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Levofloxacin and Ciprofloxacin in the treatment of urinary tract infection

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Abstract

Background: Urinary tract infections (UTIs) are one of the most frequent bacterial infections acquired in both hospital and community.

Aim: To compare between levofloxacin and ciprofloxacin in the management of urinary tract infections would typically be to compare and assess the safety, efficacy, and tolerability of these two antibiotics in treating UTIs caused by common bacterial pathogens.

Patients and methods: This systematic review and meta-analysis search were carried out across multiple databases, involving Cochrane Library, PubMed, and Embase, to identify relevant randomized controlled trials (RCTs). The included data from four studies conducted between 2003 and 2012, with a total of 1127 patients.

Results: Two studies reported (Headache) and all can be used. A no significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 = 0%, P=0.32). The combined mean difference and ninety-five percent CIs was 0.78 (0.35 to 1.72). The combined result demonstrates statistically no significant difference between groups regarding (Headache) (Z= 0.62, P=0.54).

Two studies reported (Dizziness) and all can be used. A significant heterogeneity was detected. Therefore, a random-effect model was used for analysis (I^2 = 73%, P-value equals 0.05). The combined mean difference and ninety-five percent CIs was 0.43 (0.12 to 1.53). The combined result demonstrates statistically insignificant distinction among groups regarding (Dizziness) (Z-value equals 1.30, P-value equals 0.19).

Conclusion: Both levofloxacin and ciprofloxacin are effective in treating UTI, with no significant difference in clinical success rate, microbial eradication rate, or adverse event rate.

Key words: UTIs; Headache; Dizziness.

Introduction

Urinary tract infections (UTIs) are among the most frequent bacterial infections that can be contracted in both the hospital and the community. Levofloxacin and ciprofloxacin are fluoroquinolones that are frequently utilized to manage urinary tract infections **(1).**

Each year, approximately 150 million people globally are affected by urinary tract infections. Investigations have indicated that forty to fifty percent of females worldwide will experience urinary tract infections at least once during their lifetimes, and females are significantly more susceptible to these infections. urinary tract infections are equally harmful to males, particularly in terms of reproductive function **(2).**

Levofloxacin and ciprofloxacin are the most frequently utilized medications for the management of acute pyelonephritis (AP) and cUTIs. urinary tract infections may result in a significant reduction in the total number of sperm once they have migrated to the accessory gland, and bilateral infections are more detrimental **(3).**

Levofloxacin and ciprofloxacin are antimicrobial agents that are anticipated to expand their applications due to their underlying effects on neuroinflammation, which modulate hematopoietic stem cell transplantation and even inhibit SARS-CoV-2 replication **(4).**

The objective of the investigation was to assess and compare the safety, efficacy, and tolerability of levofloxacin and ciprofloxacin for the management of urinary tract infections caused by common bacterial pathogens.

Patients and methods

This systematic review and meta-analysis search were carried out across multiple databases, involving Cochrane Library, PubMed, and Embase, to identify relevant randomized controlled trials (RCTs). The included data from four studies conducted between 2003 and 2012, with a total of 1127 patients. The studies were geographically distributed, involving populations from China, California, New Jersey, and other parts of the United States. The patient pool comprised individuals with a confirmed diagnosis of acute or chronic UTIs.

Inclusion Criteria: Adult patients (18-75 years) diagnosed with acute or chronic UTIs, comparative RCTs involving levofloxacin and ciprofloxacin, studies reporting detailed clinical and microbiological outcomes and clear documentation of adverse events.

Exclusion Criteria: Non-randomized studies or observational data, studies involving pediatric populations or other antibiotic comparisons and incomplete or unpublished data

Data Sources and Collection

Data were extracted from the included studies using standardized forms, focusing on: Baseline patient demographics (age, gender, underlying conditions). Clinical endpoints (e.g., success rates at end-of-therapy and post-therapy). Microbiologic eradication rates (before and after therapy). Adverse events (e.g., headache, nausea, dizziness). The mean age of participants across all studies was 37.5 years (range: 18–75). Gender distribution was reported in two studies, with 439 males and 965 females.

