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Bibliografía

1. Elborn JS. Cystic fibrosis. Lancet. 2016;388:2519–31, http://dx.doi.org/10.1016/S0140-6736(16)00576-6.
2. Castellani C, Assael BM. Cystic fibrosis: a clinical view. Cell Mol Life Sci. 2017;74:129–40, http://dx.doi.org/10.1007/s00018-016-2393-9.
3. http://www.ema.europa.eu/; 2022 [consulted 04.5.22].
4. Taylor-Cousar JL, Munck A, McKone EF, van der Ent CK, Moeller A, Simard C, et al. Tezacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del. New Engl J Med. 2017;377:2013–23, http://dx.doi.org/10.1056/NEJMoa1709846.
5. Rowe SM, Daines C, Ringshausen FC, Kerem E, Wilson J, Tullis E, et al. Tezacaftor-ivacaftor in residual-function heterozygotes with cystic fibrosis. New Engl J Med. 2017;377:2024–35, http://dx.doi.org/10.1056/NEJMoa1709847.
6. Castellani C, Linnane B, Pranke I, Cresta F, Sermet-Gaudelus I, Peckham D. Cystic fibrosis diagnosis in newborns, children, and adults. Semin Respir Crit Care Med. 2019;40:701–14, http://dx.doi.org/10.1055/s-0039-1697961.
7. Paterson I, Johnson C, MacGregor G. Tezacaftor-ivacaftor use in routine care of adults with cystic fibrosis: a medicine use evaluation. Eur J Hosp Pharm. 2021, http://dx.doi.org/10.1136/ejhpharm-2020-002676, ejhpharm-2020-002676.
8. Heltshe SL, Mayer-Hamblett N, Burns JL, Khan U, Baines A, Ramsey BW, et al. *Pseudomonas aeruginosa* in cystic fibrosis patients with G551D-CFTR treated with ivacaftor. Clin Infect Dis. 2015;60:703–12, http://dx.doi.org/10.1093/cid/ciu944.
9. Volkova N, Moy K, Evans J, Campbell D, Tian S, Simard C, et al. Disease progression in patients with cystic fibrosis treated with ivacaftor: data from national US and UK registries. J Cyst Fibros. 2020;19:68–79, http://dx.doi.org/10.1016/j.jcf.2019.05.015.
10. Neerincx AH, Whiteson K, Phan JL, Brinkman P, Abdel-Aziz MI, Weersink E, et al. Lumacaftor/ivacaftor changes the lung microbiome and metabolome in cystic fibrosis patients. ERJ Open Res. 2021;7:00731–2020, http://dx.doi.org/10.1183/23120541.00731-2020.

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Chronic ESBL-*Klebsiella pneumoniae* prostatitis treated with once-daily tigecycline monotherapy in home hospitalization

Tratamiento con tigeciclina administrada una vez al día en monoterapia de una prostatitis crónica causada por Klebsiella pneumoniae *productora de beta-lactamasas de espectro extendido*

Dear Editor,

We present the case of a 79-year-old male with a history of low-risk myelodysplastic syndrome diagnosed in 2013, currently without specific treatment. He required a resection of the terminal ileum due to hemorrhagic ileitis in 2014. Afterwards, he presented several episodes of urinary tract infections (UTI). The first consisted of an acute prostatitis in 2015 caused by an extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae*. Thereafter, he suffered from prostatic and seminal vesicle abscesses requiring bilateral orchiectomy in 2016. Abscesses were drained, and the patient received empirically linezolid and meropenem. Treatment was switched to ertapenem according to culture results, for a total of 21 days. No new episodes of prostatic or seminal vehicle abscesses have been observed. In 2017, he was admitted twice for sepsis secondary to prostatitis due to the ESBL-*K. pneumoniae*. In November 2020, he was diagnosed with voiding syndrome, being prescribed two months of fosfomycin-trometamol 3 g every 48 h with good tolerance. Minimum inhibitory concentration (MIC) was < 16 mg/L at the beginning of the treatment, with development of resistance after the antibiotic course (MIC > 256 mg/L). In December 2020, he was admitted because of persistence of lower UTI symptoms with the presence of ESBL-*K. pneumoniae*, being treated with ertapenem 1 g/24 h for one week.

