# Rational analysis of adverse drug reactions cases in Northland of China.

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## Abstract

**Objective: To learn about ADRs of antibacterial drugs in our Hospital and to provide references for rational drug use.**

**Methods: Conduct retrospective studies, classification statistics, analysis and assessment on 469 ADR reports of antibacterial drugs collected between January 2015 and December 2016 in the hospital. Register ADR's names, levels, results, drugs' names, routes of administration, patients' ages, gender, and his/her original disease.**

**Results: 45 kinds of drugs were involved among the 469 ADR reports, with a larger proportion of drugs for children (29.54%); the major route of administration was intravenous (73.26%); lesion of skin and its appendages were main clinical manifestations (61.35%), which was 25.00% of the total number; Levofloxacin and Azithromycin have ADR incident rates.**

**Conclusion: Causes for ADRs of antibacterial drugs are complex, so medical workers should enhance the supervision over the antibacterial drugs, deepen their understanding of ADRs, and take necessary interventions to reduce or avoid the occurrence of ADRs as much as possible.**

## Introduction

Infectious diseases are common clinically and antibacterial drugs play an important part in various infectious diseases since they had the most clinical consumption [1-3]. With increased types of antibacterial drugs of different specifications, the incidence rate of ADR has been increasing up to now [4,5]. This research analysed 469 ADRs reports of antibacterial drugs, serving as references for rational use of antibacterial drugs. Though we have found that many ADRs reports or research had reported their own numbers or characteristics, however, the number of some antibiotics was different and the interaction of the drug and the patient was varied greatly from others, thus we make a report of ADRs in our hospital by utilizing the ADRs data from the incidence department of our hospital.

## Materials and Methods

### General materials

469 ADR reports of antibacterial drugs from those being reported to National Center for ADR Monitoring by our Hospital between January 2015 and December 2016, all of which met the diagnostic criteria for ADRs.

### Methods

Retrospective analysis was conducted by gender, age, kinds of antibacterial drugs, routes of administration, ADR-involved organs or systems, major clinical manifestations, prognosis and alike [6,7]. The classification criteria for antibacterial drugs consult' Clinical Guide to Pharmacopoeia of the People's Republic of China (Chemical Drugs and Biological Products Volume)' as reference. Types of ADR-involved organs or systems are based on WHO Adverse Reaction Terminology. Relevance evaluation of ADR under the criteria which are set by CFDA National Center for ADR Monitoring, China.

### Statistical methods

SPSS 20.0 was used to process the data, and verify the enumeration data with $\chi^2$. The difference showed statistical significance ($P<0.05$).

## Results

### General conditions

Among the 469 ADR cases of antibacterial drugs, there were 231 males (49.3%) and 238 females (50.7%), female patients had higher incident rate of ADRs than male patients did, the difference had statistical significance ($P<0.05$); patients' ages ranged from four months old to 86 y old, and 153 patients were at least 60 y old (32.6%) and the number was more than that of other age groups, the difference had statistical significance ($P<0.05$, Table 1).

## Routes of administration

Among the 469 ADR cases of antibacterial drugs, 312 cases adopted intravenous injection (66.5%), followed by oral dosing, local application, intramuscular injection, subcutaneous injection, and vaginal medication (Table 2).

*Table 1. General characteristic of the enrolled patients.*

| Gender | Ages | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | <10 | 10~19 y | 20~29 | 30~39 | 40~49 | 50~59 | 60~69 | ≥ 70 |
| Male | 51 | 12 | 36 | 17 | 32 | 15 | 37 | 31 |
| Female | 47 | 23 | 38 | 29 | 28 | 36 | 18 | 19 |
| In total | 98 | 35 | 74 | 46 | 60 | 51 | 55 | 50 |

*Table 2. Adverse reactions report by the classification of delivery system.*

| Delivery system | Number of cases | Proportion (%) |
|---|---|---|
| Intravenous | 312 | 66.5 |
| Oral administration | 68 | 14.5 |
| Local application | 32 | 6.8 |
| Intramuscular route | 28 | 6.0 |
| Subcutaneous injection | 18 | 3.8 |
| Vaginal medication | 11 | 2.4 |
| In total | 469 | |

## Types of antibacterial drugs

Among the 469 ADR cases, cephalosporins was the major part, with 152 cases in total (32.4%), followed by 25 kinds, including β-lactams, β-lactamase inhibitors, fluoroquinolones, nitroimidazoles, macrolides, glycopeptides, and Penicillins (Table 3).

