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Original Article

Speed of recovery in adult patients with community-acquired pneumonia; moxifloxacin versus levofloxacin

Jamal Wadi Al Ramahi[1,2], Mustafa Ramadan [2], Waad Jaber[2], Lamya Abushanab[3], Mohammad Mughrabi[3], Noor Alshamayleh[3], Ahmad Mulhem[3], Dania Momani[1], Mohammad Obaidat[3], Ghayda Haddad[1], Basma Khalil[2], Anas Zahran[4], Esraa Odat[4], Nadeen Kufoof[4], Haneen Arabiat[4], Amr Diab[2], Antonio Anzueto[5]

[1] Al Khalidi Hospital and Medical Center. Amman, Jordan. An Affiliate with Lahey Health Center. Boston, MA, United States
[2] Al Takhassusi Hospital, Amman, Jordan
[3] Jordan Hospital and Medical Center, Amman, Jordan
[4] Arab Medical Center, Amman, Jordan
[5] Internal Medicine Department, University of Texas Health Science Center, San Antonio, TX, United States

Abstract

Introduction: To evaluate the speed of recovery in CAP-treated adults with Moxifloxacin versus levofloxacin.
Methodology:A retrospective multicenter study between January 14, 2010 - March 23, 2017. Patients' records with the diagnosis of community-acquired pneumonia (CAP), age ≥ 18 and ≤ 60 years old, susceptible bacteria to the prescribed fluoroquinolone, completed three days of antimicrobial therapy and who were switched from parenteral to the oral form for the same antimicrobial agent were included.
Results: 701 charts were reviewed, 367 were excluded; not on respiratory fluoroquinolones (RFQ), age > 60 or < 18 years old, not enough data, prior antimicrobials, hospital-associated pneumonia, < 3 days of therapy, and one pregnant woman. 334 patients were Included; 167 levofloxacin and 167 moxifloxacin, with 68.5% males (P = 0.259), no significant difference in comorbidities (P > .05), but increased diabetes mellitus in moxifloxacin-treated patients (P = 0.012). No significant difference in Pneumonia Severity Index (PSI). Multivariate and univariate analysis demonstrated that day 3 rate of improvement; levofloxacin-treated patients 75.9% (95% CI, 69.9 to 81.8), and 84.0% (95% CI, 78.1 to 89.9) for Moxifloxacin (difference -8.1%, 95% CI, -16.5 - .003, P = 0.058). And day 5 rates of improvement in Levofloxacin-treated patients was 91.9%, (95% CI, 88.3 – 95.6), and 95.5% (95% CI, 91.8 - 99.2) for moxifloxacin (difference -3.5%, 95% CI, -8.7 - 1.7, P = 0.184). There was no significant difference for patients with radiological diagnoses for day 3 (P = 0.832) and 5 (P = 0.929).
Conclusions: Our uni-and-multivariate analyses demonstrated that moxifloxacin exhibited no significant differences in the rates of improvement on days 3 and 5.

Key words: levofloxacin; moxifloxacin; CAP; community-associated pneumonia; speed of recovery.

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Introduction

Mortality from community-acquired pneumonia (CAP) remains unacceptably high despite the modern antimicrobial therapy. An observational study verified improvement in the treatment outcome of the included 4558 patients: mortality decreased from 9.6% in the early study period (1995–1999) to 4.1% in the late period (2010–2014), with a yearly downward trend in mortality (P for trend = 0.003), despite patients were significantly older (P < 0.05), had more co-morbidities, worse PSI scores, septic shock, and frequently required intensive care unit admission [1]. To improve CAP outcome, an antimicrobial prescribing strategy was used to evaluate the ninety-days mortality for patients admitted to the ward with CAP by simplifying the regimen into monotherapy; mortality was non-inferiority for the β-lactam monotherapy strategy compared with the combination regimen [2]. A study demonstrated that using oral clarithromycin was noninferior to its intravenous route when the speed of clinical stability was evaluated; in addition, both routes had similar 30-days mortality and length of hospital stay [3]. Another double-blind, multicenter, randomized, placebo-controlled Swiss trial, demonstrated that adding systemic steroid for admitted patients with CAP shortened time to clinical stability with similar 30 days complications in both groups [4]. The benefit of a faster recovery in the treatment of CAP

patients may translate into less suffering; less duration of treatment, less hospital stays, cost-saving, and possibly decreased complication and mortality [5,6]

