

# Comparison of the Efficacy and Safety between Doxycycline and Moxifloxacin in the Treatment of Tsutsugamushi Disease

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**Abstract: Objective:** To explore the efficacy and safety of doxycycline and moxifloxacin in the treatment of tsutsugamushi disease. **Methods:** There was a total of 80 cases of tsutsugamushi disease that were treated in Jiangsu Sihong Fenjinting Hospital from January 2017 to August 2020. The patients were divided into group A and group B, with 40 cases in each group. The patients in group A were treated with moxifloxacin whereas those in group B were treated with doxycycline. The efficacy and safety of the clinical treatment between the two groups were compared. **Results:** The effective rate was 72.5% in group A and 95.0% in group B. Compared with group A, group B was better ( $p < 0.05$ ). The time taken for the resolution of clinical symptoms, the detection indexes of liver function, and the incidence of adverse reactions were also compared between the two groups, in which group B was significantly better than group A ( $p < 0.05$ ). **Conclusion:** In the clinical treatment of tsutsugamushi disease, doxycycline has better therapeutic effect and higher safety compared to moxifloxacin. It can significantly improve the patient's liver function, reduce the probability of adverse reactions, and accelerate the patient's physical recovery.

**Keywords:** Doxycycline; Tsutsugamushi disease; Moxifloxacin; Acid base balance; Liver function

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## 1. Introduction

Tsutsugamushi disease is not common. It is an acute natural focal infectious disease. The disease is mainly caused by the tsutsugamushi bacteria that is transmitted from the bite of larval mites, especially in warm and humid areas. The clinical symptoms of tsutsugamushi disease include ulceration or eschar, major lymph node involvement, varying degrees of rash and fever, as well as a significant decrease in the number of leukocytes in the peripheral blood. Untimely treatment would induce a series of adverse reactions, resulting in organ injury and even seriously damaging the patient's health <sup>[1]</sup>. Although the incidence rate of this disease is low, with the improvement of people's living standards, outdoor activities such as fishing, picnic, and camping are becoming more popular. Therefore, the incidence of scrub typhus is increasing year by year <sup>[2]</sup>. Clinically, the drugs for tsutsugamushi disease are mainly for acute natural focal infection, but there are some differences in the treatment effect. How to improve the treatment effect and reduce the incidence of adverse reactions have become the main research direction in clinical practice. The clinical effects of doxycycline and moxifloxacin in the treatment of tsutsugamushi disease for 80 patients with the disease treated in Jiangsu Sihong Fenjinting Hospital were comprehensively analyzed and studied so as to provide support for the clinical treatment of the disease and further theoretical research.

## 2. Materials and methods

### 2.1. General information

There was a total of 80 cases of tsutsugamushi disease treated in Jiangsu Sihong Fenjinting Hospital from January 2017 to August 2020. The patients were divided into group A and group B, with 40 cases in each group. The inclusion criteria were patients that had met the diagnostic and treatment criteria for tsutsugamushi disease with a history of field activities, had clinical manifestations of tsutsugamushi disease, such as eschar, ulcer, and major lymph node involvement, tested positive for tsutsugamushi disease, as well as those whose family members and they themselves understood and agreed to this study. The exclusion criteria were patients with contraindications, learning disabilities, and other infectious diseases that were treated with quinolones, tetracycline, rifampicin, and macrocyclic visfatin before treatment. In group A, there were 24 male and 16 female patients, age ranging from 18 years old to 69 years old, with an average age of  $40.15 \pm 3.25$ ; the shortest onset time was 2 days and the longest was 14 days, with an average of  $5.60 \pm 0.95$  days; the minimum eschar diameter was 2mm while the maximum was 11mm, with an average of  $5.16 \pm 1.25$  mm; there were 11 cases of conjunctival hyperemia and 29 cases of major local lymph node involvement. In group B, there were 22 male and 18 female patients, age ranging from 19 years old to 68 years old, with an average age of  $41.22 \pm 3.14$ ; the shortest onset time was 2 days while the longest was 15 days, with an average of  $5.10 \pm 0.96$  days; the minimum eschar diameter was 2mm while the maximum was 11mm, with an average of  $5.08 \pm 1.16$  mm; there were 13 cases of conjunctival hyperemia and 27 cases of major local lymph node involvement.

### 2.2. Methods

During the treatment, patients in both group A and B were instructed to have full bed rest; high calorie and high nutrition diet intervention were provided along with the maintenance of water electrolyte balance and acid-base balance.

Patients in group A were treated with moxifloxacin hydrochloride tablets along with the above supportive treatment. They were to take the tablets once a day, 0.4 g each time for 7 days. Meanwhile, patients in group B were treated with doxycycline hydrochloride tablets, 50 mg on the first day, twice a day, and then 100mg to 200 mg once a day along with the same aforementioned supportive treatment.

### 2.3. Observation indicators

- (1) Clinical efficacy. ① Full recovery: Complete resolution of clinical symptoms along with the return of body temperature and leukocyte level to normal values; ② Remarkable effect: Clinical symptoms basically resolved and body temperature as well as leukocyte level tend to be normal; ③ Effective: Resolution of some clinical symptoms, body temperature showing a downward trend, and improvement of leukocyte level; ④ Invalid: Clinical symptoms remained the same without worsening or any resolution, high body temperature, and low leukocyte level. Total effective rate = (full recovery + remarkable effect + effective) / total x 100%.
- (2) Comparison of the time taken for the resolution of clinical symptoms.
- (3) Changes of liver function indexes before and after treatment, which include aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, and platelet count.
- (4) The adverse reactions experienced by the patients in both the groups were compared, including diarrhea, abdominal pain, vomiting, nausea, rash, and other symptoms.

