2. Kristopher Siu L, Kuo-Ming Y, Jung-Chung L, Chang-Phone F, Feng-Yee C. *Klebsiella pneumoniae* liver abscess: a new invasive syndrome. Lancet Infect Dis. 2012;12:881–7.
3. Esper RC, Luis J, Hernández S, Alberto C, Pérez P, Daniel L, et al. Síndrome de absceso hepático secundario a *Klebsiella pneumoniae* hipermucoviscosa con involucro pulmonar. Gac Med Mex. 2013;149:102–7.
4. Podschun R, Ullmann U. *Klebsiella* spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev. 1998;11:589–603.
5. Siu LK, Yeh KM, Lin JC, Fung CP, Chang FY. *Klebsiella pneumoniae* liver abscess: a new invasive syndrome. Lancet Infect Dis. 2012;12:881–7.
6. Kim JK, Chung DR, Wie SH, Yoo JH, Park SW, Korean Study group for Liver abscess. Risk factor analysis of invasive liver abscess caused by the K1 serotipe *Klebsiella pneumoniae*. Eur J Clin Microbiol Infect Dis. 2009;28:109–11.
7. Foo NP, Chen KT, Lin HJ, Guo HR. Characteristics of pyogenic liver abscess patients with and without diabetes mellitus. Am J Gastroenterol. 2010;105:328–35.
8. Rodríguez-Lagos FA, Ferrer-García JC, Ramón-Capilla M, Sánchez-Juan C. Absceso hepático por *Klebsiella pneumoniae* en un paciente diabético. Endocrinol Nutr. 2013;60:106–9.
9. Martín Sánchez A, Acosta de Bilbao F, Peña Quintana P, Pérez Marín JC, Suárez Cabrera M, Calvo Hernández LM, et al. Absceso hepático piógeno por *Klebsiella pneumoniae*. Revisión de Abscesos Hepáticos (1998–2003). Revista Canarias. Méd Quir. 2004:1.
10. Hui J, Yang M, Cho D, Li A, Loke T, Chan J, et al. Pyogenic liver abscesses caused by *Klebsiella pneumoniae:* US appearance and aspiration findings. Radiology. 2007;242:769–96.

Gema Barbeito-Castiñeiras[a,*], María Jesús Ladra González[b], María Jesús Domínguez Santalla[c], Carmen Rivero Velasco[d]

[a] *Servicio de Microbiología y Parasitología, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[b] *Servicio de Cirugía General y Digestiva, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[c] *Servicio de Medicina Interna, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, A Coruña, Spain*
[d] *Servicio de Medicina Intensiva, Complexo Hospitalario Universitario de Santiago de Compostela, A Coruña, Spain*

* Corresponding author.
E-mail address: Gema.Barbeito.Castineiras@sergas.es
(G. Barbeito-Castiñeiras).

2529-993X/

First case of ceftazidime/avibactam administration in home care. ESBL producing *Klebsiella pneumoniae* bacteremia☆

Primer caso de administración de ceftazidima/avibactam en hospitalización a domicilio. Bacteriemia por Klebsiella pneumoniae *BLEE multirresistente*

Dear Editor,

The increase in nosocomial infections caused by multi-drug resistant Gram-negative bacilli has necessitated the development of new antibiotics. In recent months, the FDA approved 2 new antibiotics, ceftolozane/tazobactam and ceftazidime/avibactam, for the treatment of intra-abdominal infections (together with metronidazole) and urinary tract infections.[1] Since June 2016, ceftazidime/avibactam has been approved in Europe for the treatment of nosocomial pneumonia, including those cases associated with mechanical ventilation and infections caused by Gram-negative aerobic microorganisms, with limited treatment options.[2] There is no documented evidence on the use of these drugs in the hospital at home (HAH) setting, a treatment modality that is not only less expensive, but also drastically reduces the possibility of intrahospital transmission of the bacteria.

We report the first case of ceftazidime/avibactam administration in a hospital at home programme. It discusses a 62-year-old patient with hypertension who had recently been diagnosed (February 2016) with acute myeloblastic leukaemia and was undergoing treatment with chemotherapy. He was admitted to haematology for a consolidation cycle, and had as a complication persistent bacteraemia caused by multidrug resistant extended-spectrum beta-lactamase (ESBL) *Klebsiella pneumoniae* secondary to sacral ulcer. Initially he received empirical treatment with imipenem/cilastatin and colistin. Given that his fever persisted and his blood cultures were positive again, the antibiogram was extended and showed sensitivity only to ceftazidime/avibactam and resistance even to ceftolozane/tazobactam (minimum inhibitory concentration of 8). Therefore, in view of the results, despite the fact that it was not among the approved indications at that time (it is now), it was decided to start treatment with ceftazidime/avibactam. Given his clinical stability, HAH services were contacted to complete treatment. They continued administering 2/0.5 g/8 h of ceftazidime/avibactam, which required pump infusion and 2 home visits (the drug is stable diluted and unrefrigerated for 12 h[1]). No outstanding incidents or related side effects occurred, and his monitoring rectal swab and blood cultures became negative.

