Review of clinical experience of Intravenous fosfomycin at Royal Bolton Hospital.

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Introduction

Intravenous (IV) fosfomycin is a broad spectrum bactericidal antibiotic[1] which has seen a recent resurgence because of increasing antimicrobial resistance and the limited number of effective alternative treatment options[2]. There is a lack of clinical experience in using IV fosfomycin in the UK. Royal Bolton Hospital has introduced IV fosfomycin to its antibiotic formulary as a restricted agent. In this small series we have reviewed our use of IV fosfomycin at Bolton with the aim to share our learning and improve our understanding in the role of IV fosfomycin. Our study aimed to look at the patient population who were prescribed IV fosfomycin, which indications it was being prescribed for, dosing regimes, and clinical outcomes.

Method

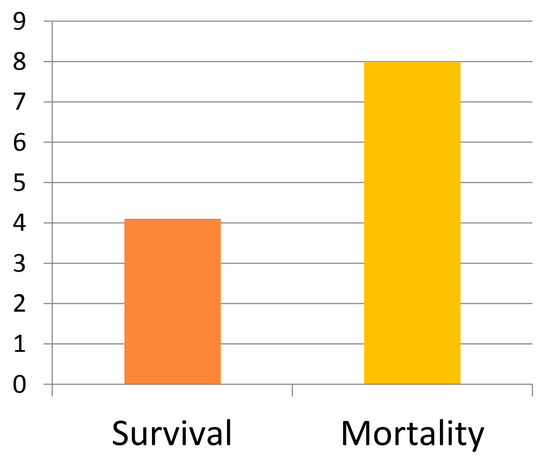
Patients who had been prescribed IV fosfomycin were identified from microbiology records between September 2016 and April 2017. Available case notes and online laboratory systems were used to record co-morbidity scores, indications, pathogens isolated, dosing regimes, renal function, reasons for IV fosfomycin use (primary therapy and allergy, salvage, or salvage and allergy) and outcome.

Results

Out of the 21 records analysed there were 7 deaths and 14 patients survived the inpatient episode. In the mortality group all deaths had the infection being treated by the fosfomycin as the main or contributing cause of death.

1. Patterns of clinical use

a) Charlson co-morbidity index



The patients in our mortality group had a higher mean Charlson co-morbidity index[3] than patients in the survival group. A higher score indicates more co-morbidities.

b) Infections treated

Fosfomycin was used to treat a wide range of infections including respiratory tract infections (n=9), urinary tract infections (n=3), infection of unknown origin (n=3) and other sources such as prostatitis, osteomyelitis, post-operative wound site infection and cholecystitis. Causative organisms were identified in 7 clinical episodes.

Infection being treated	Pathogen isolated
Mortality group	
Osteomyelitis	*Escherichia coli* (AmpC)
Unknown source	*Proteus mirabilis*
Community acquired pneumonia	*Pseudomonas aeruginosa*
Survival group	
Infective exacerbation of chronic obstructive pulmonary disease	*Pseudomonas aeruginosa*
Prostatitis	*Escherichia coli (ESBL)*
Urosepsis	*Escherichia coli (ESBL)*
Infected dynamic hip screw	*Enterobacter cloacae, Enterobacter kobei, Proteus mirabilis*

2. Indications

We looked at why fosfomycin was chosen as an antibiotic for each patient, grouping decisions as 'primary and/or allergy', 'salvage' or 'salvage and allergy'.

Reason for fosfomycin use	Overall (n=21)	Mortality (n=7)	Survival (n=14)
Primary and allergy	8 (38.1%)	1 (12.5%)	7 (87.5%)
Salvage	3 (14.3%)	2 (66.6%)	1 (33.3%)
Salvage and allergy	10 (47.6%)	4 (40.0%)	6 (60.0%)

3. Dosing

Bolton uses the summary of product characteristics[4] (SPC) and Nottingham University Hospitals guidelines[5] for dosing and renal adjustment. Incorrect dosing was identified in 4 patients, all with renal impairment.

Patient CrCl	Regime received	Correct regime	Dose	Outcome
17	4g BD	2g TDS	Overdose	Survived
34	Two 8g stat doses	One 8g stat then 4g TDS	Overdose	Mortality
22	2g TDS	3g TDS	Underdose	Mortality
34 then 18	4g TDS then 4g BD	4g TDS then 2g TDS	Overdose	Mortality

In total 37.8% of patients in our study were prescribed dual therapy. In the survival cohort 35.7% of patients had mono therapy with IV fosfomycin, 57.1% patients had dual therapy with IV fosfomycin and a range of agents, and 7.2% patients initially had monotherapy which was then converted to dual therapy. In the mortality cohort all but 1 patient (85.8%) had dual therapy treatment.

Conclusion

Fosfomycin is an antibiotic which has been shown in other studies to have equal clinical effectiveness as other comparable antibiotics. Our results suggest that mortality with fosfomycin is linked to higher patient co-morbidities and its use as a salvage antibiotic for infections in complex patients. We consider IV fosfomycin as a reasonable option for difficult-to-treat infections when there is resistance or allergy to more mainstream agents.

References. 1) Michalopoulos A, Livaditis I, Gougoutas V. The revival of fosfomycin. International Journal of Infectious Diseases 2011;15(11): e732-9. 2) Grabein B, Graninger W, Bano J, Liesenfeld D. Intravenous fosfomycin – back to the future. Systematic review and meta-analysis of the clinical literature. Clinical Microbiology and Infection 2017;23: 363-372. 3) Charlson M, Pompei P, Ales K, MacKenzie C. A new method of classifying prognostic co-morbidity in longitudinal studies: development and validation. Journal of Chronic diseases 1987;40(5): 373-83. 4) Summary of Product Characteristics, Fomicyt solution for infusion, accessed 21/11/17 https://www.medicines.org.uk/emc/medicine/28971. 5) Clarkson A, Horton-Smith C, Sonnex K, Guideline for the use of IV fosfomycin for exacerbations of Cystic Fibrosis, Nottingham University Hospital 2017.