With the emergence and spread of drug resistant pneumococci, commonly used agents in the treatment of CAP patients like β-lactam, macrolides, doxycycline and Trimethoprim/ Sulfamethoxazole became less popular, and were largely replaced by respiratory fluoroquinolones (RFQ) [7,8]. Their relative safety, suitable dosing regimen, ability to rapidly ameliorate clinical symptoms, low resistance profile, association with lower mortality and the decrease length of hospital stay, in the treatment of pneumococci and other respiratory pathogens made them the alternative agents for CAP therapy in patients with increased risk of resistant pathogens [9-12]. We published an earlier study demonstrating that treatment of CAP patients with a respiratory quinolone monotherapy (here moxifloxacin or levofloxacin) was associated with significantly (P = 0.004) shorter hospital stay [12]. A clinical trial by Anzueto and co-workers focused on studying the difference in the speed of recovery for CAP patients of the two RFQ (moxifloxacin and levofloxacin) in elderly patients (≥65 years old). They found that patients treated with moxifloxacin had faster clinical recovery than levofloxacin (P = 0.01) during treatment days 3 – 5, however, there was no difference at days 5 and 21 after completion of therapy (P = 0.2) [13].

In this retrospective study, our aim was to examine whether CAP speed of recovery reported in the first 3 – 5 days for moxifloxacin in patients over the age of 65 years is different from levofloxacin treatment in younger population i.e. ≥ 18 years to ≤ 60 years old, using real world data.

Methodology

Study design

A retrospective multicenter study in four hospitals (two community and two teaching hospital), located in Amman – Jordan, charts were reviewed for the period; January 14, 2010 - March 23, 2017. The participating hospitals encompass 800 beds (570 beds in the two teaching hospitals). The protocol and the working teams in Jordan were approved in each hospital by the IRB (internal review board-ethics committee). Patients were included in the review after they were treated and discharged from the hospital. Medical records were reviewed for the diagnosis of community acquired pneumonia (according to International Classification of DiseasesICD - 9), CAP, pneumonia, lower respiratory tract infection. Pharmacy records were reviewed for patients for whom moxifloxacin or levofloxacin was prescribed for CAP treatment, whether given parenteral or oral routes. Charts recruitment for moxifloxacin treatment arm was extended two months, as more charts were found with levofloxacin.

Inclusion and Exclusion Criteria

Patients' records were included if they were ≥ 18 and ≤ 60 years old and they were on parenteral or oral moxifloxacin or levofloxacin therapy. Patients had to have completed at least three days of antimicrobial therapy with be the same agent, whether oral or parenteral. Patients were excluded if they had healthcare-associated pneumonia, ventilator associated pneumonia, hospital-associated pneumonia, or if they were pregnant women, or in case of resistance to the used antimicrobial agent if cultures and antimicrobial susceptibility were available. Other conditions of exclusion were; complete endobronchial obstruction, suspected tuberculosis or fungal infection and/or patients who were switched between the two studied antimicrobial agents or who were treated with other quinolones (Figure 1). The recruited patients were classified according to Pneumonia Severity Score (PSI).

CAP Definition

Patients who had symptoms and signs of CAP including cough, fever, chills, rigors, chest pain, dyspnea and sputum production (mucopurulent, scant or watery), gastrointestinal symptoms including nausea, vomiting, diarrhea, mental status changes, respiratory rate ≥ 24 breaths/minute, tachycardia, audible rales or bronchial sounds. Laboratory evaluation: leukocytosis with a left shift or leukopenia. The presence of an infiltrate on a plain chest radiograph or a chest CT is considered the "gold standard" for CAP diagnosing when clinical and microbiologic features are supportive (see CAP definition). Microbiological diagnosis includes a sputum culture [14], urinary antigen testing, and or positive blood culture.

Definition of Recovery (Improvement)

Patients were judged to be improved according to the following criteria: oral temperature ≤ 37°C, heart rate ≤ 100 beats/minute, respiratory rate ≤ 24 breaths/minute, systolic BP ≥ 90 mmHg, arterial oxygen saturation ≥ 90% or PO_2 ≥ 60 mmHg on room air, ability to maintain oral intake, and normal or baseline mental status. Clinical improvement is evaluated according to the clinical stability criteria published by IDSA/ATS [15].

Outcome measure

The primary outcome measure was to test the speed of recovery for patients with CAP, considered as the comparative cumulative proportions of improvement on day 3 and day 5 from the start of levofloxacin or moxifloxacin therapy, and for patients with radiological diagnosis. The secondary measures were the daily differences in the proportion of the recovered patients, the length of hospital stay, and proportions of recovered patients with mild-moderate and severe PSI risk classes.

