REVIEW ARTICLE

Effectiveness and safety of levofloxacin in the treatment of community-acquired pneumonia: A systematic review and meta-analysis

DOI: 10.29063/ajrh2025/v29i2.19

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Abstract

This study was conducted to evaluate the efficacy and safety of levofloxacin in the treatment of community-acquired pneumonia (CAP), and to provide a more reliable medication guide for the treatment of community-acquired pneumonia. Clinical studies of levofloxacin for CAP were searched through online literature databases, and the final literature for analysis was identified after screening by inclusion and exclusion criteria. The quality of the literature was assessed according to the risk of bias assessment criteria of the Cochrane system. Literature information was extracted and meta-analysis was performed using RevMan software. The observational indicators were clinical cure rate, microbiologic (bacteriologic) success rate, adverse event rate, and mortality rate. After screening, a total of 8 papers were included in the study, totaling 2,272 study subjects, of which 1,155 patients who received levofloxacin treatment were considered as the study group. 1117 patients who received other antimicrobial drugs were considered as the control group. The literature was evaluated to have a low risk level and a high reference value. The results of meta-analysis showed that there was no significant difference in the clinical cure rate, microbiologic (bacteriologic) success rate, adverse event rate and mortality rate between the study group and the control group (P>0.05).As a result of the study, it was concluded that: levofloxacin has significant efficacy and safety in the treatment of CAP, and other antimicrobial drugs (e.g., moxifloxacin) have comparable efficacy and higher safety than levofloxacin, which provides a more diversified solution for the treatment of CAP. *(Afr J Reprod Health 2025; 29 [2]:181-189).*

Keywords: Levofloxacin; Community-acquired pneumonia; Adverse events

Résumé

Cette étude a été menée pour évaluer l'efficacité et l'innocuité de la lévofloxacine dans le traitement de la pneumonie communautaire (PAC) et pour fournir un guide médicamenteux plus fiable pour le traitement de la pneumonie communautaire. Les études cliniques sur la lévofloxacine pour le traitement de la PAC ont été recherchées dans des bases de données documentaires en ligne, et la littérature finale à analyser a été identifiée après sélection selon des critères dout-'inclusion et d'exclusion. La qualité de la littérature a été évaluée selon les critères d'évaluation du risque de biais du système Cochrane. Les informations de la littérature ont été extraites et une méta-analyse a été réalisée à l'aide du logiciel RevMan. Les indicateurs d'observation étaient le taux de guérison clinique, le taux de réussite microbiologique (bactériologique), le taux d'événements indésirables et le taux de mortalité. Après sélection, un total de 8 articles ont été inclus dans l'étude, totalisant 2 272 sujets d'étude, parmi lesquels 1 155 patients ayant reçu un traitement à la lévofloxacine ont été considérés comme le groupe d'étude. 1 117 patients ayant reçu d'autres médicaments antimicrobiens ont été considérés comme groupe témoin. La littérature a été évaluée comme ayant un faible niveau de risque et une valeur de référence élevée. Les résultats de la méta-analyse ont montré qu'il n'y avait pas de différence significative dans le taux de guérison clinique, le taux de réussite microbiologique (bactériologique), le taux d'événements indésirables et le taux de mortalité entre le groupe d'étude et le groupe témoin (P > 0,05). l'étude, il a été conclu que : la lévofloxacine a une efficacité et une sécurité significatives dans le traitement de la PAC, et d'autres médicaments antimicrobiens (par exemple, la moxifloxacine) ont une efficacité comparable et une sécurité plus élevée que la lévofloxacine, qui fournit une solution plus diversifiée pour le traitement de la PAC. *(Afr J Reprod Health 2025; 29 [2]: 181-189).*

Mots-clés: Lévofloxacine ; Pneumonie communautaire ; Événements indésirables

Introduction

Based on the location of acquisition, pneumonia can be divided into two types: community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP).CAP is typically characterized as a lower respiratory tract infection that is acute and non-hospital acquired. The incidence of CAP is high worldwide. According to a Chinese study, CAP has a major negative impact on the country's public

health, with an annual incidence rate of 7.13 cases per 1,000 people[1]. There are 915,500 cases of CAP in Americans 65 and older per year, and the 2011 healthcare costs related with CAP were more than $10 billion[2].With a higher incidence in men than in women, the incidence of CAP in Europe is roughly 1.07–1.2 cases per 1,000 people per year, rising to 14 cases per 1,000 people per year in those 65 years of age and older[3]. The risk of CAP is higher in children under the age of five, adults 65 years of age and older, especially those who have comorbid conditions.

