Original Article

Efficacy and safety of moxifloxacin injection in treatment of acute exacerbation of chronic bronchitis

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ABSTRACT

Objective: To evaluate the clinical efficacy and safety of moxifloxacin injection in the treatment of acute exacerbation of chronic bronchitis (AECB) in daily clinical practice. **Patients and Methods:** From May 2009 to March 2011, a total of 1026 cases with AECB were collected from 43 hospitals in eight cities. All the patients were treated with moxifloxacin (400 mg qd) intravenously. Whether to use oral or sequential therapy was decided by the physicians according to the clinical efficacies. Patient conditions such as combined uses of drugs, efficacies and adverse events were recorded and analyzed. **Results:** The cure rate of infection was 83.03%, and the total effective rate of moxifloxacin injection was 93.80%. The efficacies were statistically different among subgroups with different ages, complications, forced expiratory volume in 1 s (FEV_1%), and combined uses of drugs, respectively. Multivariable logistic regression analysis showed that the advanced age (≥65 years) and severe obstructive pulmonary disease (FEV_1 <50%) were significantly correlated with the clinical efficacies. A total of 15 cases of adverse events were recorded, and the incidence rate was 1.23%. **Conclusion:** Moxifloxacin injection can effectively control the infection of AECB patients with fewer adverse events.

Key words: Efficacy, moxifloxacin injection, multi-center, safety

INTRODUCTION

Chronic bronchitis is a worldwide disease with high incidence and disability rates and it ranks the fourth position of death

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causes worldwide. A study shows that the prevalence rate of chronic bronchitis among people above 40 years old in China reaches up to 8.2%.[1] Repeated acute exacerbation of chronic bronchitis (AECB) reduces life quality of patients, promotes pulmonary dysfunction, and increases the fatality rate. AECB may be caused by multiple factors, and the most popular one is an infection of bacteria, virus, and atypical pathogens. If the symptom becomes worse, especially when purulent sputum is available, antibiotic treatment shall be positively used. Empirical antifungal treatments shall cover major pathogens for AECB.[2] Moxifloxacin has a good antibacterial activity for major pathogens of AECB and has been widely used for AECB treatment. However, with growing of AECB patients' ages, variations of pathogenic bacteria spectrum and an increase of drug-resistant bacteria, large-sample studies should be performed to prove the clinical efficacy and safety of moxifloxacin for the treatment of AECB. In this study, we performed a prospective, open, and noninterventional multi-center clinical trial to assess the clinical efficacy and safety of moxifloxacin (Avelox®) injection for treatment of AECB and to analyze the influencing factors. We hope to provide the clinical evidence and references for the treatment of AECB with moxifloxacin injection.

PATIENTS AND METHODS

Study design

From May 2009 to March 2011, a total of 1206 patients from 43 hospitals in 8 cities were observed. The diagnosis, examination, and individualized treatment of these patients were conducted by their doctors. Observation period covered the whole process of moxifloxacin treatment. Sequential therapy and oral medication were recorded.

Subjects enrolled and exclusion criteria

Enrolled criteria

Diagnosed with AECB, age ≥18 years, treated with moxifloxacin injection, either inpatients or outpatients, without consideration of disease severity or usage of moxifloxacin tablets in the following treatment. All enrolled patients received moxifloxacin injection treatment. During treatment, moxifloxacin injection may be changed to oral medication or sequential therapy.

Exclusion criteria

With infections of other locations besides respiratory system treated with other antibacterial drugs, or with mechanical ventilation therapy, or without informed consent.

Observation index and effectiveness judgment

Therapeutic method and combined medication: Moxifloxacin (400 mg) was intravenously injected once every day; the course of treatment was decided by their doctors and the concomitant medication process was recorded.

Observation index:

1. Cure time: Time that takes from moxifloxacin treatment to disappearance of the symptoms;
2. Improvement time: Time that takes from moxifloxacin treatment to when patients felt improved;
3. Fever reduction time: Time that takes in reducing the body temperature to normal level;
4. Efficacy evaluation of moxifloxacin by the doctors;
5. Leukocyte count before and after moxifloxacin treatment.

Per protocol Set (PPS) was used for result statistics. Main variables could be measured and there was no serious violation of criteria. Adverse event analysis was used as main safety indexes. The clinical efficacy was evaluated as curative, effective, improved, and according to clinical research guide for antibiotic drugs issued by China Ministry of Health, clinical effect shall be valued as curative, effective, improved, and nonresponsive.

Statistical analysis

Conclusive statistics was used for demographic data, AECB history and treatments, and concomitant medication. Mean value, standard deviation, minimum value, median, and maximum value were used for continuous variables. Categorical variables were analyzed using categorical counting and frequency (percentage) calculation. Chi-square test was used for comparison of cure rates between subgroups. Influencing factors for cure rates were analyzed by logistic regression analysis.

RESULTS

Among the 1206 patients, 1096 were taken into PPS data, including 735 males (67.0%) and 361 females (32.9%). The average age was 66.4 ± 13.1 years. As per Anthonisen classification, type I patients covered 25.3%, type II 26.4%, and type III 48.3%. As per the severity of AECB; mild, moderate, and severe patients accounted for 11.4%, 58.3%, and 30.3%, respectively. Of the patients, 748 cases did not receive any other antibacterial treatment within recent 14 days, and 32.1% patients had a history of hormone treatment.

Totally 813 patients received only intravenous injection and 283 patients underwent sequential therapy. The dosage of both treatments was 400 mg per day and the course of treatment was 3-14 days (median: 8 days).

