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Review

Fluoroquinolone-based versus β-lactam-based regimens for complicated intra-abdominal infections: a meta-analysis of randomised controlled trials ☆

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ABSTRACT

Complicated intra-abdominal infections (cIAIs) are common and confer significant morbidity, mortality and costs. In this era of evolving antimicrobial resistance, selection of appropriate empirical antimicrobials is paramount. This systematic review and meta-analysis of randomised controlled trials compared the effectiveness and safety of fluoroquinolone (FQ)-based versus β-lactam (BL)-based regimens for the treatment of patients with cIAIs. Primary outcomes were treatment success in the clinically evaluable (CE) population and all-cause mortality in the intention-to-treat (ITT) population. Subgroup analyses were performed based on specific antimicrobials, infection source and isolated pathogens. Seven trials (4125 patients) were included. FQ-based regimens included moxifloxacin (four studies) or ciprofloxacin/metronidazole (three studies); BL-based regimens were ceftriaxone/metronidazole (three studies), carbapenems (two studies) or piperacillin/tazobactam (two studies). There was no difference in effectiveness in the CE (2883 patients; RR = 1.00, 95% CI 0.95–1.04) or ITT populations (3055 patients; RR = 0.97, 95% CI 0.94–1.01). Mortality (3614 patients; RR = 1.04, 95% CI 0.75–1.43) and treatment-related adverse events (2801 patients; RR = 0.97, 95% CI 0.70–1.33) were also similar. On subset analysis, moxifloxacin was slightly less effective than BLs in the CE (1934 patients; RR = 0.96, 95% CI 0.93–0.99) and ITT populations (1743 patients; RR = 0.94, 95% CI 0.91–0.98). Although FQ- and BL-based regimens appear equally effective and safe for the treatment of cIAIs, limited data suggest slightly inferior results with moxifloxacin. Selection of empirical coverage should be based on local bacterial epidemiology and patterns of resistance as well as antimicrobial stewardship protocols.

1. Introduction

Intra-abdominal infections (IAIs) encompass a wide spectrum of diseases, ranging from simple acute appendicitis to feculent diverticulitis and penetrating intra-abdominal injuries. Traditionally, uncomplicated IAIs are those that are limited to a hollow viscous. Complicated IAIs (cIAIs) are generally defined as infections that extend into a normally sterile area of the abdomen such as the peritoneal cavity, mesentery, retroperitoneum, another abdominal organ or the abdominal wall [1–3]. A source control procedure is recommended for nearly all patients with cIAI (Grade B recommendation, based on moderate quality evidence according to the 2010 Surgical Infection Society/Infectious Diseases Society of America guidelines) [4] and therefore cIAIs have also been described as IAIs that require a source control procedure (such as surgery or percutaneous drainage) [1]. By definition, these include secondary and tertiary peritonitis (localised or diffuse).

The microbiology of cIAIs largely depends on the source of the infection and prior exposure of the patient to antimicrobial agents. In a large multicentre observational study in Europe, the appendix

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was the most common source of cIAI (37% of cases), followed by postoperative surgical site infection (15.9%), colonic perforation (15%), cholecystitis (13.4%) and gastroduodenal perforation (7.3%) [5]. When cultures are obtained, the isolated organisms usually include Enterobacteriaceae (mainly *Escherichia coli* and, to a lesser extent, *Klebsiella pneumoniae, Pseudomonas aeruginosa* and others), whilst Gram-positive cocci (mainly *Enterococcus* spp., *Streptococcus* spp. and *Staphylococcus aureus*), anaerobes (mainly *Bacteroides* spp.) and fungi are somewhat less common [5–7]. Patients with hospital-acquired infections have a higher prevalence of multidrug-resistant strains, such as extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae and glycopeptide-resistant *Enterococcus* spp. [5–7].

The susceptibility of bacteria responsible for cIAIs to antimicrobial agents is constantly evolving [8], thus so are the recommendations for empirical coverage in affected patients. In addition to source control, current recommendations by the Surgical Infection Society for empirical coverage in lower-risk patients include cefotaxime or ceftriaxone with metronidazole, cefoperazone/sulbactam (not available in the USA), ertapenem, moxifloxacin or ciprofloxacin/metronidazole; for higher-risks patients they include piperacillin/tazobactam, cefepime, doripenem, imipenem/cilastatin and meropenem [1]. Second-line agents include a combination of older and newer antimicrobials of different classes, including β-lactams (with or without a β-lactamase inhibitor), monobactams, carbapenems and fluoroquinolones [1].

Recent reports have documented increasing resistance of Enterobacteriaceae to fluoroquinolones around the world [9–13]. In this context, we sought to systematically review the available published evidence comparing a fluoroquinolone (FQ)-based versus a β-lactam (BL)-based regimen for the empirical treatment of patients with cIAIs and to synthesise the data using the methodology of meta-analysis.