Outcomes: The primary outcomes were: Clinical Success Rates: Defined as the resolution of symptoms and infection during or after therapy. Microbiologic Eradication Rates: Defined as the absence of bacterial pathogens in post-treatment cultures and adverse Events: Including headache, dizziness, nausea, and other reported side effects.

Statistical Analysis

Review Manager version 5.4.1 has been utilized to conduct all data analyses. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The odds ratio for binary results has been determined using a ninety-five percent confidence interval (CI). For continuous results, we computed the mean difference with a ninety-five percent confidence interval. A fixed-effect model with the Mantel-Haenszel method has been utilized to compute the overall impact, which has been estimated with a ninety-five percent confidence interval, in the absence of heterogeneity among investigations. Alternatively, the random-effects model utilizing the method of DerSiomonian and Laird has been selected. The I^2 test and Q statistic have been utilized to assess the heterogeneity among investigations, which describes the degree of variability in the effect estimates. A P-value of less than 0.05 was regarded as significant.

Results

A total of 4 studies were selected for the current analysis, including a total of 1127 patient. The publication year ranged from 2003 to 2012. 1 study was conducted in each of the following: china, California, United States and New Jersey. Demographic data of involved investigations are demonstrated in **Table 1**.

Author, year	year	country	Study period		Study design	Sample Size		
			from	to		Levofloxacin	Ciprofloxacin	Total
Zhi-Chao Zhang, 2012	2012	China			randomized, controlled non-inferiority trial	209	199	408
WILLIAM BUNDRICK, 2003	2003	California			double-blind, active-control trial	136	125	261
Howard A. Klausner, 2007	2007	United States	2005	2006	double-blind, parallelgroup, randomized, noninferiority trial	146	165	311
Janet Peterson,2008	2008	New Jersey			A multicenter, double-blind, randomized, noninferiority study	537	556	147

Table 2. Patient's characteristics

The mean participants' age in studied groups was 37.5ranging from 18to 75 years, and gender was reported in 2 studies with 439 male and 965 female as shown in table 2.

Author, year	Age (year)						sex					
	Levofloxacin			Ciprofloxacin			Levofloxacin			Ciprofloxacin		
	mean	SD	total	mean	SD	total	male	female	total	male	female	total
Zhi-Chao Zhang, 2012	33.4	8.1	209	33.5	8.5	199						
WILLIAM BUNDRICK, 2003												
Howard A. Klausner, 2007	38.9	17.96	146	39.4	17.05	165	8	138	146	4	161	165
Janet Peterson,2008							207	330	537	220	336	556

Acute pyelonephritis:

Clinical success rates end of therapy:

Two studies reported (**Clinical success rates end of therapy)** and all can be used. A significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 93%, P-value equals 0.0002). The combined mean difference and ninety-five percent confidence intervals was 2.39 (1.61 to 3.54). The combined result demonstrates statistically significant distinction among groups regarding (**Clinical success rates end of therapy**) (Z = 4.35, P <0.0001).

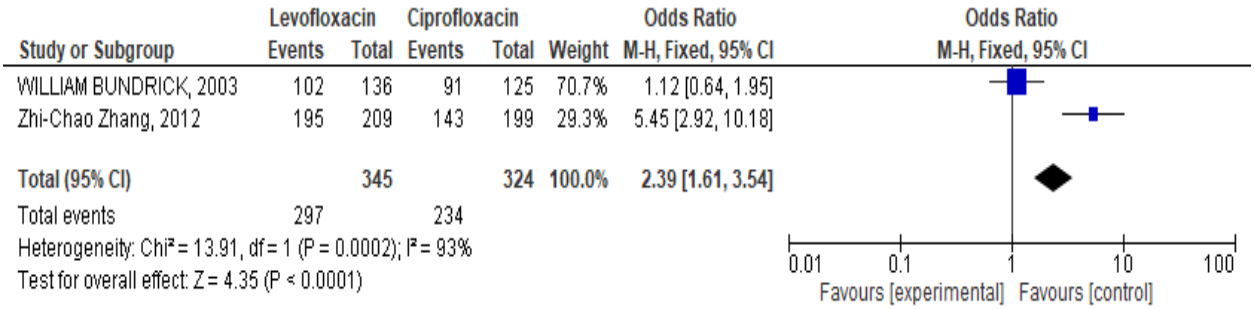

Figure 1. Forest plot of Clinical success rates end of therapy demonstrates statistically significant difference between Levofloxacin and d Ciprofloxacin groups.

