

A Prospective, Randomized, Double Dummy, Placebo-controlled Trial of Oral Cefditoren Pivoxil 400 mg Once Daily as Switch Therapy after Intravenous Ceftriaxone in Acute Pyelonephritis: An Interim Analysis

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Background: Acute pyelonephritis (APN) is common and often initially treated with initial intravenous (IV) antibiotics followed by oral agent, especially fluoroquinolones. Unfortunately, *Escherichia coli* (*E. coli*) and other uropathogens are increasingly resistant to fluoroquinolones and there are limited treatment options left. Cefditoren pivoxil has shown excellent *in vitro* activity against *E. coli*. This study was designed to assess the efficacy of cefditoren pivoxil as a switch therapy after intravenous ceftriaxone in APN.

Methods: A prospective randomized controlled trial in patients with presumptive diagnosis of APN was conducted at Srinagarind Hospital, Thailand during December 2010 to July 2011. A daily 2 gram IV ceftriaxone was given as an initial antibiotics in both groups. After Day 3, the patients who were satisfied the criteria of switch therapy, were randomized to either the control or study group. Group A (control) were given oral placebo 4 tablets once daily with meal plus IV ceftriaxone. Group B (study) were given oral

cefditoren pivoxil (100 mg) 4 tablets once daily with meal plus intravenous placebo. The total duration of antibiotics was 10 days. At the end of treatment, clinical and bacteriological outcomes were assessed. The outcomes of both groups were compared by using the proportion test. Furthermore, recurrent of APN was evaluated at 2 weeks after the end of treatment.

Results: This interim analysis included 70 patients (plan for 82 patients). There were no statistically significant differences in baseline characteristics and resolution of acute symptoms between the two groups. The most common pathogen in urine and blood cultures was *E. coli*, which was accounted for 82.28% and 82.35% of the isolates, respectively. Clinical cure was observed in 33 of 35 (94.30%) patients in the group A and in 35 of 35 (100%) patients in the group B (p-value = 0.15, 95% CI; -0.13 to 0.02). Urine bacteriological eradication was found in 61.80% and 58.80% in the group A and group B, respectively (p-value=0.80, 95% CI; -0.20 to 0.26). No recurrent APN was observed in either of the groups. The most frequently reported drug related

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clinical adverse effects for both groups were digestive symptoms, including diarrhea and nausea and there was no significant difference between the two treatment groups.

Conclusion: These data suggested that an intravenous ceftriaxone followed by oral cefditoren pivoxil 400 mg once daily is a potential option as an effective and safe antibiotic for treatment of acute pyelonephritis.