2. Methods

2.1. Data sources

A systematic review of the MEDLINE (PubMed) database, Cochrane Library and ClinicalTrials.gov (https://clinicaltrials.gov/) was performed to identify relevant trials for the meta-analysis. The primary search was conducted with the following pattern: (fluoroquinolone* OR quinolone* OR ciprofloxacin OR moxifloxacin OR levofloxacin) AND (penicillin* OR penicilin* OR cephalosporin* OR beta-lactam* OR carbapenem* OR monobactam* OR piperacillin OR ticarcillin OR cefuroxime OR cefotaxime OR ceftriaxone OR ceftazidime OR cefepime OR cefoperazone OR ceftolozane OR aztreonam OR imipenem OR ertapenem OR meropenem OR doripenem) AND (appendicitis OR diverticulitis OR cholecystitis OR peritonitis OR perforation OR intra-abdominal OR intraabdominal). No restriction was set on the year of publication. We also sought to identify potentially useful studies in the references of the relevant articles. The search process was last updated in March 2018. The study was not fully registered in PROSPERO owing to a technical malfunction.

2.2. Study selection

Two investigators (MNM and NAT) independently searched the literature and examined relevant studies for potential inclusion in the meta-analysis. To be considered eligible, a study should be a randomised controlled trial (RCT) examining the effectiveness and/or safety of a FQ-based regimen compared with a BL-based regimen for the treatment of adult patients with cIAI. Studies on paediatric patients were excluded due to the different pathophysiology (appendiceal perforation is the source of cIAI in the vast majority of paediatric patients) and safety profile of antimicrobials in this population [14–16]. Non-randomised studies were excluded. Additional antimicrobial agents could be used in the trials. Studies written in English, French, Spanish, German, Italian or Greek were considered eligible. Unpublished studies reported as abstracts in conferences were not included in this review [17]. Studies comparing regimens that are currently not recommended for the treatment of patients with cIAI based on the 2017 Surgical Infection Society revised guidelines on the management of IAI [1] were also excluded.

In the event that multiple studies reported on overlapping patient populations (e.g. two studies from the same institution), only data from the largest study or (if sample sizes were similar) the one with the longer follow-up were analysed. Every effort was made to identify overlapping populations by recording each study's investigators and affiliated institutions as well as the study period.

2.3. Data extraction

Two reviewers (MNM and NAT) independently extracted the relevant data. Any disagreement was resolved by consensus in communication with all investigators. A review of each trial was performed to assess the quality of reporting and the risk of bias using two methods: a modified Jadad score, assessing details of randomisation, generation of random numbers, details of double-blinding procedure, information on withdrawals and allocation concealment [18]; and the Cochrane Risk of Bias Tool, assessing selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias [19]. A trial was considered to be of high quality when it had a modified Jadad score of $\geq$3.

Data were extracted in duplicate spreadsheets by two individual investigators (MNM and NAT). Data regarding the study design, clinical setting, patient population, number of patients [by intention-to-treat (ITT) and those clinically evaluable (CE) and microbiologically evaluable (ME)], antimicrobial agents and doses used, clinical and microbiological outcomes, safety and mortality were recorded. The ITT population comprised patients who received at least one dose of the study medications. The CE population comprised patients who appropriately completed the treatment protocol, had complete follow-up and for whom full data on treatment outcomes were available. The ME population was a subset of the CE population whose infections were also documented microbiologically.

2.4. Definitions and outcomes

The definition of each individual study was accepted for the definition of cIAI, as long as it was in line with the general definition by the Surgical Infection Society (infections that extend into a normally sterile area of the abdomen, such as the peritoneal cavity, mesentery, retroperitoneum, another abdominal organ or the abdominal wall, and that require a source control procedure) [1]. Secondary peritonitis due to infected peritoneal dialysis catheters was excluded owing to the differences in pathophysiology and management [20].

Primary outcome measures for this meta-analysis were treatment success at the test-of-cure visit (defined as sustained resolution or improvement of clinical symptoms and signs attributed to the cIAI, with the absence of surgical site infection requiring systemic antimicrobial treatment in the CE population) and all-cause mortality (ITT population). Secondary outcomes included treatment success in the ITT and ME populations as well as the incidence of treatment-related adverse events (AEs), severe AEs and withdrawal due to AEs (as defined in each study).

