

Best Practice Message

December 2021

Focus on Antimicrobial Resistance: Non-antibiotic urinary tract infection prophylaxis

Practice changing moments

- To reduce the risk of antimicrobial resistance consideration should be made to alternatives for UTI prophylaxis
- In most patients Hiprex® (now fully funded) is a suitable option for UTI prophylaxis
- In males, ruling out of alternative diagnoses such as prostatitis, prior to starting prophylaxis for UTI, must be done

Risks with antimicrobial prophylaxis

While most agents are well tolerated, some antibiotics can have severe adverse drug reactions which can appear with long-term use, such as the emergence of resistant bacteria, pulmonary effects by nitrofurantoin or tendinopathies and QTc prolongation with fluoroquinolones. Disruptions to the gut microbiome can also occur with systemic antibiotic use. The most well known issue of this would be *C. difficile* infection, which can be life-threatening.

Patients who experience recurrent urinary tract infections may be started on antibiotic prophylaxis for this purpose, however, prior to initiation consideration to antibiotic-sparing measures should be made.

Alternatives to antimicrobial agents for recurrent urinary tract infections in women

Methenamine hippurate (Hiprex)¹ – Hiprex is an agent which is converted to formaldehyde in an *acidic* urine. There is no risk of resistance developing to formaldehyde², however it does require an acidic pH to be converted. It is therefore not effective in patients taking urinary alkalinisers such as Ural® or sodium bicarbonate. Some bacteria can produce urease which may increase the urinary pH enough to render Hiprex ineffective. This is most commonly *Proteus sp.* Vitamin C is commonly suggested to aid with acidifying the urine pH but, up to 12g per day may be required.³

Caution is required in patients with uncontrolled gout due to the risk of precipitation of uric acid crystals and consideration of patients who are catheterised as the retention in the bladder may not be long enough to be effective. Hiprex is contraindicated in patients taking sulphonamides such as co-trimoxazole due to crystalluria, patients with renal impairment (eGFR<10mL/min) due to the risk of hippurate crystalluria and in hepatic impairment (Child-Pugh class B or greater) due to the production of ammonia.

Topical oestrogens⁴ – Menopause brings about a reduction of vaginal oestrogen which can increase the vaginal pH and alter the microbiome. Topical oestrogen can improve the antimicrobial capacity of the uroepithelium and affect microbial growth. In postmenopausal women a trial of topical oestrogen can be utilised to reduce the incidence of urinary tract infections and adverse effects are typically mild. Systemic absorption of vaginal oestrogen is considered to be low so there is no need for additional progestins. The use of low dose vaginal oestrogens is considered safe in women who have had breast cancer, however, it may be appropriate to consult with an oncologist.

Non-funded prophylactic agents

Cranberry – Cranberry based products have been used for centuries to treat urinary tract disorders. This is thought to be due to the presence of proanthocyanidins which inhibit mobility of *P. aeruginosa*, *E. coli*, and *P. mirabilis* as well as provide an anti-adherence effect. There is a lack of convincing evidence that cranberry based products affect the number of recurrent UTIs a patient will experience. However, other studies have shown that in young to middle aged women there may be a reduction in recurrence rate⁵.

D-Mannose – D-Mannose is a monosaccharide which has been shown to reduce adhesion of bacteria to uroepithelial cells⁶. Studies conducted in the use of D-mannose have generally shown a benefit in reducing recurrence, however, these studies have typically been of poor quality with small sample sizes. It is well tolerated in most patients, and could be considered if the patient wants to trial its use.

Recurrent urinary tract infections in men

It is very uncommon for men to have recurrent urinary tract infections without an underlying cause which would require evaluation by a urologist due to the potential for urinary tract obstruction or prostatic hypertrophy. If a male patient is experiencing frequent UTIs with the same organism consideration should be made as to whether the patient has prostatitis.

While there would not be a pharmacological issue with using Hiprex in male patients, current studies looking at recurrent UTI treatment are typically focussed on female patients so consideration to the generalisability of the studies is warranted.

Tools available:

- Child-Pugh score calculator: <https://www.mdcalc.com/child-pugh-score-cirrhosis-mortality>

References:

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