant placement, sex, history of periodontal disease, smoking, diabetes, bisphosphonate therapy, immunosuppressant diseases, and self-reported allergy to penicillin
- implant-related factors, such as implant manufacturer, type, length and width, torque on insertion, implant placement timing (immediate socket placement versus conventional healed alveolar ridge), immediate versus delayed loading protocol, location of implant placement, additional surgical procedures such as sinus elevation procedure (direct and indirect osteotome), and bone augmentation.

When applicable, date and reasons for implant failure were recorded. Failure was defined as the removal of an implant for any reason. Early failure was defined as implant loss prior to prosthesis (typically under 3 months) and late failure defined as implant loss after prosthetic connection. Infection was defined as suppuration with either pain and /or bleeding and was determined by a single examiner (DF). When infection was noted in the early healing period (< 2 months), implant removal was often chosen to avoid further damage to the site, and after recovery a new implant was placed. When late infections were noted (after prosthetics), a variety of procedures was used, including debridement, gingivectomy, subgingival minocycline application, and systemic antibiotics.

Data management and statistical analysis

A logistic regression model was fitted to the data. Selection of variables into the final logistic regression model was carried out in steps. First, a bivariate analysis was performed between implant failure and each explanatory variable. Pearson's chi-squared test was employed to examine the relationship between categorical variables such as penicillin allergy and implant failure (yes/no). Fisher's exact test was applied if assumptions for chi-squared test were not met. As the second step, all variables with a *P* value equal or less than .1 were entered into a multivariate model. This modeling enabled an estimate of the odds ratio (OR) with adjustment to possible confounders. The variables entered in the model were self-reported allergy to penicillin, immediate implantation, implant site, smoking, guided bone regeneration, and baseline bone loss considering penicillin allergy as the main variable. Goodness of fit of the regression model was tested using the Hosmer-Lemeshow test. The level of statistical significance was .05 using the SPSS statistical package (version 20.0, IBM).

Implant survival was analyzed by calculating the percentage of surviving implants as a function of time. The cumulative survival rate (CSR) was calculated according to the life table method. Kaplan Meier analysis was used to test if there was a significant difference between survival rate of implants placed for penicillin-allergic and non-allergic groups. Cox proportional hazard model was fitted to data.

RESULTS

Of the total 5,576 dental implants studied, 5,106 (91.6%) were placed in patients with no history of self-reported allergy to penicillin, and 470 implants (8.4%) were placed in patients with self-reported allergy to penicillin. The mean patient age at the time of surgery was 60 years old with a range of 20 to 89 years. There was no significant difference in age at time of placement with regard to failure rate, with the mean ± standard deviation (SD) age of failed site of 53.8 ± 12.7 years as compared to mean ± SD age of surviving implant of 54.1 ± 12.6 years. Of note was a difference in failure rate between implant types. Of the 4,591 Straumann implants placed, 0.7% failed, and of the 985 Nobel Biocare implants placed, 1.7% failed; the association with implant failure was significant at *P* value equal to .002. However, when entered into multivariate analysis, the effect of implant type on failure disappeared. Distribution of implant site and jaw can be seen in Table 1. There were 3,046 maxillary implant sites and 2,530 mandibular implant sites. A statistically significant difference in implant failure rate by area of

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Table 1a Frequency of implants by site placed in maxilla

	Frequency	Percentage
Central	403	13.2
Lateral	433	14.2
Canine	232	7.6
First premolar	494	16.2
Second premolar	568	18.7
First molar	649	21.3
Second molar	246	8.1
Third molar	21	0.7
Total	3,046	100.0

Table 1b Frequency of implants by site placed in mandible

	Frequency	Percentage
Central	48	1.9
Lateral	149	5.9
Canine	64	2.5
First premolar	215	8.5
Second premolar	513	20.3
First molar	975	38.5
Second molar	519	20.5
Third molar	47	1.9
Total	2,530	100.0

Table 2 Implant level descriptive information on potential confounders and their association with implant failure

