ISSN 2616-5791 Vol. 6, Issue 3: 8-13, DOI: 10.25236/AJMHS.2025.060302

Main problems of clinical use of cefotaxime sodium for injection in China and its countermeasures

Haishi Yu[1,a], Juan Yu[1,b], Jieli Guang[1,c*], Hongxi Li[1,d], Jinrong Bai[1,e], Yujiao Gao[1,f], Ping Chang[1,g], Yan Feng[1,h], Fengyuan Li[1,i]

[1]Yunnan Normal University Hospital, Yunnan Normal University, Kunming, China
[a]yuhaishi@ynnu.edu.cn, [b]1054743236@qq.com, [c]1244423741@qq.com, [d]77149423@qq.com, [e]396638550@qq.com, [f]694055914@qq.com, [g]ping610113@163.com, [h]386942141@qq.com, [i]1980602762@qq.com
**Corresponding author*

Abstract: *This paper provides an in-depth discussion of the major problems in the clinical use of cefotaxime sodium for injection in China. Analysis of the relevant literature reveals that the need for skin testing before the use of cefotaxime sodium is controversial, and that inappropriate dosage and solvent use are the main problems in the current application of this drug in China. In view of these problems, this paper puts forward corresponding countermeasures and suggestions to solve them, including strengthening the training of medical personnel, optimising the dosage regimen, and standardising the choice of solvents. By revealing the main problems of clinical use of cefotaxime sodium for injection in China and exploring the countermeasures and suggestions, this paper will provide research results for optimising and improving China's antimicrobial drug management policy and improving the health of the whole population, thus contributing to the construction of "Healthy China".*

Keywords: *cefotaxime sodium for injection; clinical use; skin test controversy; dosage; solvent choice*

1. Introduction

Cefotaxime Sodium is a third-generation cephalosporin antibiotic widely used for the treatment of respiratory, urinary tract and central nervous system infections due to its broad-spectrum antimicrobial activity and good tissue permeability [1]. It has been clinically used in China for more than 40 years since it was first marketed in Germany in 1980, and as a class A cephalosporin in the *National Drug Catalogue for Basic Medical Insurance, Workers' Compensation Insurance and Maternity Insurance (2024)*, it has a broad antimicrobial spectrum, is stable and safe. However, despite their remarkable efficacy, there are still controversies and irregularities in the clinical use of cephalosporins, mainly in the three aspects of skin test operation, dosage adjustment and solvent selection. The only cefotaxime sodium formulations currently approved in China are powdered injections [2]. In Chinese clinical practice, excessive concern about allergy risk among healthcare professionals has led to misuse of skin tests, which may delay treatment and increase healthcare costs. In addition, optimization of dosing regimens and solvent stability studies based on PK/PD principles have not yet been adequately landed [3]. Therefore, by collating the results of existing studies, this paper summarizes the major problems in the clinical use of cefotaxime sodium for injection in China, and puts forward practical countermeasures and suggestions, with a view to providing valuable information for the rational and safe use of this drug in the clinic, promoting the rational and safe use of cefotaxime sodium, and ultimately improving the therapeutic efficacy and safety of patients.

2. Major Problems of Clinical Use of Cefotaxime Sodium for Injection in China

2.1. The need for a skin test before use is controversial

Although the Pharmacopoeia of the People's Republic of China (2020 Edition) and the Guiding Principles for the Clinical Application of Antimicrobial Drugs (2015 Edition) do not have a clear requirement on the need for cephalosporin antimicrobial drug allergy testing [4], in order to clarify the mechanism of drug allergic reactions and the clinical significance of skin testing, standardize the screening of the history of allergy to β-lactam antimicrobial drugs and the clinical practice of skin testing,

ISSN 2616-5791 Vol. 6, Issue 3: 8-13, DOI: 10.25236/AJMHS.2025.060302

guarantee patient safety and promote the rational application of antibacterial drugs, the National Health and Health Commission organized the Expert Committee on Clinical Application of Antibacterial Drugs and Evaluation of Bacterial Drug Resistance to formulate the Guiding Principles for Skin Tests of Antibacterial Drugs of β-lactam Class (2021 Edition) [5]. The Guiding Principles for Skin Tests of β-lactam Antimicrobial Drugs (2021 Edition) pointed out that the clinical predictive value of routine skin tests for allergic reactions prior to cephalosporin administration is not supported by sufficient evidence-based medical evidence, and that the instructions for most cephalosporin antimicrobial drugs do not require that cephalosporins be routinely subjected to skin tests prior to drug administration. Routine skin testing prior to cephalosporin administration is not recommended and is only required in the following cases. (i) Patients with a clear history of penicillin or cephalosporin type I (fast-acting) allergy. (ii) Where skin testing is specified in the drug insert.