Diabetes mellitus, cardiovascular illness, and chronic liver disease are the most prevalent comorbid conditions that raise the risk of CAP[4,5]. The risk of CAP is higher in immunocompromised individuals than in the general population[6]. In a multicenter survey of 54 nations, it was discovered that around one-fifth of CAP patients were either immunocompetent or immunodeficient[3]. Moderate CAP is often treated in hospital wards, mild CAP in outpatient clinics, and severe CAP in intensive care units (ICU)[3]. The severity of the disease and the environment in which it is treated have a significant impact on the death rate of CAP patients. Globally, the death rate of CAP patients treated in outpatient clinics is less than 1%, compared to the ranges of 4% to 18% for patients treated in hospital wards and up to 50% for those treated in intensive care units[7-9]. The age of the patient is also an important factor in CAP mortality. A study showed that the mortality rate of CAP patients <65 years old is about 5%, 65-79 years old is about 8%, and ≥80 years old is about 14%[10].

Streptococcus pneumoniae and Mycoplasma pneumoniae are the most common pathogens associated with CAP. Macrolides and fluoroquinolones are recommended by the Infectious Diseases Society of America/American Thoracic Society (IDSA) for the antimicrobial therapy of CAP[11]. However, increasing antimicrobial resistance poses an important challenge to the clinical practice of CAP[12]. Levofloxacin is a fluoroquinolone antimicrobial drug commonly used in clinical practice. According to the results of relevant surveys, the global resistance rate of levofloxacin among Streptococcus pneumoniae is less than 1%[13,14] In recent years, levofloxacin at 750 mg/dose has been gradually used in the treatment of CAP, and has been shown to have better efficacy[15,16]. However, levofloxacin may cause adverse reactions in the cardiovascular system, gastrointestinal system and other aspects, which makes the overall safety of the treatment reduced. However, the current clinical attention to levofloxacin treatment of CAP is mainly focused on increasing the dose to strengthen the efficacy, ignoring the possible adverse effects of levofloxacin, which has led to a continuous increase in the incidence of levofloxacin-induced adverse effects in recent years, resulting in a decrease in the overall therapeutic effect.

In order to give a more accurate and thorough reference for levofloxacin's potential therapeutic usage in the treatment of CAP, this study will launch a systematic evaluation and meta-analysis of the drug's efficacy and safety.

Methods

Literature inclusion and exclusion criteria

Inclusion criteria: (1) Type of study: randomized controlled trial or cohort study. (2) Year of study: studies published since 2010. (3) Study subjects: CAP patients treated with levofloxacin with a clear diagnosis. (4) Therapeutic measures: one of the two groups of CAP patients received levofloxacin treatment.

Exclusion criteria: (1) Incomplete study data. (2) Repeatedly published literature. (3) Unavailability of full text.

Retrieval strategy

The terms "levofloxacin, community-acquired pneumonia" were used to search PubMed, Web of Science, and other databases. To keep track of references and prevent omissions, a combination of subject and free words was used.

Literature screening and data extraction

Two researchers independently conducted the literature review and data extraction, with a third

researcher making decisions in the event of a dispute. The acquired records were added to Endnote X 9.1, and those with the same title, the same authors and the same year of publication were checked, and then the documents after checking were screened according to the title and the abstract for the first time, and the irrelevant documents were excluded, and then read the full text for the second time. Two researchers extracted data according to the contents of the documents, including the title of the included documents, nationality of the authors, basic information of the research subjects, sample size, treatment measures, outcome indicators and measurement tools, authors, nationality, type of disease, basic information about the study population, sample size, treatment measures, outcome indicators, and measurement tools.

