

Discusión

En nuestra práctica clínica, hemos observado que la incidencia de hipopotasemia debida al tratamiento con ceftolozano/tazobactam podría ser superior a la descrita en los ensayos clínicos (<3%)^{2,3}. En nuestro hospital, 3 de los 10 pacientes tratados con ceftolozano presentaron hipokalemia.

Del resto de fármacos prescritos solo está descrita la hipokalemia en las fichas técnicas de linezolid (1-10%) y fluconazol (0,01-0,1%), ambos prescritos en el primer paciente. Este paciente estaba en tratamiento con linezolid y fluconazol desde hacía casi 4 semanas sin haber presentado hipopotasemia previamente.

Aplicando el algoritmo de Naranjo se obtuvieron unos grados de imputabilidad de PROBABLE para el primer y segundo caso y SEGURO para el tercero. Los 3 casos fueron notificados al Sistema Español de Farmacovigilancia.

A raíz de nuestra experiencia, consideramos muy conveniente monitorizar el PS en los pacientes tratados con ceftolozano/tazobactam.

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Prevalence and risk factors for fosfomycin resistance among *Escherichia coli* strains isolated from males with community febrile urinary tract infection



Prevalencia y factores de riesgo de resistencia a fosfomicina en cepas de *Escherichia coli* aisladas de hombres con infección del tracto urinario febril comunitaria

Dear Editor,

Escherichia coli is responsible for most febrile urinary tract infections (FUTI) in men the majority of which are acute prostatitis (AP).¹ Fluoroquinolones (FQ) achieve high prostatic concentrations and are considered the first choice in patients with AP.² *E. coli* is becoming increasingly resistant to FQ limiting its empirical use.³ Given the lack of new antimicrobials it is necessary to reevaluate already existing agents.

Fosfomycin, a bactericidal antibiotic that targets peptidoglycan formation, is active against most *E. coli* causing FUTI, including extended-spectrum beta-lactamase producing *E. coli* (ESBL-EC) strains.⁴ Fosfomycin trometamol achieves reasonable intraprostatic concentrations and has been used in the treatment of chronic prostatitis caused by multidrug-resistant bacteria.⁵ We aimed to assess the prevalence, trends and risk factors associated to fosfomycin resistance (FR) in *E. coli* from males with a community FUTI.

An ambispective cross-sectional study was performed at a primary care hospital. Data were recorded retrospectively from January 2008 to October 2009 and prospectively from then to December 2015. FUTI was defined as an armpit temperature $\geq 38^\circ\text{C}$ together with UTI symptoms. When urinary symptoms were absent, diagnosis was accepted if no other infections were found. Variables reviewed included: age, dementia, diabetes mellitus, chronic kidney or heart failure, cirrhosis, neoplastic or lung disease, use of immunosuppressive agents, the Charlson score, any antibiotic intake in the previous 30 days, prior UTI and existence of urinary abnormalities. A healthcare-associated FUTI

was considered in case of: hospitalization in the previous 90 days; residence in a long term care facility; outpatient care, therapy, or invasive urinary tract procedures, 30 days before the FUTI and presence of an indwelling urethral catheter. Urine samples were obtained from midstream urine or from urinary catheters and cultured on MacConkey agar. Positive urine cultures were defined by bacterial growth $\geq 10^3$ CFU/mL. Identification of *E. coli* was performed by biochemical methods. Antimicrobial susceptibility was tested by agar diffusion (CLSI criteria). Intermediate and resistant strains were grouped together.

The study included 385 males with a community FUTI due to *E. coli*. Eight (2.1%) isolates were FR and 377 (97.9%) fosfomycin susceptible (FS). Resistance to FQ ($p=0.006$), amoxicillin-clavulanate ($p=0.01$), cefuroxime ($p=0.03$), ceftriaxone ($p=0.024$) and gentamicin ($p=0.015$) was more frequent in FR strains. Among the 29 (7.5%) ESBL-EC, 27 (93.1%) were FS. In the univariate analysis FR was associated to older age ($p=0.048$), dementia ($p=0.028$) and recent FQ use ($p=0.036$). The frequency of FR remained stable over the study while there was an increase in the proportion of ESBL-EC (chi square for linear trend 17.4; $p<0.001$) (Fig. 1).