Clinical success rates posttherapy:

Two studies reported (**Clinical success rates posttherapy)** and all could be utilized. A significant heterogeneity has been identified. Consequently, a random-effect model was used for analysis (I^2 = 95%, P-value less than 0.00001). The combined mean difference and ninety-five percent confidence intervals was 2.32 (1.58 to 3.40). The combined result demonstrates statistically significant difference between groups regarding (**Clinical success rates posttherapy**) (Z = 4.30, P <0.0001).

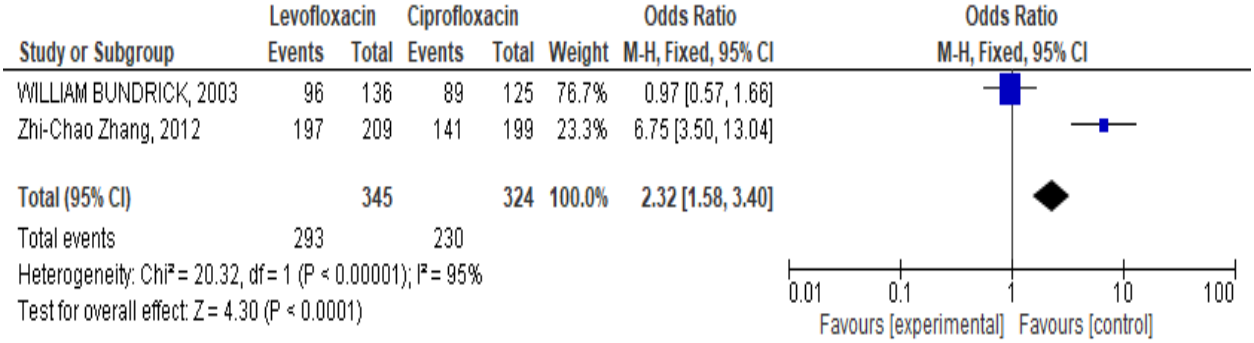

Figure 2. Forest plot of Clinical success rates posttherapy shows statistically significant distinction among Levofloxacin and d Ciprofloxacin groups.

Microbiologic Eradication rate:

Two studies reported (**Microbiologic Eradication rate)** and all can be used. A significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis

(I^2 equals 85%, P-value equals 0.01). The combined mean difference and ninety-five percent confidence intervals was 1.63 (1.16 to 2.30). The combined result demonstrates statistically significant difference between groups regarding (**Microbiologic Eradication rate**) (Z-value equals 2.81, P-value equals 0.005).

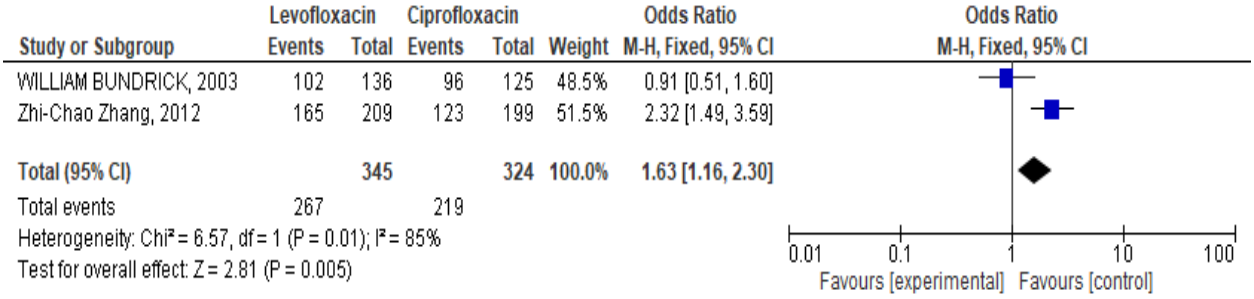

Figure 3. Forest plot of Microbiologic Eradication rate shows statistically significant distinction among Levofloxacin and d Ciprofloxacin groups.