Literature quality assessment

Two researchers independently assessed the quality using the risk of bias assessment scale from the Cochrane Handbook version 5.1.0[17]. The evaluation covered the creation of random sequences, allocation concealment, blinding of subjects and investigators, blinding of outcome measures, completeness of outcome data, selective reporting of results, and other bias risks, each of which was rated as "high risk," "unclear," or "low risk." Each signal was given a risk rating of "high," "unclear," or "low.". If the original study fully met the above criteria, the quality of the literature was graded as A, if it met some of the criteria it was graded as B, and if it did not meet all of the above criteria it was graded as C.

Observation indicators

(1) Clinical cure rate. (2) Microbiologic (bacteriologic) success rate. (3) Adverse event rate. (4) Mortality rate.

Statistical methods

Relative risk (RR) and 95% confidence intervals (CI) were employed for statistical analysis using Review Manager 5.3 software, whereas mean difference (MD) and CI were used to express measurement data. The heterogeneity of the included studies was examined using the chi-square test, with a test level of =0.1. The fixed-effects model was used to examine the absence of heterogeneity (I^2<50%), the random-effects model was used to analyze the existence of heterogeneity (I^2≥50%), and the funnel plots were further plotted to determine the publication bias. I2 quantified heterogeneity. The statistical significance of the difference was set at P<0.05.

Results

Search results

According to the results of keywords search, 68 pieces of related literature were initially found; 60 pieces were left after EndNote checking; and 8 pieces of literature were finally included after screening by reading the full text and according to the inclusion and exclusion criteria[18-25] for meta-analysis, see Figure 1.

Basic characteristics of the included literature

A total of 2,272 study subjects were included in the eight literatures, of which 1,155 patients treated with levofloxacin were uniformly labeled as the study group, and 1,117 patients treated with other drugs were uniformly labeled as the control group. See table 1.

Quality assessment of the included literature

The current study included literature with a low risk rating and a high reference value. See Figure 2

Meta-analysis results

Clinical cure rate

A fixed-effects model was chosen for the analysis because there was no evidence of heterogeneity across the six publications' clinical cure rates (I^2 = 0%). Figure 3 demonstrates that there was no clinical cure rate difference between the study group and the control group that was statistically significant (P>0.05).