However, a scholarly survey on the implementation of the Guiding Principles for Skin Testing of β-lactam Antimicrobial Drugs (2021 Edition) in some medical institutions in China found that the percentage of medical institutions that cancelled the routine skin testing of cephalosporins after the promulgation of the Guiding Principles for Skin Testing of β-lactam Antimicrobial Drugs (2021 Edition) increased from 17.86% to 58.93%, and 32.14% of medical institutions did not cancel the routine skin testing of cephalosporins [6]. This indicates that medical personnel in China are concerned about β-lactam-induced allergic reactions, and cephalosporins are still widely used in China. The misuse of skin tests is still driven by excessive anxiety about allergic reactions, leading to waste of healthcare resources and delays in patient treatment. There is still resistance to the implementation of this guideline in China. This phenomenon diverges from the international consensus: the American Academy of Allergy, Asthma and Immunology (AAAAI) recommends skin testing only in high-risk populations, whereas several European studies have demonstrated the limited predictive value of routine skin testing [7].

The implementation of β-lactam antimicrobial skin tests in different regions and medical institutions in China still varies widely [8]. Huo et al. analyzed and explored the differential stance of courts in different regions on cephalosporin antibiotic skin tests based on statistical data from judicial decisions [9]. They found that in the absence of conclusive evidence supporting the validity of skin tests for cephalosporin antibiotics, established medical practice and expert opinion could not adequately prove that the failure of a medical institution to perform a skin test constituted negligence. Accordingly, they proposed that the focus should be shifted to the implementation of preventive measures and emergency treatment programmes, rather than focusing solely on whether or not skin tests were performed.

2.2. Inappropriate dosage for the method used

Cefotaxime sodium is a time-dependent antibiotic, and its efficacy is closely related to the time (%T>MIC) at which the blood concentration exceeds the minimum inhibitory concentration (MIC) [3]. According to the basic principle of the Guiding Principles for Clinical Application of Antimicrobial Drugs (2015 version) [10] on the number of times of administration, "To ensure that the drug can exert maximum efficacy in the body and kill the pathogenic bacteria of the infected foci, it should be administered according to the principle of combining pharmacokinetic and pharmacodynamic principles. Penicillins, cephalosporins and other β-lactams, erythromycin, clindamycin and other time-dependent antimicrobials should be administered several times a day. Concentration-dependent antimicrobials such as fluoroquinolones and aminoglycosides may be administered once a day".

The New Pharmacology (18th Edition) [11] on the dosage of cefotaxime sodium reads, "Adults 2- 6 g a day in 2-3 intravenous injections or intravenous drips; for severe infections 2- 3 g every 6- 8 hours, with a maximum dose of not more than 12 g a day. For the treatment of uncomplicated Streptococcus pneumoniae pneumonia or acute urinary tract infections, 1 g every 12 hours. For neonates aged≤ 7 days, 50 mg/kg every 12 hours, and for those born >7 days, 50 mg/kg every 8 hours. The dose may be increased to 75 mg/kg every 6 hours for the treatment of patients with meningitis, all administered intravenously".

At the same time, the drug inserts of cefotaxime sodium of five pharmaceutical companies were randomly reviewed, and the adult dosage was taken as a representative for statistical purposes (Table 1), which shows that there are differences in the dosage of the drug in the drug inserts of different companies.

ISSN 2616-5791 Vol. 6, Issue 3: 8-13, DOI: 10.25236/AJMHS.2025.060302

Table 1: Usage and dosage of cefotaxime sodium in five Chinese pharmaceutical companies based on the drug inserts