Subgroup analyses were also performed stratifying the studies based on specific antimicrobials (for FQs: moxifloxacin,

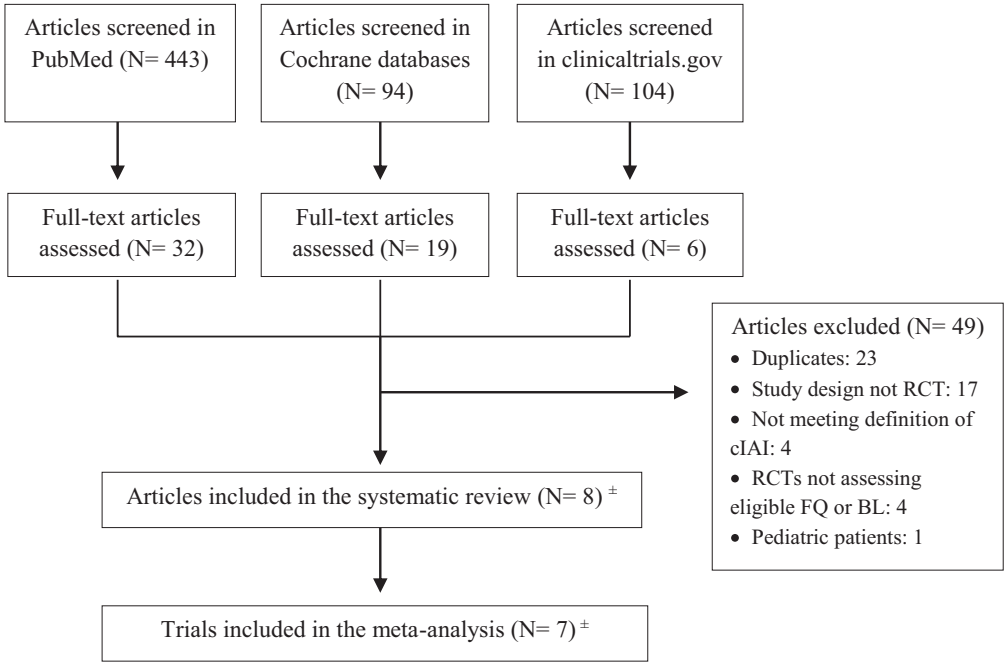

Fig. 1. Flow diagram of the study selection process. RCT, randomised controlled trial; cIAI, complicated intra-abdominal infection; FQ, fluoroquinolone; BL, β-lactam.
* No additional studies were identified in the references of relevant articles.
± One of the articles [31] reported on part of the population analysed in another larger trial (2 of 32 centres) [30]; for the meta-analysis, data from the smaller study were used only for subgroup analyses where the larger trial did not provide data, otherwise these two studies were considered as one trial.

ciprofloxacin/metronidazole, other FQ regimen; and for BLs: carbapenems, ceftriaxone/metronidazole, piperacillin/tazobactam), the source of infection (appendix, stomach/duodenum, small bowel, colon) and the microbiology of the isolated bacteria (*E. coli, P. aeruginosa, K. pneumoniae*, Gram-negative aerobes, Gram-positive anaerobes, *Bacteroides fragilis*). Only data for subgroup analyses pooling more than one study were reported.

2.5. Data analysis and statistical methods

Statistical analyses were performed with Review Manager [21]. Heterogeneity between trials was assessed using a χ^2 test ($P < 0.10$ was defined to indicate significant heterogeneity) or I^2. Publication bias was assessed using Egger's funnel plot method [22]. Pooled risk ratios (RRs) and 95% confidence intervals (CIs) for all primary and secondary outcomes were calculated by the DerSimonian–Laird random-effects model [23].

3. Results

The study selection process is depicted in Fig. 1. The search process generated 641 articles, of which 7 trials (enrolling 4125 patients) were eligible for this meta-analysis [24–30]. One of the excluded studies [31] reported on part of the population analysed in another larger trial (2 of 32 centres) [30]; for the meta-analysis, data from the smaller study were used only for subgroup analyses where the larger trial did not provide data (i.e. clinical effectiveness for complicated appendicitis), otherwise these two studies were considered as one trial. Three trials investigating ampicillin/sulbactam [32], alatrofloxacin [33] and clinafloxacin [34] were excluded since those agents are not currently considered first-line for patients with cIAI. The characteristics of the included trials are presented in Table 1. All of the studies were multicentre RCTs, and all but one [29] were double-blinded and of high quality (Jadad score ≥3). Quality assessment of the trials based on the Cochrane Risk assessment tool is presented in Supplementary Table S1. All analysed trials enrolled adult (age >18 years) patients and compared intravenous (i.v.) FQs versus BLs; in 3 trials i.v. antimicrobials could be switched to oral when the patient's condition was stable. One phase 3 study comparing the safety and efficacy of moxifloxacin versus ertapenem in paediatric patients was excluded [35]. The FQ regimen consisted of moxifloxacin (four RCTs) or ciprofloxacin plus metronidazole (three RCTs). The BL regimen consisted of carbapenems (ertapenem in one RCT and imipenem/cilastatin in another), piperacillin/tazobactam (two RCTs) or ceftriaxone plus metronidazole (three RCTs).