Possible confounder			Association with implant failure (*P*)
History of periodontal diseases	Yes = 249, percentage failed = 2.4%	No = 5,327, percentage failed = 0.8%	Significant (.021†)
Smoking status > 15 cigs/day	Yes = 125, percentage failed = 3.2%	No = 5,451, percentage failed = 0.8%	Significant (.023†)
History of diabetes	Yes = 102, percentage failed = 0.0%	No = 5,474, percentage failed = 0.9%	Not significant
Immediate implantation	Yes = 687, percentage failed = 1.7%	No = 4,889, percentage failed = 0.8%	Significant (.009*)

*Chi-squared test.
†Fisher's exact test.

Table 3 Cross tabulation of penicillin allergy and implant failure

Allergy to penicillin	Implants (n)	Failures (n)	Failures (%)*
Positive	470	10	2.1
Negative	5,106	39	0.8
Total	5,576	49	0.9

*Chi-squared test; $P = .002$.

Table 4 Cross tabulation of implant failure as a function of both penicillin allergy and immediate implantation

Penicillin allergy	Immediate implants (n)	Immediate implant failures (n)	Immediate implant failure (%)*
Yes	57	6	10.5
No	630	6	1.0
Total	687	12	1.7

*Fisher's exact test; $P < .001$.

implant placement was seen ($P = .002$). The region with the highest percentage of failure was the area of second molars (22.4% of all failures).

Nonsignificant findings in bivariate analysis were as follows: age at time of placement, bisphosphonate use, bruxism, diabetes, immediate loading, and sinus elevation (OSFE or LW). Table 2 presents descriptive information on potential significant confounders as well as their relationship with implant failure. Bivariate analysis of implant failure as a function of self-reported penicillin allergy, failure rate, and immediate implantation are shown in Tables 3 and 4, respectively, and discussed below.

Based on initial analysis, the following variables were significant and therefore considered for multivariate analysis: penicillin allergy, implant type, smoking,

Table 5 Multivariate logistic regression of implant failure

		95% CI for OR		
Variable	**B (SE)**	**Lower**	**Point estimate**	**Upper**
Constant	−5.42 (0.48)	NA	NA	NA
Self-reported allergy to penicillin	1.14 (0.37)	1.5	3.1	6.4
Immediate implantation	1.12 (0.39)	1.4	3.1	6.6
Guided bone regeneration	0.82 (0.30)	1.2	2.3	4.1
Implant site	1.70 (0.74)	1.3	5.7	24.7
Baseline bone loss > 1 mm	1.16 (0.43)	1.3	3.2	7.5

$R^2 = 0.1$ (Hosmer-Lemeshow). Model χ^2 (12) = 54.5, $P < .001$
CI, confidence interval; NA, not applicable; OR, odds ratio; SE, standard error.

periodontal disease history, immediate socket placement, guided bone regeneration, and implant location. The variables that remained significant after multivariate analysis were: allergy to penicillin, immediate socket placement, guided bone regeneration, implant location, and base bone < 1 mm. No significant relation between penicillin allergy and baseline bone loss was found; however, since the *P* value was < .1, this variable (baseline bone loss) was included in the final logistic regression model. Results of the multivariate logistic regression, showing ORs, are presented in Table 5.

Self-reported penicillin allergy and implant failure

Out of 5,106 implants placed in the non-allergic group, it was found that 0.8% failed, whereas 2.1% of implants placed in the self-reported penicillin-allergic group failed (Table 3). The implant failure rate between the two groups was significantly different ($P = .002$), with penicillin-allergic patients demonstrating a greater chance for failure with an OR of 3.1 (95% confidence interval [CI]: 1.5 to 6.4) when compared to patients who were able to utilize penicillin and controlling for other variables (Table 5).