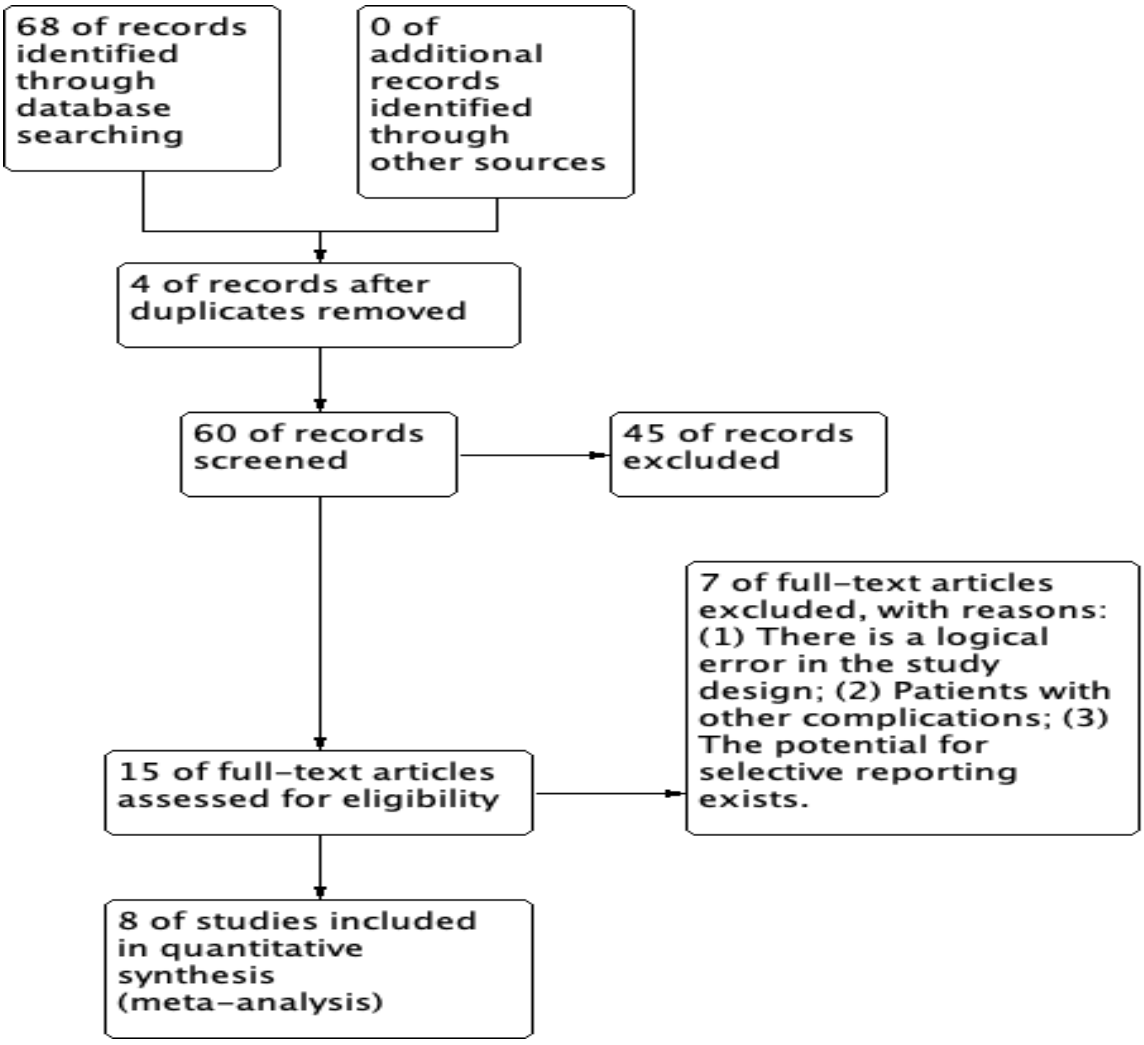

Figure 1: Flow of the study

Table 1: Basic characteristics of literature

Author and date of publication	Research group (treatment with levofloxacin)	Control group (treatment with other drugs)	Observed indicators
Sun T 2014[21]	40	37	(1)(3)
Oldach D 2013[22]	67	65	(1)(3)
Bradley JS 2007[23]	405	134	(1)(2)(3)
Yuan J 2017[24]	171	356	(1)(2)(3)
Querol-Ribelles JM 2005[25]	250	209	(4)
Mokabberi R, 2010[26]	30	35	(3)
Liu Y 2015[27]	52	140	(1)(2)(3)
Anzueto A 2006[28]	140	141	(1)(2)(3)(4)