Chronic pyelonephritis:

Clinical success rates end of therapy

Two studies reported (**Clinical success rates end of therapy)** and all can be used. A significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 76%, P-value equals 0.04). The combined mean difference and ninety-five percent confidence intervals was 1.10 (0.69 to 1.75). The combined result demonstrates no statistically significant distinction among groups regarding (**Clinical success rates end of therapy**) (Z-value equals 0.42, P-value equals 0.68).

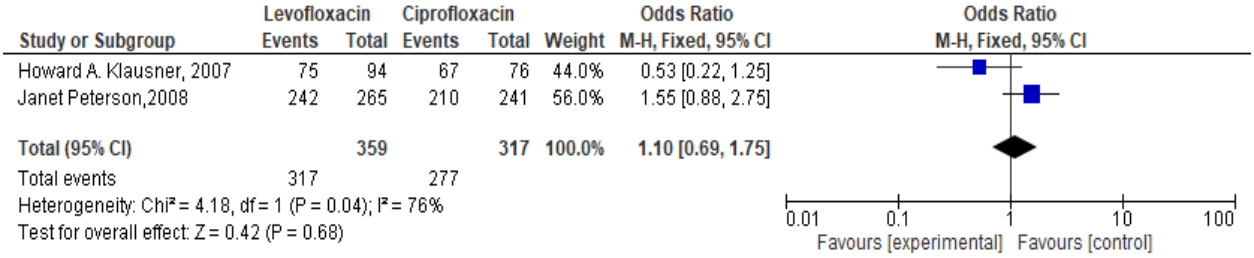

Figure 4. Forest plot of Clinical success rates end of therapy shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Clinical success rates posttherapy:

Two studies stated (**Clinical success rates posttherapy)** and all could be utilized. A non-significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 0%, P-value equals 0.38). The combined mean difference and ninety-five percent confidence intervals was 0.93 (0.58 to 1.49). The combined result shows statistically insignificant distinction among groups regarding (**Clinical success rates posttherapy**) (Z = 0.31, P =0.75).

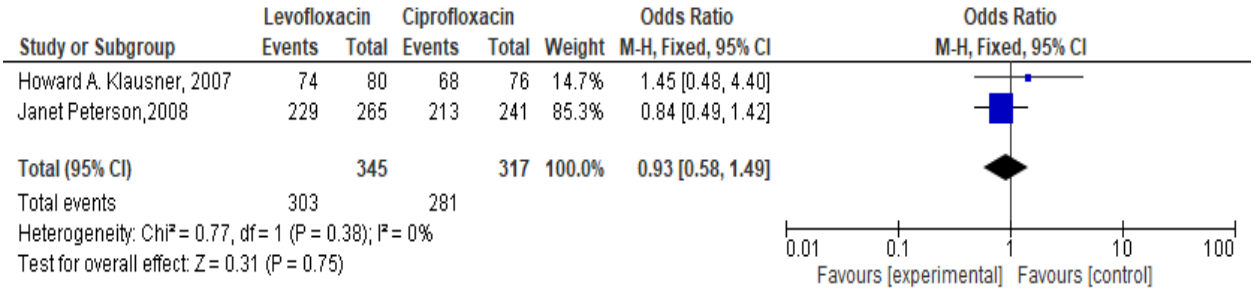

Figure 5. Forest plot of Clinical success rates posttherapy shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Microbiologic Eradication rate end of therapy:

Two studies reported (**Microbiologic Eradication rate end of therapy)** and all can be used. A non-significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 60%, P-value equals 0.12). The combined mean difference and ninety-five percent confidence intervals was 0.91 (0.59 to 1.41). The combined result shows statistically insignificant distinction among groups regarding (**Microbiologic Eradication rate end of therapy**) (Z-value equals 0.42, P-value equals 0.68).

