

S022

2-hour Symposium

Resurrecting old antimicrobial agents

Sparing carbapenems by revived old antibiotics (mecillinam, temocillin, fosfomycin)

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The increasing prevalence of infections caused by ESBL-producing Enterobacteriaceae (EPE) internationally has resulted in escalating clinical use of carbapenems, often because ESBL production is linked to aminoglycoside, fluoroquinolone and trimethoprim resistance. As a consequence, carbapenemase-resistant Enterobacteriaceae have emerged and become a potential threat to these last-line antimicrobial agents. In order to preserve the future of carbapenems as valuable reserve agents for patients with life-threatening infections, alternative agents have been actively sought amongst the “forgotten antibiotics”. These include fosfomycin, temocillin and mecillinam. Of these, the greatest experience has been had with fosfomycin as the trometamol salt. This agent has a unique mechanism of action and a long history of use as single-dose therapy for the treatment of uncomplicated urinary tract infection. Extension to the treatment of urinary tract infection caused by EPE was an obvious step and a recent meta-analysis of published experience suggests that it can produce satisfactory rates of clinical and microbiological success. The optimum dosing regimen for patients with complicated EPE urinary infection has not been determined, although three once-daily doses of 3g have been most commonly used. By contrast, experience in treating sepsis caused by EPE with the IV formulation of fosfomycin is very limited, and true efficacy in that setting has yet to be established. Another old agent, temocillin, has the potential to treat invasive EPE infection, and published experience to date has shown good results in both animal models and serious EPE infections in humans. Work on optimising the dosing regimen using PK-PD, including the use of continuous infusion, continues. Another suggested option for treating lower UTI caused by EPE is pivmecillinam, the prodrug of mecillinam. Like fosfomycin, this agent has been widely used in a limited range of countries for uncomplicated UTI, due to its activity against TEM-1 producing *E. coli*. A recent prospective comparative study from Norway, however, has suggested that efficacy may be suboptimal. Further studies are needed before confidence can be placed in pivmecillinam for EPE urinary tract infection. In summary, fosfomycin trometamol is a very suitable oral agent for EPE urinary tract infection, and temocillin offers a useful alternative to carbapenems for serious EPE infections. Efforts should be placed into getting both these agents registered in more countries around the globe.