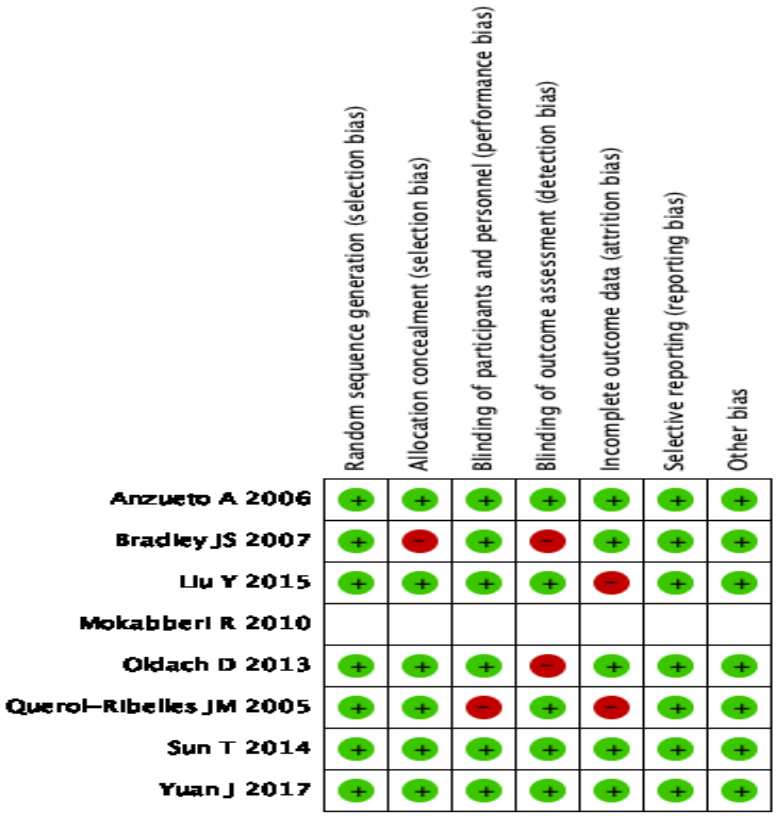

Figure 2: Literature quality evaluation chart

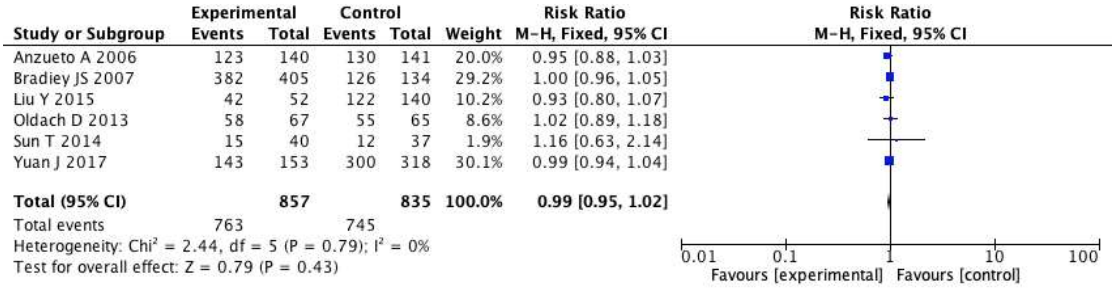

Figure 3: Clinical cure rate

Microbiology (Bacteriology) Success Rate

Four publications reported microbiological (bacteriological) success rates of patients, and I^2 analysis showed no heterogeneity among the publications (I^2 =0%), which were analyzed using a fixed-effects model. Figure 4 illustrates that there was no statistically significant difference between the study group and the control group in terms of microbiologic (bacteriologic) success rates (P>0.05).

Adverse event rate

Seven publications reported the incidence of adverse events in patients.I^2 analysis showed no heterogeneity among the publications (I^2 =0%) and was analyzed using a fixed-effects model.