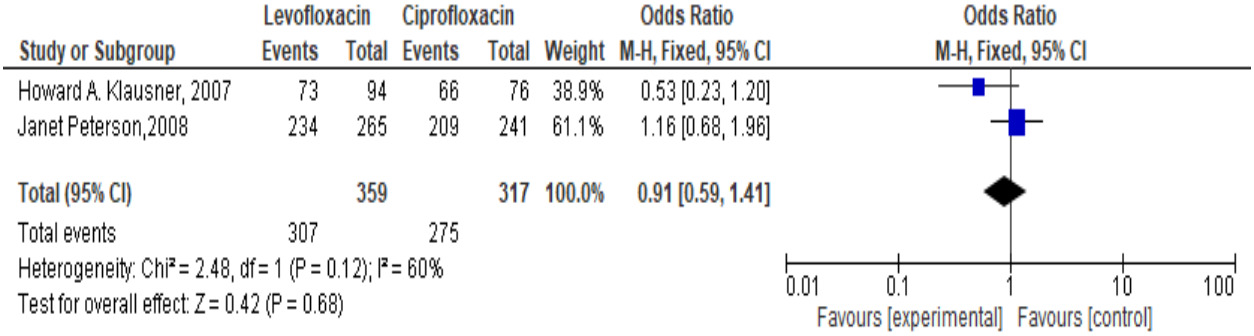

Figure 6. Forest plot of Microbiologic Eradication rate end of therapy shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Microbiologic Eradication rate posttherapy:

Two studies reported (**Microbiologic Eradication rate posttherapy)** and all can be used. A non-significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 = 0%, P=0.82). The combined mean difference and ninety-five percent confidence intervals was 0.76 (0.47 to 1.25). The combined result shows statistically insignificant distinction among groups regarding (**Microbiologic Eradication rate posttherapy**) (Z-value equals 1.08, P –value equals 0.28).

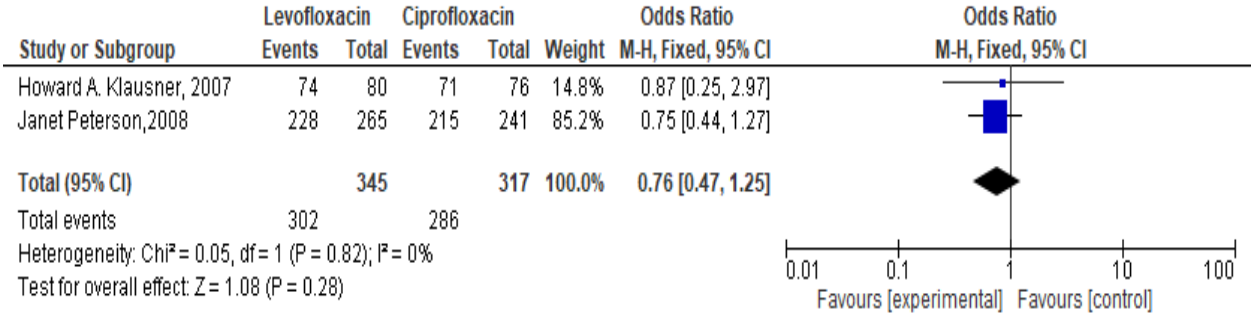

Figure 7. Forest plot of Microbiologic Eradication rate posttherapy shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Adverse events:

Headache:

Two studies reported (**Headache**) and all can be used. A no significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 0%, P-value equals 0.32). The combined mean difference and ninety-five percent confidence intervals was 0.78 (0.35 to 1.72). The combined result demonstrates statistically no significant difference between groups regarding (Headache) (Z-value equals 0.62, P-value equals 0.54).

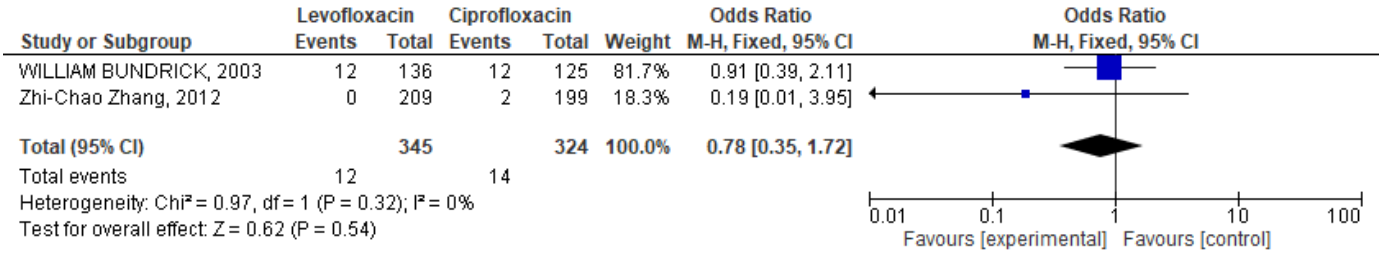

Figure 8. Forest plot of Headache shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Dizziness:

Two studies reported (Dizziness) and all can be used. A significant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 73%, P-value equals 0.05). The combined mean difference and ninety-five percent confidence intervals was 0.43 (0.12 to 1.53). The combined result demonstrates statistically no significant difference between groups regarding (Dizziness) (Z-value equals 1.30, P-value equals 0.19).