## 2.4. Statistical methods

The clinical data of group A and group B were calculated using Statistical Package for the Social Sciences (SPSS) version 18.0 software. The measurement data were tested with t-test, and the counting data were tested with chi-square ( $\chi^2$ ). If  $p$  value is below 0.05, it indicates that the data difference between group A and group B is statistically significant.

## 3. Results

### 3.1. Comparative analysis of the clinical efficacy between the two groups

The effective rate was 72.5% in group A and 95.0% in group B. Compared with group A, group B was better ( $p < 0.05$ ) (Table 1).

**Table 1.** Comparative analysis of the clinical efficacy between the two groups

Group	Full recovery	Remarkable effect	Effective	Invalid	Total effective rate
A (n = 40)	8 (20.0)	7 (17.5)	14 (35.0)	11 (27.5)	29 (72.5)
B (n = 40)	18 (45.0)	11 (27.5)	9 (22.5)	2 (5.00)	38 (95.0)
$X^2$					7.4397
$p$ value					0.0064

### 3.2. Time taken for the resolution of clinical symptoms between the two groups

The time taken for the resolution of clinical symptoms in group B was significantly better than that in group A ( $p < 0.05$ ) (Table 2).

**Table 2.** Time taken for the resolution of clinical symptoms in both groups

Group	Normal temperature	Relief of headache	Eschar shedding	Liver is functioning normally
A (n = 40)	2.58±0.99	4.67±1.36	6.9±1.34	15.36±3.08
B (n = 40)	2.28±0.94	4.18±1.42	6.51±1.24	12.16±2.03
t	1.390	1.576	1.351	5.486
$p$ value	0.169	0.119	0.181	0.000

### 3.3. Changes of liver function indexes between the two groups before and after treatment

There was no significant difference in the liver function indexes between group A and group B before treatment ( $p > 0.05$ ). However, after the two groups were treated with different drugs, the indexes of liver function in group B were significantly lower than those in group A ( $p < 0.05$ ) (Table 3).

**Table 3.** Changes of liver function indexes in the two groups before and after treatment

Group	ALT		AST		ALP		Total bilirubin	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
A (n = 40)	130.36 ± 48.66	75.99 ± 19.24	179.83 ± 51.22	86.67 ± 14.64	182.15 ± 27.06	137.17 ± 35.43	40.13 ± 10.76	22.32 ± 5.88
B (n = 40)	132.70 ± 57.62	57.62 ± 17.22	176.98 ± 54.37	47.74 ± 10.22	185.26 ± 31.26	108.65 ± 41.36	41.69 ± 11.33	17.67 ± 6.22
t	0.196	4.500	0.241	13.790	0.476	3.312	0.631	3.436
p value	0.845	0.000	0.810	0.000	0.636	0.001	0.530	0.001

### 3.4. Comparative analysis of the incidence of adverse reactions between the two groups

There was one case of rash, one case of diarrhea, one case of vertigo, three cases of vomiting, and two cases of nausea among the patients in group A. The incidence of adverse reactions was 20.0%. There was one case of diarrhea and one case of nausea among patients in group B. The incidence of adverse reactions was 5.0%. The difference was statistically significant ( $p < 0.05$ ,  $\chi^2 = 4.114$ ).

## 4. Discussion

Tsutsugamushi disease is caused by tsutsugamushi bacteria that is usually transmitted during field activities. The release of toxin in the body would lead to inflammatory reactions and organ injuries. If treatment is not given in a timely manner, it may cause serious infection and even threaten the life of patients. The clinical manifestations of tsutsugamushi disease include enlarged lymph nodes, elevated body temperature, eschar, and abnormal liver functions. Anti-infectives are usually used to kill the Oriental body of tsutsugamushi disease and achieve the purpose of treatment [3-5]. Moxifloxacin and doxycycline which can inhibit the synthesis of bacterial protein body along with their bacteriostatic effect are the main drugs used in clinical practice. Moxifloxacin is a fluoroquinolone antibiotic, which has a significant effect in the treatment of mycoplasma, chlamydia, and anaerobic bacteria [6]. However, in the treatment of tsutsugamushi disease, the therapeutic effect of moxifloxacin is still controversial, and doxycycline is known to be better and safer [7-9].

In this study, the effective rate of group A was 72.5% while in group B, the effective rate was 95.0%. Compared with group A, group B was better ( $p < 0.05$ ). The recovery time of clinical symptoms for the patients in group B was significantly better than that in group A ( $p < 0.05$ ). There was no difference in the liver function indexes between group A and group B before treatment ( $p > 0.05$ ); however, after both the groups were treated with different drugs, the indexes of liver function in group B were significantly lower than those in group A ( $p < 0.05$ ). There was a case of rash, a case of diarrhea, a case of vertigo, three cases of vomiting, and two cases of nausea among the patients in group A; the incidence of adverse reactions was 20.0%. There was a case of diarrhea and a case of nausea among the patients in group B; the incidence of adverse reactions was 5.0%. The difference was statistically significant ( $p < 0.05$ ,  $\chi^2 = 4.114$ ).

In conclusion, in the treatment of tsutsugamushi disease, doxycycline has significantly better treatment effect and safety compared to moxifloxacin. In addition, with doxycycline, the recovery time of patients' clinical symptoms is shorter with improved liver functions.

## Disclosure statement

The author declares that there is no conflict of interest.

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