Penicillin allergy and infection rate

There were 48 sites with a postoperative infection incident, resulting in an overall infection rate of 0.9% per implant. In the non-allergic group, 32/5,106 sites developed infection, resulting in an infection rate of 0.6%. In patients with self-reported allergy to penicillin, 16/470 sites developed infection, giving rise to an infection rate of 3.4%. The infection rate in penicillin-allergic patients was about six-times higher than the rate of infection in the non-allergic group when all implant case types were included ($P < .05$).

Penicillin allergy and immediate implantation failure

A total of 687 implants (12.3%) were placed immediately into fresh extraction sockets, and of these 12 implants failed, resulting in a failure rate of 1.7%. The remaining 4,889 implants were placed in healed ridges, and of these 37 implants failed, resulting in a failure rate of 0.8%. The difference in implant failure rate between immediate placement and placement into healed ridges was statistically significant ($P = .009$) (Table 4).

Within the subset of 687 implants immediately placed in extraction sockets, 630 implants were in the non-allergic group (91.7%) while 57 implants were in the penicillin-allergic group (8.3%). In the non-allergic group, 6 out of 630 immediately placed implants failed, resulting in a failure rate of only 1%. In the penicillin-allergic group, 6 out of 57 immediately placed implants failed, resulting in a failure rate of 10.5%, such that the

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Table 6 Life table as a function of penicillin allergy

Start time (months)	No penicillin allergy			Penicillin allergy		
	N	Events	CSR	N	Events	CSR
0	5,069	21	0.9955	465	8	0.9812
6	4,145	4	0.9945	379	0	0.9812
12	3,907	1	0.9942	348	0	0.9812
18	3,493	4	0.9929	314	0	0.9812
24	2,783	0	0.9929	258	1	0.9772
30	2,435	2	0.9921	225	1	0.9725
36	2,194	1	0.9916	189	0	0.9725
42	1,847	1	0.9910	174	0	0.9725
48	1,426	1	0.9902	139	0	0.9725
54	1,169	1	0.9893	106	0	0.9725
60	965	0	0.9893	93	0	0.9725
66	761	2	0.9864	74	0	0.9725
72	609	0	0.9864	43	0	0.9725
78	475	1	0.9840	30	0	0.9725
84	330	0	0.9840	26	0	0.9725
90	240	0	0.9840	22	0	0.9725
96	168	0	0.9840	16	0	0.9725
102	122	0	0.9840	15	0	0.9725
108	59	0	0.9840	6	0	0.9725
114	44	0	0.9840	4	0	0.9725
120	23	0	0.9840	3	0	0.9725
126	11	0	0.9840	2	0	0.9725

CSR, cumulative survival rate at end of interval; events, number of terminal events (implant failure); N, number entering interval.

Table 7 Summary of survival rates

Allergy to penicillin	Number of failures	1-year survival rate (%)	5-year survival rate (%)	10-year survival rate (%)
Positive (n = 465)	10	98.1	97.3	97.3
Negative (n = 5,069)	39	99.5	98.9	98.4

failure rate for immediate implant placement into fresh extraction sockets was 10-times higher in the penicillin-allergic group compared to the non-allergic group (Fisher's exact test, $P < .001$) (Table 4).

Descriptive survival analysis at implant level

Among the cohort of 5,576 implants, there were 32 (0.5%) failures during the surgical phase (before loading) and only 17 (0.3%) failures after loading.

When evaluating implant failure in the non-allergic group, 53.8% (21/39) were found to occur during the first 6 months following implant insertion, while in the penicillin-allergic group this amount was 80.0% (8/10) (Table 6). According to the life table analysis, the CSRs at the implant level, at 1-, 5- and 10-years were 98.1%, 97.3%, and 97.3%, respectively in the penicillin-allergic group, and 99.5%, 98.9%, and 98.4%, respectively in the non-allergic group (Table 7). Kaplan Meier (Log rank)