3.1. Primary and secondary outcomes

The clinical outcomes of the included trials are presented in Table 1. Overall, there was no difference in clinical effectiveness between patients treated with a FQ-based versus a BL-based regimen in the CE population (2883 patients; RR = 1.00, 95% CI 0.95–1.04; $I^2 = 56\%$; Fig. 2a). Similarly, there was no difference in the ITT population (3055 patients; RR = 0.97, 95% CI 0.94–1.01; $I^2 = 13\%$; Fig. 2b) or the ME population (2191 patients; RR = 0.98, 95% CI 0.95–1.02; $I^2 = 16\%$; Fig. 2c). All-cause mortality was similar among the two groups (3614 patients; RR = 1.04, 95% CI 0.75–1.43; $I^2 = 0\%$; Fig. 3a), as were overall treatment-related AEs (2801 patients; RR = 0.97, 95% CI 0.70–1.33; $I^2 = 73\%$; Fig. 3b), severe AEs (2338 patients; RR = 1.16, 95% CI 0.87–1.56; $I^2 = 44\%$) and withdrawal due to AEs (3380 patients; RR = 1.07, 95% CI 0.86–1.33; $I^2 = 0\%$; Fig. 3c). Publication bias was not observed (Fig. 4).

3.2. Subgroup analyses

Subgroup analyses based on specific antimicrobials mostly replicated the findings of the original analysis; the only difference was significantly lower effectiveness of moxifloxacin versus BL comparators in the CE (1934 patients; RR = 0.96, 95% CI 0.93–0.99; $I^2 = 1\%$; Fig. 2a), ITT (1743 patients; RR = 0.94, 95% CI 0.91–0.98; $I^2 = 0\%$; Fig. 2b) and ME population (1484 patients; RR = 0.96,

Table 1
Characteristics and outcomes of randomised controlled trials (RCTs) included in the meta-analysis

Study	Study design	Study quality	FQ regimen[a]	BL regimen[a]	Infection source	Enrolled patients	Clinical effectiveness				Treatment-related AEs	Withdrawal due to AEs
							CE	ITT	ME	Mortality		
Cohn et al., 2000 [28]	MC DB RCT	3	i.v. CIP + MTR	i.v. TZP	Appendix 42%, colon 21%	459	73.9% vs. 62.9%	75.0% vs. 68.9%	77.5% vs. 70.8%	5.5% vs. 4.5%	NR	6.0% vs. 7.2%
De Waele et al., 2013 [PROMISE study] [26]	MC DB RCT	4	i.v. MFX	i.v. ETP	Appendix 50%, GD 15%, diverticulitis 6%	804	89.5% vs. 93.4%	81.9% vs. 86.9%	86.5% vs. 90.2%	5.4% vs. 3.1%	18.9% vs. 19.0%	2.7% vs. 1.5%
Malangoni et al., 2006 [24]	MC DB RCT	4	i.v. MFX/p.o. MFX	i.v. TZP/p.o. AMC	Appendix 60%, GD 5%, SB/colon 14%	681	79.8% vs. 78.1%	NR	78.0% vs. 77.3%	1.8% vs. 2.1%	24.9% vs. 27.5%	10.3% vs. 8.6%
Solomkin et al., 1996 [25]	MC DB RCT	3	i.v. CIP + MTR	i.v. IPM/CIL	Appendix 25%, GD 4%, SB 15%, colon 42%	691	83.8% vs. 80.5%	82.0% vs. 82.2%	88.3% vs. 88.5%	4.5% vs. 8.9%	NR	NR
Solomkin et al., 2009 [DRAGON study] [27]	MC DB RCT	5	i.v. MFX	i.v. CRO + MTR	Appendix 77%, GD 11%, SB 4%, colon 2%	364	90.2% vs. 96.5%	87.2% vs. 91.2%	89.4% vs. 95.9%	0 vs. 0	4.4% vs. 5.0%	2.2% vs. 1.7%
Wacha et al., 2006 [30]	MC DB RCT	4	i.v. CIP + MTR	i.v. CRO + MTR	Appendix 33%, GD 15%, SB 11%, colon 21%	531	90.6% vs. 87.9%	84.9% vs. 84.8%	91.2% vs. 87.6%	5.9% vs. 6.1%	15.3% vs. 16.1%	15.4% vs. 16.7%
Weiss et al., 2009 [AIDA study] [29]	MC OL RCT	2	i.v. MFX/p.o. MFX	i.v. CRO + MTR/p.o. AMC	Appendix 53%, GD 11%, SB 8%, colon 17%	595	80.9% vs. 82.3%	71.6% vs. 76.9%	78.9% vs. 81.3%	4.2% vs. 5.1%	19.0% vs. 12.2%	15.9% vs. 14.2%

FQ, fluoroquinolone; BL, β-lactam; CE, clinically evaluable population; ITT, intention-to-treat population; ME, microbiologically evaluable population; AE, adverse event; MC, multicentre; DB, double-blind; OL, open-label; i.v., intravenous; CIP, ciprofloxacin; MTR, metronidazole; TZP, piperacillin/tazobactam; MFX, moxifloxacin; ETP, ertapenem; p.o., oral; AMC, amoxicillin/clavulanic acid; IPM/CIL, imipenem/cilastatin; CRO, ceftriaxone; GD, gastroduodenal; SB, small bowel; NR, not reported; q12h, every 12 h; qd, once daily; q6h, every 6 h; q8h, every 8 h.

