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Use of Antibiotic Prophylaxis in Ear Surgery

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A prospective, double-blind, randomized, placebo-controlled study was performed to evaluate the effect of antibiotic prophylaxis in ear surgery. The present study reports on the results of 750 patients, half of whom received cefuroxime for 1 day, the other half, placebo. All postoperative infections occurring within 2 weeks after the intervention were recorded, together with several preoperative and perioperative parameters. It is concluded that exploratory tympanoplasties (including stapedotomy) and "dry perforation" tympanoplasties should be considered "clean" operations according to the American National Research Council and do not benefit from antibiotic prophylaxis. On the other hand, tympanoplasties performed on draining ears and on ears with cholesteatoma should be considered "dirty" operations for which antibiotic prophylaxis may decrease the postoperative infection rate by factor 3. All postoperative infections healed without sequels under proper treatment, except for three that resulted in graft necrosis—one in the placebo group and two in the cefuroxime group. In consequence, prophylaxis may not be mandatory in the dirty group, although the authors advocate its use for the sake of patient and surgeon comfort.

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INTRODUCTION

The ubiquitous use of antibiotics over the years has dramatically reduced the morbidity and mortality of infectious diseases. Yet the present era is characterized by the emergence of resistant strains of bacteria that may become responsible for serious health problems.[1] The cost of both the overuse of antibiotics and the treatment of the infections with multiresistant germs is also becoming a matter of concern. Therefore health care policy should focus on how to establish a rational attitude toward antibiotics. A safe reduction in the use of antibiotics can be based only on solid comparative studies with evidence authoritative enough to be able to convince not only the academic people but also the physician "in the field."

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Antibiotics are widely used in a prophylactic scheme for surgery. The guidelines of the American National Research Council (NRC) for general surgery restrict the prophylactic use of antibiotics to specific types of surgery and in any case for a period not exceeding 24 hours.[2] For ear surgery no consensus exists concerning whether to administer antibiotics or not. Still, many ear surgeons give antibiotics for 5 or 7 days.

To the best of our knowledge, only one prospective trial has been published to evaluate the use of antibiotic prophylaxis in ear surgery, and it reported no benefit of the prophylactic use of antibiotics.[3]

MATERIALS AND METHODS

A prospective, double-blind, placebo-controlled, and randomized study was carried out to evaluate the prophylactic effect of the antibiotic cefuroxime. The study design was approved by the Ethical Committee of St. Augustinus Hospital.

All patients undergoing ear surgery from January 1, 1993, to June 1, 1995, entered the study. Patients undergoing otoneurosurgery or cochlear implant surgery, patients who had taken systemic antibiotics during the week preceding the operation, patients with diabetes or immunodeficiency, and patients who needed endocarditis prophylaxis were excluded. Randomization was performed by computer in balanced sets of 50 cases (25 placebo + 25 cefuroxime). Blinding was performed by the hospital pharmacist (A.V.), who kept the randomization scheme and delivered consecutively numbered vials to the anesthesiologist. The anesthesiologist administered the blinded vial. The postoperative evaluations were carried out by the ear, nose, and throat (ENT) residents. In case of infection the study coordinator (P.G.) had to confirm the findings and keep a record of them in the patient's study file.

Cefuroxime was administered (1.5 g intravenously [IV]) at the moment of induction (approximately 30 minutes before incision) and 6 hours later. In case of operations lasting longer than 6 hours, a third injection of 1.5 g was given 12 hours after the first one. The placebo was blinded and given in the same scheme.

The surgical procedures were carried out according to the general rules of sterility. Surgery for otosclerosis was performed by means of the stapedotomy technique with a whole-Teflon prosthesis interposition.[4,5] Most tympanoplasties made use of the tympanoossicular allograft technique, for which the grafts were processed according to the stringent legal procedures as defined by the Belgian Law on Tympanoossicular Allograft Banks.[6,7] The postoperative packing contained an antibiotic ointment (oxytetracyclin and polymyxin B).

At the time of surgery the administrative data of the patients were recorded, together with the name of the surgeon, the type of surgery, the time of antibiotic administration, and the du-

ration of the surgery. The patients were evaluated 2 and 7 days after surgery and at the first ambulatory control (basically, 14 days after surgery).

Postoperative infection was defined by one of the following features: fever, wound inflammation, wound secretion, myringitis, or otitis media. In case of infection, the case was marked as such; different parameters were carefully noted (such as site, symptoms, and signs of infection), and a bacteriologic swab was taken. The surgeon was allowed to break the code of the drug and prescribe proper antibiotic therapy. The fate of the ear (at least 3 months later) was also recorded.