In February 2021, he was readmitted with astheny, general malaise, dysuria and vesical tenesmus, low-grade fever (37.5 °C) and perianal discomfort, being diagnosed of recurrent prostatitis. A new course-treatment of ertapenem (1 g/24 h) was started (glomerular filtration rate 31 mL/min/1.73 m^2). After 3 days, urine culture showed ESBL-*K. pneumoniae* susceptible to carbapenems, without other potential alternatives. Clinical follow-up was satisfactory, with resolution of voiding symptoms and improvement of analytical parameters including glomerular filtration rate. However, on the 13th day of treatment, the patient presented neutropenia (initial neutrophils 5.8 × 10^3 u/mcl, nadir 0.43 × 10^3 u/mcl), and diarrhea, which caused hypernatremia, hypokalemia, hypomagnesemia, and hypocalcemia. Intravenous fluids and electrolyte replacement were required. *Clostridioides difficile* associated diarrhea was ruled out, so side effects were attributed to ertapenem. Treatment was firstly switched to tigecycline 100 mg followed by 50 mg/12 h. After the change, a significant improvement was noticed. Diarrhea went away, ion values were corrected, and neutropenia improved (although one dose of filgrastim was administered). After 48 h with tigecycline, the patient was discharged to home hospitalization with tigecycline 100 mg/24 h for 14 days to complete 4 weeks of antibiotic treatment. The patient did not present any recurrence nine months after this episode, with negative control urine cultures. Unfortunately, semen culture was not requested at any time.

We present the first case of chronic prostatitis due to ESBL-*K. pneumoniae* treated with once-daily tigecycline. This approach resolved the adverse events caused by ertapenem and allowed the patient to be early discharged.

Carbapenems are associated with diarrhea, neutropenia or astheny.[1] In our case, ertapenem caused numerous adverse events, with a probable causal relationship according to the Naranjo Scale. Due to the absence of therapeutic alternatives, need for prolonged antibiotic duration, penetration issues, risk of adverse effects and possibility of discharge, tigecycline was chosen as a potential alternative.[2]

Tigecycline is a third generation tetracycline whose use in UTI is controversial due to its limited urinary excretion (5–35%).[3,4] However, it may be an alternative in the treatment of prostatitis.[2]

In terms of pharmacokinetics, tigecycline presents an excellent tissue penetration, showing a high volume of distribution (7–9 L/kg).[5–7] Prostate penetration depends on the lipophilicity and degree of ionization of the drug. Tetracyclines, due to their high lipophilicity, penetrate up to 90–100% in the prostatic tissue, although specific data for tigecycline are lacking.[5–7] Other interesting characteristics include its long elimination half-life (42 h), allowing the once-daily administration.[7,8] This dosing has shown optimal therapeutic levels (maximum concentration 1.5 mg/L), considering that, for *Enterobacterales*, its pharmacokinetic/pharmacodynamic index is the area under the curve/MIC ≥ 15–20. These concentrations guarantee sufficient levels based on the established cut-off of 0.5 mg/L.[5–8] However, this approach is experimental with very limited clinical evidence.[7,8]

Tigecycline has demonstrated clinical and microbiological cure in complicated UTIs (77.4–78.6% and 85.7%, respectively).[3,9] Concerning prostatitis, some cases have demonstrated its clinical effectiveness without safety issues.[3,6,9,10]

In our case, the use of tigecycline for the treatment of ESBL-*K. pneumoniae* prostatitis optimized tolerability, avoiding ertapenem-associated adverse effects while maintaining clinical effectiveness. Once-daily administration regimen allowed early hospital discharge to home hospitalization, reducing the risk of nosocomial complications, and improving patient's quality of life.

Conflict of interest

There is no conflict of interest or source of funding for the present study.

