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Scientific letters

Ceftobiprole, a new option for multidrug resistant microorganisms in the outpatient antimicrobial therapy setting

Ceftobiprole, una nueva opción de tratamiento para microorganismos multirresistentes en el ámbito del tratamiento antimicrobiano domiciliario

Ceftobiprole is a broad spectrum fifth-generation cephalosporin. Ceftobiprole is approved in several European countries for the treatment of community-acquired pneumonia and hospital-acquired pneumonia, excluding ventilator-associated pneumonia. Respiratory infections in patients with bronchiectasis have special characteristics because they are frequently caused by *Haemophilus influenzae*, *Pseudomonas aeruginosa*, respiratory viruses, and less frequently, *Moraxella catarrhalis*, *Staphylococcus aureus*, and Enterobacteriaceae.[1] The high number of exacerbations leads to high antibiotic pressure. Ceftobiprole is stable for up to 24 h at 25 °C and protected from light, which allows for potential administration in OPAT.[2,3] There is limited experience and research data of its use at home. The specific characteristics of our OPAT programme have been described previously.[4]

We present the case of a 32-year-old male patient diagnosed with cystic fibrosis at the age of 5 (homozygous for the CFTR gene with the delta-F508 mutation) and colonized with multidrug-resistant (MDR) *Pseudomonas aeruginosa*, and methicillin-susceptible *Staphylococcus aureus* (MSSA) since 1995. A bipulmonary transplant was performed in October 2019 (8 months previously) with multiple subsequent complications. Mucoid phenotype *Pseudomonas aeruginosa* resistant to quinolones, piperacillin-tazobactam, aminoglycosides, ceftazidime, cefepime, and carbapenems was isolated in a sputum culture three months before. Susceptibility to ceftazidime/avibactam, ceftobiprole, and ceftolozane/tazobactam are not test routinely in our hospital. The patient was admitted at the beginning of June 2020 with fever and respiratory symptoms. Procalcitonin and C-reactive protein were compatible with a bacterial aetiology. Nevertheless, a cytomegalovirus serology and viral load were requested to rule out possible reactivation. Blood and sputum cultures were taken, without making identification. Urinary antigens for *Legionella* and *Streptococcus pneumoniae* were negative. Empirical treatment was started with piperacillin-tazobactam 4 g every 8 h, with no improvement after three days. A CT scan showed alveolar infiltrates compatible with an infectious cause. Taking into account the resistance pattern of *Pseudomonas aeruginosa*, we decided to start empirical treatment with ceftobiprole 500 mg over 2 h, every 8 h. Within 48 h, the patient became afebrile, the respiratory parameters improved, and acute phase reactants normalized. Since the patient was clinically stable, it was proposed that he continue antibiotic therapy at home in our OPAT programme. Ceftobiprole was prepared daily, diluted in 0.9% saline solution at a concentration of 3 mg/mL, then refrigerated. The antibiotic solution was administered by electronic pump over 2 h every 8 h. Three days after being discharged, the patient became asymptomatic, and ceftobiprole was stopped after 7 days of therapy. He showed no adverse events and no changes in the control analysis carried out at home. We examined him in the pneumology clinic one month later, with no clinical incidents. After 3 months of follow-up by telephone, he has shown no new episodes of infection.

To our knowledge this is the first case report providing a clinical and safety evaluation of ceftobiprole in OPAT. The stability of the drug using an elastomeric pump has not been tested.

