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ANALYSIS ON 113 CASES OF ADVERSE REACTIONS CAUSED BY B-LACTAM ANTIBIOTICS

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Abstract

The objectives of this study were to learn about the characteristics and rules of the occurrence of adverse reactions caused by lactam antibiotics and provide a reference for clinical drug use. Methods: A retrospective study was made to analyse the 113 case reports of adverse reactions caused by β-lactam antibiotics collected in our hospital between 2007 and 2009. Results: 113 cases of ADR involved 17 kinds of β-lactam antibiotics, headed by ceftriaxone sodium. The most common manifestation was skin and accessory damage; nervous system and gastrointestinal system damage were also easier to find, and the administration route was mainly intravenous infusion. Conclusion: The clinical application of β-lactam antibiotics should pay attention to adverse reaction monitoring and rational drug use to reduce the incidence of adverse reactions.

Key words: adverse drug reactions; β-lactam antibiotics

Introduction

β-lactam antibiotics are antibacterial drugs widely used in clinical, referring to the antibiotics, which molecules contain β-lactam rings, including penicillin, cephalosporin, etc. World Health Organisation survey shows that antibiotic use in China is far higher than the international level (Kong et al., 2010). With continuous marketing of drugs and antibacterial spectrum expansion, the application range is increasingly wider and adverse reactions are also increasing, and they should be concerned (Qin et al., 2009).

Data and methods

113 case reports in our hospital between 2007 and 2009 were collected according to the ADR standards in National Adverse Drug Reaction Monitoring Center to make statistics and analysis on patients' age, gender, clinical manifestations of adverse reactions, administration routes, etc.

Results

Distribution of gender and age

Distribution of gender: 52 males and 61 females, without significant difference; distribution of age is shown in Table 1.

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Table 1: Distribution of age

Age (years old)	N	Proportion (%)
<10	11	9.73
11~20	13	11.50
21~30	9	7.96
31~40	10	8.85
41~50	16	14.16
51~60	22	19.47
>60	32	28.33
Total	113	100.00

It can be seen from the table that as patients' age increases, the incidence of adverse reactions also increases. Elderly patients usually have many diseases: body functions gradually deteriorate, liver and kidney functions decrease, leading to drug accumulation and adverse reactions, and they also have strong sensitivity to drug side effects. So, the incidence of adverse reactions is very high among the elderly. This suggests that the focus should be more on the elderly when monitoring the adverse reactions of drugs.

ADR involving drug varieties and proportions

The 113 case reports involve 17 antibiotics, headed by ceftriaxone sodium, and seconded by penicillin sodium, as shown in Table 2.

Table 2: ADR involving drug varieties and proportions

Drug name	Occurrence frequency	Proportion (%)
Ceftriaxone sodium	32	28.32
Penicillin sodium	15	13.27
Cefotaxime sodium	11	9.73
Cefazolin	7	6.19
Ampicillin sodium	6	5.31
Ampicillin	6	5.31
Ceftazidime	5	4.42
Cefalexin	5	4.42
Amoxicillin	4	3.54
Mezlocillin	4	3.54
Cefoperazone sodium	4	3.54
Cefoperazone sodium + sulbactam sodium	4	3.54
Azlocillin	3	2.65
Oxacillin sodium	3	2.65
Amoxicillin + clavulanic acid	2	1.77
Cefixime	1	0.88
Piperacillin sodium + tazobactam	1	0.88
Total	113	100.00

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Ceftriaxone sodium is a third generation cephalosporin antibacterial drug, which kills bacteria by inhibiting bacterial cell wall synthesis, and has strong effect on Gram-negative bacteria. It is widely used in clinical for the treatment of pneumonia, bronchitis, urinary tract and other infections (Chen et al., 2003). Due to its wide use in clinical, the adverse reactions caused by ceftriaxone sodium gradually increase. Cephalosporins have no immunogenicity and do not cause allergic reactions, but their high polymer impurities are the main allergen. The high polymers degraded from the drugs once introduced into body irreversibly combine with protein, peptides and other macromolecular carriers in body, and cause antigen-antibody reactions, thereby causing allergy (Li, 2011).

Administration routes

In the 113 cases, the adverse reactions are mostly caused by intravenous infusions. Oral administration and intramuscular injection also cause adverse reactions, as shown in Table 3.

Table 3: Classification of drug administration routes

Administration route	N	Proportion (%)
Intravenous infusion	99	87.62
Oral administration	13	11.50
Intramuscular injection	1	0.88
Total	113	100.00

Past allergy history

It is shown in Table 4.

Table 4: Past allergy history

Allergy history	N	Proportion (%)
Yes	24	21.24
No	46	40.71
Unknown	43	38.05
Total	113	100.00

Clinical manifestations of ADR

ADR involves 8 systems in human body, and the most common is skin and accessory damage, followed by cardiovascular system, digestive system, etc. The reason may be that these drugs really cause serious damage to skin and accessory, and the digestive system, or that allergic reactions, gastrointestinal reactions, fever and other symptoms are easy to observe and find, while the damage to blood system and urinary system are usually difficult to find and directly observed. So, the cases of blood and urinary systems are relatively fewer (Zhang et al., 2009). Therefore, in clinical medication, patients should be more keenly and closely observed and minor or small symptoms should not be ignored, as shown in Table 5.

