- **CLINICAL REVIEW**

Management of recurrent urinary tract infection

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Recurrent lower urinary tract infection (rUTI) is defined as three or more episodes of UTI during a 12-month period, or two infections in a six-month period. Recurrent UTI may be due to relapse of the original organism and implies treatment failure or to reinfection with the same or different organism, with the latter being much more common. The woman's lifetime risk of at least one UTI is around 50 per cent. In a study involving college students with their first UTI, 27 per cent had at least one culture-confirmed recurrence within the six months following the initial infection, and 2.7 per cent had a second recurrence over the same period[1].

In the majority of women with simple acute lower UTI, the diagnosis is made on clinical grounds, supported by point-of-care dipstick urinalysis. The test strips that used for urinalysis detect leucocyte esterase (produced by segmented leucocytes) and nitrite (produced by uropathogens by converting nitrates). However, women with rUTI warrant further investigations especially in the presence of persistent haematuria, atypical organisms (Proteus, Pseudomonas, Enterobacter and Klebsiella) and persistent infection despite appropriate antibiotic therapy. Urine microscopy, urine culture (including fastidious organisms such as Mycoplasma hominis, Ureaplasma urealyticum and Chlamydia trachomatis), ultrasound scan of the urinary tract, diagnostic cystoscopy and renal function blood tests could facilitate treatment and exclude underlying causes.

Women with rUTI should be given advice about behavioural and personal hygiene measures to reduce the risk of UTI, such as drinking enough fluids to avoid dehydration, not delaying habitual and post-coital urination and not douching or wearing occlusive underwear[3]. The use of contraceptive diaphragms with spermicides should be discouraged. Vaginal flora changes with the reduction of oestrogen levels after the menopause. The vaginal pH increases and the level of Lactobacilli dramatically decreases, allowing bacteria to grow and act as uropathogens. Oestrogen therapy can reverse the changes that occur in the vaginal microbiome after the menopause[2]. Vaginal oestrogens, but not systemic oestrogens, have been shown to reduce the number of UTIs in post-menopausal women with rUTI[3].

When compared to placebo, continuous antibiotic prophylaxis for 6–12 months reduces the rate of UTI; however, there is no difference in the UTI incidence upon discontinuation of therapy[4]. In women with rUTI related to intercourse or another trigger, a single dose when exposed to the trigger might be as effective as continuous daily therapy in preventing UTI with less side effects. Another alternative option is self-start therapy, that involves providing patients with instructions and materials (urine reagent strips and antibiotics) that allow them to both diagnose and treat their UTI at the onset of symptoms. The choice of antibiotics should be based on local guidelines considering the frequency and resistance of different uropathogens, but Nitrofurantoin, Trimethorpim and Cefalexin are the most commonly used.

Methenamine hippurate is hydrolysed to formaldehyde in acidic environments such as the distal tubules of the kidney. Formaldehyde is bacteriocidal and works by denaturing bacterial proteins and nucleic acids. Its efficacy was shown to be non-inferior to low dose prophylactic antibiotics in a recent RCT[5]. However, more information is needed on safety and long-term effectiveness.

Cranberry products have been used for many years for the prevention of UTIs. Proanthocyanidins (PACs), a component of cranberries, inhibit the adherence of p-fimbriated E. coli on uroepithelial cells of the bladder, preventing the adherence of bacteria to the mucosal surface of the urinary tract and thereby inhibiting bacterial proliferation. Although these biological mechanisms have been demonstrated in vitro, clinical studies conducted so far have not conclusively demonstrated efficacy in preventing rUTI. Nevertheless, a recent systematic review showed that cranberry products may be effective in preventing UTI recurrence[6]. D-mannose is a monosaccharide that can also inhibit the adherence of E. coli to the surface of urinary tract cells. A small RCT has demonstrated significant reduction of infections compared to no treatment[7]. To date, clinical evidence on the effectiveness of D-mannose for preventing rUTI is spare and of low quality.

The use of probiotics, especially Lactobacilli, has been proposed for preventing recurrent UTI in women; they also have a good safety profile. However, there is inconclusive evidence for the efficacy of probiotics in UTI prevention[8]. Vitamin C is often recommended as a supplement that can prevent recurrent UTI. In vitro data suggest that it can have a bacteriostatic effect in the urine, but there is a lack of strong clinical evidence[9].

Vaccination represents an alternative preventative approach to UTIs. However, it is well-known that UTIs fail to elicit a protective host immune response and there is substantial diversity between uropathogens. Thus, different vaccination strategies have been developed. Although a number of vaccines have been developed (Uromune, UroVaxom, Solco-Urovac, ExPEC4V), their long-term efficacy is not proven[10].

References

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