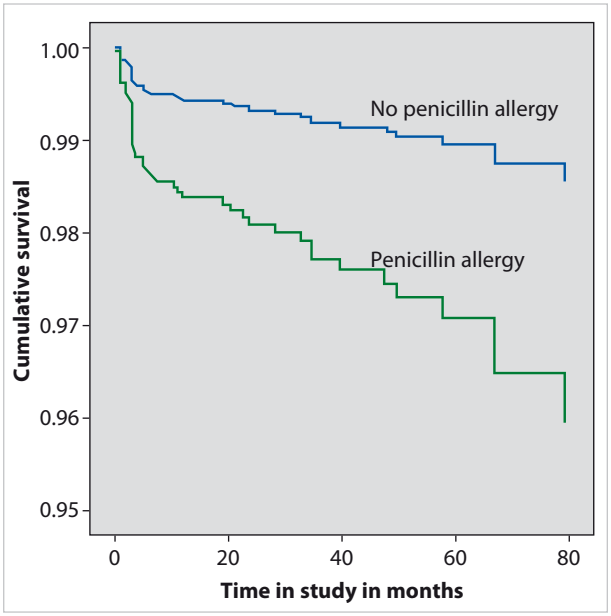

Fig 1 Cumulative survival as a function of penicillin allergy.

test showed there was significant difference ($P = .002$) between survival of implants placed in the penicillin-allergic group compared with the non-allergic group (Fig 1).

According to a univariate Cox regression analysis of the implants that had not yet failed in the penicillin-allergic cohort at the end of the 10-year follow-up, it was found that the penicillin-allergic cohort had a 2.8-times higher probability to fail by the next time point (6 months) compared to the non-allergic cohort (hazard ratio = 2.8; 95% CI, 1.4 to 5.6).

DISCUSSION

There have been numerous studies looking at different implant-related, patient-related, and surgery-related factors that may impact implant surgery outcomes; however, there are fewer studies looking at the potential impact of an allergy to penicillin on implant therapy outcome. One of the proposed methods to minimize infection following implant surgery is the prescription of antibiotics.[2,4,21] The choice of antibiotic requires that it cover a reasonable bacterial spectrum to limit potential pathogens from colonizing in the vicinity of the surgical sites.[1] However, antibiotic administration in conjunction with implant surgery either prophylactically or postoperatively has been a matter of controversy in implant literature due to the conflicting data on their efficacy as reported in various studies, as well as the adverse side-effects of antibiotic use and increased risk of antibiotic-resistant bacteria.[10,13] In a recent prospective, double-blind, randomized, controlled trial comparing amoxicillin in 27 test patients versus placebo in 28 control patients, it was noted that 2 g of amoxicillin given orally, 1 hour preoperatively, resulted in higher dental implant survival rates (100% vs 82%) ($P = .05$).[7]

In the present study, the reported OR indicates a potential tripling of failure rate (3.1 times) including all implant case types in patients allergic to penicillin that increased to a 10-times higher failure rate in immediate implant in sockets; however, due to low numbers of implant failures, this result should be interpreted with caution. In a study by Wagenberg and Forum,[15] it was found that of 1,925 immediately placed implants in fresh extraction sockets, there was a 3.3-times higher risk of implant failure for patients who were unable to take amoxicillin postsurgically compared to those who could receive amoxicillin. A recent systematic review of implant survival after 1 year of use for implants placed into fresh extraction sockets showed that among factors analyzed (reasons for extraction, antibiotic use, position of implant, type of loading), only the regimen of antibiotic use affected the survival rate significantly, with lower failure rates in groups that received a course of postoperative antibiotics.[22] The results of this study support the above studies and expand those findings to all case types, as well providing an analysis of infection risk.