Discussion

It can be seen from the distribution of gender that male is slightly less than female. The distribution of ages shows that the proportion of patients >60 years old is high, probably because liver and kidney functions in the elderly decrease, and

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perhaps because the elderly patients usually suffer from many diseases and need drug combination, thus increasing the risk of adverse reactions. Therefore, special populations should be considered at drug use. Unknown allergy history cannot indicate no allergy history. But medical care staff did not ask and did not pay attention patients' unknown allergy history, apparently increasing the incidence of adverse reactions. Therefore, doctors should ask for patient's allergy history and family allergy history in details, to try to avoid the occurrence of adverse reactions. For administration routes, the incidence of adverse reactions caused by intravenous infusion is high, same as in the related report (Zhao et al., 2004). This development is so,

Table 5: ADR involving systems and clinical manifestations

Involved organ / system	n	Proportion (%)	Clinical manifestations
Skin and accessory	71	62.83	Rash, pruritus, herpes, edema, limb pain, phlebitis
Cardiovascular system	15	13.27	Chest tightness, palpitation, blood pressure decrease, arrhythmia
Digestive system	9	7.96	Nausea, vomiting, diarrhea, abdominal pain, loss of appetite, dry mouth, bloody stool
Respiratory system	6	5.31	Shortness of breath, chest tightness, shortness of breath, difficult breathing, asthma, cough
Nervous system	5	4.42	Dizziness, headache, fatigue, dysphoria, memory loss
Systemic symptoms	4	3.54	Chills, high fever, allergic shock
Urinary system	2	1.77	Frequent urination, urgent urination, hematuria, proteinuria, renal dysfunction
Blood system	1	0.88	White blood cell decrease, bleeding spots

because intravenous infusion directly sends the drug into the blood, so as to enter human body circulation to cause many direct incentives of ADR. Thus, appropriate administration routes should be selected at drug use. Oral administration or intramuscular injection is better than intravenous infusion, and the monitoring of ADR caused by intravenous infusion should be strengthened. The incidence of adverse reactions caused by oral administration is lower than that caused by intravenous infusion, but it is also a kind of systemic administration method, and oral administration is mostly for outpatients and they cannot be monitored at any time. Therefore, doctors should pay more attention to patient's allergy history, tell patients about the possible adverse reactions and ask patients to come to the hospital when any symptom occurs so as to reduce and avoid the occurrence of adverse reactions (Yu et al., 2008).

It can be seen from Table 5 that the types of ADR are mostly skin and accessory damage, with the main symptoms of maculopapule, rash, drug rash, pruritus, etc., belonging to drug allergy. And because they are easy to observe, they are more reported (Yang, 2010). The mechanism is that antibacterial drugs, as exogenous antigens, combine with protein in body to form whole antigens, to make human body produce specific antibodies, so as to cause allergic reactions (Zhu et al., 2010). Secondly, adverse reactions in cardiovascular system mainly manifested as chest tightness, palpitation, arrhythmia and other symptoms. Adverse reactions in digestive tract are also very common, manifested as nausea, vomiting, abdominal pain, diarrhoea, etc. (Sui 2011). Appropriate antibiotics should be selected according to the types of pathogens and the antibacterial spectrum of the drugs. Patients should also select the drugs according to their own conditions, and certainly, dose and administration times should be proper, bearing in mind that overdose may also cause adverse reactions (Huang et al.2010; Wang 2010). Before drug use, doctors should carefully ask for patient's allergy history and make skin test, and after drug use, the doctor should monitor patient's conditions, know the adverse reactions of antibiotics well, rationally use antibiotics, increase clinical treatment effects, and reduce the incidence of adverse reactions.

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References

1. Kong, KF, Schneper L, Mathee, K. (2010). Beta-lactam antibiotics: from antibiosis to resistance and bacteriology. APMS, 118 (1): 1-36.
2. Sui Lingjuan. (2011) Analysis on adverse reactions caused by macrolide antibiotics. Guide of China Medicine. **9(9)**.
3. [Huang Jinmin, Zhou Benhong. (2010) Analysis on antibiotic abuse and preventive measures. Journal of China Traditional Chinese Medicine Information.**2 (16)**: 74-75.
4. Wang Wan. (2010) Investigation and analysis on irrational use of antibiotics in our hospital. China Modern Medicine. **17 (18)**: 141-142.
5. Qin Song, Yu Hao, Sun Xiaoyang. (2009). Analysis on 619 case reports of adverse reactions caused by β-lactam antibiotics. Pharmaceutical and Clinical Research, **17 (6):** 505-508.
6. Chen Xinqian, Jin Youyu, Tang Guang. (2003). New Pharmacology. Edition 15. Beijing: People's Medical Publishing House: 61-62.
7. Li Xiangrong. (2011) Two cases of adverse reactions caused by intravenous infusion of ceftriaxone sodium. Chin J of Clinical Rational Drug Use, **4 (5B)**.
8. Zhang Minhong, Wang Haibao, Pei Meng.(2009). Retrospective analysis on 463 case reports of adverse reactions caused by antibacterial drugs. Strait Pharmaceutical Journal. **21 (4):** 171.
9. Zhao Chunjing, Jiang Chengli, Cao Yali. (2004). Analysis on 133 case reports of adverse reactions caused by β-lactam antibiotics . Adverse Drug Reactions Journal. **6 (4):** 235.
10. Yu Li, Li Yanying, Li Jinbao, Zhao Zhifeng. (2008) Analysis on 348 case reports of adverse reactions caused by β-lactam antibiotics. Evaluation and Analysis of Drug-Use in Hospitals of China. **8(10).**
11. Yang Jurong. (2010) Analysis on 158 cases of adverse reactions caused by β-lactam antibiotics. Modern Medicine and Health. **26(23)**.
12. Zhu Pengxiang, Zhang Qi. (2010) Analysis on 168 case reports of adverse reactions caused by antibacterial drugs in our hospital. China Pharmacy. **21 (46)**.