Statistical methods

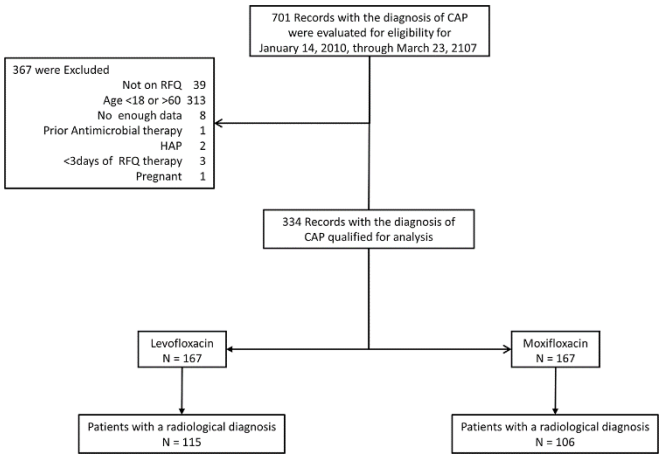
Sample size calculation was based on a previous knowledge, Bayesian statistics. Statistical values were considered for; $\alpha = 0.05$, Power (1 – Beta) = 0.9, Beta = 0.1 and the expected success for Levofloxacin and Moxifloxacin to be 0.9, with maximum difference of $\delta = 0.1$. The total sample size was calculated to be 310 patients, 155 patients for each arm. The sample size was increased about 8% to account for some possible missing major data from some charts, a total of 334 patients' charts were considered for the review, 167 patients per each arm. Multivariate and univariate linear regression analysis was used to calculate the primary outcome measure; the difference in improvement between levofloxacin and moxifloxacin on days 3 and 5. Cumulative curve was used to evaluate the time to event (improvement) for the two RFQ-treated patients until day 10, and for day 5 in the radiologically diagnosed patients**.** A Bar chart was constructed to demonstrate the daily absolute difference between the two RFQ-treated patients. Continuous variables were analyzed by ANOVA, and t-student test. Fischer exact test and Pearson Chi Square (χ^2) to detect significant differences among comorbidities, laboratory, radiological diagnoses and PSI among different antimicrobial therapy groups. Mann-Whitney U test to detect the differences for ranks in categorical data. Two-tailed P-value < 0.05 is considered significant. Statistical package for social sciences (SPSS), version 20 was used, and a web page application for the sample size calculation: (*http://www.nss.gov.au/nss/home.nsf/pages/Sample+size+calculato*r).

Results

701 records were reviewed, 367 were excluded; 39 were not on RFQ, 313 either age > 60 or < 18 years old, 8 not enough data, 1 prior antimicrobials use, 2 hospital-associated pneumonia, 3 less than 3 days of therapy, and one pregnant woman (Figure 1). Three-hundred and thirty-four patients were eligible for inclusion, they were hospitalized in between January 14, 2010 and March 23, 2107; 167 levofloxacin and 167 moxifloxacin, demographic characteristics are summarized in (Table 1), with 68.5% males and 31.5% females with no significant gender difference in the levofloxacin (P = 0.259) or moxifloxacin (P = 0.840) groups. Diabetes mellitus was significantly more prevalent in patients treated with moxifloxacin (P = 0.012). There was a trend towards increased bronchial asthma in moxifloxacin (P = 0.055), and malignancy in the levofloxacin group (P = 0.067). Cough was more frequent in the moxifloxacin than levofloxacin group (140, 154, P = 0.014), as well as shortness of breath (92, 12, P = 0.016) respectively. Chills and rigors were reported in 129 (38.6%) and fever in 248 (74.3%) of patients, both combined in (38%) of patients, fever was significantly more in levofloxacin- than moxifloxacin-treated patients (132, 116, P = 0.03) respectively. Other associated symptoms were not significantly different between the study groups. Other antimicrobials (β-lactams, β-lactam/β-lactamases inhibitors, glycopeptides, macrolides and aminoglycosides) that were combined with quinolones were statistically not different in both arms (P > 0.5).

Positive radiological examinations were similar for both agents, levofloxacin 115 (34.4%) and moxifloxacin 106 (31.7%) P = 0.772. There was no significant difference in PSI risk classes for patients treated with either agent (P = 0.445), even when analyzed as low, medium or severe (P = .381).

Figure 1. Flow chart of the reviewed records for the CAP-diagnosed patients who were treated with the study RFQ: Levofloxacin or moxifloxacin.