serial number	drug name	Dosage	manufacturer (of a product)
1	Cefotaxime sodium for injection	Adults and children over 12 years of age: General infection: 1g once, twice daily, intramuscularly or intravenously. Severe infection: 2 g once, twice daily, intramuscularly or intravenously or intravenously. Severe infections: 2-4g once every 8-12 hours intravenously or intravenously, not to exceed a daily dose of 12g.	Shenzhen Xinlitai Pharmaceutical Co.
2	Cefotaxime sodium for injection	Adults 2-6g a day in 2-3 IV or IV drips; for severe infections 2-3g every 6-8 hours, maximum dose not to exceed 12g a day. For treatment of uncomplicated Streptococcus pneumoniae pneumonia or acute urinary tract infections, 1g every 12 hours.	Shanghai ShangPharma Xinya Pharmaceutical Co.
3	Cefotaxime sodium for injection	Adults 2-6g a day in 2-3 IV or IV drips; for severe infections 2-3g every 6-8 hours, maximum dose not to exceed 12g a day. For treatment of uncomplicated Streptococcus pneumoniae pneumonia or acute urinary tract infections, 1g every 12 hours.	Kunming Jida Pharmaceutical Co.
4	Cefotaxime sodium for injection	Adults and children over 12 years of age: General infection: 1g once, twice daily, intramuscularly or intravenously. Severe infection: 2 g once, twice daily, intramuscularly or intravenously or intravenously. Severe infections: 2-4g once every 8-12 hours intravenously or intravenously, not to exceed a daily dose of 12g.	Ruiyang Pharmaceutical Co.
5	Cefotaxime sodium for injection	Adults and children over 12 years of age: General infection: 1g once, twice daily, intramuscularly or intravenously. Severe infection: 2 g once, twice daily, intramuscularly or intravenously or intravenously. Severe infections: 2-4g once every 8-12 hours intravenously or intravenously, not to exceed a daily dose of 12g.	Beijing Taiyang Pharmaceutical Co.

In the recent literature, the dosage of cefotaxime sodium reported by Liu et al. [12] in "1 case of anaphylactic shock caused by cefotaxime sodium" was "5.0 g of cefotaxime sodium for injection should be added to 250 ml of 0.9% sodium chloride solution in outpatient clinic and given by intravenous drip once/d"; Lv [13] reported in the article "Analysis of two cases of adverse reactions caused by intravenous cefotaxime sodium", the dosage of cefotaxime sodium in the two cases was "0.9% sodium chloride injection 250 ml, cefotaxime sodium for injection 1.0 g× 6 sticks, intravenous injection". China needs to strengthen clinical training on the principles of PK/PD and clarify and standardize the dosage of this drug, and push companies to update their drug inserts based on reasonable dosage.

2.3. Improper use of solvents

As a third-generation cephalosporin antibiotic, the clinical efficacy of cefotaxime sodium is closely related to the choice of solvent medium. Several studies have shown that there are significant differences in the chemical stability of the drug in different solvents, which directly affects its bioavailability and the incidence of adverse reactions. Earlier studies have found that the degradation rate of cefotaxime sodium is significantly faster when glucose injection is used as a solvent medium compared to sodium chloride injection [14]. The β-lactam ring in the molecular structure of cefotaxime sodium is susceptible to hydrolysis in acidic environments, which is the main pathway for its degradation.

In China, Xue et al. monitored 1,671 inpatients using cefotaxime for injection in Shanxi Children's Hospital from September 2015 to April 2016, and 348 cases, or 20.83% of the total number of monitored cases, were solubilized with 10% dextrose injection, 1,322 cases, or 79.11% of the total number of cases, were solubilized with 0.9% sodium chloride injection, and 1 case, or 0.06% of the total number of cases, were solubilized with 5% dextrose The results showed that there were 1 case of adverse effects between different solution groups[15]. The results showed that there was a statistically significant difference in the

ISSN 2616-5791 Vol. 6, Issue 3: 8-13, DOI: 10.25236/AJMHS.2025.060302

incidence of adverse reactions between the different solution groups, and it is recommended that 0.9% sodium chloride injection be used as the solvent if permitted, so as to reduce the degradation products of cefotaxime during the infusion process. This suggests that the potential risks of low-concentration dextrose solvents have been generally avoided in clinical practice. The analysis revealed a common misconception among Chinese primary care physicians: 58.6% of respondents believed that "glucose is more suitable for rehydration in children", without realizing that its acidic environment (pH 3.2-5.5) accelerates drug degradation [16].

3. Main recommendations for countermeasures

Aiming at the main problems existing in the clinical use of cefotaxime sodium, this paper puts forward the following solution countermeasures and suggestions to improve the safety and effectiveness of the drug.

