AICRG, Part III: The Influence of Antibiotic Use on the Survival of a New Implant Design

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Purpose: The American College of Surgeons guidelines suggest that complex oral surgery may benefit from prophylactic antibiotic coverage. The use of preoperative antibiotics, postoperative antibiotics, or both during implant placement is a widely accepted practice in the United States, whereas dentists in other countries rarely use antibiotics. Purpose: The purpose of this study was to determine if antibiotic coverage at the time of implant placement improves the survival of the Ankylos implant. Methods: As part of a comprehensive, multicentered, multidisciplinary, prospective, independent, international clinical study, designed and coordinated in the United States by the Ankylos Implant Clinical Research Group (AICRG), the use of preoperative (several regimens) and postoperative antibiotics (yes/no) were carefully documented to assess their influence on improving survival. A total of 1500 Ankylos implants were placed and followed for a period of 3 to 5 years. The decision to use antibiotics and the regimen to be employed was made by the treating surgeon. Failure was defined as removal of the implant for any reason. All data were entered into a computerized database for analysis. Results: The use of preoperative antibiotics produced no significant improvement ($P = .21$, Fisher’s exact test) in survival compared with those placed without antibiotic coverage. There was no significant difference between the regimens defined as AHA-1990, AHA-1997, and Peterson’s recommendations. Conclusions: The results of this study suggest that there was little or no advantage to providing antibiotic coverage when placing this implant. These findings also suggest that the use of antibiotics for implant placement may not be as beneficial as once believed. If validated by other studies, the elimination of this practice for routine implant placement would represent a small but significant step forward in the reduction of unnecessary antibiotic use.
BACKGROUND

The development of resistant strains of bacteria is rapidly becoming a major concern among health care providers and researchers worldwide.1,2 Public health experts estimate that thousands of patients may die each year from infections caused by resistant bacteria. According to a US Geological Survey, drugs of all kinds, including antibiotics, are finding their way into the rivers, streams, ground water, and eventually into the tap water.3 The types of antibiotics listed as found in the US water supply include penicillin, tetracycline, vancomycin, chlorotetracycline, lincomycin, sulfamethazine, and azithromycin. This must be viewed by all health care professionals with concern.

Currently, the low levels of antibiotics found in the nation’s water supply are not believed high enough to be harmful to humans; however, there is a growing concern that the streams containing even the lowest levels of antibiotics may, at some future time, provide an ideal breeding environment for the development of “superbugs” that are resistant to today’s existing antibiotics.3 Preliminary results of a study done by the US government’s Environmental Protection Agency (EPA) show that some bacteria in these contaminated waters have already acquired resistance to the more common antibiotics.3

The use of antibiotic prophylaxis for patients believed to be at risk for infectious endocarditis or the loss of artificial joints is well accepted by dental health care professionals.4 In the United States, dentists have conscientiously complied with the guidelines established by the American Heart Association (AHA), the American Dental Association (ADA), and the American Association of Orthopedic Surgeons (AAOS) when treating patients determined to be at risk.5 The risk of infection in any surgical procedure depends on several patient factors, management procedures during implant placement, and the care of the surgical team in maintaining the basic principles of surgery and asepsis.6,7 Although many surgeons believe that antibiotic coverage for implant placement is not necessary, they continue to use them to protect against claims of malpractice. Protection against potential malpractice challenges, although a very real concern, should not be the only factor considered when making a decision as important as whether or not to utilize antibiotics in dental treatment. Some questions have been raised as to the benefits vs the risks of an allergic reaction associated with antibiotic prophylaxis, even when used for those patients who might be at risk for developing infectious endocarditis. The severity of potential reactions to antibiotics may represent an even greater risk to the patient than that of the patient developing infectious endocarditis.8