RFQ: Respiratory fluoroquinolones.

Table 1. Comparison between treatment groups of the demographic characteristics.

Characteristic of Patients	Number (Percentage) of Patients per the used Antimicrobials		P-value
Study Antimicrobial	Levofloxacin 167 (100%)	Moxifloxacin 167 (100%)	--
Gender (N, (%)			
Male 229 (68.5%)	107 (64.0)	122 (73)	.259 **
Female 105 (31.5%)	60 (36.0)	45 (27)	.840 **
Age mean (years) and SD	41.96 (11.25)	42.55 (10.93)	.626[&]
Co-Morbidities			
Bronchial asthma	7 (4.2)	17 (10.2)	.055
Tobacco smoking	73(43.7)	64 (38.3)	.374
COPD	7 (4.2)	5 (3.0)	.414
Mechanical Ventilation	23(13.7)	5 (3.0)	.77
Diabetes mellitus	5 (3.0)	42 (25.1)	.012
Kidney disease	4 (2.4))	9 (5.4)	.414
Immunosuppression	7 (4.2)	5 (3.0)	1.0
Malignancy	1 (0.6)	1 (0.6)	.067
Asplenia	2 (1.2)	1 (0.6)	1.0
Lung Abscess	2 (1.2)	1 (0.6)	1.0
Other chronic Lung diseases	1 (0.6)	5 (3.0)	.893
Others*	1 (0.6)	13 (7.7)	1.0
[$]Radiological diagnosis	115 (34.4)	106 (31.7)	.772[&]
Frequency of Symptoms	132 (79.0)	116 (69.4)	.06
Fever	78 (46.7)	91 (54.5)	.189
Sputum	70 (41.9)	65 (38.9)	.656
Chest pain	64 (38.3)	65 (38.9)	1.0
Chills/Rigors	140 (83.8)	154(92.2)	.027
Cough	92 (55.0)	112(67.0)	.033
Shortness of Breath	11 (6.5)	12 (7.1)	1.0
Vomiting	11 (6.5)	27 (10.1)	1.0
Other Symptoms	**25 (14.9)**	**27 (10.1)**	**.88**
PSI Risk Class			
I	100 (59.9%)	105 (62.9%)	
II	37 (22.1%)	32 (19.1%)	
III	15 (9)	21 (12.6%)	.445**
IV	0 (0.0%)	1 (0.6%)	
IV	10 (6%)	6 (3.6%)	
V	5 (3%)	2 (1.2%)	
Use of other antimicrobial agents			
β -lactams	86 (51.4)	88	.913
β-lactams, β-lactamase inhibitor	51 (30.5)	44	.467
Glycopeptides	25 (14.9)	25 (14.9)	1.0
Macrolides	6 (3.6)	3 (1.8)	.502
Aminoglycosides	3 (1.8)	1 (0.6)	.623
Antifungal	1 (0.6)	3 (1.8)	.623
Others Unspecified[$$]	5 (3.0)	5 (3.0)	1.0
Mean duration of therapy (Days)	4.27 (SD = 2.3)	4.58 (SD = 4.58)	.2
Length of hospital stays (Days)	4.32 (SD = 4.765)	4.45 (SD = 7.146)	.850

P-value, two-sided tailed by Fischer Exact test, Except where indicated by ANOVA[&] or Pearson chi square test**; CAP: Community-associated pneumonia; HAP: Hospital associated pneumonia; COPD: chronic obstructive pulmonary disease; PSI: Pneumonia severity score; SD: standard deviation; *Others for Levofloxacin and Moxifloxacin: Hypertension (0, 5), coronary artery (0,1) disease (0,1), epilepsy, ulcerative colitis (0,2) and meningitis (0,1), HIV (1, 1), skin disease (0, 1), Alcohol drinking (0, 1), others were tested by Pearson chi square test as independent pairs; [$]The rest (33.9%), either the results were not available or few plain radiology did not give the diagnosis, in either case diagnosis was based on clinical grounds; [$$]Other Unspecified: antimicrobials that were used for other reason like nitrofurantoin, metronidazole and antivirals.

Table 2. Clinical Outcome Comparisons for all patients on day 3 and day 5 among patients prescribed the RFQ Levofloxacin or Moxifloxacin.