The biology behind the higher failure rates in penicillin-allergic patients is not known. It can only be speculated that it could relate to the suboptimal antimicrobial efficacy of the alternative antibiotics (such as clindamycin) or even that such antibiotics could have direct detrimental side effects on wound healing. Interestingly, clindamycin has been reported to have negative effects on osteoblasts in vitro.[23]

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The difference in implant failure rates between immediate implantation in extraction sockets and conventional implant placement in healed ridges was statistically significant irrespective of penicillin allergy status. However, the failure rate for immediate implantation into fresh extraction sockets was further increased in the penicillin-allergic group compared to the non-allergic group. Furthermore, a drastically increased failure rate for immediately placed implants was linked to the higher infection rate in patients who were unable to use penicillin due to self-described allergy. Immediate implantation could pose higher risks of implant failure due to the presence of oral infection at the time of tooth extraction and the potential for plaque colonization of the micro-rough surface since the implant is not fully placed in bone. However, this should be interpreted with caution, as there are other factors such as buccal wall integrity, gap distance, implant design and geometry, and provisional loading that may also play a role in implant failure in immediate implantation cases.[24-26]

The rate of patients reporting penicillin allergy in this report is higher than the actual number of patients with true allergy, with about 10% being truly allergic.[27] Nonetheless, this does affect antibiotic selection, and in light of the finding of this report and other analyses[14] it may be advised to consider allergy testing prior to implant treatment, especially if immediate socket placement or bone grafting is planned.

It remains important to understand that implant failure is a multifactorial phenomenon with several risk factors involved. Penicillin allergy alone as a risk indicator does not cause implant failure; however, it can contribute to failure when other risks are present as well. Of the other factors considered, the following were also significant in multivariate analysis and warrant further analysis: site and baseline bone < 1 mm. Site is an important confounder as there was a higher rate of failure in second molars, and this could be attributed to the placement of shorter implants due to close proximity to vital anatomical structures such as maxillary sinus and inferior alveolar nerve, free standing position of the implant in this region due to absence of adjacent posterior tooth, and lower quality of bone.

The results of this study should be interpreted with caution due to the small number of implant failures studied. Randomized, controlled clinical trials would be required for conclusive evidence.

CONCLUSION

Within the limitations of this retrospective study, the following conclusions can be drawn.

Implants in patients unable to take penicillin due to self-reported allergy were 3.1-times more likely to suffer implant failure than those placed in patients who were able to receive penicillin, when all implant sites were evaluated ($P = .002$). The failure rate for immediate implantation in extraction sockets was 10-times higher (10.5% vs 1.0%) in the penicillin-allergic group ($P < .001$).

The infection rate in the penicillin-allergic group was about 6-times higher than the rate of infection in non-allergic group (3.4% vs 0.6%, $P < .05$).

There was a trend of more "early" implant failure within the first 6 months of implant insertion in the penicillin-allergic group.

The results of this study further elucidate the importance of pre- and postoperative use of antibiotics in their ability to reduce the rate of implant failure and infection, especially in the case of immediate implantation. Future studies including larger sample sizes of implant failures as well as randomized, controlled clinical trials will be beneficial. The results of this study also show that clindamycin is not as effective as penicillin in reducing the adverse effects of failure and infection. Since most patients who report allergy are not truly allergic, penicillin allergy testing may be advised in at-risk cases. Further research is required to find an effective alternative to penicillin for improved oral rehabilitation in the penicillin-allergic population.