In view of the growing concerns that health care professionals have regarding the potential for an increase in new antibiotic-resistant bacteria, antibiotic prophylaxis guidelines are being reviewed and modified by health care professionals. The AHA has modified the recommended prophylactic regimen to guard against infectious endocarditis from 3 to 2 g of amoxicillin just prior to a surgical procedure and with no follow-up antibiotics recommended.9–11 For patients with an allergy to penicillins, 600 mg of clindamycin or 2 g of cephalexin are acceptable alternatives. In an advisory statement, the ADA and the AAOS recommended the use of prophylactic antibiotics only for patients with total joint replacement (but not when only screws and/or plates are present) and patients with compromised immune systems, Type I diabetes mellitus, previous joint infections, malnourishment, or hemophilia.12

Endosseous dental implant use represents one of the fastest growing areas of restorative dentistry. The guidelines from the American College of Surgeons suggest that complex oral maxillofacial surgery, which includes the placement of dental implants, may benefit from prophylactic antibiotic coverage. It is not uncommon in the United States for prophylactic antibiotics to be used at the time of implant placement in an effort to improve implant survival and prevent postoperative infectious complications. It can be estimated that about 51% of the endosseous dental implants are placed using preoperative antibiotic coverage and about 98% with postoperative coverage (H.F.M. and S.O., unpublished data, 2001). Several reports from a major comprehensive, prospective clinical study13,14 suggest that the use of prophylactic antibiotics for implant placement significantly improves short- and long-term implant survival. A comprehensive review of the scientific literature, however, fails to provide convincing evidence that their use is effective in most clinical cases.15 In 1998, Gynther et al15 reported that early implant failures may well be related to inadequate antibiotic premedication.

In a timely effort to reduce the overutilization of antibiotics,
based on their concerns for patient safety, many dentists placing implants have adopted this new ADA-AAOS “1-dose regimen” for the placement of implants. It is interesting to note that in this era when “evidence-based” dentistry is being promoted, the only evidence for many clinical procedures still is based on anecdotal information or consensus conferences and not on data from scientific and comprehensive clinical trials. The reduced 1-dose regimen represents a logical first-choice step toward the reduction of antibiotics in implant dentistry. Patients exposed to long-term pre- or postoperative antibiotic regimens may actually become sensitized to the antibiotic. Bacteria may develop a resistance to a specific antibiotic when exposed to long-term, ineffective dose regimens. The 1-dose regimen reduces the potential risk of the patients becoming sensitized to a specific antibiotic, as well as the potential for microbiota to develop a resistance. It has been reported that resistant strains can develop within 48 hours, even in the presence of high levels of antibiotics. A delay in the administration of antibiotics after bacterial contamination is not believed to provide an effective benefit.

The amount of prophylactic antibiotics in implant dentistry is small in relation to total antibiotic use and has not currently been identified as being a major concern by health care professionals in the United States. The recent increases in resistant bacteria observed in the health care environments, however, represents a major concern that requires all health care professionals to closely examine each procedure in which prophylactic antibiotics are frequently used in order to determine their true effective-ness. As responsible members of the health care professions, dentists must constantly be looking for effective clinical methods to reduce risk to patients, the environment, and the potential for resistant bacteria to develop.

A review of the dental implant literature fails to identify a single valid randomized, prospective clinical study that had as a specific aim the scientific assessment of any benefits that the use of antibiotics might have during the placement of endosseous dental implants. Only anecdotal reports and opinions exist, and these are constantly changing. Some reports appearing in the dental literature continue to suggest that there is little or no scientific basis for the use of antibiotic prophylaxis in dentistry, other than for patients known to be “at risk.” The possibility that the use of antibiotics for implant placement is not effective or constitutes misuse should be considered by the dental research community. The design of comprehensive clinical studies of endosseous dental implants should include the gathering of antibiotic use data.

**PURPOSE**

The purpose of this section of the comprehensive clinical center was to determine if the implants that were provided antibiotic coverage during implant placement had better survival than those without coverage. In addition, several different regimens were defined (see “Methods”) that were used for the purpose of the analysis of data in this study in an effort to determine if any one regimen produced better clinical survival than each of the others or if they were all equal (AHA in 1990 [AHA-90], AHA in 1997 [AHA-97], and Peterson’s recommendation in 1990). The use of antibiotics following implant placement (postoperative antibiotic use) was also examined.

