Dalbavancin was effective and safe after one year of treatment in a complicated osteoarticular infection caused by methicillin-resistant *Staphylococcus aureus*

Sir,

Osteomyelitis is a subacute/chronic infectious process that is often perpetuated by the presence of contaminated osteosynthesis material, which cannot always be removed due to the surgical risk involved. The success rate in chronic infection after removal and with prolonged antimicrobial treatment is less than 40%, leading to suppressive antibiotic strategies which in more than 50% of cases are withdrawn due to toxicity. Dalbavancin is a long-acting lipopeptide that has demonstrated outstanding in vitro activity against resistant Gram-positive bacteria. There is evidence for the effectiveness and safety of dalbavancin in biweekly dosing schedules. This could be useful in the treatment of infections that require prolonged treatment in home care units. However, we were unaware of the presence of side effects in suppressive treatments. We present the case of a young patient with infantile cerebral palsy, with functional dependence and a coxofemoral infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA), perpetuated by the migration of a Harrington bar used for vertebral fixation that invaded the coxofemoral joint. Intravenous dalbavancin was administered at a dose of 1,500 mg every 15 days for one year. Clinical and analytical parameters were determined to assess efficacy and safety.

A 41-year-old male with a history of chronic ischaemic-anoxic motor ischaemic encephalopathy of perinatal origin with total body involvement and tetraparietal expansion, symptomatic epilepsy since the age of 13–14 years, related to the encephalopathy. He has had a gastrostomy tube for more than 10 years due to swallowing spasticity with propulsive defaecation and aspiration pneumonia. Severe neuropathic scoliosis and operated in 1996 with Harrington bars and Luque wires. From July 2018 to March 2019 the patient developed up to four episodes of fever, lumbar pain, right coxalgia, wound on the external and upper thigh and a palpable collection (figure 1). In all of them, blood tests revealed leukocytosis with left shift, as well as elevated CRP levels. The CT scan showed Harrington bar migration, coxofemoral joint invasion and contiguous collection (figure 2). In the culture of the collection, MRSA was isolated in all episodes in association with *Proteus mirabilis* with different antibiogram phenotypes (figure 1, table 1). On up to three occasions the case was brought to the attention of the Spine Unit of the Traumatology and Orthopaedic Surgery Department, which rejected the removal of osteosynthesis material due to the high surgical risk involved. Suppressive treatment was started for 6 weeks, keeping the patient afebrile and with a progressive decrease in biomarkers (CRP). The suppressive treatment regimens were initially combinations of linezolid 600 mg every 12 hours associated with ceftriaxone 2g every 24 hours iv, in the first cycle of treatment the patient developed thrombopenia and cholestasis. Subsequent treatment regimens were performed with daptomycin 10 mg/kg/day and ertapenem 1 g/24h. After the third episode of clinical recurrence, the case was discussed again with the Spine Unit who accepted the surgical revision. The Harrington Bar that caused the invasion of the coxofemoral joint was removed. The contralateral one and the Luque wires, which were included in the spinal arthrodesis, were maintained.

Two months after removal, the patient returned to the emergency department with fever 38.5ºC, a spontaneous fistula with abundant purulent content, leukocytosis with left deviation and a CRP of 18.6 mg/dl. In the culture of the purulent material, MRSA with the same phenotype was reisolated. Suppressive treatment with dalbavancin 1500 mg every 15 days was started, with early clinical improvement, and the patient remained afebrile, and CRP decreased. During the months of

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Monitoring of temperature, CRP and liver function parameters. At review in December 2020 and January 2021, he remained asymptomatic.