Parametric and nonparametric statistics were used to describe the different variables. Student's *t*-tests were used to compare parametric data. Chi-squared tests with Yates correction and Fisher Exact Tests were used to compare nonparametric data. The level of significance was set at 5 % ($P < 0.05$). The present study's design was able to detect a reduction in postoperative infection by factor 3 or more. All statistics were performed on a personal computer with the Statistica program for Windows version 4.1.

RESULTS

Seven hundred fifty cases entered the trial; 50.7% received cefuroxime, and 49.4%, placebo. The overall infection rate was 3.9%; 2.6% required systemic antibiotics, and 0.4%, topical antibiotics; 0.9% did not require antibiotics. Most infections were wound infections (1.9%), 1.4% were ear infections (external otitis or otitis media), and 0.6% were called "infections of unknown origin." The causative agents were *Staphylococcus aureus* (1% of the total study population), *Staphylococcus epidermidis* (0.1%), *Pseudomonas aeruginosa* (0.6%), and *Proteus mirabilis* (0.4%). The infections rate was 4.7% in the placebo group compared with 3.1% in the cefuroxime group. Therefore cefuroxime prophylaxis protects the patient against postoperative infections by factor 1.5, which is not statistically significant. The time course of this protection (Fig. 1) shows a protective effect of cefuroxime by factor 3 during the first week after surgery (13 infections in the placebo group versus 4 in the cefuroxime group) but steadily decreasing afterward. This early protection by factor 3 is statistically significant ($P < 0.05$).

Sixty-two percent of the cases received the first dose within 2 hours before incision (Fig. 2). Thirty-eight percent received the first dose after incision, which is too late, according to the guidelines of the NRC. Yet the incidence of postoperative infections did not differ between these groups. Figure 3 shows the age distribution of the study group. The infected cases occurred over all patient ages. Figure 4 shows the duration of the surgical procedures. The infected ears were ears with operation times averaging 3.4 hours, compared with 2.1 hours for the noninfected ears ($P < 0.0001$). Figure 5 shows the types of surgery. All infections occurred in the tympanoplasty group, which was statistically significant ($P < 0.005$). All infections healed without sequels under proper therapy (either local care or antibiotic therapy) except for three cases that resulted in graft necrosis—one case in the placebo group and two in the cefuroxime group.

The relative risk of different preoperative conditions of the ears is depicted in Figure 6, which shows a low risk (<5%) for normal tympanic membranes and dry perforations and a high risk (>10%) for wet perforations and cholesteatomas.

No adverse events were recorded, except in one case in which the patient had a mild allergic reaction while receiving cefuroxime (prevalence = 0.3%) that prompted discontinuation of the drug.

DISCUSSION

The Antwerp School of Otology was established by the late Jean Baron Marquet whose major contributions to ear surgery are acknowledged worldwide. Otosclerosis operations are performed according to the calibrated-hole stapedotomy procedure.[4,5] Tympanoplasties are mainly performed with the use of tympanoossicular allografts.[6,7]

Until the present study was initiated, it was a custom to administer antibiotics during an entire week to prevent postoperative infections. As the guidelines of the NRC were discussed, some elements of otosurgery were considered to be too particular to make these guidelines applicable without further debate. The introduction of a foreign material (Teflon prosthesis) in the middle ear with "free access" (stapedotomy hole) to the inner ear may turn a possible infection into a serious threat for irreversible sensorineural damage. The use of tympanoossicular allografts is different from fascia and may be considered a

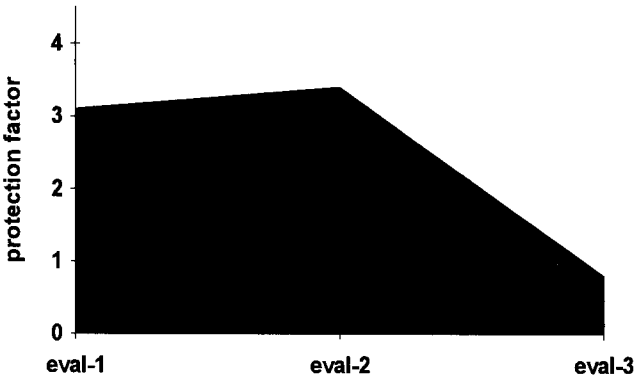

Fig. 1. The protective effect of cefuroxime compared with placebo, expressed as a ratio of frequency of postoperative infections in the placebo group to frequency of postoperative infection in the cefuroxime group. Eval-1 = 2 days after surgery; eval-2 = 7 days after surgery; eval-3 = first ambulatory control (basically 14 days after surgery).