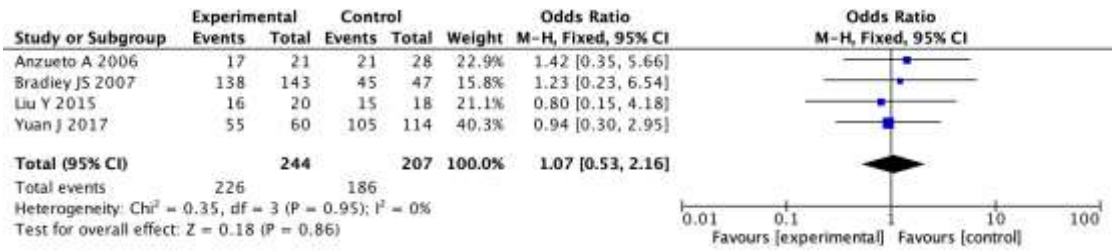

Figure 4: Microbiology (Bacteriology) Success Rate

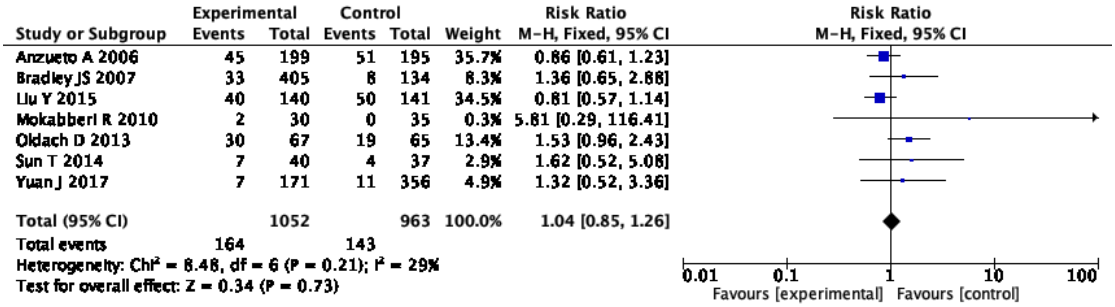

Figure 5: Incidence of adverse events

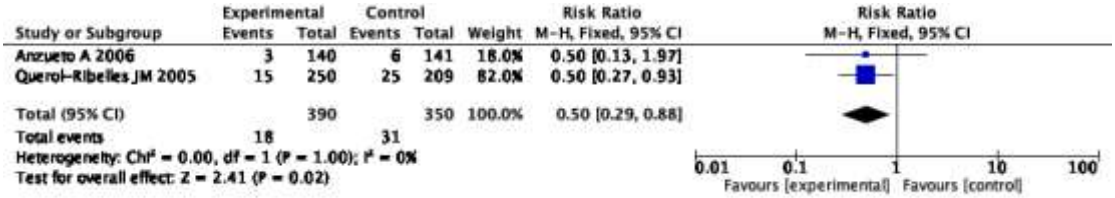

Figure 6: Mortality

According to Figure 5, there was no statistically significant difference between the study group and the control group's incidence of adverse events (P>0.05).

Mortality rate

Two publications reported patient mortality rates.I^2 analysis showed no heterogeneity seen across the literature (I^2 =0%) and was analyzed using a fixed-effects model. According to Figure 6, there was no statistically significant difference between the study group and the control group's incidence of adverse events (P>0.05)

Discussion

Levofloxacin is a commonly used drug for the treatment of CAP. The results of the TRUST 2001-2005 study in the United States showed that the sensitivity rate of common pathogens of CAP such as Streptococcus pneumoniae, Haemophilus influenzae, and Catamoeba to levofloxacin was more than 99%[26]. However, since the use of levofloxacin varies around the globe, leading to different resistance to levofloxacin, it is worth studying whether the efficacy of levofloxacin for CAP has decreased and whether it is the drug of choice for the treatment of CAP. In this study, we screened and carried out a meta-analysis of eight papers on levofloxacin for CAP, which were from 2005 to 2017, which can represent the changes in the effectiveness of levofloxacin for CAP over a 12-year period. The results of the eight papers showed that levofloxacin and other drugs for CAP achieved high clinical cure rates, microbiologic (bacteriologic)

success rates, and lower adverse event rates and mortality rates, confirming that levofloxacin can still play a significant role in the treatment of CAP and has not been affected by the increase in drug resistance of CAP flora. Meanwhile, other antimicrobial drugs represented by moxifloxacin have played an increasing effect in the treatment of CAP. And the outcomes of meta-analysis demonstrated that there was no discernible difference between levofloxacin and other medications in terms of the clinical cure rate, microbiological (bacteriological) success rate, adverse event rate, and death rate. This indicates that levofloxacin is no longer the only choice for the treatment of CAP, and that antimicrobial drugs such as moxifloxacin can play an essentially equal role to levofloxacin in the treatment of CAP, providing a diversified solution for the clinical treatment of CAP.

