Letter to the Editor

Empirical therapy and teicoplanin use in periprosthetic joint infections

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To the Editor,

With the help of improved health care the life expectancy of an individual is increased, and so is the need for prostheses. Recent technology has enabled many people to obtain prostheses, but this also leads to an increase in prosthesis-related infection (1). Periprosthetic joint infection (PJI) requires a multidisciplinary approach, including the correct diagnosis, good surgical care, and appropriate antibiotic treatment. Surgical interventions include debridement and retention, one- or two-stage exchange, and sometimes even arthrodesis or amputation. The duration of the antibiotic therapy differs according to the etiologic agent, surgical intervention type, and laboratory and clinical response of the patient, so the antibiotic therapy can last from 4–6 weeks to several months (2). Several antibiotics, especially those with gram-positive coverage, are used for first-line treatment. Teicoplanin is among the frequently used antibiotics because of its gram-positive coverage and the advantage of once daily use. Because the target coverage of empirical therapy is affected by different parameters and many times gram-negative coverage is also provided, empirical therapy does not seem to be standard in routine practice in all centers. In this retrospective study we aimed to review our experience of treatment, particularly the use of teicoplanin, of a series of PJI cases.

We performed a cross-sectional observational study. Patients who were diagnosed with acute PJI and followed in the Ankara Atatürk Training and Research Hospital between January 2014 and July 2015 were included. The hospital is a tertiary-care referral hospital and admits difficult-to-treat PJI cases. The PJI diagnosis was based on the criteria stated by the clinical practice guidelines of the Infectious Diseases Society of America and cases of acutely warm, swollen, painful, erythematous joints were

diagnosed as "acute PJI" (2,3). The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Ethical committee approval was not needed because of the study design. Demographic findings and details of the management of PJI were obtained from the database of the hospital and the researchers' records of the patients. Microsoft Excel was used for statistical analysis. Results are given in numbers and percentages.

Twenty-two patients with the diagnosis of acute PJI, either early acute or delayed acute (4), were included: 13 (59%) women and nine (41%) men, with a median age of 68 years (39–87 years). Ten (45%) patients had PJI of the hip, while the remaining patients had PJI of the knee (n = 12, 55%). All patients (100%) presented with warm, swollen, and painful joints. None of them had wound discharge. Median laboratory values were as follows: white blood cell (WBC) count, 7800/μL (5800–15,660/μL); C-reactive protein (CRP), 35 mg/L (5–93 mg/L); and erythrocyte sedimentation rate, 55 mm/h (30–107 mm/h). Five (24%) patients had diabetes mellitus, one (5%) had rheumatoid arthritis, and three (14%) had malignancy. All but one of the patients had previous interventions for the treatment of PJI: either debridement and retention (n = 2, 0.9%) or one-stage (n = 2, 0.9%) or two-stage exchange operations (n = 17, 77%). The causative agents of PJI are shown in Table 1. Fifteen (68%) patients received empirical antibiotic therapy. Details of antibiotic therapies for the management of PJI were available for 19 patients (Table 2). In five (23%) patients, rifampicin was added to therapy. Five patients (23%) needed changes in antibiotic therapy in follow-up: from ampicillin sulbactam + ciprofloxacin to teicoplanin + sulbactam cefoperazone (n = 4, 18%) and from teicoplanin + ciprofloxacin to antifungal therapy (n = 1, 5%) according to either clinical unresponsiveness

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Table 1. Causative agents of PJI (n = 22).

	n (%)
Gram-positive	9 (41)
Staphylococcus aureus	2
Coagulase-negative staphylococci	6
Enterococcus faecalis	1
Gram-negative	6 (27)
Escherichia coli	3
Other gram-negative bacteria	3
Fungi	1 (5)
Non-*albicans Candida*	1
Unknown	6 (27)

or culture results. Other than one patient who needed multiple operations and suppressive antibiotic therapy, the other patients responded to therapy (96%). When those two who were under antifungal therapy and under suppressive therapy were excluded, the median duration of antibiotic treatment for two-stage operations was 6 weeks (4–8 weeks), while it could be prolonged up to 6 months for one-stage operations. The patient whose treatment was changed to antifungal therapy needed multiple debridement after a two-stage exchange operation. Previously he was under teicoplanin plus ciprofloxacin therapy because of a PJI caused by *Enterococcus faecalis*. That PJI was under control and the prosthesis was removed, but non-*albicans Candida* was cultured from tissue and synovial fluid samples of the patient in the second stage of the operation. Two more cultures of synovial fluid showed the same organism afterwards. Antifungal therapy was started with amphotericin B (4 weeks), followed by voriconazole (1

months), and later continued with fluconazole for up to 1 year in duration. He recovered without any sequelae.

In our study, the median WBC count was within normal limits and CRP levels were increased only by 6- to 7-fold, which was unhelpful for definitive diagnosis. Main findings for PJI diagnosis were based on some clinical findings like pain, warmth, swelling, and redness of the affected joint and in addition to these either purulence of synovial fluid or growth of the etiologic agent from tissue or synovial fluid culture. Delayed diagnosis can cause harmful effects to prostheses. Clinical findings guided our prompt diagnosis. The empirical therapies of PJI mainly included broad-spectrum antibiotics because of the possible nosocomial source of infection in patients who had multiple operation histories. As seen in our results, almost one-third of the patients had gram-negative etiology and the agent was unknown in many patients. Thus, the empirical treatment had gram-negative coverage as well. Teicoplanin was the most preferred antibiotic for gram-positive coverage, with a successful outcome. Still, one patient needed suppressive antibiotic therapy while another patient experienced fungal PJI after a long-term broad-spectrum treatment.

There are limitations of this study. It was a retrospective study and the relation between therapy duration and exact clinical and laboratory response was not closely monitored. Although we have records, the details of synovial fluid analysis and surgical interventions were not available for all subjects and this retrospective study cannot state the success of medical therapy alone. The details of surgical interventions were lacking for some patients. Synovial fluid analysis was done for all patients but the detailed results were not available for all patients.

In conclusion, although there are many advantages of teicoplanin use in PJI (good soft tissue and bone concentrations, administration once a day in outpatient parenteral therapy, tolerability, safety) and it is even

Table 2. Empirical antibiotic therapies for PJI (n = 19).

	n (%)
Teicoplanin ± one of the following: Ciprofloxacin/sulbactam cefoperazone/imipenem/piperacillin tazobactam	9 (47)
Ampicillin sulbactam ± ciprofloxacin	4 (21)
Ertapenem	2 (11)
Daptomycin	1 (5)
Fusidic acid	1 (5)
Trimethoprim-sulfamethoxazole	1 (5)
Cefazolin	1 (5)

suggested for the prophylaxis (4), randomized, controlled, prospective studies (which are already planned by the authors of this study, according to results of a current observational study) are needed for documenting its advantages in cases of PJI.

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