A history of colonization or infection with resistant gram-negative bacilli in the previous 12 months, previous hospitalization with exposure to broad-spectrum antibiotics, and cystic fibrosis, among others, have been reported in the literature to increase the risk of resistant gram-negative bacilli. A recently published consensus statement based on a Delphi survey of expert opinion recommends the use of empirical therapy against resistant gram-negative bacilli, including *Pseudomonas aeruginosa*, in patients with any of these risk factors.[1] Ceftobiprole could be a good option in this scenario due to its broad spectrum of activity. There are no recommendations in cases without improvement using an initial antipseudomonal beta-lactam in the absence of an aetiological diagnosis. In such cases, the strategy should be based on previous clinical experience and local epidemiological data. One study reported the activity of ceftobiprole against a large set of clinical isolates obtained from hospitalized patients in the United States in 2016 that caused serious infections, including pneumonia, in which 72.7% of 1,017 isolates of *Pseudomonas aeruginosa* were susceptible to ceftobiprole.[5] In an unpublished observational study including respiratory, skin, genitourinary tract, body fluid, and gastrointestinal clinical isolates from Europe isolated in 2018, the rate of susceptibility to ceftobiprole in 376 *Pseudomonas aeruginosa* isolates ranged from 59% to 76.3%.[6] In the presented case, ceftazidime/avibactam and ceftolozane/tazobactam would have been good empirical treatment options against *Pseudomonas aeruginosa*. The decision to use ceftobiprole was taken in the absence of precise data on susceptibility data to *Pseudomonas aeruginosa* in our setting, considering its high activity against MSSA and MRSA, and the possibility to be used in OPAT.

More data are needed to demonstrate the safety and efficacy of ceftobiprole and specific use in the outpatient setting.

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Conflicts of interest

LELC has served as scientific advisor for Novartis, speaker for MSD, Pfizer, Angelini, ViiV, Gilead and Correvio, and has served as trainer for MSD and ViiV. The rest of authors have no conflicts of interests to declare.

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Obturator internus pyomyositis: not everything is septic arthritis☆

Piomiositis del músculo obturador interno: no todo es artritis séptica

Pyomyositis is a bacterial infection of the striated muscle, which usually develops into a muscle abscess. It mainly affects the large muscles of the lower limbs,[1,2] and its location in the obturator internus muscle (OIM) is exceptional, little documented and a real diagnostic challenge.

We present the case of a 15-year-old adolescent boy, who came to the Emergency Department with a one-week history of fever, pain in the right gluteal region and a limp. He did not report any trauma, recent intense physical exercise or any previous infectious process. On examination, an antalgic position was observed with the right hip in flexion, external rotation and abduction. Blood tests showed 70.6% of neutrophils without leukocytosis (7.6·10$\hat{9}$/l) and CRP of 8.9 mg/dl. X-rays of the pelvis and hips were performed without relevant findings and an ultrasound of the hip revealed joint effusion. The patient was admitted with clinical suspicion of septic arthritis.

Arthrocentesis was performed, with negative gram stain and culture results. Blood cultures were positive for methicillin-sensitive *Staphylococcus aureus* (MSSA), and treatment with intravenous cloxacillin was started. An abdominal ultrasound study was completed, which ruled out appendicitis, and an MRI of the hip showed oedema of the peritrochanteric soft tissues without signs of septic arthritis. A follow-up MRI repeated five days later revealed an abscess measuring 6 × 1.5 × 5.5 cm in the OIM with probable associated pelvic osteomyelitis (Fig. 1). Ultrasound-guided drainage of the collection was performed, obtaining 12 cm^3 of purulent fluid and culture isolation of MSSA (identical sensitivity to blood cultures). In turn, antibiotic treatment was extended with vancomycin and clindamycin, after withdrawing cloxacillin.

The clinical response and test results were favourable, but without complete resolution in successive follow-up MRIs, so it was decided to prolong parenteral treatment for six weeks, the first four weeks in hospital, and at discharge, two more weeks with weekly dalbavancin combined with oral clindamycin.

Primary pyomyositis is an infrequent condition, which is observed mainly in tropical climates, although in recent decades it has notably increased in our setting, associated above all with situations of immunosuppression.[2–4]

Its pathogenesis is not completely known, but it has traditionally been associated with local trauma (15-50%) or strenuous physical exercise.[1–5] It usually originates from haematogenous dissemination, with gram-positive bacteria being responsible for practically all cases, and *Staphylococcus aureus* being the most frequent microorganism.[2,4]

Obturator internus pyomyositis (OIP) is an extremely rare condition of which few cases have been described in the literature. However, its incidence has been increasing in recent years.[3,5] It is more common in children,[1,5] and usually manifests with fever, pain in the hip or thigh, limp and antalgic position with the hip in flexion, external rotation and abduction.[1,5] In half of the cases, it is complicated by infection of adjacent muscles or pelvic osteomyelitis,[1,5] as occurred in our case.

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