It should be noted that although there was no statistically significant difference in the incidence of adverse events between levofloxacin and other medications used to treat CAP, the incidence of adverse events caused by levofloxacin was higher than that of other medications, indicating that there is a need to emphasize the safety of levofloxacin in the treatment of CAP. Previous studies have pointed out that, with the widespread use of levofloxacin in the clinic, its adverse reactions are also increasing, and the adverse reactions of levofloxacin are mainly concentrated in the damage of central and peripheral nervous system, systemic damage, musculoskeletal muscle system, metabolic and nutritional disorders, neurological disorders, damage of the hepatic and biliary system, and so on, and the adverse reactions of the central nervous system caused by levofloxacin are one of the most common and serious adverse reactions, accounting for about one percent of the overall adverse reactions. The central nervous system adverse reaction is one of the most common and serious adverse reactions, accounting for about 17.95%-40% of the overall adverse reactions[27, 28]. The central and peripheral nervous system damage is mainly manifested as grand mal seizures, extrapyramidal disease, convulsions, local numbness, etc.; the systemic damage is mainly manifested as anaphylaxis, metamorphic reaction, anaphylactic reaction, high fever, etc.; the musculoskeletal muscle system damage is mainly manifested as tendonitis, tendon damage, arthralgia, rhabdomyolysis, etc.; the other damage is mainly manifested as hypoglycemia, phlebitis, coagulopathy, hepatitis, Liver function abnormality, renal function abnormality, eruption, insomnia, leukopenia, thrombocytopenia, etc. The guideline for the use of antimicrobial drugs of the Ministry of Health of China pointed out that levofloxacin has chondrotoxicity, and should be avoided in children over 18 years old and pregnant women. CAP has a large number of pediatric patients, and the use of levofloxacin for treatment should be cautious. Meanwhile, some Chinese researchers have noted that the frequency of levofloxacin side effects is highly correlated with age, and that the frequency of side effects in persons over 60 is 2.3 times higher than that in those under 60. Neurological diseases, Parkinson's syndrome, epilepsy and other past medical history are also high-risk factors to induce levofloxacin adverse reactions. It can be seen that levofloxacin treatment should be used with caution and dose control in CAP patients with past medical history of neurological diseases, children or elderly CAP patients over 65 years of age, and pregnant women with CAP, and should be closely observed during the course of treatment, and treated promptly in the event of an adverse reaction.

However, there are many limitations to improve this study. For example, the sample size of our included studies was generally small, and the subjects were from different countries, who had different diagnostic and inclusion criteria for CAP, and different dosages of levofloxacin, which are potential causes of clinical heterogeneity and methodological heterogeneity. In addition, all the included studies were in English, and there was no literature in other languages, which may lead to the risk of language bias that studies published in other language forms were not included. Additionally, these restrict the conclusions of the assessment of the effectiveness and safety of levofloxacin in the treatment of CAP because extended follow-up data were not included. All of the above factors may affect the results of Meta-analysis in this paper.

Strengths and limitations of the study

This study demonstrates that levofloxacin is safe and effective in the treatment of CAP, but it does not show absolute advantages. This reminds us that in the context of the increasing incidence of CAP, it is necessary to continue to explore drugs with higher clinical benefits for CAP, so as to bring better benefits to patients with CAP. At the same time, this study also has some limitations. If the number of included studies is small, the research conclusions may be biased to a certain extent. The research on other languages except English is insufficient, and it is impossible to focus on the relevant studies of other languages to improve the credibility of the conclusions of this study. These limitations will be addressed on a case-by-case basis in the future.

Conclusion

Levofloxacin still has significant effectiveness in the treatment of CAP, and other antimicrobial drugs represented by moxifloxacin have gradually shown excellent effects in the treatment of CAP, providing diversified options for the clinical treatment of CAP. Compared with other drugs, although levofloxacin does not lead to significant adverse reactions in the treatment of CAP, its potential predisposing factors still deserve attention.

Conflicts of Interest

The authors report no conflict of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Funding

Not applicable.

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