[a] Antibiotic dosing index. FQs: i.v. CIP 400 mg q12h, i.v. MFX 400 mg qd, p.o. MFX 400 mg qd. BLs: i.v. TZP 3.375 g q6h, i.v. ETP 1 g qd, i.v. IPM/CIL 500 mg q6h, i.v. CRO 2 g qd, p.o. AMC 500 mg q8h (in [24] 800 mg/114 mg q12h). Metronidazole: i.v. MTR 500 mg q6h (in [29,30] 500 mg q8h, in [27] 500 mg q12h).

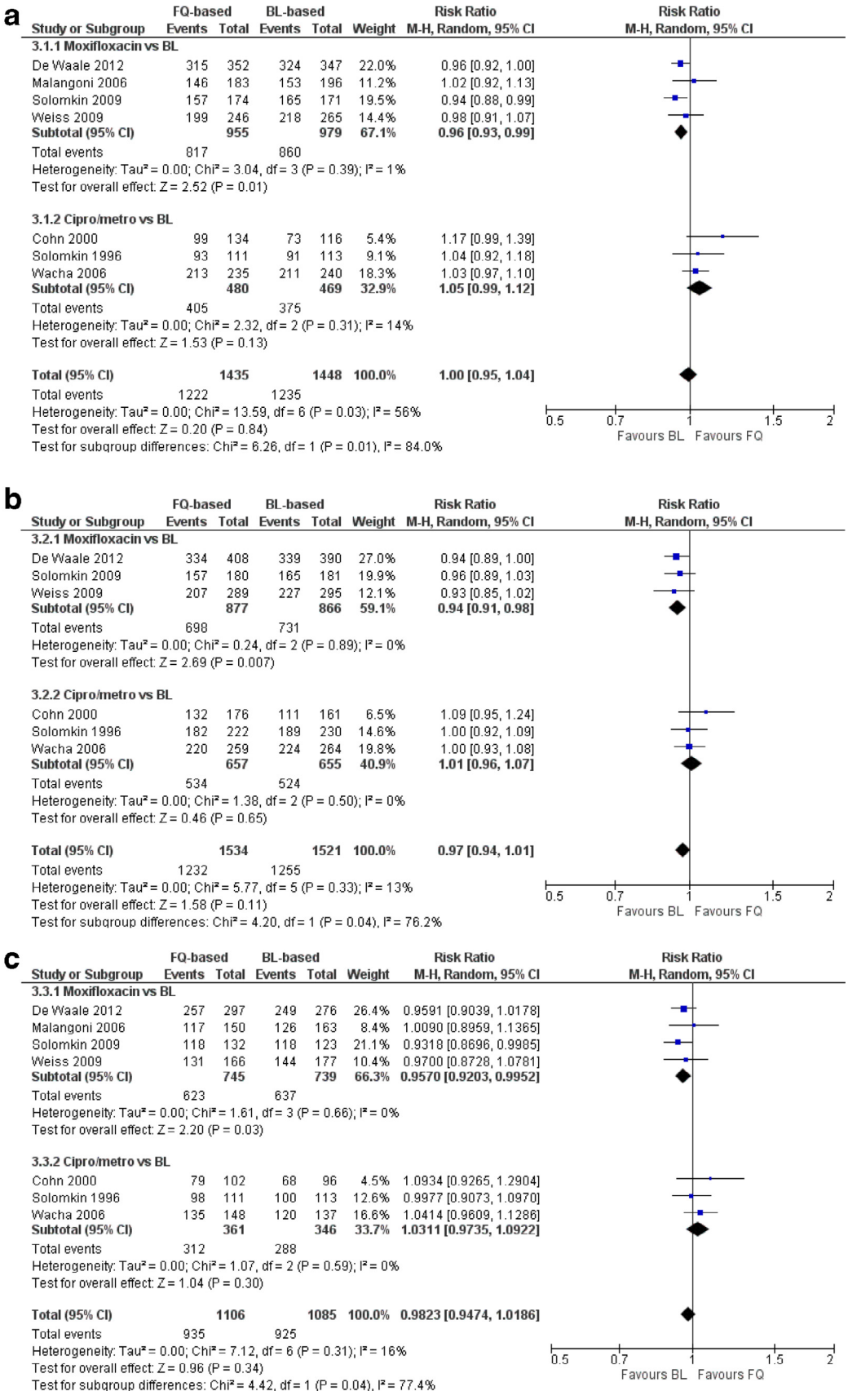

Fig. 2. Forest plots depicting risk ratios (RRs) of clinical effectiveness of fluoroquinolone (FQ)-based versus β-lactam (BL)-based regimens for complicated intra-abdominal infections, stratified by FQ type in the (a) clinically evaluable, (b) intention-to-treat and (c) microbiologically evaluable populations. Vertical line, 'no difference' line between compared treatments; horizontal