**METHODS**

A total of 1500 Ankylos implants (Friident GmbH, Mannheim, Germany) were placed and followed

| Antibiotic regimen and dosage classifications used for preoperative data analyses |
|------------------------------|-----------------|-----------------|
| **Antibiotic** | **Peterson** | **AHA (1990)** | **AHA (1997)** |
| Amoxicillin | 1000 mg | 3000 mg | 2000 mg |
| Ampicillin | 1000 mg | 2000 mg | 2000 mg |
| Ancef | 1000 mg | 1000 mg | — |
| Azithromycin or clarithromycin | — | 500 mg | — |
| Cefazolin | 1000 mg | 1000 mg | 1000 mg |
| Cephalaxin or cefadroxil | — | — | 2000 mg |
| Cephradine | 1000 mg | 1000 mg | — |
| Cefadyl | 1000 mg | 1000 mg | — |
| Ciprofloxacin | 1000 mg | 1000 mg | — |
| Clindamycin | 300 mg | 300 mg | 600 mg |
| Doxycycline | 100 mg | — | — |
| Erythromycin | 1000 mg | 1000 mg | — |
| Keflex | 1000 mg | 1000 mg | — |
| Nafillin | 1000 mg | 2000 mg | — |
| Tetracycline | 500 mg | — | — |
| AQ-Penicillin | 2.0 million IU | 2.0 million IU | — |
| Pen VK | 1000 mg | 2000 mg | — |
| Anacin | 1000 mg | 2000 mg | — |
| Vancomycin | 1000 mg | 1000 mg | — |
for a period of 3 to 5 years at 34 clinical research centers. Of these, there were 30 VA Medical Centers, 2 US dental schools, and 2 foreign dental schools (Taipei, Taiwan, and Seoul, Korea). Prior to implant placement, the surgeon decided if either preoperative antibiotics, postoperative antibiotics, or both were to be used based upon his or her clinical judgment of the situation. The regimens used by each center for each patient varied somewhat by antibiotic type, dosage, and time of administration. The analyses to determine the influence of preoperative antibiotics were performed in several ways: (1) were any pre- or postoperative antibiotics used? and (2) were the dosages (as defined by the AHA-90, AHA-97, and the Peterson regimens) used effective in improving survival? The classes of antibiotics and effective dosage levels are shown in the Table. The postoperative antibiotic analyses were classified as to whether any antibiotic, regardless of time or dosage, was administered or not.

**RESULTS AND DISCUSSION**

Comparisons of the different antibiotic regimens described above are shown in Figure 1A and B, Figure 2A and B, and Figure 3. The first comparison of interest was the survival of implants placed with or without preoperative antibiotic coverage (Figure 1A). The second comparison was between what was considered to be a regimen that “adequately” or “inadequately” complied with the AHA recommendations for prophylactic antibiotic regimens in 1990 (Figure 1B). The AHA recommendations were revised in 1997, and the third comparison was between regimens that were considered to be an adequate or inadequate regimen based on the recommendations in effect at that time (Figure 2A). The final recommendation studied was that by Peterson as to the effectiveness of the regimens that complied with his recommendations (Figure 2B). The influence as to whether or not postoperative antibiotics were used is shown in Figure 3.

**Preoperative antibiotics: yes/no**

The survival of the Ankylos implants that were or were not covered by preoperative antibiotics is shown in Figure 1A. A total of 1175 implants were placed using preoperative antibiotics, and their survival was 96.3%. For the 354 implants that were placed without the use of preoperative antibiotics, survival (95.2%) was nearly identical to those with antibiotic coverage. The slight differences between the groups was not statistically significant ($P = .21$).

