

Is it currently reasonable to offer short, 14-day antibiotic therapies after a surgical synovectomy in native joint septic arthritis?

Gjika *et al*¹ recently reported the non-inferiority of 2-week versus 4-week antibiotic therapy after systematic surgical washing (with or without synovectomy) in the management of septic arthritis. Although this randomised, controlled trial adds important new insights to the management of patients with infectious arthritis, it has several drawbacks that limit generalisation of the results.

First, the patients included in this study were not representative of a usual population of native joint septic arthritis patients. These patients had mainly septic arthritis affecting the small joints (metatarsophalangeal, metacarpophalangeal and proximal interphalangeal joints in 85% of cases). Moreover, in most cases, contamination occurred after direct inoculation following skin invasion (bite/scratch or post-traumatic), with only 4% of patients with systemic signs of infection. Finally, patients were included on the basis of having been treated with surgical drainage, the indications for which are largely centre dependent. These characteristics are probably explained by the monocentric design of the study. Native joint septic arthritis affects mainly large joints, such as the knees, ankles or hips in more than 70% of the cases. Moreover, haematogenous seeding is by far the most frequent type of inoculation (95%), with concomitant bacteraemia occurring in about 50% of the cases.²⁻⁴ The joints involved, as well as the bacterial species found in this study, clearly differ from those observed following systemic contamination: 50% of the pathogens were Gram-negative rods (25%) (with >10% *Pasteurella* sp.) or *Streptococcus* sp. (25%), with less than one-third the result of staphylococcal infection. This bacterial distribution is not representative of the type of septic arthritis either referred to emergency departments or managed in rheumatology/infectious disease departments.²⁻⁴ Importantly, the bacterial inoculum and virulence factors associated with haematogenous inoculation are very different from those found in direct inoculation through a bite or direct skin trauma. Underrepresentation of the bacteria capable of persistence and slow metabolism activity, such as *Staphylococcus aureus*, which more readily lead to relapses, may have artificially explained the non-inferiority and very high rate of cure without relapse, despite the short-term antibiotherapy observed by the authors. Moreover, the median final assessment was 2 months, while the classic, gold-standard definition of recovery without relapse in osteoarticular infections is 1 year.⁵ The authors reported three relapses (two of which occurred with *S. aureus* infection) over this short period of systematic follow-up. Few results are available on the radiological and functional evolution of the patients (one-third of the patients had follow-up X-ray) in the midterm and long term. This is even more important knowing the high prevalence of structural damage and functional sequelae reported in prospective series.⁶

From a methodological point of view, the authors calculated that 48 patients needed to be included in each arm, with a non-inferiority margin of 10%. This low number of subjects required was based on the hypothesis of a high healing goal of 96% at 2 months. If we consider a 1-year cure of 90%, closer to the objectives of other large, non-inferiority trials on antibiotic treatment of osteoarticular infections,^{5,7} with the same margin of error at 10% and the same power (1- β) of 80%, the number of patients needed would have been 112 patients in each group. In an ongoing study comparing 3 weeks versus 6 weeks of antibiotic

therapy in native septic joint arthritis (SHASAR, NCT0371692), the number of subjects required to demonstrate non-inferiority in the per-protocol analysis, with a 5% loss of patients included during follow-up, was calculated as 175 patients in each group.⁸ In addition, the authors did not explain why the number of subjects included (77 in each arm) was much higher than planned. Finally, subgroup analyses were performed in patients with hand and wrist involvement, although this was not initially planned (not declared on clinicaltrials.gov). Furthermore, these subgroup analyses were the only ones presented in the protocol population. It would have been interesting to report the results for the primary endpoint in the whole per-protocol population, as recommended in a non-inferiority study, to avoid the risk of overestimating efficacy, and not just present the results for hand and wrist involvement.⁹

Overall, even if these results are of great interest in an era of decreasing antibiotic treatment duration for ecological and economic reasons, it seems difficult to generalise and transpose the results of this study to daily practice for the management of native joint septic arthritis, and the conclusions drawn from this trial must be limited to patients with small joint infection caused by direct inoculation.

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