lines, 95% confidence interval (CI); squares, point estimates; size of squares, weight of each trial in the meta-analysis; diamond shape, pooled RR plus 95% CI.

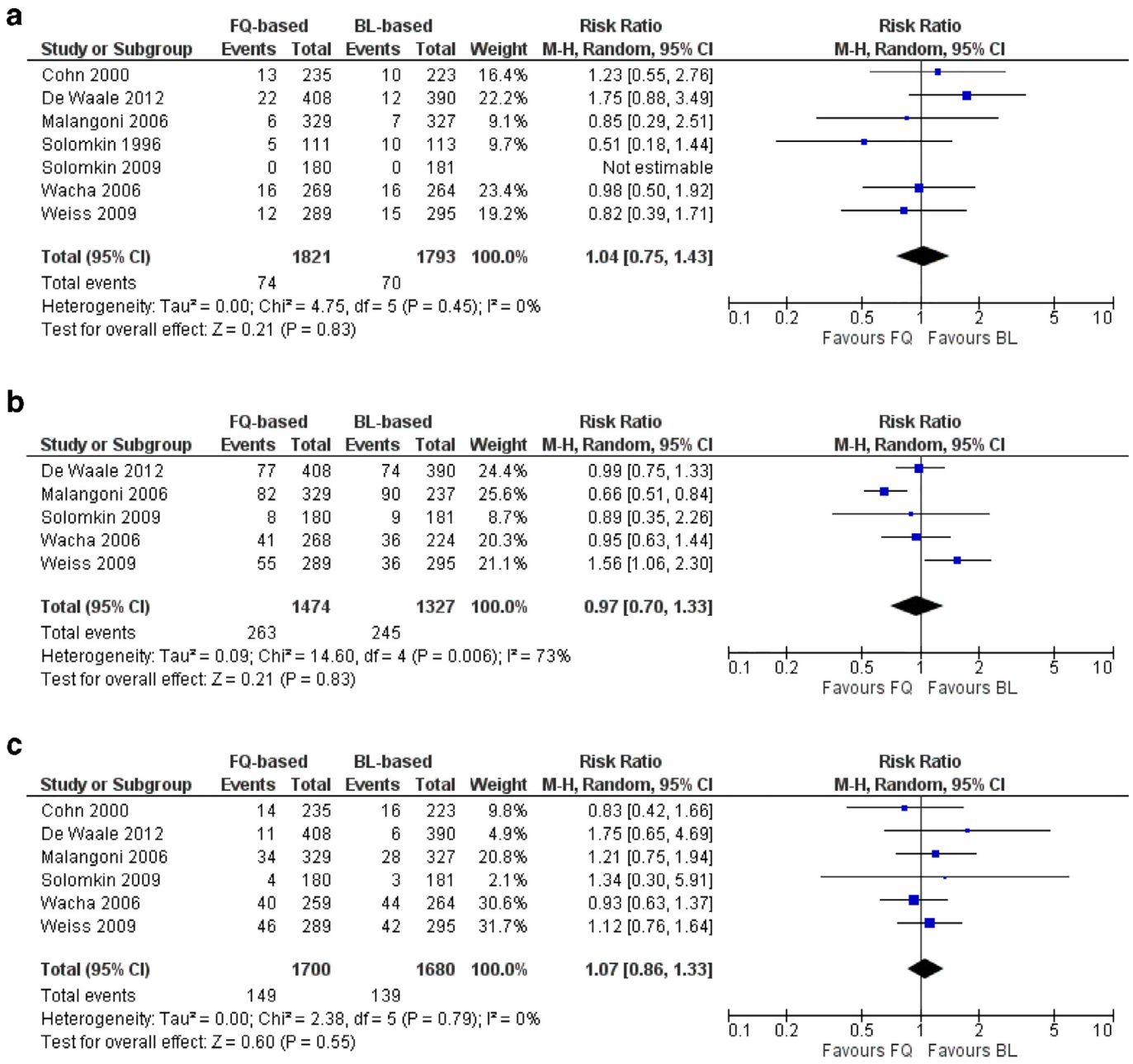

Fig. 3. Forest plots depicting the risk ratios (RRs) of (a) all-cause mortality, (b) treatment-related adverse events and (c) withdrawal due to adverse events associated with fluoroquinolone (FQ)-based versus β-lactam (BL)-based regimens for complicated intra-abdominal infections. Vertical line, 'no difference' line between compared treatments; horizontal lines, 95% confidence interval (CI); squares, point estimates; size of squares, weight of each trial in the meta-analysis; diamond shape, pooled RR plus 95% CI.

