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Optimal dosage and duration of pivmecillinam for the treatment of uncomplicated lower urinary tract infections: a systematic review and meta-analysis

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Background: Lower urinary tract infections (UTIs) are among the most prevalent bacterial infections affecting people of all ages. Pivmecillinam (PIV) has been used for over 30 years, although the optimal PIV dosage and duration regime remains unknown. We conducted a systematic review and meta-analysis to compare efficacy and safety of different PIV regimes in the management of lower uncomplicated UTIs.

Material/methods: We searched Medline, Embase and the Cochrane Library. We included randomized clinical trials (RCTs) with adults or children with symptoms suggestive of uncomplicated UTI that compared different PIV regimes or PIV versus other antibiotics. Meta-analyses were conducted using fixed-effect model for the following outcomes: clinical or bacteriological cure, reinfection, relapse, failure and adverse events. We categorized PIV regimes into high-total dosage (2900 mg to 16800 mg), moderate-total dosage (1900 mg to 2800 mg) and low-total dosage (600 mg to 1800 mg) regimes (e.g. total dosage of 3600mg: 400mg 3x for 3 days). Risk of bias was evaluated using the Cochrane tool.

Results: We included 23 RCTs in the quantitative synthesis (5733 patients). No difference in clinical cure was found in PIV high versus moderate (short-term: 2 studies, 818 patients, RR 1.01 [0.90; 1.14], p=0.813; long-term: 1 study, 487 patients, RR 1.09 [0.96; 1.23], p=0.174) or PIV high versus low total dosage comparisons (short-term clinical cure: 1 study, 125 patients, MD 0 [-0.44; 0.45], p=1). For bacteriological cure, comparisons of high versus moderate total PIV dosage (short-term: 2 studies, 691 patients, RR 1.05 [0.99; 1.10], p=0.056; long-term: 1 study, 523 patients, RR 1.05 [0.98; 1.13], p=0.131) as well as high PIV versus low total PIV dosage (short-term: 2 studies, 124 patients, RR 1.02 [0.89; 1.18], p=0.759; long-term: 1 study, 53 patients, RR 1.13 [0.91; 1.40], p=0.247) showed a trend in favour of the total high dosage treatment (meaning at least a minimum dosage of e.g. 400 mg x3 for 3 days = 3600 mg total dosage). Results for relapse, reinfection and failure were inconclusive and statistically not significant. Patients treated with PIV total high dosages were 40% (2 studies, 835 patients, RR 1.40 [0.98; 1.98], p=0.062) and 44% (2 studies, 195 patients, RR 1.44 [0.73; 2.83], p=0.293) more likely to report mild to moderate adverse events than those treated with moderate or low total PIV dosages, respectively.

Conclusions: There is insufficient evidence to support the use of an optimal PIV therapy regime for lower uncomplicated UTIs. Evidence is limited due to high risk of bias, poor reporting and old study data. In order to give guidance on patient care for clinicians, who are in need of definitive recommendations in clinical practice, data suggest that 3-days treatment durations of 400 mg three times daily can safely be recommended.