Clinical Outcome	The Respiratory Fluoroquinolones Outcomes Evaluated for The Analyzed Patients Numbers (%)					
	Day 3			Day 5		
	Levofloxacin	Moxifloxacin	*P**	Levofloxacin	Moxifloxacin	*P**
Improved	126 (75.4%)	141 (84.4%)		153 (91.6%)	160 (95.8%)	
Partially improved	19 (11.4%)	20 (12%)	0.022	2 (1.2%)	5 (3%)	0.104
Failed, switched, added	20 (12%)	5 (3.0%)		8 (4.8%)	0 (0.0%)	
Death	0 (0.0%)	0 (0.0%)		1 (0.6%)	0 (0.0%)	

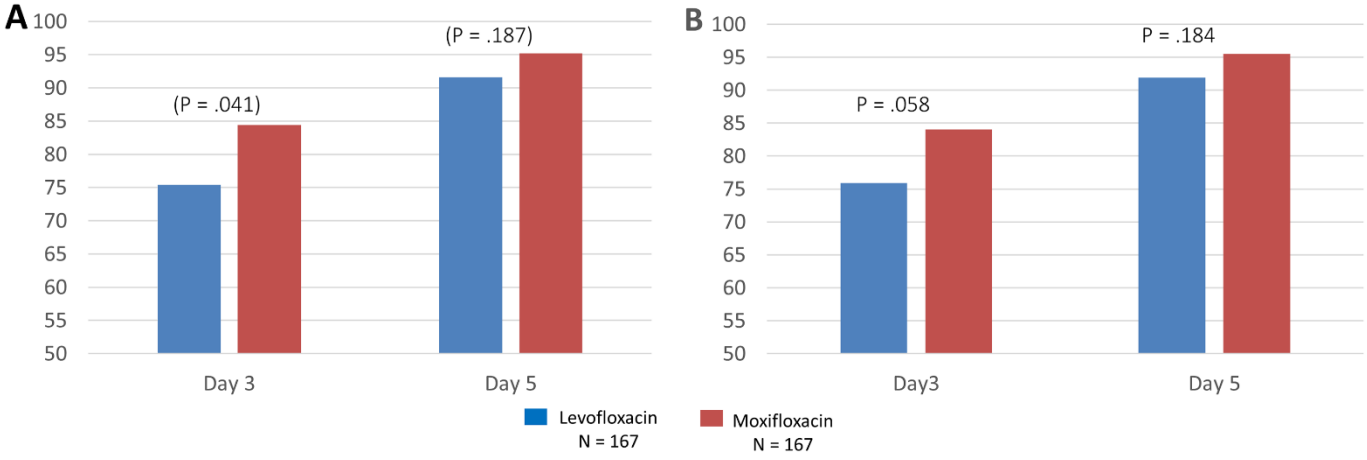
Number of analyzed patients for levofloxacin 167 and moxifloxacin 167; No available data for day 3 for Levofloxacin 2 and Moxifloxacin 1, and for day 5 Levofloxacin 3 and Moxifloxacin 2; *2-tailed P-value for 3 and 5 days were tested by Mann-Whitney U test.

Table 3. Clinical Outcome Comparisons for patients with radiological diagnoses on day 3 and day 5 among who were prescribed the RFQ levofloxacin or moxifloxacin.

Clinical Outcome	The Respiratory Fluoroquinolones Outcomes Analyzed for Patients with A Radiological Diagnoses of CAP Numbers (%)					
	Day 3			Day 5		
	Levofloxacin	Moxifloxacin	*P**	Levofloxacin	Moxifloxacin	*P**
Improved	93 (80.8)	88 (83.0)		108 (93.9)	101 (95.3)	
Partial improved	9 (7.8)	14 (13.2)	.537	1 (0.87)	4 (3.8)	0.622
Failed, Switched, Added	12 (10.4)	3 (2.8)		5 (4.3)	0	
Death	0	0		1 (0.87)	0	

Number of patients with radiological diagnosis for levofloxacin 115 and moxifloxacin 106.

Figure 2. Rates of improvement for day 3 and day 5 (the primary outcome) for CAP-treated patients with levofloxacin or moxifloxacin. (A) Unadjusted analysis, and (B) multivariate analysis.



Significance was adjusted for multiple comparisons by Bonferroni.