95% CI 0.92–1.00; $I^2 = 0\%$; Fig. 2c). Subgroup analyses based on the source of infection only revealed a difference for complicated appendicitis, where based on data from three trials moxifloxacin was less effective than BLs (1296 patients; RR = 0.95, 95% CI 0.90–0.99; $I^2 = 0\%$). Subgroup analyses based on the isolated bacteria did not reveal any statistically significant differences between FQ- and BL-based regimens. All trials except one were of high quality, and sensitivity analysis of the high-quality trials replicated the initial findings. The pooled results of all original and subgroup analyses are presented in Supplementary Table S2.

4. Discussion

In the present study, all published RCTs comparing a FQ-based regimen versus a BL-based regimen for the empirical treatment of adult patients with cIAI were systematically reviewed. Overall, the two classes of antimicrobials were equally effective and safe. Limited evidence from subgroup analyses suggested slightly lower clinical effectiveness of moxifloxacin compared with a BL-based regimen in the overall population (based on four trials) [24,26,27,29] as well as in the subset of patients with complicated appendicitis (three trials) [24,26,29].

Antimicrobial therapy for cIAIs is prescribed empirically. Recently, the Surgical Infection Society and the Infectious Diseases Society of America as well as the World Society of Emergency Surgery published guidelines on this issue, suggesting that FQs and BLs alone or, when needed, in combination with metronidazole are equally effective [1,36]. The choice of therapy is physician-oriented and is based on local bacterial epidemiology, the infection site, acquisition (community-acquired, healthcare-associated or hospital-

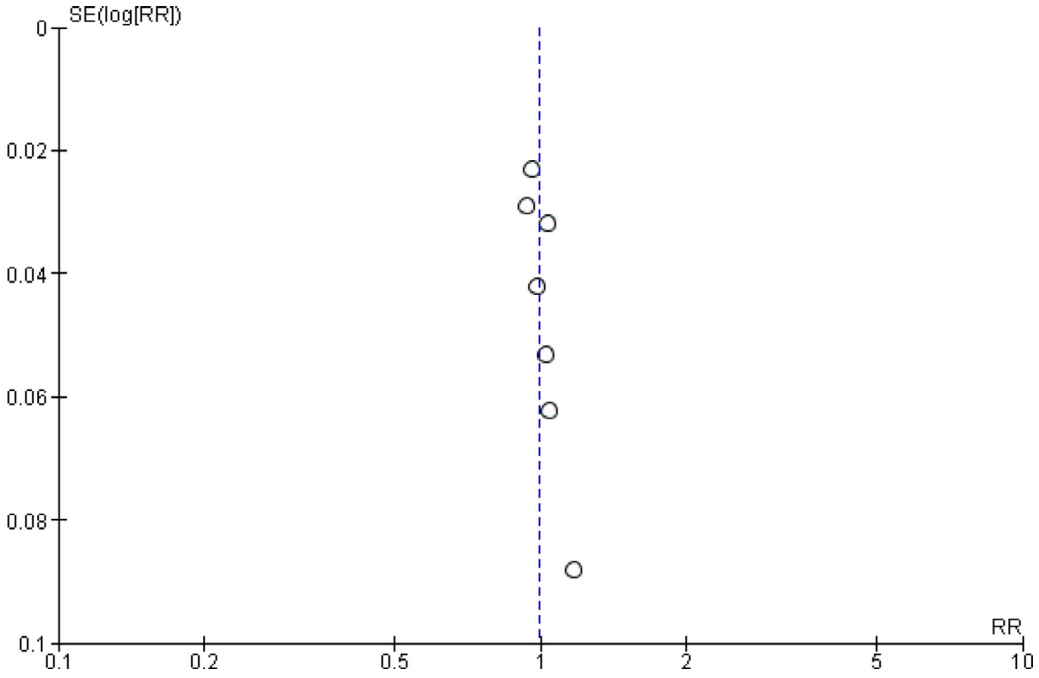

Fig. 4. Funnel plot depicting treatment effect estimate and standard error of the analysed trials with regards to clinical effectiveness in the clinically evaluable population. RR, risk ratio.

acquired) and the risk of treatment failure and death [37,38]. The findings of this analysis confirm the majority of the recommendations regarding antibiotic treatment for patients with cIAIs. In terms of treatment duration, a recent landmark trial reported equal outcomes in 518 patients with cIAI receiving a fixed, short course of antibiotics (3–5 days) versus a longer course extending until after the physiological derangements had resolved (5–10 days), provided they had achieved adequate source control (either operatively or percutaneously) [39]. The main limitations of this trial included inadequate statistical power to reject the null hypothesis as well as an 18% protocol non-adherence rate [39,40]. Ad-hoc analyses focusing on high-risk patients or those receiving percutaneous drainage (as opposed to operative source control) replicated the initial findings [41–45].