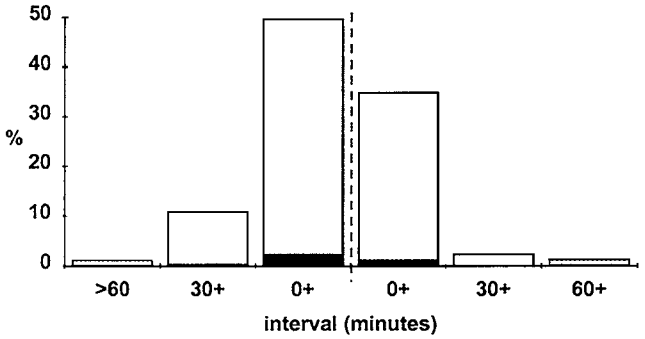

Fig. 2. Histogram of the time of administration of the prophylactic drug with respect to the surgical incision. Dashed line = moment of incision; X axis = three time frames of 30 minutes before and after incision; black bars = infected ears; white bars = noninfected ears.

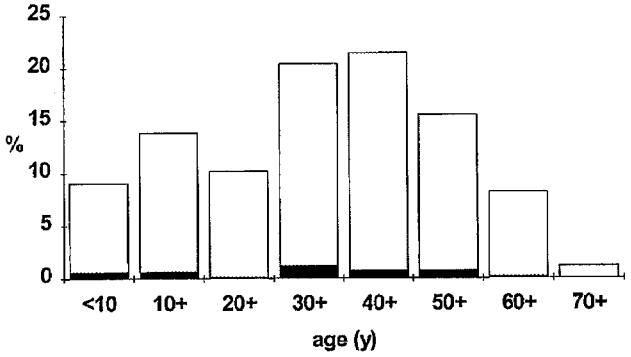

Fig. 3. Histogram showing the age distribution per decade. Black bars = infected ears; white bars = noninfected ears.

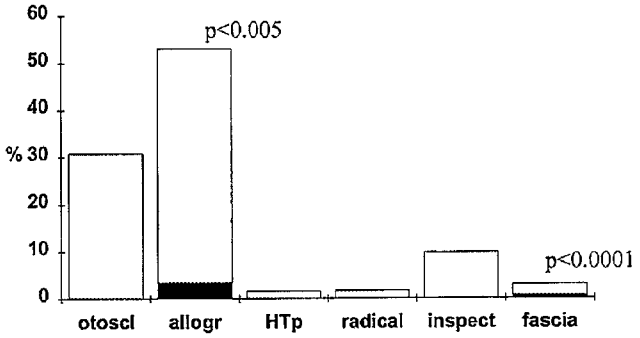

Fig. 5. Histogram of the different kinds of surgery. Black bars = infected ears; white bars = noninfected ears; otoscl = otosclerosis; allogr = tympanoplasty using tympanoossicular allografts; HTp = tympanoplasty using a partial tympanic allograft to restore a small drum perforation; radical = radical mastoidectomy; inspect = middle ear inspection (tympanotomy) with no reconstruction; fascia = tympanoplasty with a fascia graft in underlay.

transplantation requiring extra precautions. The risk of bacterial contamination may be higher than in general surgery because of the open contact of the middle ear with the nasopharynx and because the outer ear canal is not sterilized before surgery.

Hence the present study was set up to verify whether antibiotic prophylaxis is advantageous in ear surgery. It was taken for granted that prophylaxis should in any case be limited to a short perioperative period. Cefuroxime was chosen as the study drug because of its activity against gram positive and many gram negative strains and because of good penetration in the meninges and, in consequence, in the perilymphatic fluid of the inner ear. Cefazolin might also be a drug of choice, although its gram negative activity is slightly less, as is its perilymphatic penetration.

The results of the present study show no antibiotic protection either in otosclerosis operations or in dry perforation tympanoplasties. The incidence of postoperative infections in these two groups is low (<5%) and well in the range of the clean surgery as defined by the NRC. Thus the authors propose to define these two types of ear surgery as clean ear surgery that does not justify antibiotic prophylaxis.

In contrast, antibiotics, when given as in the present study design, may decrease the incidence of early postoperative infections by factor 3 (which is statistically significant) in draining ears and cholesteatomas. The incidence of postoperative infections in these groups is high (>10%), which is in line with the dirty surgery of the NRC. Probably the duration of these interventions strongly contributes to the risk of postoperative infections, because most infections occurred in operations that had lasted longer than 2 hours (average duration, 3.4 hours).