Hospital-acquired infections are the sixth leading cause of death both in the United States and in Europe.[3] Those caused by Gram-negative bacteria have a special capacity for acquiring new mechanisms of resistance to antibiotics, especially if they are under antibiotic pressure. Since few new antibiotics have been developed in recent years, few treatment options are available to fight these infections. Cases of nosocomial bacteraemia caused by Gram-negative bacteria account for 30% of these infections. The most common microorganisms include species of *Klebsiella*, as in our case. The increase in resistance to broad-spectrum cephalosporins and carbapenems is also a particularly significant problem.[3] Among cases of nosocomial bacteraemia caused by *K. pneumoniae*, in the United States, 27.1% were resistant to third-generation cephalosporins, and 10.8% were resistant to carbapenems, with even higher rates of resistance in Europe.[3] Therefore, in this regard it is essential to have new therapeutic weapons such as ceftazidime/avibactam, an antibiotic approved on 25 February 2015. This antibiotic is active against a broad group of Gram-negative bacteria, *Enterobacteriaceae* and even *Pseudomonas aeruginosa*. However, it is minimally active against *Acinectobacter*, anaerobes and Gram-positive bacteria.[4] It is well tolerated (the most common side effects reported in the REPRISE study were gastrointestinal, in the same proportion in the 2 branches of the study–with and without ceftazidime/avibactam–with no other significant side effects).[5] In addition, it has demonstrated activity against *K. pneumoniae* carbapenemase, or KPC,[6] class A carbapenemases, encoded by plasmid genes, which would explain its greater capacity for spreading. Moreover, it should be noted that the antibiotic treatment directly observed in HAH units in Spain has proven to

☆ Please cite this article as: Torres-del-Pliego E, Delgado-Mejía E, Gil-Alonso L, del Mar-Periáñez-Párraga L. Primer caso de administración de ceftazidima/avibactam en hospitalización a domicilio. Bacteriemia por *Klebsiella pneumoniae* BLEE multirresistente. Enferm Infecc Microbiol Clin. 2017;35:322–323.

be safe, effective and probably more economical (there are no clear data that confirm this).[7] In addition, another advantage demonstrated in this case in particular–and to date not studied–is the potential for home administration of the antibiotic. This would significantly decrease the potential for transmission of the bacterium.

In conclusion, administration of ceftazidime/avibactam in the HAH setting in selected cases would drastically decrease costs deriving from hospital admission, as well as complications related to hospital stay; would not undermine the treatment indicated for the patient; and would help control intrahospital transmission. Therefore, we believe that its home use should be considered under suitable circumstances.

Funding

The authors declare that they did not receive funding to complete this study.

References

1. Highlights of prescribing information for Avycaz (ceftazidime and avibactam). Available in: http://www.allergan.com/assets/pdf/avycaz_pi [accessed February 2015].
2. European Medicines Agency (Internet). Committee for Medicinal Products for Human Use. Available in: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/04/news_detail_002518.jsp&mid=WC0b01ac058004d5c1 [accessed 28.04.16].
3. Peleg AY, Hooper DC. Hospital-acquire infections due to gram-negative bacteria. N Engl J Med. 2010;362:1804–13.
4. Liscio JL, Mahoney MV, Hirsch EB. Ceftolozane/tazobactam and ceftazidime/avibactam: two novel β-lactam/β-lactamase inhibitor combination agents for the treatment of resistant Gram-negative bacterial infections. Int J Antimicrob Agents. 2015;46:266–71.
5. Carmeli Y, Armstrong J, Laud PJ, Newell P, Stone G, Wardman A, et al. Ceftazidime-avibactam or best available therapy in patients with ceftazidime-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* complicated urinary tract infections or complicated intra-abdominal infections (REPRISE): a randomised, pathogen-directed, phase 3 study. Lancet Infect Dis. 2016;16:661–73.
6. Toussaint KA, Gallagher JC. β-lactam/β-lactamase inhibitor combinations: from then to now. Ann Pharmacother. 2015;40:86–9.
7. Mirón-Rubio M, González-Ramallo V, Estrada-Cuxart O, Sanroma-Mendizábal P, Segado-Soriano A, Mujal-Martínez A, et al. Intravenous antimicrobial therapy in the hospital-at-home setting: data from the Spanish Outpatient Parenteral Antimicrobial Therapy Registry. Future Microbiol. 2016;11:375–90.