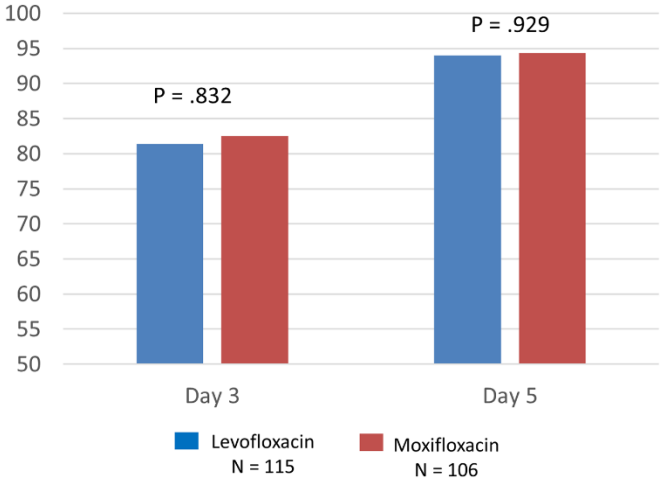
Sputum production was described in 169 (50.6%) of patients; though cultures were requested in 95 (28.4%) patients; 66 (69.4%) showed no growth, and 30.6% grew different microorganisms (5 *Haemophilus influenzae*, 3 *Staphylococcus aureus*, 1 *Streptococcus pneumoniae* and 20 grew various microorganisms). Blood cultures were collected in 114 (45.9%) febrile patients; 110 (96.5%) patients with no growth and four blood cultures grew different microorganisms, and no urinary antigens were requested.

Other associated phenomena were not significantly different (P > 0.05), like sputum production, chest pain, chills and rigors, vomiting, leukopenia < 4000, thrombocytopenia and hypoglycemia.

Outcome

Patients' outcome such as improved, partially improved, failed/switched/added antimicrobial agent and death are summarized in (Table 2), where day 3 demonstrated significant difference in favor of moxifloxacin (P = 0.022), but not day 5. For the radiological diagnosed CAP patients (Table 3), there were no significant differences detected for day 3 and day 5 (P > 0.5). The total number of the improved patients on day 3, levofloxacin 126 (75.4%) and moxifloxacin 141 (84.4%), (difference = 15 (9%), P = 0.041), and for day 5 levofloxacin were 153 (91.6%), and moxifloxacin group were 159 (95.2%), (difference = 6 (3.6%), P = 0.187) (Figure 2A). In a multivariate analysis (Pillai's trace for RFQ was .810 (P < 0.0001) denoting significantly contributing to the model) the primary outcome showed that on day 3 the

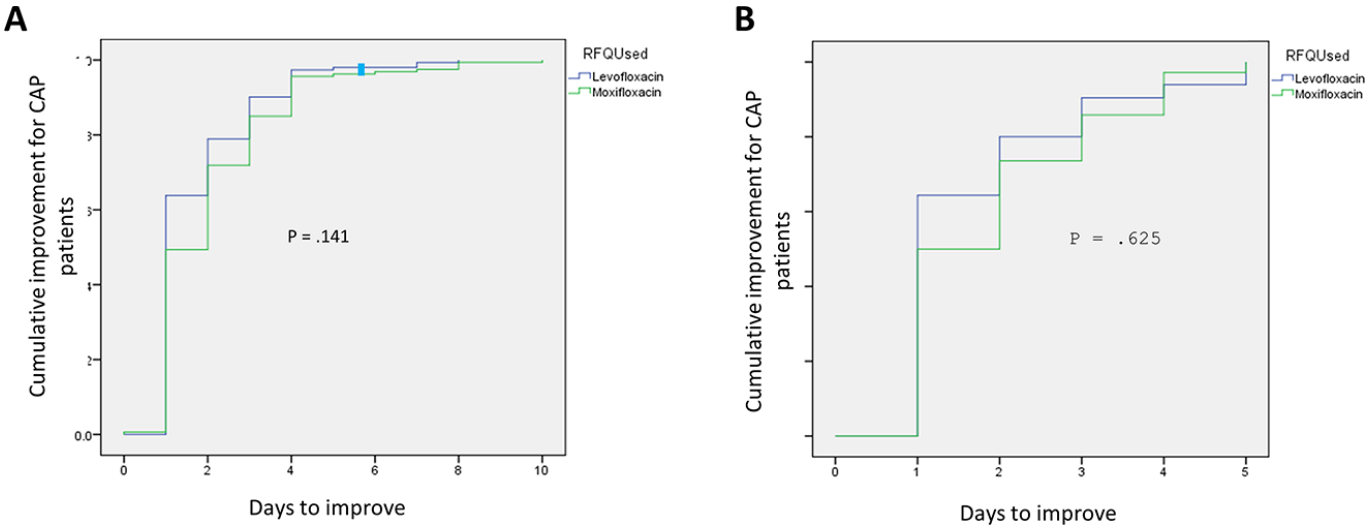
Figure 3. Multivariate analysis of the rates of improvement for radiologically diagnosed CAP patients for day 3 and day 5, who were treated with levofloxacin or moxifloxacin.



