Reply to Krause et al

TO THE EDITOR—We have read with interest the letter by Krause et al [1] highlighting some important aspects of our recent publication [2]. Their interesting remarks deserve some comments.

Prosthetic joint infections (PJIs) are a highly complex process that involves different specialists in its management [3]. Not only the microbiological outcome is of importance, but also the patient’s functional prognosis and life expectancy [4, 5]. In recent years, Zimmerli et al’s algorithm [6] for PJI has been most useful in identifying the more suitable patients for debridement, antibiotics, and implant retention (DAIR). However, the decision of removing the prosthesis in patients not meeting Zimmerli’s criteria is not straightforward. DAIR offers the opportunity of curing and keeping the implant, thus saving the patient’s bone stock, improving the likelihood of a better functional status, and also reducing healthcare costs [5]. Importantly, the removal of a recently cemented prosthesis should be balanced with the risks of a complex and bleeding surgery, which may be not be advisable in older and fragile patients, in whom DAIR may control the infection [3]. Furthermore, the decision of following a DAIR strategy does not necessarily prevent the possibility of a further prosthesis removal as salvage therapy, if finally the outcome is not favorable.

All these factors, together with Zimmerli’s criteria [6], are taken into account in the everyday clinical practice. From a realistic point of view, our case series, by far the largest published to date, answers the question of what is the likelihood of curing and retaining the implant of a patient with PJI by Staphylococcus aureus where a DAIR decision has been made. In this regard, we would like to stress that 48% of patients not meeting Zimmerli’s criteria were still cured and kept their prosthesis. Also, our results show that the overall prognosis of methicillin-resistant S. aureus PJI and methicillin-susceptible S. aureus PJI was similar, thus challenging the contraindication of performing DAIR on the former patients, as long as rifampin may be administered.

In regard to this antibiotic, the recommendation for using 450 mg twice daily by Zimmerli et al was based on empirical experience, but not on pharmacokinetic/pharmacodynamic studies. Thus, it should be noted that the recently published guidelines of the Infectious Diseases Society of
America recommend a slightly modified dose of 300–450 mg twice daily [3]. In fact, the most appropriate regime of rifampin in difficult-to-treat S. aureus infections is not well established and the debate remains open. The area under the curve (AUC)/minimum inhibitory concentration ratio seems to correlate better with the activity of rifampin [7], and thus 2 aspects must be taken into consideration. First, the most appropriate fraction of the daily dose: a fasting single morning dose seems to offer the best pharmacokinetic profile. It has been reported that the drug transport of rifampin is saturable, thus giving place to nonlinear increases in the Cmax and the AUC for single doses beyond 300–450 mg [8]. Second, the total daily dose: the values of AUC0–12 h after a dose of 450 mg and 600 mg are 30.7 μg×mL⁻¹×h and 40.2 μg×mL⁻¹×h to 57.3 μg×mL⁻¹×h, respectively, suggesting a similar pharmacokinetic profile for 450 mg twice daily and 600 mg once daily [9]. In any case, it is unlikely that the use of a 600 mg once-daily regimen in our patients could play a relevant role in the rate of failures observed in our series.

Finally, Table 4 of our work already states that the rate of failure among patients where no polyethylene exchange was performed was 56% [2]. Krause et al [1] ask for the specular data of this information: the polyethylene was not exchanged in 33% of patients finally presenting with failure vs 21% of patients who evolved favorably (P = .021). We would like to remark that, in spite of the retrospective nature of our study, most parameters reached an almost complete fulfillment, the exchange of removable components being the exception.

Notes

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