Evaluating the Use of Cefuroxime for the Treatment of Outpatient Pyelonephritis at an Indian Health Service Hospital

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BACKGROUND

- Oral β-lactams are not recommended over sulfamethoxazole-trimethoprim (SMX/TMP) and fluoroquinolones (FQ) ciprofloxacin and levofloxacin due to inferior efficacy and higher relapse rate.[1] In 2014, the local antibiogram for this facility found 95% susceptibility with cefuroxime against E. coli compared to 70% susceptibility with SMX/TMP (Table 1) . Based on the antibiogram findings, the antibiotic order set for treatment of outpatient pyelonephritis was updated to include cefuroxime as a first line agent (Figure 1).
- Though there is limited literature on cefuroxime treatment for outpatient pyelonephritis, a 2019 study found no difference in 30-day readmission for step-down β-lactams compared to FQ and SMX/TMP therapies (98% vs. 96%, P=0.38) with shorter hospital stay in the β-lactam group (8.2 vs. 9.5 days, P=0.02). [2]
- This data analysis on cefuroxime for treatment of outpatient pyelonephritis came as a result of the antibiotic order set implemented in 2015 (Figure 1).

OBJECTIVE & METHODS

- This project was the end result of a PI project that implemented antibiotic order sets for pyelonephritis. Cefuroxime was designated as first line therapy. We evaluated the failure rate of cefuroxime therapy for acute uncomplicated pyelonephritis.
- The primary measure of failure rate was 30-day reinfection rates defined as requiring secondary antimicrobial treatment or inpatient hospitalization. Secondary endpoints included cefuroxime failure rate in patients with a one-time IV antibiotic dose and an emergence of ESBL isolates in urine cultures without a prior history of ESBL growth.
- Patients with a diagnosis of pyelonephritis from January 1st, 2015 to June 11, 2021 were included. Patients who required initial inpatient hospitalization and pediatric patients were excluded.
- Manual chart reviews were performed by fourth year student pharmacists and verified by two clinical pharmacists. Data collection included 30-day reinfection rates, emergence of ESBL isolates, duration of therapy, one time intravenous (IV) antibiotic administration with a cephalosporin or aminoglycoside, urine culture and susceptibility, increased risk (genitourinary abnormalities and diabetes), white blood cell count, and symptoms.

Table 1. Abridged Local Antibiogram (2014) Leading to Order Set Change

Gram Negative	# Isolates	Amoxicillin/ Clavulanate	Cefuroxime	Cefazolin/ Cephalexin	Ciprofloxacin	SMX/ TMP
E. coli	345	87	**94**	91	89	**64↓**
E. cloacae	8	-	**-**	-	100	**88↑**
P. aeruginosa	10	-	**-**	-	80	**-**
P. mirabilias	16	94	**81↓**	81↓	69	**69**
K. pneumoniae	52	94	**94**	96	96	**92**
Shigella	7	100	**-**	-	100	**0**

RESULTS

Figure 1. Pyelonephritis Order Set

Pyelonephritis
1st Line:
[] Cefuroxime 500mg BID for 14 days

alternative:
[] Ciprofloxacin 500mg PO BID x7 days (contraindicated in pregnancy)

Pyelonephritis (ESBL hx past year)
[] Amox/Clav 875/125mg BID + cefixime 400mg daily x14 days

Table 2. Baseline Data

Characteristic	All patients ± SD (N=198)	Cefuroxime Treatment Failure Group ± SD (N=29)
Age	44 ± 19	44 ± 19
Sex		
Female no. (%)	190 (96)	29 (100)
Male no. (%)	8 (4)	0 (0)
Total Isolates	162	24
E. coli no. (%)	112 (69)	17 (71)
ESBL no. (%)	15 (9)	3 (13)
Duration of therapy	12.3 ± 3	12.5 ± 3
Ethnicity		
Native Americans no. (%)	198 (100)	29 (100)

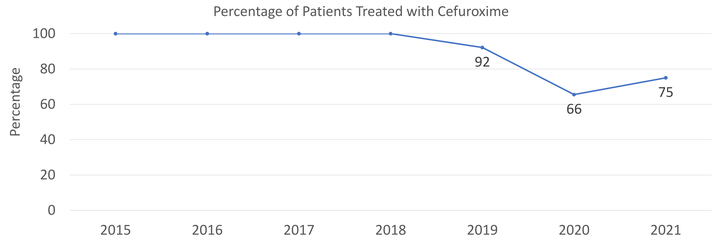

Chart 1. 182 patients (91.9%) received oral cefuroxime therapy for the treatment of outpatient pyelonephritis. 5% patients received treatment with FQs, which are recommended as first line therapy when local resistance is <10%.

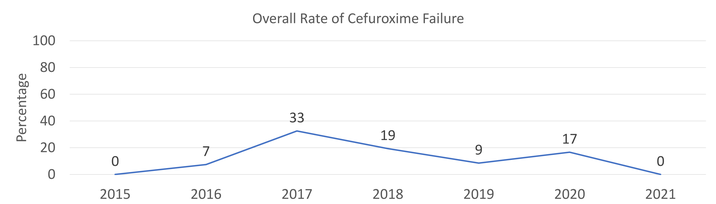

Chart 2. There were 32 patients with treatment failure in the studied time frame, of which 29 received cefuroxime therapy.

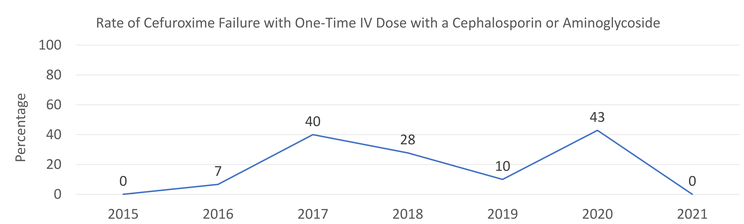

Chart 3. 91 patients (50%) received a one time IV dose with a cephalosporin or an aminoglycoside, of which 21 patients (23%) experienced treatment failure.

DISCUSSION

- This descriptive data analysis showed a 16.4% failure rate with cefuroxime therapy and 23% of the failure among patients who received a one-time IV antibiotic dose in the ER. ESBL isolates after cefuroxime therapy were seen in 28 patients, of which 23 patients did not have a prior history of ESBL.
- Limited literature suggests non-inferiority with β-lactams compared to FQ and SMX/TMP therapies. [2] Guidelines for the treatment of uncomplicate pyelonephritis recommend caution with β-lactams due to inferior efficacy and higher relapse rates. [3] This recommendation comes largely from a study comparing a 3 day regimen of cefpodoxime with a 3 day regimen of ciprofloxacin. This trial found a treatment failure, defined as requiring antimicrobial treatment during a 30 day follow up, of 7% for ciprofloxacin compared with 18% with cefpodoxime. [4]
- The failure rate is consistent with research showing cefuroxime does not reach target minimum inhibitory concentration needed for bacteriostasis. [5]
- Data analysis on outpatient pyelonephritis prior to 2015 was not performed. Therefore, a limitation of the project is a lack of baseline data on previous antibiotic use to compare against the results of this project.

CONCLUSION

- This review suggests a lower rate of bacteriological cure of acute uncomplicated pyelonephritis with cefuroxime therapy with or without a one-time IV antibiotic dose with a cephalosporin or aminoglycoside.

DISCLOSURES

- This material is the result of work supported with resources and the use of facilities at the Whiteriver Indian Hospital located in the Phoenix Area of the Indian Health Services. The contents do not represent the views of the Indian Health Services of the United States Government. The authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: All authors have nothing to disclose.

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