The protective effect of antibiotics lasts for 1 week (Fig. 1), which gives additional evidence that such a short prophylactic scheme has a good efficacy. Yet it is not "full protection." The ears are protected against infections (mainly wound infections) that do little harm and that can be easily treated if necessary without any serious sequels. Therefore it does not seem to be mandatory to give this type of prophylaxis at all. Yet, the authors do advocate the use of antibiotics in the aforementioned cases to minimize the discomfort of an infection for both patient and surgeon. Indeed, for the final outcome it does not make any difference whether prophylaxis (1 day) is given to all and treatment (7 to 10 days) to a few, or prophylaxis to no one and treatment to three times more patients. Also, the total amount of antibiotics given in each of the two schemes is roughly the same. For instance, if 100 patients get pro-

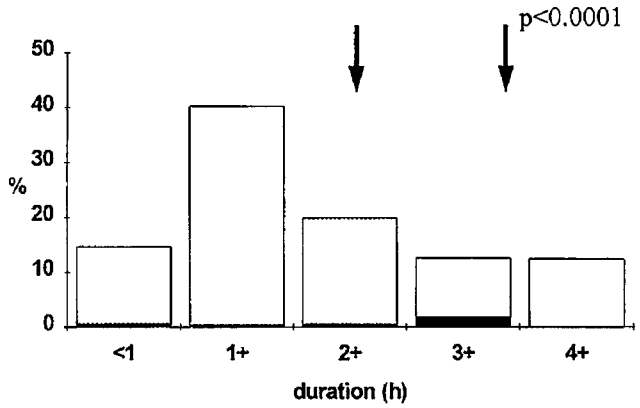

Fig. 4. Histogram of the duration of the interventions per hour. Black bars = infected ears; white bars = noninfected ears; arrows represent duration of intervention in the noninfected (left) and the infected (right) ears.

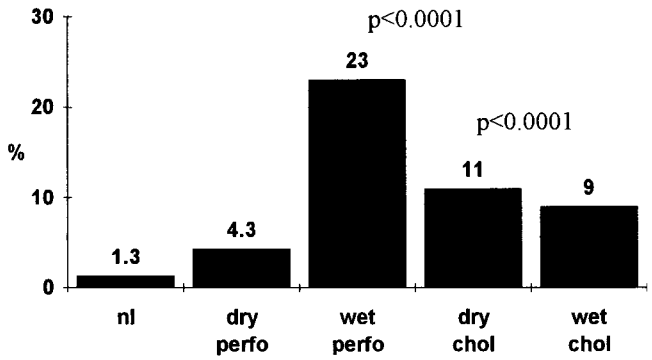

Fig. 6. Histogram of the perioperative state of the ear. nl = Normal (intact drum and ventilated middle ear); perfo = drum perforation; chol= cholesteatoma; wet = draining.

phylaxis (100 daily doses), approximately 8 require treatment for postoperative infection (8 × 7 days = 56 daily doses), which makes a total of approximately 156 doses. If no prophylaxis is given (0 daily doses), approximately 24 patients will require treatment (24 × 7 days = 168 daily doses), which makes a total of 168 doses. In consequence, the choice of whether prophylaxis should be given does not depend on these factors; therefore other factors will determine the choice. Since any infection is a burden both for the patients and their physician and necessitates additional visits to the physician, the authors believe that in the absence of other criteria, prophylaxis may be advocated to reduce the number of postoperative infections.

Antibiotic prophylaxis as given in the present study does not protect against those very rare postoperative infections that result in total graft necrosis. In the present study these infections were caused by aggressive gram-negative germs that were susceptible only to piperacillin, aminoglycosides, and quinolones. Nevertheless, the authors do not believe these drugs should be used for prophylactic purposes; specifically, piperacillin and the aminoglycosides should not be used because of their cost and side effects, and the quinolones, because of their alleged high potential to generate resistant bacterial strains. We believe the ecologic and economical advantages of this restrictive and rational prophylactic scheme is worth the cost of one case of graft necrosis in every 250 cases. Yet, this statement is open for debate, and we invite the microbiology experts to comment on this.

CONCLUSION

The authors state that otosclerosis and dry perforation tympanoplasties should be considered clean surgery according to the NRC and that, in consequence, antibiotic prophylaxis is not needed. In contrast, draining ears and cholesteatomas should be considered dirty surgery, according to the NRC, for which antibiotic prophylaxis is not mandatory in terms of survival of the graft but in which prophylaxis is justifiable in terms of comfort and cost-benefit ratio when taking into account all costs related to an infection.

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