Significance was adjusted for multiple comparisons, Bonferroni.

improvement in levofloxacin-treated patients was 75.9% (SE = .030, 95% CI, 69.9 - 81.8), moxifloxacin-treated patients 84.0% (SE = .030, 95% CI, 78.1 - 89.9%), with marginal mean difference (Levofloxacin - Moxifloxacin) of -8.1% (SE = .043, 95% CI, -16.5 - .3%, P = 0.058) adjusted for multiple comparisons by Bonferroni. And day 5 the improvement in levofloxacin-treated patients was 91.9% (SE = .019, 95% CI, 88.3 - 95.6), moxifloxacin-treated patients 95.5% (SE = .019, 95% CI, 91.8% - 99.2%) with marginal means difference (Levofloxacin - Moxifloxacin) of -3.5% days (SE = .027, 95% CI, -8.7% - 1.7%, P = 0.184) adjusted for multiple

Figure 4. Cumulative curve for the recovery of all RFQ-treated CAP patients until day 10 (A), and those with radiological diagnosis until day 5 (B).



Censored (beyond day 10): Levofloxacin 4, Moxifloxacin 3; One death on day 5 in Levofloxacin; RFQ: respiratory fluoroquinolones; P-value by log rank.

comparisons by Bonferroni (Figure 2B). For the outcomes days 3 and 5, univariate analysis was similar, no significant differences between the two RFQ (P = 0.058 and .184 respectively).

Levofloxacin-treated 115 and moxifloxacin-treated 106 with radiologically diagnosed CAP patients were analyzed for the outcomes; the rates of improved patients were 81.4% and 82.5% (P = 0.832) for day 3 outcome respectively. For day 5 outcome levofloxacin improvement rates was 94%, and moxifloxacin was 94.3% (P = 0.929) (Figure 3).

Multivariate analysis for nested age group (here decades of age) did not reveal statistical significance differences between the two antimicrobial agents for day 3 and day 5 (P > 0.05). Secondary measures; cumulative (1- Kaplan Meier survival) curve demonstrated no significant difference for the time to event (improvement) between the two therapeutic agents (Log Rank, P = 0.141) until day 10 (Figure 4 A), or for patients with positive radiological diagnosis until day 5 (P = 0.625) (Figure 4B). The estimates for the PSI risk classes (analyzed as low, medium and high-risk classes) were also not significant (P = 0.302 by Log Rank test) for both RFQ. The mean duration of therapy for levofloxacin was 4.27 (SD = 2.30) days and moxifloxacin 4.58 (SD = 4.58) days (P = 0.200). Length of hospital stays 4.32 (SD = 4.765) days and 4.45 (SD = 7.146) days (P = 0.850) for levofloxacin and moxifloxacin respectively.

Discussion

The main findings of this study for day 3 outcome in the unadjusted analysis, moxifloxacin speed of recovery demonstrated a marginal significant difference (P = 0.041), and when analyzed as outcome ranks: improved, partially improved, failed-switched-added agent, and death (P = 0.022). However, on adjusted analysis no statistically significant difference was detected but tendency (P = 0.058) and for outcome ranks no significant tendency (P = 0.104). This tendency was also observed in the multivariate analysis of radiologically diagnosed patients who were treated with levofloxacin or moxifloxacin for day 3 outcome (P = 0.087), but ranks differences were not significant (P = 0.537). For Day 5 outcome the analyses predicted no significant statistical differences between both treated groups of patients, whether all patient diagnosed with CAP or patients with radiological diagnoses (P > 0.1), as well as ranks (P = 0.622) (Tables 2, and 3). Furthermore, secondary outcomes analyzed including the difference between both antimicrobials on day-by-day basis, or the cumulative improvement over the first 10 days for all CAP patients and the first 5 days for patients with radiological diagnoses were statistically not significant (P > 0.1) (Figures 4 A, B)