Elisa Torres-del-Pliego [a,*], Elena Delgado-Mejía [a], Leire Gil-Alonso [a], Leonor del Mar-Periáñez-Párraga [b]

[a] *Unidad de Hospitalización a Domicilio, Hospital Universitario Son Espases, Palma de Mallorca, Balearic Islands, Spain*
[b] *Servicio de Farmacia, Hospital Universitario Son Espases, Palma de Mallorca, Balearic Islands, Spain*

* Corresponding author.
E-mail address: elisatorresdelpliego@gmail.com
(E. Torres-del-Pliego).

2529-993X/

Comparative activity of tedizolid against clinical isolates of linezolid-resistant coagulase-negative staphylococci and methicillin-resistant *Staphylococcus aureus*☆

Actividad comparativa de tedizolid frente a Staphylococcus *coagulasa negativos resistentes a linezolid y* Staphylococcus aureus *resistentes a meticilina*

Tedizolid phosphate is an antibiotic from the oxazolidinone group that was recently approved for the treatment of acute bacterial skin and soft-tissue infections caused by Gram-positive cocci.[1] This second-generation drug has higher activity *in vitro* than its analogue linezolid.[2–4] Although the breakpoints for susceptibility to tedizolid against *Staphylococcus* were recently established,[5] its activity against linezolid-resistant (LR) isolates has not been well studied. Our objective was to evaluate *in vitro* the susceptibility to tedizolid of methicillin- and linezolid-resistant coagulase-negative *Staphylococcus* (LR-CNS) and methicillin-resistant *Staphylococcus aureus* (MRSA). Our secondary objective was to compare the susceptibility of our isolates to other antibiotics used as an alternative in MRSA infections.

Susceptibility *in vitro* to tedizolid was studied in 22 LR-CNS and 33 MRSA isolates in the Department of Microbiology at Hospital Universitario San Cecilio in Granada, Spain, from 2007. Nine of the LR-CNS isolates were recovered from a previous study conducted by Sorlozano et al.[6] Identification was performed using MALDI-TOF (Bruker Daltonics®, Germany) and all isolates underwent a study of the minimum inhibitory concentration (MIC) against tedizolid, linezolid, vancomycin, ceftaroline and daptomycin through the disk diffusion method with a gradient strip (Liofilchem®, Italy). All LR isolates also underwent a study of the MIC against erythromycin, clindamycin, chloramphenicol and streptogramin A, and the different profiles of resistance linked to different mechanisms of resistance to linezolid were evaluated[7]: point mutations in the V domain of 23S ribosomal RNA (*rrn* gene), presence of the *cfr* gene or mutations in the genes that encode the L3 and L4 proteins of the 50S ribosomal subunit. All isolates were seeded in Mueller-Hinton agar with a 0.5 McFarland inoculum and incubated for 24 h at 37 °C. Methicillin resistance was confirmed using 5 μg cefoxitin. The MIC of the different antibiotics was interpreted according to the EUCAST recommendations (v. 6.0). All redundant isolates with a period less than 5 days for a single patient were excluded. In addition, a clonality study was conducted using pulsed-field gel electrophoresis (PFGE)[6] on the isolates that had signs of epidemiological outbreak: isolates that were grouped in time and space.[8]

A total of 55 isolates from 30 men (54.5%) and 25 women (45.5%), from different locations, were analysed: 29 blood culture samples (13 *S. aureus*, 7 *Staphylococcus epidermidis* and 9 *Staphylococcus hominis*), 15 respiratory samples (15 *S. aureus*) and 11 samples from exudates (5 *S. aureus* and 6 *S. epidermidis*).

The epidemiological relationship of the patients infected with LR-CNS was as follows: 9 of the patients infected with *S. hominis* between 2007 and 2008 were admitted to the intensive care unit (n = 8) or the emergency department (n = 1). All other patients infected with LR-CNS (*S. epidermidis*, n = 13) were admitted to different departments between 2009 and 2015: general surgery (n = 2, 2009–2013), internal medicine (n = 3, 2010–2015), gastroenterology (n = 1, 2009), vascular medicine (n = 2, 2009–2014), nephrology (n = 3, 2011–2015), anaesthesia (n = 1, 2010) and emergency medicine (n = 1, 2013). The clonality study for the *S. hominis* isolates that had signs of epidemiological outbreak confirmed

DOI of refers to article: http://dx.doi.org/10.1016/j.eimc.2016.08.004
☆ Please cite this article as: Pérez-Parra S, Peña-Monje A, Recio JL, García-García F. Actividad comparativa de tedizolid frente a *Staphylococcus* coagulasa negativos resistentes a linezolid y *Staphylococcus aureus* resistentes a meticilina. Enferm Infecc Microbiol Clin. 2017;35:323–324.