3.1 Strengthening training and education of medical personnel

Strengthening the training and education of medical staff is the key to resolving skin test disputes. Medical institutions should regularly organize medical staff to study the Guiding Principles for Skin Testing of β-lactam Antimicrobial Drugs (2021 Edition) to ensure that they fully understand and follow the latest clinical guidelines. Through training, medical staff should master the recognition and treatment of allergic reactions to cephalosporins and reduce unnecessary skin test operations, thus avoiding patients from missing the best time for treatment. In addition, medical institutions should establish a comprehensive emergency plan for allergic reactions to ensure rapid and effective treatment in the event of an allergic reaction.

3.2 Standardizing and optimizing medication regimens

Standardizing and optimizing the dosing regimen and dose adjustment are important measures to ensure the efficacy of cefotaxime sodium. Strengthening medication monitoring and feedback, medical institutions should establish a monitoring system for the use of antimicrobial drugs, real-time monitoring of the clinical use of cefotaxime sodium. Through prescription review and medication analysis, the irrational use of medication is detected and corrected in a timely manner, forming closed-loop management. Medical personnel should formulate a personalized medication plan according to the specific conditions of the patient, combined with pharmacokinetic and pharmacodynamic principles. For example, for patients with serious infections, medication should be administered in strict accordance with the dosage and frequency recommended by the guidelines to ensure that the drug reaches an effective concentration in the body. At the same time, medical institutions are encouraged to carry out clinical pharmacological studies on cefotaxime sodium, focusing on the impact of different dosing regimens on efficacy and safety. Drug supervision and management authorities should establish a mechanism for dynamic updating of drug instructions, requiring manufacturers to revise the instructions in a timely manner based on the latest clinical research evidence. It is recommended that an expert committee be set up to unify and validate controversial dosages and eliminate discrepancies between different enterprises.

3.3 Standardize the selection and use of solvents

Standardizing solvent selection and use is an effective way to reduce drug degradation and adverse reactions. A solvent selection review system should be established, solvent pH should be included in the pre-prescription review system, and prescriptions for glucose solvents should be mandatorily intercepted (except for cases explicitly permitted by the instructions). In clinical practice, 0.9% sodium chloride injection should be preferred as the solvent for cefotaxime sodium to reduce the degradation of the drug during infusion. Medical institutions should establish clear specifications for the use of solvents and clearly label the recommended solvent type and method of use in the drug insert. Medical personnel should regularly monitor the stability of drugs in solvents to ensure their effectiveness and safety. In addition, intelligent early warning systems can be developed. For example, the real-time infusion monitoring and sensing system is equipped with an infusion alarm device based on sensor technology and intelligent analysis mechanisms. It can automatically identify the specifications of the infusion bag, monitor the remaining liquid volume in real time, and promptly alert users when the infusion is completed. Simultaneously, the relevant information is transmitted via a wireless receiver and an intelligent controller to the nursing station monitoring center and the remote monitoring center, enabling nursing

ISSN 2616-5791 Vol. 6, Issue 3: 8-13, DOI: 10.25236/AJMHS.2025.060302

staff to keep track of the patient's infusion status anytime and anywhere [17].

4. Conclusion

After summarizing and collating the existing literature, it is shown that there are three core problems in the clinical use of cefotaxime sodium for injection in China. Firstly, the misuse of skin test is common, although the Guiding Principles for Skin Tests of β-lactam Antimicrobial Drugs (2021 Edition) clearly opposes the routine skin test, a relatively large number of healthcare institutions have not yet implemented it, which leads to the waste of healthcare resources and delay in treatment. Secondly, the dosage and administration are not standardized. Differences in the instructions of different companies and the neglect of PK/PD principles by medical personnel have led to the frequent administration of single large doses, which reduces the efficacy and increases the risk of drug resistance. Thirdly, improper choice of solvent, and the misuse of dextrose injection (with a low pH) in primary healthcare institutions, which accelerates the degradation of the drug and triggers undesirable reactions such as phlebitis.

To address the above problems, this article suggests that multi-dimensional interventions are needed. First, strengthen the training of medical personnel, popularize the latest skin test guidelines and emergency procedures for allergic reactions, and reduce non-essential skin tests. Second, unify the standardization of medication, promote the dynamic updating of manuals by the pharmacological supervisory department, and formulate an individualized dosing regimen based on the principles of PK/PD, as well as strengthen the monitoring of clinical use of medication. Third, standardize the use of solvents, and block prescriptions for glucose solvents by means of the prescription auditing system; and improve primary pharmacy guidance. Glucose solvent prescriptions, giving priority to 0.9% sodium chloride injection, while improving pharmacological guidance at the grassroots level. These measures will systematically improve the rational use of cefotaxime sodium and help optimize the antimicrobial drug management policy and patient safety.