Bibliografía

1. Vardakas KZ, Kalimeris GD, Triarides NA, Falagas ME. An update on adverse drug reactions related to β-lactam antibiotics. Expert Opin Drug Saf. 2018;17:499–508, http://dx.doi.org/10.1080/14740338.2018.1462334.
2. Lipsky BA, Byren I, Hoey CT. Treatment of bacterial prostatitis. Clin Infect Dis. 2010;50:1641–52, http://dx.doi.org/10.1086/652861.
3. Brust K, Evans A, Plemmons R. Tigecycline in treatment of multidrug-resistant Gram-negative bacillus urinary tract infections: a systematic review. J Antimicrob Chemother. 2014;69:2606–10, http://dx.doi.org/10.1093/jac/dku189.
4. Nix D, Matthias K. Should tigecycline be considered for urinary tract infections? A pharmacokinetic re-evaluation. J Infect Dis. 2008;198:1243–6, http://dx.doi.org/10.1093/jac/dkq116.
5. Bates D, Parkins M, Hellweg R, Gibson K, Bugar JM. Tigecycline treatment of urinary tract infection and prostatitis: case report and literature review. Can J Hosp Pharm. 2012;65:209–15, http://dx.doi.org/10.4212/cjhp.v65i3.1144.
6. Priore EL, Livermore DM, Buetti N, Jent P, Pelzer N, Casanova C, et al. Successful treatment of acute prostatitis caused by multidrug-resistant *Escherichia coli* with tigecycline monotherapy. Open Forum Infect Dis. 2020;7:1–2, http://dx.doi.org/10.1093/ofid/ofz551.
7. Cunha BA, Baron J, Cunha CB. Once daily high dose tigecycline – pharmacokinetic/pharmacodynamic based dosing for optimal clinical effectiveness: dosing matters, revisited. Expert Rev Anti Infect Ther. 2017;15:257–67, http://dx.doi.org/10.1080/14787210.2017.1268529.
8. Baron J, Cai S, Klein N, Cunha B. Once daily high dose tigecycline is optimal: tigecycline PK/PD parameters predict clinical effectiveness. J Clin Med. 2018;7:49, http://dx.doi.org/10.3390/jcm7030049.
9. Liu YX, Le KJ, Shi HY, Zhang ZL, Cui M, Zhong H, et al. Efficacy and safety of tigecycline for complicated urinary tract infection: a systematic review. Transl Androl Urol. 2021;10:292–9, http://dx.doi.org/10.21037/tau-20-959.
10. Drekonja DM, Johnson JR. Tigecycline treatment for urinary tract infections: case report and literature review. J Chemother. 2011;23:168–70, http://dx.doi.org/10.1179/joc.2011.23.3.168.

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Streptococcus oralis, un patógeno oportunista en la queratopatía cristalina

Streptococcus oralis, *an opportunistic pathogen in crystalline keratopathy*

Caso

Paciente de 55 años con diabetes mellitus tipo 2 y microangiopatía en tratamiento con metformina (850 mg dos veces al día). También presentaba glaucoma de ángulo abierto, una retinopatía diabética asociada a edema macular por la que había recibido 14 inyecciones intravítreas en el ojo derecho (OD) y 8 inyecciones en el ojo izquierdo (OI) con aflibercept (40 mg/ml), así como desprendimiento de retina en OI que requirió vitrectomía pars plana (23 g y endoláser por pequeños desgarros paravasculares). Además, refería uso frecuente de lentes de contacto diarias. El paciente sufrió empeoramiento progresivo de la agudeza visual en OD con hiperemia conjuntival y fotofobia. A la exploración del OD, se observó la córnea deslustrada, así como 2 úlceras corneales laterales (3 × 2 mm) y otra en región medial con forma de semiluna. Se tomaron muestras de raspado corneal para estudio microbiológico.

Se sembró la muestra de raspado corneal en agar tripticasa soja con 5% de sangre de cordero (Becton Dickinson, Franklin Lakes, NJ, EE.UU.), agar Saboraud con cloranfenicol (BD™) y agar chocolate, además de cultivo específico para detección de *Acanthamoeba* spp. Para el cultivo de *Acanthamoeba* spp. se emulsionaron 1-2 colonias de *Escherichia coli* o *Enterobacter aerogenes* en una solución Page hasta conseguir una turbidez homogénea y posteriormente inocular 0,2 ml de esta solución en una placa de Petri. Posteriormente se inoculó la muestra en este medio y se visualizó cada 24-48 h, observándose crecimiento a los 4 días (fig. 1b, ejemplo de creci-