The overall prevalence of FR was comparable with that previously reported in Spain⁶ and lower when focusing in ESBL-EC strains.^{6,7} The low frequency of FR in *E. coli* despite extensive use of fosfomycin has been attributed to a decreased bacterial fitness.⁸ However, Spanish studies have suggested the existence of a correlation between fosfomycin consumption and FR in *E. coli* isolates, mainly in ESBL-EC.^{6,9} Resistance to fosfomycin is generally related to chromosomal mutations in the target or in the transporter genes and less frequently to plasmid modifying enzymes, mainly the *fosA3*.⁴ The *fosA3* genes, commonly located on a conjugative plasmid that also carries a CTX-M, are widespread in East Asia.⁴ A high proportion of the analyzed ESBL-EC strains were susceptible to fosfomycin. Interestingly, only 25% of the FR *E. coli* isolates were ESBL-EC suggesting that the *fosA* genes are not spread in our environment. However, this could change in case of dissemination of the *fosA3* genes, which have already been detected in Europe.¹⁰

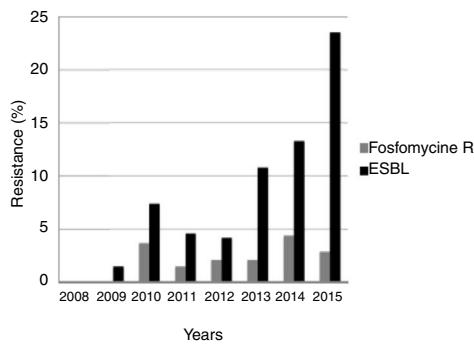


Fig. 1. Trends in fosfomycin resistance and ESBL production in *E. coli* isolated from males with febrile urinary tract infection over the study period.
Abbreviations: R: resistant; ESBL: extended-spectrum beta-lactamase.

We found that older age, dementia and FQ consumption were associated to FR. Nursing home residence has been described as a predictor of FR in ESBL-EC.⁶ Further studies are required to fully evaluate the risk factors of FR in *E. coli*.

Our study suggests that FR has not increased over time. Most *E. coli* isolates were FS including ESBL-EC. Risk factors for FR should be considered when prescribing fosfomycin to males with a FUTI.

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Fatal multi-drug-resistant *Acinetobacter baumannii* pneumonia in Maputo, Mozambique: A case report



Neumonía con desenlace fatal por *Acinetobacter baumannii* multirresistente en Maputo, Mozambique: reporte de un caso

Acinetobacter baumannii is one of the six most important multidrug-resistant (MDR) microorganisms isolated in hospitalised patients worldwide, having an extraordinary capacity to spread to different areas.¹ In the last three decades *A. baumannii* has acquired resistance to antibiotics including carbapenems and even polymyxins, representing a challenge for achieving effective antibacterial treatment.^{1,2} In the global priority list of antibiotic-resistant bacteria of the World Health Organisation, *A. baumannii* is considered the most critical pathogen.³ Knowledge of the epidemiology and antibacterial susceptibility profile of *A. baumannii* is still incomplete in many parts of the world including Africa. Here, we report a fatal pulmonary infection by MDRA *A. baumannii* in Maputo, Mozambique.

In 2014, a woman in her 20s, with HIV infection on antiretroviral treatment for the preceding 12 months, was admitted to the Maputo Central Hospital with cough, dyspnoea and seizures of acute presentation. Physical examination revealed: a Glasgow score of 15/15, temperature 38.2 °C, blood pressure 180/120 mmHg, heart rate 100 bpm, and respiratory rate 24 rpm. Thick and thin smear tests for malaria were negative. Laboratory analyses during

hospitalisation showed anaemia (haematocrit 24.9% and haemoglobin 8.3 g/dL), leukopenia (white blood cell count $2.9 \times 10^9/L$), elevated transaminases (AST 157 IU and ALT 726 IU), and kidney failure (maximum creatinine and urea levels were 363 $\mu M/L$ and 29.4 $\mu M/L$ respectively); the estimated glomerular filtration (Cockcroft-Gault Equation) was 18.8 mL/min. Chest X-ray was performed and only a cardiomegaly was reported. The nadir CD4 count was 192 cells/mL. Sputum Gram stain and blood culture were not performed. The patient received penicillin, cotrimoxazole, and oxygen but died on day 14 of hospitalisation. Pre-mortem clinical diagnoses were: HIV/AIDS, Kaposi's sarcoma, dilated cardiomyopathy, kidney failure, and pulmonary hypertension. The patient was not intubated or in mechanical ventilation.

The case was included in the CaDMIA project, a validation study of a minimally invasive autopsy (MIA) protocol against the complete diagnostic autopsy (CDA).^{4,5} A universal screening for several key pathogens was conducted, and microbiological analysis were performed according to the histopathological findings.^{4,5} The autopsy revealed a severe pyogenic pneumonia (Fig. 1). Serum samples tested positive for antibodies against HIV with a viral load of 182 copies/mL. Lung samples resulted negative for tuberculosis, *Cryptococcus*, *Toxoplasma gondii*, *Pneumocystis jirovecii* and respiratory viruses by PCR testing. *A. baumannii* was isolated from brain, lung and liver samples. Gram negative bacilli were visible in the Gram stain of histological lung samples (Fig. 1), brain, and liver. *A. baumannii* was also identified by 16S rRNA PCR in plasma, brain,