Moxifloxacin is one of the currently recommended agents for the treatment of cIAIs in lower-risk patients [1]. The current findings, based on four RCTs (1934 patients), suggest slightly lower success rates in patients treated with moxifloxacin versus BLs in the CE, ITT and ME populations as well as the subset of patients with complicated appendicitis. The relative difference was low (1–7% in the CE population), did not translate into higher mortality, and data for further subgroup analyses were limited. In contrast to our findings, an industry-sponsored pooled analysis of a subset of patients from the same four RCTs (1024 patients) by the original investigators concluded that moxifloxacin is equally as effective and safe as comparators (CE population, 85.3% vs. 88.4%, $P > 0.05$; ITT population, 73.7% vs. 77.7%, $P > 0.05$) [46]. This pooled analysis focused on the subset of patients characterised as having 'secondary peritonitis' and mainly included patients with complicated appendicitis (52%) and perforated gastroduodenal ulcer (19%). On personal communication (MNM), the lead investigator described the analysed population as having generalised peritonitis and therefore likely a more severe form of the disease. A recently published multicentre, double-blind RCT on 451 paediatric patients also indicated that moxifloxacin was less effective than ertapenem for the treatment of cIAI (84.6% vs. 95.5% clinical success in the modified ITT population; $P < 0.01$) [35]. Of note, 95% of the enrolled children underwent appendectomy, highlighting the high relative incidence of complicated appendicitis in this population. It should also be noted that that study was primarily focused on the safety profile of moxifloxacin, since FQs are generally avoided in the paediatric population owing to potential cardiac and musculoskeletal toxicity. In light of the above findings, further research is warranted to delineate whether the slightly lower efficacy of moxifloxacin is limited to patients with complicated appendicitis or extends to all subgroups.

In this study, there was no difference in the safety profile of the compared groups. A recent meta-analysis compared the safety of FQs versus other antimicrobials and reported FQs to be associated with significantly more central nervous system-related adverse effects than (BL and other) comparators [47]. Compared with BLs, FQs were associated with more gastrointestinal adverse effects than cefuroxime but less than amoxicillin/clavulanate [47].

This meta-analysis has certain limitations. First, antimicrobial resistance is a moving target, constantly evolving with different patterns in different regions, which may impair the generalisability of the findings. Second, IAIs encompass a wide range of infections with different bacterial patterns depending on the source (gastroduodenal versus appendix versus colon) and, as such, it is possible that certain antimicrobials perform better for upper or lower gastrointestinal infections and worse for other infections, but cumulatively they appear equal. Relevant data from subgroup analyses based on infection source were limited. Third, the enrolled patients were not stratified by severity of illness, and overall mortality was 4%, suggesting that the most severely ill patients were under-represented in the analysed trials [48], and extrapolation of the current findings in this population should be performed with caution. Last, source control is of paramount importance in patients with cIAI and is difficult to standardise [49]; however, there is indirect evidence that this may not translate into a difference in clinical outcomes [43].

This study is the most comprehensive analysis on this topic to date and, as such, it bears significant clinical implications. Three databases were searched, studies published in six languages were considered, and the widely adopted PRISMA guidelines were followed [50,51]. High-quality RCTs were included and the

methodology of meta-analysis was used to pool their results. Subgroup analyses were performed based on specific antimicrobials, source of infection and isolated pathogens. The results provide evidence that in this era of rapidly increasing antimicrobial resistance, combinations of ceftriaxone/metronidazole, ciprofloxacin/metronidazole and carbapenems have an equal role in antimicrobial stewardship protocols for the treatment of cIAIs.

In conclusion, this meta-analysis suggests that ciprofloxacin/metronidazole is as effective as ceftriaxone/metronidazole and carbapenems for the treatment of cIAIs, whilst moxifloxacin monotherapy had slightly inferior outcomes, especially in complicated appendicitis. Empirical antimicrobial treatment of patients with cIAIs should be selected in light of the local bacterial epidemiology and patterns of resistance. Future research may focus on patients with healthcare-associated cIAIs and the critically ill, and clinical outcomes should ideally be stratified by infection source.

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Competing interests

MEF has participated on advisory boards for AstraZeneca, InfectoPharm, Tetraphase, Shionogi and Xellia, has received lecture honoraria from Cipla, Merck and Pfizer, and has received research support from Shionogi, Tetraphase, Helperby and Xellia. All other authors declare no competing interests.

Ethical approval

Not required.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2019.01.004.

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