

Intravesical Instillations

Antibiotic Bladder Irrigation

Antibiotic irrigation of the bladder for prophylaxis and/or treatment provides some potential advantages over oral and parenteral routes. These include direct drug delivery to the site of infection and bypass of gastrointestinal tract which avoids collateral consequences and side effects such as gastrointestinal upset.

Gentamicin has been the antibiotic most studied for bladder irrigation.^{114–116} There have been no randomized controlled trials performed to date, and all reports have been case series in individuals with complicated UTIs. Reports have included findings from in vitro, animal, and human studies. Bladder instillation regimens have included gentamicin solutions with concentrations ranging from 40–80 mg gentamicin with 50 mL normal saline; instillation volumes of 30 to 60 mL with at least a 1-hour or overnight dwell have been recommended. No elevated serum gentamicin levels were recorded, and all studies reported a meaningful reduction in UTIs while instillations were performed. Specialists may use this therapy in select patients, despite the lack of evidence from robust comparison studies. Limited current evidence supports the safety of gentamicin bladder instillations.

Colistin

Colistin is a polymyxin molecule that damages the lipopolysaccharide component of gram-negative bacteria, leading to increased membrane permeability and eventual cell death.^{117,118} Giua et al¹¹⁸ reported intravesical colistin use in 3 different critically ill patients with multidrug-resistant *Acinetobacter*. The intravesical treatment regimen was 100,000 UI colistin in 50 mL normal saline 3 times daily for 90 minutes for 7 days (2 patients) and 2 days (1 patient). All 3 patients were successfully treated. Although there are not sufficient data to recommend this treatment, it may be considered in a patient who has very limited treatment options.

PREVENTION

The goal of prophylaxis is to prevent or suppress subsequent infections. Although this is most commonly accomplished with antibiotics, alternative nonantibiotic options exist as well.

Antibiotic Prophylaxis

Both the European Association of Urology and the Society of Obstetricians and Gynaecologists of Canada recommend ensuring a negative urine culture before starting prophylactic antibiotics.³² Table 7 displays recommended postcoital and continuous antibiotic regimens. Postcoital prophylaxis should be offered to women who have UTIs temporally related to sexual intercourse. These women will take a single dose of an antimicrobial agent immediately after intercourse.⁶ Postcoital therapy decreased recurrence rates compared with placebo (0.3 vs 3.6 patient-years, $P = 0.001$) and was equally as efficacious as continuous daily therapy.^{44,119} This strategy has decreased costs, likely fewer medication side effects, and decreased risk of antibiotic resistance.^{4,119}

With continuous prophylaxis, a patient takes a single, daily antibiotic dose.⁶ Compared with placebo, continuous prophylaxis decreases recurrences by up to 95%.²⁰ The duration of these regimens ranges from 6 months (based on observations that UTIs tend to cluster and recur within 3 months) to at least 2 years; regimens have been extended to 5 years in some reports.^{96,102,113,131} A Cochrane systematic review of antibiotics for prevention of rUTI in nonpregnant women found that antibiotics given continuously for 6 to 12 months were considerably more effective than placebo in preventing rUTI (RR, 0.15; 95% CI, 0.08–0.28).⁴⁴ Although low-dose prophylaxis with antibiotics may inhibit emergence of bacteria while on therapy, this inhibition may not extend when the antibiotic is discontinued.^{44,132} Several studies have found that 50% to 60% of women become reinfected within 3 months of discontinuing prophylaxis,^{102,113,133} perhaps due in part to intravesical bacterial persistence.^{134–136} Antibiotic prophylaxis may increase the risk of bacterial resistance. This document supports reevaluation of continuous antibiotic prophylaxis at 3 months to determine the efficacy and side effects. Antibiotic prophylaxis is rarely continued beyond 6 months, although it may have to be restarted if UTIs recur.

Estrogen

Vaginal estrogen should be used whenever possible in hypoestrogenic women with rUTI because it clearly decreases UTI recurrence. In a randomized, double-blind, placebo-controlled trial of 93 postmenopausal women assigned to topically applied

TABLE 7. Recommended Antibiotic Prophylaxis Regimens^{20,44,119–130}

Antibiotic Regimens for Prevention		
	Dose	UTIs Per Year
Continuous		
Trimethoprim daily	100 mg	0–1.5
Trimethoprim/sulfamethoxazole daily	40 mg/200 mg	0–0.2
Trimethoprim/sulfamethoxazole every 3 d	40 mg/200 mg	0.1
Nitrofurantoin monohydrate/macrocrystals daily	50 mg	0–0.6
Nitrofurantoin monohydrate/macrocrystals daily	100 mg	0–0.7
Cephalexin daily	125 mg	0.1
Cephalexin daily	250 mg	0.2
Fosfomycin every 10 d	3 g	0.14
Postcoital		
Trimethoprim/sulfamethoxazole	40 mg/200 mg	0.3
Trimethoprim/sulfamethoxazole	80 mg/400 mg	0
Nitrofurantoin monohydrate/macrocrystals	50–100 mg	0.1
Cephalexin	250 mg	0.03

Adapted from Hooton.²⁰