Dalbavancin is a long-acting lipopeptide with a fatty acid chain responsible for its long-estimated half-life of up to 14 days, which has demonstrated extraordinary in vitro activity against resistant Gram-positive strains, specifically MRSA, where it has a MIC$_{50}$ of 0.03 mg/l and a MIC$_{90}$ of 0.12 mg/l, being 10 times more potent than vancomycin and 10 times more...
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| Table 1 | Staphylococcus aureus isolation with the same phenotype in all cultures (July and August 2018, January 2019). Proteus mirabilis isolation with different phenotypes. |
|---------|---------------------------------------------------------------------------------------------------|
| **Staphylococcus aureus** | **MIC** | **Interpretation** | **Proteus mirabilis (1st isolate)** | **MIC** | **Interpretation** | **Proteus mirabilis (2nd ans 3rd isolates)** | **MIC** | **Interpretation** |
| Penicillin | > 8 | Resistant | Amoxicillin | > 8 | Resistant | Amoxicillin | > 8 | Resistant |
| Amoxicillin/clavulanic | > 8/16 | Resistant | Amoxicillin/clavulanic | > 8/2 | Resistant | Amoxicillin/clavulanic | ≤ 8/2 | Susceptible |
| Oxacillin | 4 | Resistant | Cefoxime | ≤ 0,5 | Susceptible | Cefoxime | ≤ 0,5 | Susceptible |
| Gentamicin | ≤ 4 | Susceptible | Cefoxitin | ≤ 0,5 | Susceptible | Cefoxitin | ≤ 0,5 | Susceptible |
| Vancomycin | 2 | Susceptible | Ceftriaxone | ≤ 0,5 | Susceptible | Ceftriaxone | ≤ 0,5 | Susceptible |
| Clindamycin | > 0,5 | Resistant | Cefepime | < 1 | Susceptible | Cefepime | < 1 | Susceptible |
| Daptomycin | ≤ 0,5 | Susceptible | Aztreonam | 0,25 | Susceptible | Aztreonam | 0,25 | Susceptible |
| Linezolid | 4 | Susceptible | Meropenem | ≤ 0,12 | Susceptible | Meropenem | ≤ 0,12 | Susceptible |
| trimetoprim sulfametoxazol | ≤ 1/19 | Susceptible | Piperaclil-Tazobactam | ≤ 8/4 | Susceptible | Piperaclil-Tazobactam | ≤ 8/4 | Susceptible |
| Levofloxicin | > 2 | Resistant | Ciprofloxacin | 2 | Resistant | Ciprofloxacin | 0,5 | Susceptible |
| Dalbavancin | 0,06 | Susceptible | Gentamicin | 16 | Resistant | Gentamicin | ≤ 0,12 | Susceptible |
| | | | Amikacin | 8 | Intermediate | Amikacin | ≤ 0,12 | Susceptible |

Potent than linezolid [1, 2]. It has a protein binding of 93%, its elimination half-life is 372 hours (333–405) and it maintains a concentration of more than 8 mg/L for one month, both after infusion at a dose of 1000 mg on the first day, adding 500 mg a week, and maintaining a dose of 1500 mg every two weeks [3].

In clinical studies in skin and soft tissue infection, no differences were found with respect to sequential therapy with vancomycin and linezolid [4]. In the comparative study on skin and soft tissue infection, the primary efficacy and safety endpoints between different dalbavancin strategies. No differences were found at 14 days in the 20% reduction in erythema 48–72 hours after initiation of therapy, in clinical success or in adverse effects between the fractionated treatment schedule of 1,000 mg first dose with a second 500 mg per week or a single dose schedule of 1,500 mg [5], with both doses included in its data sheet. Dalbavancin is also active in the bacterial population embedded in the biofilm. Experimental models suggest that dalbavancin is distributed in bone, skin and joint tissue at concentrations above the MIC of S. aureus over long periods of time even after a significantly reduced dosing regimen [6], which would suggest prolonged treatment strategies with lower than standard doses while maintaining effectiveness [7].

In clinical studies in skin and soft tissue infection, there is no evidence that dalbavancin is distributed in bone, skin and joint tissue at concentrations expected to exceed the MIC for S. aureus over long periods of time after a significantly reduced dosing regimen [7], which would even suggest prolonged treatment strategies with lower than standard doses while maintaining effectiveness. There is also evidence of little or no toxicity during prolonged treatment in patients who have had toxicity with other drugs previously and in whom osteosynthesis material cannot be removed [8, 9].

Suppressive therapy was maintained for 1 year after removal of part of the osteosynthesis material with excellent tolerance and the patient remained asymptomatic 6 months after the end of treatment. The long half-life, which even allows removal of permanent vascular access in prolonged treatment, the in vitro activity against all Gram-positive bacteria, the activity in biofilm and its excellent tolerability make this antibiotic an extraordinarily useful tool in home hospitalisation units in general and particularly in suppressive strategies in comorbid patients when the implant cannot be removed.

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**CONFLICTS OF INTEREST**

The authors declare that they have no conflict of interest.

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