The intention for the inclusion of ≤ 60 years old patients is to avoid skewing of the results toward older age groups, provided that the search for CAP patients, many patients were found > 60 - 65 years old, the decision not to include this age category was set at the implementation of the protocol to avoid any potential buffering effect for the speed of recovery of a close elder age group. , and it was found that it contrasted with Anzueto and coworkers study for patients with age ≥ 65 years old [13]. Unfortunately, attempt to isolate a pathogen to guide therapy was poor, even among patients with fever (74.3%), sputum production (50.6%), or both symptoms combined (38%), despite pathogen-guided treatment was reported to have the better outcome compared with empiric treatment [16]. Nonetheless, it seems that the few properly isolated microorganisms from the respiratory secretions did not convince the treating physicians to de-escalate treatment focusing on the isolated microbial agent though some of those microorganisms are usually associated with CAP, [17-19]. However, former studies attempted to culture a causative microorganism from CAP patients was met with low recovery rates, as low as 38% using the conventional culture methods, thus might have added to the decreased enthusiasm to culture respiratory secretions [20-24]. However, employing the current molecular testing raised the yield up to 87%, and the detected etiological agents were viruses, followed by bacterial pathogens, commonly *Streptococcus pneumoniae* which remain the commonest agent causing bacterial CAP [25-27], but this methodology was not available during the study time in the participating hospitals. Nonetheless, in this study the etiologic agent seems to be less determinant than the host factors (PSI) for the outcome and the absence of a complete microbial study did not invalid the presented results.

In our patient series, possibly due to the admitted low-severity risk patients and the short term follow up, all-cause mortality was low, where one patient died by day 5 in the Levofloxacin group, he had malignancy and was on mechanical ventilator. The nature of our retrospective study has no control over the risk stratification and hospital admission, which may have resulted in falsely low mortality among this subset of patients, though a study by Ruhnke WG and co-workers found that the 30 days mortality was markedly reduced due pneumococcal vaccination, influenza vaccination, and guidelines-instructed antimicrobial therapy [28].

Also, antimicrobial adherence and treatment within 6 hours' time frame, and implementation of standardized care bundle in the emergency room, significantly reduce risk and the risk of death in admitted patients (P = 0.02), including 18 – 79 years old age patients [29,30].

Though our study design was retrospective, a real world data demonstrated tendency in favor of moxifloxacin for the speed of improvement, our study was with, but not exactly in line with an earlier prospective study by Anzueto et al, that showed significant difference in that regard [13], and other studies that demonstrated the same effect in acute exacerbations of COPD [31,32], including a real life prospective non-interventional study that demonstrated a faster speed of recovery of moxifloxacin compared with macrolides [33]. Our finding (tendency) may be explained based on younger age group, and lower risk group. No significant differences were found for the cumulative improvement curves, including 10 days of follow up (beyond the outcome) for all patients (P = 0.141), and for 5 days in the radiologically diagnosed patient (P = 0.625) respectively (Figure 4 A, B), and the Bar chart representing the absolute daily recovered patients for the two RFQs did not reach statistical difference (P = 0.165).

The limitation of our retrospective study mostly comes from the small sample size of the patients with radiological diagnoses, 34.4% for levofloxacin and 31.7% for moxifloxacin, that decreased the power of the study. There was no control on hospital admissions risk stratification (PSI) for the included patients, abundance of low-risk patients may have had a tempering effect on the analysis of the measured improvement rates difference, since those patients may improve with either regimen equally [34]. Furthermore, the multiple antimicrobials use in the treatment of low-risk patient may have added a dilution effect for difference between the two fluoroquinolones. Few records were found to have cultures and susceptibility, and analysis in this regard could not be done. In addition, no data was collected on the time between presentation with the CAP diagnosis and the start of the RFQ treatment [35], and *Legionella* as well aspneumococcal urinary antigen were not requested, though the former antigen test was available for the practicing physicians in the participating hospitals. Some adequate points for this study is that patients with established radiological diagnoses who presented clinically as CAP were analyzed as a subgroup. The choice of age limit 60 was to exclude many patients with age > 60 - 65; the intent was not to have a buffering effect and data skewness from the elder age group. Analyzing patients as age categories (decades) may have had shed light if age influenced the speed of recovery of the studied respiratory fluoroquinolones.

Conclusion

Our multivariate and univariate analysis demonstrated that moxifloxacin exhibited no significant differences (though tendency) for the rates of improvement examined on day 3 and not for 5. This study, though was different in its design from a previously published study that evaluated both quinolones for community-associated pneumonia in older age groups (> 65 years), where moxifloxacin significantly showed less time to recovery than levofloxacin, that benefit may not be extended to young patients as in our study.

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Corresponding author

Jamal Ahmad Wadi MD
Adjunct, Assistant Professor of Infectious Diseases, School of Medicine, The University of Jordan.
Office 11, 3rd Floor, Jordan Hospital Medical Center
29 Adeeb Wahbeh Street, Amman – Jordan 11118.
Telefax: +962 6 568 6551
Email: jamalwadimd@yahoo.com

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