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GENTAMICIN BLADDER INSTILLATIONS DECREASE SYMPTOMATIC URINARY TRACT INFECTIONS AND ORAL ANTIBIOTIC USE IN PATIENTS ON INTERMITTENT CATHETERIZATION

Hypothesis / aims of study
Recurrent urinary tract infections (UTI) are a significantly morbid and costly clinical problem in patients with neurogenic bladder (NGB). Strategies for preventing UTIs in this population are lacking in evidence. The use of a variety of prophylactic bladder instillations, including intravesical gentamicin is described in the literature, but only in small cohorts. The use of daily intravesical gentamicin instillations for the prevention of UTIs is a common clinical strategy for neurogenic bladder patients on intermittent catheterization (ISC) in our institution. We sought to determine if gentamicin bladder instillations reduce the rate of symptomatic UTI's, reduce the use of oral/intravenous antibiotics, and/or reduce the frequency of telephone encounters with their treating urologist.

Study design, materials and methods
We queried our Institutional Review Board approved Neurogenic Bladder database to identify eligible subjects. Inclusion criteria included NGB of any etiology managing their bladder drainage exclusively with ISC for 6 months before and 6 months after initiating prophylactic intravesical gentamicin instillations. Providers used a compounded formulation of 480mg gentamicin diluted in 1L normal saline. A gravity instilled dose of 30-60ml (14.4-28.8mg) of the solution is instilled into the bladder after drainage of urine is complete during patient's last evening catheterization, or when catheterization interval is longest, typically once daily, up to twice per day. Exclusion criteria included short-term instillations only, < 6 months follow up, discontinuation of ISC (>4 weeks of indwelling catheter or urinary diversion). Symptomatic UTIs were defined as a patient complaint of symptoms consistent with UTI (cloudy/foul smelling urine, fevers, chills, increase in bladder spasms or leakage) combined with antibiotic treatment. Descriptive statistics were used to evaluate demographic characteristics and paired variables were evaluated before and after gentamicin instillations. For comparisons between gentamicin cohort and excluded patient cohort, Wilcoxon rank sum test and general chi-square test/Fisher exact test were used for continuous and categorical variables, respectively. For pre-post gentamicin comparisons on UTI prevention strategies, use of antibiotics, telephone encounters and ED/Hospital visits for UTI, Wilcoxon signed-rank test and McNemar test were used for continuous and categorical variables, respectively. For organism comparisons, considering the dependence between organisms belonging to the same culture or the same patient, GEE model was used in order to take unknown correlation into account.

Results
Of 50 subjects identified, 22 met inclusion criteria after chart review. Of the 28 excluded subjects, 11 were excluded due to <6 months follow up, 11 due to short-term use of gentamicin only, 5 due to indwelling catheters, and 1 for urinary diversion. Included subjects had a median age of 37.5 years and were 59.1% male. 63.6% had a spinal cord injury, 13.6% multiple sclerosis, with median time since injury/diagnosis of 14 years. Age, race, sex, neurologic condition and comorbitities were not significantly different between included and excluded NGB patients.

Patients had fewer symptomatic UTI's (4 vs 1 episodes, p<0.004) and used significantly less oral antibiotic prophylaxis after gentamicin instillations were initiated (p=0.03). Patients also had significantly fewer courses of treatment with oral antibiotics (3.5 vs 1, p<0.01); and telephone encounters for UTI's (3 vs 0, p=0.03) after starting gentamicin washes. Days of antibiotic therapy changed from 15 days before gentamicin to 5 days after gentamicin (excluding days on oral prophylaxis), but this did not reach significance. The proportion of multidrug resistant organisms decreased, and the rate of gentamicin resistance did not change. Two antibiotic-related adverse events were reported in patients pre-gentamicin (diarrhea and thrush) and two post-gentamicin (vaginal yeast infection and diarrhea) with only one of these (vaginal yeast infection) being gentamicin related.

Interpretation of results
This is the largest reported series of adult patients in the outpatient setting using gentamicin instillations for management of recurrent urinary tract infections. The use of gentamicin instillations appears to improve antibiotic stewardship and decrease resistant organisms in this at-risk population. Antibiotic resistance and adverse events are rare in patients using daily gentamicin installations

Concluding message
Gentamicin bladder instillations significantly decrease symptomatic UTI episodes and oral antibiotic use in patients with NGB on ISC. Larger, prospective, placebo-controlled (saline instillations) trials should be conducted to confirm these effects

Table 1: Comparison of 22 Neurogenic Bladder Patients Before and After 6 Months of Intravesical Gentamicin Instillations

	Before Gentamicin	After Gentamicin	p-value
Use of Oral Antibiotic Prophylaxis	6 (54.6%)	1 (10.0%)	0.03
Use of Methenamine Hippurate	3 (27.3%)	4 (40.0%)	0.32
Use of Cranberry Extract	1 (9.1%)	1 (10.0%)	> 0.99
Symptomatic UTI (median (range))	4 (IQR 2 – 5)	1 (IQR 1 – 1)	0.004
Courses of Oral Antibiotics	3.5 (IQR 3 – 4)	1 (IQR 1 – 2)	0.01
Days of Antibiotic Therapy	15 (IQR 7 – 24)	5 (IQR 1- 10)	0.06

Courses of IM or IV Antibiotics	3 (27.3%)	1 (10.0%)	0.16
Telephone Encounters for UTI	3 (IQR 1 – 5)	0 (IQR 0 – 1)	0.03
ED/Hospital Visits for UTI	3 (27.3%)	1 (10.0%)	0.32
Multi-drug Resistant Organisms	21/36 (58.3%)	8/17 (47.1%)	0.04 Odds Ratio 2.83 95% CI (1.03, 7.79)
Gentamicin Resistant Organisms	2/33 (6.1%)	0/11 (0%)	NA

Disclosures
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