Evaluation of an outpatient 5-day course of levofloxacin in males with a urinary tract infection: A subgroup analysis of a previously published trial

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INTRODUCTION

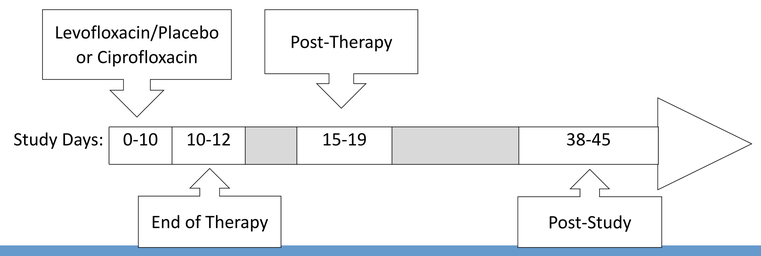
- Current guidelines classify urinary tract infections (UTIs) in males as complicated and recommend longer treatment duration than females[1]
- Clinical trials demonstrating efficacy of antimicrobials in urinary tract infections have typically enrolled a majority of female patients[2]
- Peterson and colleagues conducted a multicenter, double-blind, randomized, non-inferiority study of primarily outpatient subjects comparing levofloxacin 750 mg IV/PO daily for 5 days to ciprofloxacin 400 mg IV/500 mg PO twice daily for 10 days in both male and female patients with complicated UTIs (cUTIs) and acute pyelonephritis[3]
- However, the published results of this study combined data from both male and female subjects in the analysis

OBJECTIVE

- To evaluate clinical success rates in males who received 5 days of levofloxacin or 10 days of ciprofloxacin compared to their female counterparts with cUTI

METHODS

- De-identified, patient-level data was obtained from a previously conducted clinical trial [3] through the Yale University Open Data Access (YODA) Project
- Multicenter, double-blind, randomized, non-inferiority study comparing levofloxacin 750 mg once daily for 5 days and 400/500 mg IV/PO ciprofloxacin twice daily for 10 days
- The current study was a post-hoc, subgroup analysis of male and female patients at least 18 years old, institutionalized or ambulatory, diagnosed with a cUTI
- Patients were evaluated at end of therapy (EOT), post-therapy (PT), and post-study (PS) for clinical success rates
- Chi-square and Fisher's Exact tests with contingency tables were utilized for the categorical data of clinical success rates
- Alpha = 0.05



INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria

- At least 10^5 colony-forming units of 1 or 2 uropathogens
- One of the following: dysuria, increased urinary frequency, urgency, WBC > 12,500/mm^3 or ≥ 10% bands, temperature ≥ 100.4^{0}F within previous 24 hours

Exclusion Criteria

- Uncomplicated UTI
- Acute Pyelonephritis*
- Chronic Pyelonephritis
- Complete obstruction
- Need or history of surgery or lithotripsy within 7 days of study entry
- Need for additional antimicrobial therapy for a coexisting infection or for the presenting UTI
- Pathogen known to be resistant to the study medication
- Received more than 1 dose of any antibacterial for the treatment of the UTI within 5 days of study entry (unless patient received at least 72 hours of a non-fluoroquinolone antibiotic and were deemed a clinical failure)
- Renal or perirenal abscess
- Acute or chronic bacterial prostatitis
- Epididymitis
- Pregnancy

*Additional exclusion criteria added for current study

RESULTS

- 427 patients with cUTI met all inclusion criteria and were analyzed in the modified Intent-To-Treat (mITT) group (224 male, 203 female)
- 350 (189 male, 161 female) adhered to the study protocol and were included in the microbiologically evaluable (ME) group
- Approximately half of the patients in the mITT population were males and the majority of subjects were white (78%), over the age of 60 (62.5%), infected with *E. coli* (59%), and treated in the community (98%)
- Clinical success rates for males and females with cUTI were similar in both the mITT and ME populations at EOT and PT (p > 0.05)
- For male patients with a catheter, clinical success rates were higher in the levofloxacin group compared with ciprofloxacin (91.3% and 56.3%, respectively), p = 0.019
- Additional complicating factors yielded significantly different results

"This study, carried out under YODA Project #2015-0514, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.."

RESULTS

Table 1. Comparison of clinical success rates between male and female patients with cUTI.

EOT	Levofloxacin			Ciprofloxacin		
	Males	Females	p	Males	Females	p
mITT	87/105 (83%)	95/118 (81%)	0.730	92/119 (77%)	66/85 (78%)	1.00
ME	79/91 (87%)	88/94 (94%)	0.141	84/98 (86%)	59/67 (88%)	0.817

PT	Levofloxacin			Ciprofloxacin		
	Males	Females	p	Males	Females	p
mITT	80/105 (76%)	96/118 (81%)	0.411	93/119 (78%)	70/85 (82%)	0.485
ME	74/91 (81%)	81/94 (86%)	0.428	84/98 (86%)	61/67 (91%)	0.342

Table 2. Comparison of clinical success rates within complicating factor groups, in the ME male population at EOT, based upon antibiotic received.

	Catheter	No catheter	p
Levofloxacin	21/23 (91.3%)	58/68 (85.3%)	0.723
Ciprofloxacin	9/16 (56.3%)	75/82 (91.5%)	0.002
	Neurogenic bladder or urinary retention	No neurogenic bladder or urinary retention	p
Levofloxacin	23/26 (88.5%)	56/65 (86.2%)	1.000
Ciprofloxacin	18/26 (69.2%)	66/72 (91.7%)	0.009
	No additional complicating factors	2 or more additional complicating factors	p
Levofloxacin	30/34 (88.2%)	26/30 (86.7%)	1.000
Ciprofloxacin	36/39 (92.3%)	19/27 (70.4%)	0.040

CONCLUSION

- Male patients in this analysis achieved similar clinical success rates to their female counterparts in both the 5-day course of levofloxacin and the 10-day course of ciprofloxacin
- Male patients with additional complicating risk factors may have a greater rate of clinical success with a 5-day course of levofloxacin
- Results of this study should only be applied to male patients treated in the outpatient setting
- The subgroup analysis is not powered, and therefore, a larger scale study is warranted

REFERENCES

1. Hooton TM. Uncomplicated urinary tract infection. N Engl J Med. 2012;366:1028-37.
2. Lipskv BA. Urinary tract infections in men. Epidemiology, pathophysiology, diagnosis and treatment. Ann Intern Med. 1989;110:138-50.
3. Peterson J, Kaul S, Khashab M, Fisher AC, Kahn JB. A double-blind, randomized comparison of levofloxacin 750 mg once-daily for five days with ciprofloxacin 400/500 mg twice-daily for 10 days for the treatment of complicated urinary tract infections and acute pyelonephritis. Urology. 2008;71:17-22.