Before treatment, sputum culture was positive in 20.7% of 914 patients. The detected bacteria included *Pseudomonas aeruginosa* (5.1%), *Streptococcus pneumonia* (4.9%), *Haemophilus influenza* (2.7%), *Bacillus canalis capsulatus* (2.1%), and *Moraxelle catarrhalis* (2.0%). Sputum culture was positive in 12.4% of 909 patients after treatment.

Before treatment, 486 patients had a fever, and after treatment the fever was gone in 462 patients within 1-10 days (median: 3 days). Before treatment, the leukocyte count was abnormally high in 443 patients, but after treatment it returned to the normal level in 423 patients (95.5%). A total of 1032 patients (94.3%) felt better within 10 days (median: 3 days). After moxifloxacin treatment was completed, the recovery rates and overall efficacy were evaluated by the doctors. The cure rate was 83.03%, and the effective rate of moxifloxacin was 93.80%.

Influencing factors analysis: Significant difference was found between subgroups in terms of age, forced expiratory volume in 1 s (FEV_1%), and combined medication as well as between subgroups with and without complications (all $P < 0.05$). Moxifloxacin is effective in patients <65 years old, with FEV_1 ≥50%, and without complication nor combined medication. Multi factor logistic regression analysis showed that advanced age (≥65 years old) and severe obstructive pulmonary diseases (FEV_1 <50%) were influencing the factors of moxifloxacin effectiveness. According to Anthonisen classification, there were no significant differences among the three groups ($P = 0.1876$).

Of the 1206 patients enrolled, there were 15 (1.24%) adverse events, 12 (0.995%) of which were related with moxifloxacin (0.995%). The main symptoms included abnormal spiritual state (0.415%) such as excitation, dizziness and sleep disorder, rash and itch of skin (0.166%), and phlebitis (0.166%). Among the patients with adverse effects, 12 cases recovered. There was 1 serious adverse event, and the patient died of renal insufficiency. However, we could not be sure whether it was associated with moxifloxacin.

DISCUSSION

AECB is an acute pathogenesis process characterized by worsening of respiratory symptoms (dyspnea, cough, and expectoration) over the normal range of daily changes, leading to the change of medical treatment regimens. AECB is an important part of the course of chronic bronchitis.[3] The periodical occurrence of AECB brings patients great pains and results in pulmonary function impairment; meanwhile it increases the fatality and social economic burden.[4] The goal of treating AECB is to minimize the influences of each onset, so sufficient treatment shall be given at its beginning. When dyspnea aggravates and purulent sputum or/and sputum increases, bacterial infection is often indicated. Proper empirical antifungal therapy shall be necessary.[5]

Beta-lactam or macrolides drugs are traditional drugs to treat AECB. In recent years, with the increase of *S. pneumonia*, *H. influenza*, and *M. catarrhalis* that are resistant to beta-lactam or macrolides, the effectiveness and safety of these traditional drugs have been greatly influenced. Moxifloxacin/avelox is the fourth generation fluoroquinolone antibiotic drug. It has antibacterial activity on common bacteria in respiratory tract including atypical pathogens and anaerobia and has advantages of high bioavailability, strong tissue penetration, and good compliance, etc., which has been used more and more in anti-infection treatment.

A previous clinical randomized-control study[6-9] and large-scale noninterventional GIANT study[10] showed that an oral administration of moxifloxacin was effective and safe in the treatment of AECB. The present study was the first noninterventional study of moxifloxacin injection to AECB in China. In this study, we collected the clinical data of AECB patients with the treatment of moxifloxacin injection, and 94.71% patients received hospitalized treatment with clear indications for anti-bacterial therapy. With moxifloxacin injection only or sequential therapy, the temperature of 93.45% reduced within 5 days and 94.33% patients felt improved. The infection symptom was controlled effectively, and the effectiveness rate reached 93.80%.

A study showed that the prognosis of AECB and the effectiveness of antibiotics related with the following factors significantly including co-existences of multiple symptoms (aggregation of dyspnea, purulent sputum or/and sputum), advanced ages (≥65 years old), serious obstructive pulmonary diseases, occurrence of AECB over 4 times, and combination of cardiovascular diseases.[11] It was confirmed in this study that moxifloxacin was more effective in patients with advanced ages (<65 years old) and FEV_1 ≥50% as well as in patients without complications nor combined medication. Multi factor logistic regression analysis showed the advanced age (≥65 years old) and serious obstructive pulmonary disease (FEV_1 <50%) were factors influencing the effectiveness of Moxifloxacin. The incidence of adverse events was 1.24%, similar to other random control studies.

The common bacteria in AECB are *S. pneumonia*, *H. influenza*, and *M. catarrhalis*. In this study, the positive rate of sputum culture before treatment was 20.7% and the detected bacteria included *P. aeruginosa* (5.1%), *S. pneumonia* (4.9%), *H. influenza* (2.7%), *Bacillus canalis capsulatus* (2.1%), and *M. catarrhalis* (2.0%). This result might be related with *P. aeruginosa* infection in most of our patients. In clinical practice, it is necessary to understand the existence of *P. aeruginosa* infection, the drug-resistant and epidemic information, cost of treatment, and potential compliance of patients. Based on these considerations, proper and sufficient antibiotics may be selected and the cure rate may be improved.

To sum up, this study showed that moxifloxacin injection is effective to treat AECB with fewer adverse reactions in the clinical practice. Timely, the application of moxifloxacin injection can control the symptoms of AECB effectively.

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Conflicts of interest
There are no conflicts of interest.

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