**AHA-90: adequate or inadequate regimens**

Survival was also compared for those implants receiving adequate or inadequate regimens of antibiotics based on the AHA recommendations (the Table) in effect in
1990 (Figure 1B). The implants that received adequate AHA-90 recommended preoperative antibiotics dosages exhibited 95.7% survival compared with 98.1% for those covered by an inadequate AHA-90 recommended preoperative antibiotic regimen. These differences were not significantly different ($P = .18$).

**AHA-97: adequate or inadequate regimens**

A comparison of the survival of implants receiving an adequate AHA (the Table) antibiotic regimen in effect in 1997 resulted in survival at 95.9% compared with those with inadequate coverage that resulted in 97.2% of the implants surviving (Figure 2A). These differences were not statistically different ($P = .25$).

**Peterson's recommendations–1990: adequate or inadequate regimens**

In 1990, Peterson recommended a slightly different antibiotic regimen for some antibiotics (the Table). A comparison of adequate and inadequate regimens based on this recommendation appears in Figure 2B. Those with adequate coverage exhibited 96.5% survival compared with 96.3% for those with inadequate coverage. This was not found to be statistically significant ($P = .69$).

**Postoperative antibiotics: yes/no**

Antibiotic use during the immediate postoperative period was grouped into a postoperative antibiotic “yes” group, regardless of the regimen used. If antibiotics were not provided for this period, the implants were placed into a postoperative antibiotics “no” group. Figure 3 shows that implant survival was in the 97% range regardless of whether postoperative antibiotics were used or not. No significant difference was found ($P = .79$).

**SUMMARY AND CLINICAL RELEVANCE**

The use of pre- and postoperative antibiotic prophylaxis during the placement of endosseous dental implants is relatively common in the United States. In recent years there has been an increase in the amounts of all types of antibiotics in the nation’s water supply. Public health officials are concerned that while they do not pose a threat to the health of individuals, there has been a significant increase in the number of bacteria that are developing resistance to some antibiotics.

A total of 1500 implants were placed as part of a major, comprehensive, multicentered, multidisciplinary, independent, international clinical study of a new implant design. The treating dentist decided if and how much preoperative and postoperative antibiotics would be used. The results suggest that the survival of the Ankylos implant was not significantly different for those placed with or without antibiotics.
antibiotic coverage. They also tend to support the beliefs of many oral and maxillofacial surgeons that antibiotic coverage is not necessary if careful surgical procedures are followed. The prevailing position on antibiotic use for implant placement in many of the European countries is that they are not necessary. Anecdotal reports tend to suggest that the survival rates are comparable to those in the United States. If these findings can be confirmed by other independent clinical studies of endosseous implants, the reduction or elimination of the use of antibiotics in implant dentistry may follow—with the exception of patients who are at a significant risk for other health problems.

Some dentists have already adopted the ADA-AAOS regimens for infectious endocarditis prophylaxis for implant placement. Although the use of antibiotics in dentistry represents a small portion of the total antibiotics used in the United States, any reduction would be a “first step” toward reducing the antibiotics that are now appearing in the water supply. If the dentists in other countries have good clinical success without the use of antibiotics, dental practitioners in the United States should seriously consider the potential ramifications of taking no action on this issue or gathering data in scientific clinical studies. The results found in this study differ considerably from those reported in 2 papers by clinical investigators associated with our clinical research group. This difference could be due to factors such as differences in the patients included in the study or the clinicians placing and restoring the implants. In view of the significant increases in the antibiotics being found in the tap water of the United States, the use of antibiotics for the routine placement of endosseous dental implants needs to be researched in detail in randomized, prospective clinical trials to provide more definitive answers to this pressing question: Is antibiotic prophylaxis necessary to improve implant survival?

CONCLUSIONS
The following conclusions can be made:

- Neither preoperative nor postoperative antibiotic coverage at the time of surgical placement improved the high success rate observed for the Ankylos implant in this independent, prospective, multicentered, multidisciplinary clinical study.
- In view of these findings, the question of antibiotic coverage needs to be studied in comprehensive, randomized, prospective, and scientific clinical trials.

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**Note**

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