Efficacy and safety of 3 day versus 7 day cefditoren pivoxil regimens for acute uncomplicated cystitis: multicentre, randomized, open-label trial.

BACKGROUND:

- Fluoroquinolone-non-susceptible Escherichia coli isolated from patients with acute uncomplicated cystitis are a matter of increasing concern. Cefditoren pivoxil is an oral, β-lactamase-stable, extended-spectrum cephalosporin that is effective against fluoroquinolone-non-susceptible bacteria.

OBJECTIVE

- To evaluate the clinical and microbiological efficacies of cefditoren pivoxil against acute uncomplicated cystitis and to determine the optimal duration of cefditoren treatment

METHODS

- **Design**: multicenter, open label, randomized parallel trial; Duration: 2 years
- **Inclusion criteria**: female ≥20 years old, fever < 37.58C with any cystitis symptoms, such as micturition pain, urinary frequency, urgency or lower abdominal pain with pyuria
- **Exclusion criteria**: occurrence of complicated UTIs; previous UTIs within 4 weeks of the current UTI; treatment with other antimicrobials within the previous 10 days; a previous episode of cephalosporin hypersensitivity; patients who had allergic asthma or hives; immunosuppression; current pregnancy; renal failure; or pts who were judged as ineligible for this study by investigators because of low compliance.
- **Primary outcome measure**: Determine the microbiological outcome 5-9 days after the end of administration
- **Secondary outcome measures**: clinical outcome 5–9 days after the first visit & evaluation of recurrence 4–6 weeks following treatment completion
- 104 patients received ceditoren for either
    - 3days (51 patients)
    - 7 days (53 patients)
- No power mentioned
- Data handling method was intent-to-treat

RESULTS

- Out of 104 pts 81, 70, & 87 pts were included clinical efficacy, microbiological efficacy, and evaluation of recurrence, respectively because data was missing for each measure.
- **Primary outcome measure**: There was no significant difference in % of microbiological cure rate between groups: The microbiological cure rate of the 3 day group was 82.5% (33/40) and it was 90.2% (37/41) for the 7 day group, (P=0.349).
- **Secondary outcome measures**: There was no significant difference in % of clinical cure rate & recurrence between groups: Clinical cure rates of the 3 and 7 day groups were 90.9% (40/44) and 93.2% (41/44), respectively(P=1.000). Recurrence rates at 4–6 weeks after treatment completion were 10.2% (5/49) in the 3 day group and 12.2% (6/49) in the 7 day group(P=1.000).
- **Author's conclusion:** The efficacy rates of cefditoren pivoxil were in the same range as found in studies of other oral cephems and there was no difference in the clinical and microbiological efficacies between the 3 and 7 day regimens. Our data suggest that cefditoren pivoxil is a potent agent and a 3 day regimen might be enough for uncomplicated cystitis. Further studies are necessary to evaluate differences in duration or comparisons with other drugs.

STRENGTHS

- Random assignment for each treatment group
- Parallel Controlled experiment
- Included numbers of pts missing data
- Included background
- Primary and secondary outcome measures appropriate for determining the objective
- Included causative organisms & antimicrobial susceptibilities of e.coli

LIMITATIONS

- Possible Financial conflict of interest w manufacture and research organization
- Study design was poor
    - No power
    - Small sample size
    - No stat. signif results
    - Exclusion criteria to eliminate pts who would be low compliant
    - Open label/ unblinded
- Non-comparable SOC doses or other approved drugs for this indication
- OC data was lost for recurrence data (no returned post cards) & missing for efficacies
- No data provided to account for adherence
- Non-study concomitant medications taken by patients were not reported

CONCLUSION

- Although the study showed the 3 day treatment duration was comparable to 7 day duration of treatment implying that it might be the better option because it's just as effective and can cause less resistance and side effects, the 3 day treatment may not be comparable in actual practice.
    - There was a small sample size in this study and small amount of pts had resistant bugs which may make efficacy better than what it would be in the population outside of this study. Also missing data could have greatly changed results
    - If a larger sample size were compared with this drug vs. a drug indicated for this condition, it may have made cefditoren have a lower efficacy than it really did
- Future research:
    - Since results showed a high efficacy rate with both arms with a small sample size, a trial should be done with a larger sample with a wider variety of organisms for this condition to determine if this antibiotic is really effective for this condition and if the 3day duration is really better than the 7day duration.

Reference: Sadahira T, Wada K, Araki M, Ishii A, Takamoto A, Kobayashi Y, Watanabe M, Watanabe T, Nasu Y, Kumon H; Okayama Urological Research Group (OURG).. Efficacy and safety of 3 day versus 7 day cefditoren pivoxil regimens for acute uncomplicated cystitis: multicentre, randomized, open-label trial. J Antimicrob Chemother. 2017 Feb;72(2):529-534. doi: 10.1093/jac/dkw424. PubMed PMID: 27733519.

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