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REFERENCES

1. Esposito M, Thomsen P, Ericson LE, Lekholm U. Histopathologic observations on early oral implant failures. Int J Oral Maxillofac Implants 1999;14:798–810.
2. Adell R, Lekholm U, Rockler B, Branemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10: 387–416.
3. Iho S, Tanaka Y, Takauji R, et al. Nicotine induces human neutrophils to produce IL-8 through the generation of peroxynitrite and subsequent activation of NF-kappaB. J Leukoc Biol 2003;74:942–951.
4. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: antibiotics at dental implant placement to prevent complications. Cochrane Database Syst Rev 2013;7:CD004152.
5. Keenan JR, Veitz-Keenan A. Antibiotic prophylaxis for dental implant placement? Evid Based Dent 2015;16:52–53.
6. Ring ME. A thousand years of dental implants: a definitive history--part 1. Compend Contin Educ Dent 1995;16:1060.
7. Nolan R, Kemmoona M, Polyzois I, Claffey N. The influence of prophylactic antibiotic administration on post-operative morbidity in dental implant surgery. A prospective double blind randomized controlled clinical trial. Clin Oral Implants Res 2014;25:252–259.
8. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. J Am Dent Assoc 2008;139(Suppl):3S–24S.
9. Dent CD, Olson JW, Farish SE, et al. The influence of preoperative antibiotics on success of endosseous implants up to and including stage II surgery: a study of 2,641 implants. J Oral Maxillofac Surg 1997;55(12 Suppl 5):19–24.
10. Schwartz AB, Larson EL. Antibiotic prophylaxis and postoperative complications after tooth extraction and implant placement: a review of the literature. J Dent 2007;35:881–888.
11. Ahmad N, Saad N. Effects of antibiotics on dental implants: a review. J Clin Med Res 2012;4:1–6.
12. Albrektsson T, Jansson T, Lekholm U. Osseointegrated dental implants. Dent Clin North Am 1986;30:151–174.
13. Aldrin M, Raastad R, Tvete IF, et al. Antibiotic resistance in hospitals: a ward-specific random effect model in a low antibiotic consumption environment. Stat Med 2013;32:1407–1418.
14. Chrcanovic BR, Albrektsson T, Wennerberg A. Prophylactic antibiotic regimen and dental implant failure: a meta-analysis. J Oral Rehabil 2014;41:941–956.
15. Wagenberg B, Froum SJ. A retrospective study of 1925 consecutively placed immediate implants from 1988 to 2004. Int J Oral Maxillofac Implants 2006;21: 71–80.
16. Owens WD, Felts JA, Spitznagel ELJ. ASA physical status classifications: a study of consistency of ratings. Anesthesiology 1978;49:239–243.
17. Quirynen M, Herrera D, Teughels W, Sanz M. Implant therapy: 40 years of experience. Periodontol 2000 2014;66:7–12.
18. Albouy J-P, Abrahamsson I, Berglundh T. Spontaneous progression of experimental peri-implantitis at implants with different surface characteristics: an experimental study in dogs. J Clin Periodontol 2012;39:182–187.
19. French D, Nadji N, Liu SX, Larjava H. Trifactorial classification system for osteotome sinus floor elevation based on an observational retrospective analysis of 926 implants followed up to 10 years. Quintessence Int 2015;46:523–530.
20. French D, Nadji N, Shariati B, Hatzimanolakis P, Larjava H. Survival and success rates of dental implants placed using osteotome sinus floor elevation without added bone grafting: a retrospective study with a follow-up of up to 10 years. Int J Periodontics Restorative Dent 2016;36(Suppl):S89–S97.
21. Caiazzo A, Casavecchia P, Barone A, Brugnami F. A pilot study to determine the effectiveness of different amoxicillin regimens in implant surgery. J Oral Implantol 2011;37:691–696.
22. Lang NP, Pun L, Lau KY, Li KY, Wong MCM. A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. Clin Oral Implants Res 2012;23(Suppl 5):39–66.
23. Duewelhenke N, Krut O, Eysel P. Influence on mitochondria and cytotoxicity of different antibiotics administered in high concentrations on primary human osteoblasts and cell lines. Antimicrob Agents Chemother 2007;51: 54–63.
24. Cardaropoli G, Araújo M, Hayacibara R, Sukekava F, Lindhe J. Healing of extraction sockets and surgically produced - augmented and non-augmented - defects in the alveolar ridge. An experimental study in the dog. J Clin Periodontol 2005;32:435–440.
25. Botticelli D, Berglundh T, Buser D, Lindhe J. The jumping distance revisited: an experimental study in the dog. Clin Oral Implants Res 2003;14:35–42.
26. Ho DSW, Yeung SCH, Zee KY, Curtis B, Hell P, Tumuluri V. Clinical and radiographic evaluation of NobelActive™ dental implants. Clin Oral Implants Res 2013;24:297–304.
27. Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. JAMA 2001;285:2498–2505.

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