References

[1] Carmine AA, Brogden RN, Heel RC, Speight TM, Avery GS. Cefotaxime. A review of its antibacterial activity, pharmacological properties and therapeutic use[J]. Drugs. 1983,5(3):223-89.
[2] Wang Yun, Wang Qiang, Li Xianghe, etc. . Quality evaluation of cefotaxime sodium for injection [J] . Chinese Journal of antibiotics, 2023,48(03) : 276-284.
[3] Craig WA. Pharmacokinetic/pharmacodynamic parameters: rationale for antibacterial dosing of mice and men[J]. Clin Infect Dis. 1998 Jan;26(1):1-10; quiz 11-2.
[4] Chen Xiangjun, Zhou Yi, Meng Juan, et al. Standardized management of skin test of cephalosporins in medical institutions [J] . Chinese Journal of antibiotics, 2021,46(12): 1133-1137.
[5] General Office of the National Health Commission. Circular of the General Office of the National Health Commission on the Issuance of Guidelines for Skin Tests of β-lactam Antimicrobial Drugs (2021 Edition). State Health Office Medical Letter [2021] No. 188. 13 April 2021
[6] He Miao, Zhang Haixia, Zhao Xin, etc. Investigation on the implementation of "Skin testing guidelines for β-lactam antibiotics (2021 edition)" in some medical institutions [J] . Chinese Journal of Clinical Pharmacy, 2024,000(1): 5. DOI: 10.19577/J. 1007-4406.2024.01.003.
[7] Torres J M ,Adkinson F N ,Caubet J , et al. Controversies in Drug Allergy: Beta-Lactam Hypersensitivity Testing[J].The Journal of Allergy and Clinical Immunology: In Practice,2019,7(1):40-45.
[8] Yang Linqing, Yang Li, Luo Yanni, etc. . Summary of best evidence from skin trials of β-lactam antibiotics [J]. Journal of Advanced Nursing Education, 2024,39(01): 65-70. DOI: 10.16821/J. CNKI. HSJX.2024.01.012.
[9] Huo Ting, Wang Yue. Exploring the content of duty of care from the case of cephalosporin antibiotic allergy [J]. China Forensic Science, 2022, (02): 88-93.
[10] General Office of the National Health and Family Planning Commission, Office of the State Administration of Traditional Chinese Medicine, Bureau of Drugs and Materials of the Ministry of Health, General Logistics Department of the People's Liberation Army. Notice on the issuance of the Guiding Principles for Clinical Application of Antibacterial Drugs (2015 Edition). State Health Office Medical Development [2015] No. 43. 24th July 2015
[11] Chen Xinqian, JIN Youyu, TANG Guang. New Pharmacology (18th Edition) [M]. Beijing: People's Health Publishing House,2018
[12] Liu Meichun, Ning Yaru, Liu Yingchun. Cefotaxime sodium-induced anaphylaxis: a case report [J].

ISSN 2616-5791 Vol. 6, Issue 3: 8-13, DOI: 10.25236/AJMHS.2025.060302

China Medical Review, 2009,6(10): 163-164.
[13] Lv Wenhan. Analysis of 2 cases of adverse drug reactions induced by intravenous cefotaxime sodium [J] . Chinese community physicians, 2012,28(02): 18.
[14] Zhang Ye, Xu Feng, Wu Weifeng. Study on stability and antibacterial activity of cefotaxime sodium in different injections [J] . Chinese medical journal, 2014,16(06) : 1097-1098.
[15] Xue Zhimin, Wang Hui. Safety analysis of Cefotaxime for injection in pediatrics [J] . Chinese Journal of Pharmacology and clinical medicine, 2021,21(17) : 3027-3029.
[16] Institute of Hospital Management, National Health and Wellness Commission. Report on Quality Management of Antimicrobial Drug Clinical Use (2020) [R]. Beijing: People's Health Publishing House, 2021: 56-59.
[17] Zhu Xiaoping, Gong Meifang, Shi Yan. Practical application of transfusion safety management monitoring network and high-risk early warning system [J] . China Hospital, 2013,17(06) : 14-15.