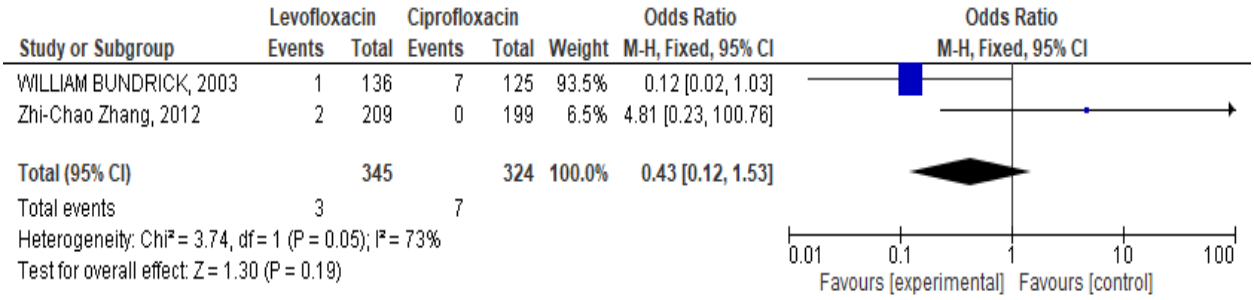

Figure 9. Forest plot of Dizziness shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Nausea:

Two studies reported (**Nausea**) and all can be used. A nonsignificant heterogeneity has been identified. Consequently, a random-effect model has been used for analysis (I^2 equals 0%, P-value equals 0.51). The combined mean difference and ninety-five percent confidence intervals was 1 (0.43 to 2.32). The combined result demonstrates statistically no significant difference between groups regarding (Dizziness) (Z= 0.01, P=1.00).

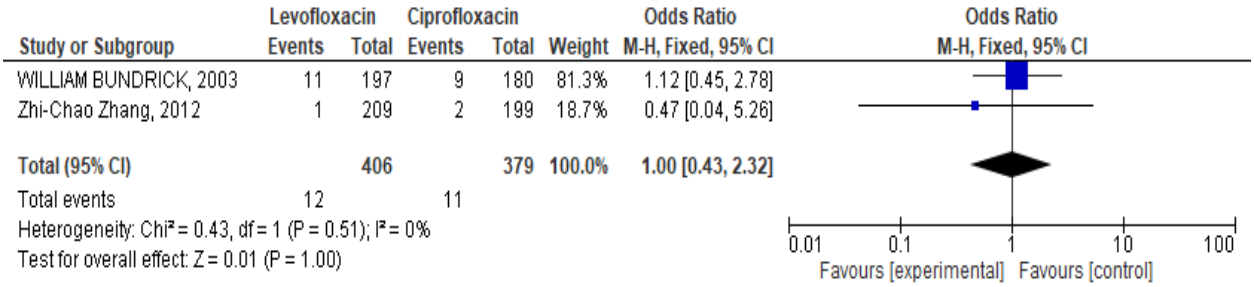

Figure 10. Forest plot of Nausea shows statistically insignificant distinction among Levofloxacin and d Ciprofloxacin groups.

Discussion

This systemic review and met analysis included total of 4 studies **(5-8)** were selected for the current analysis, including a total of 1127 patient. The publication year ranged from 2003 to 2012.

In acute pyelonephritis: Clinical success rates end of therapy and posttherapy

Two studies **(7,8)** reported the combined result demonstrates statistically significant distinction among groups regarding clinical success rates end of therapy and clinical success rates posttherapy with p value <0.0001.

In consistent with **Xue Z et al., (9)** A systematic review and meta-analysis of levofloxacin and ciprofloxacin in the management of urinary tract infection. They showed that statistically significant distinction among groups regarding clinical success rates end of therapy and clinical success rates posttherapy and also, accordance with **Mospan GA et al., (10) Alqahtani M et al., (11) Yasmeen BN et al., (12).**

In accordance with **Bundrick W et al., (8)** who intended to compare the efficacy and safety of levofloxacin and ciprofloxacin for the management of chronic bacterial prostatitis. They demonstrated that clinical success has been attained in 75.0 percent of the microbiologically

assessable levofloxacin-treated cases and 72.8 percent of the microbiologically assessable ciprofloxacin-treated cases at the following-therapy visit. This suggests that levofloxacin is clinically as effective as ciprofloxacin.

Microbiologic eradication rate

Two studies **(7)(8)** demonstrated the combined result demonstrated that there was statistically significant difference between groups regarding microbiologic eradication rate with P value =0.005.

As well, **Bundrick W et al., (8)** showed that the microbiologic eradication rates (75 percent for levofloxacin and 76.8 percent for ciprofloxacin; 95 percent confidence interval for the distinction −8.98 to 12.58). This indicated that a statistically significant distinction among groups regarding microbiologic eradication rate.

Chronic pyelonephritis: Clinical success rates end of therapy and posttherapy

Two studies **(5)(6)** reported the combined result demonstrated no statistically significant difference between groups regarding microbiologic eradication rate end of therapy and microbiologic eradication rate posttherapy.

In agreement with **Cao D et al., (13)** who conducted a meta-analysis of high-quality RCTs that compared levofloxacin and ciprofloxacin in the management of urinary tract infections, the objective was to compare the safety and efficacy of both medications. They stated that the analysis didn't reveal a significant statistical distinction in the clinical effective rate at the end of therapy or posttherapy.

In contrast to **Zhang ZC et al., (7)** stated that there was a significant statistical distinction in the end-of-therapy or posttherapy clinical effective rate; this was because of the fact that levofloxacin had a greater efficacy, a lower illness recurrence, and an adverse event rate in Chinese cases.

Microbiologic Eradication rate end of therapy and posttherapy.

Two studies **(5)(6)** reported the combined result demonstrated no statistically significant difference between groups regarding microbiologic eradication rate end of therapy and microbiologic eradication rate posttherapy with P value =0.68.

In the same line **Cao D et al., (13)** revealed that a statistically insignificant distinction has been observed among groups regarding microbiologic eradication rate end of therapy and microbiologic eradication rate posttherapy.

The microbiologically assessable population experienced the eradication of all pathogens present at the investigation entry in 75.0 percent of the levofloxacin-treated cases and 76.8 percent of the ciprofloxacin-treated cases at the end of medication therapy **Bundrick W et al., (8).**

Adverse events: Headache, Nausea, Dizziness

Two studies **(7)(8)** showed the combined result demonstrated that a statistically insignificant distinction has been observed among groups regarding Headache, Nausea and Dizziness with P value <0.05.

Accordance with **Cao D et al., (13)** demonstrated that a statistically insignificant distinction has been observed among groups regarding Headache, Nausea and Dizziness.

The two medications were comparable in terms of adverse events, and no notable severe or mortality cases have been reported. The most prevalent side effects were digestive tract symptoms (diarrhoea as well as flatulence) and central nervous system symptoms (dizziness, headache, along with nausea), which were in accordance with the previous report by **Stahlmann R et al., (14).**

Peterson et al., (6) determined that no adverse event was directly associated with the therapy, with the exception of an allergic reaction.

The previously mentioned evidence demonstrated that levofloxacin and ciprofloxacin were safe for clinical use.

The frequency of adverse reactions was not statistically heterogeneous, as demonstrated by the meta-analysis conducted by **Xue Z et al., (9)** The P-value was 0.84, and the adverse reaction rate following urinary tract infection therapy wasn't statistically significant among both medications stated in the five literatures (P-value of 0.2).

Conclusion

The safety and effectiveness of levofloxacin and ciprofloxacin are statistically equivalent, and both antibiotics are effective in the management of urinary tract infections. The end-of-therapy or posttherapy clinical success rate, microbial eradication rate, and adverse event rate did not exhibit any significant distinctions among both medications.

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