## Adverse reactions

For this group of patients, the ADR of antibacterial drugs were clinically manifested by lesion of skin and its appendages as the ADR-involved organs or systems, with 197 cases in total (31.6% Table 4).

*Table 3. Adverse reactions report by the classification of drugs.*

| Classification of drugs | Class | Number of cases | Proportion (%) | Mentioned drugs (cases) |
|---|---|---|---|---|
| Cephalosporins | 8 | 152 | 32.4 | Cefathiamidine (37), ceftezole (31), cefpiramide (25), cefprozi (18), ceftazidime (15), cefminox (14), cefdinir (7), ceftizoxime (5) |
| Other beta lactams and beta lactamase inhibitors | 3 | 131 | 27.9 | cefoperazone/sulbactam (72), piperacillin sodium/tazobactam (37), aztreonam (22) |
| Fluoroquinolones | 3 | 88 | 18.7 | Levofloxacin (45), moxifloxacin (27), ciprofloxacin (16) |
| Nitro ketone | 3 | 42 | 8.9 | Metronidazole (23), tinidazol (11), ornidazole (8) |
| Macrocyclic lipid | 2 | 26 | 5.5 | Azithromycin (14), Roxithromycin (8) Clarithromycin (4) |
| Glycopeptides | 2 | 16 | 3.4 | Vancomycin (9), norvancomycin (7) |
| Penicillins | 3 | 8 | 1.7 | Penicillin (6), Ampicillin (2) |
| Others | 3 | 6 | 1.3 | Imipenem and cilastatin (3), methacycline (2), cilindamycin phosphate (1) |
| In total | 27 | 469 | 100.0 | |

*Table 4. Adverse reactions report by the classification of organs and systems.*

| Organs or systems | Number of cases | Proportion (%) | Clinical manifestations |
|---|---|---|---|
| Skin and accessories | 162 | 27.4 | Rash, urticaria, itching, redness, skin ulcers, flushing |
| Digestive system | 135 | 22.8 | Nausea, vomiting, abdominal distension, abdominal pain, diarrhea, constipation, loss of appetite, abnormal liver function |
| Central and peripheral nervous system | 108 | 18.3 | Dizziness, headache, insomnia, hallucinations, irritability, tinnitus, tremor, numbness, convulsions |
| circulatory system | 72 | 12.2 | Chest tightness, palpitation, phlebitis |

| Respiratory system | 40 | 6.8 | Cough, wheezing, wheezing, dyspnea, laryngeal edema |
| --- | --- | --- | --- |
| Blood and hematopoietic system | 37 | 6.3 | White blood cell count increased or decreased, neutrophil count decreased, platelet count decreased |
| Musculoskeletal system | 18 | 3.0 | Joint swelling, joint pain, low back pain |
| Systemic lesion | 12 | 2.0 | Chills, fever, aches and pains, hair loss |
| urinary system | 7 | 1.2 | Frequent urination, urgency, dysuria, edema, abnormal renal function |
| In total | 591 | 100.0 | |

## *Prognosis*

Drug use was stopped after ADR of the 469 cases of antibacterial drugs occurred. 56 cases (11.9%) were cured within 24 h after supportive treatment; 378 cases (80.6%) were better within 24 h; 5 cases (1.1%) of delayed-type were worsened, and the recovery time was more than 72 h; no death or sequela.

## Discussion

It might explain the female's higher ADR rate of the antibacterial drugs than the male that the physiological characteristics made the difference [8,9]. Since females have larger fat distribution then males, the lipid-soluble drugs are easy to be kept in the body, the female has longer drug half-life than the male under the same drug dose, and the plasma-drug concentration increased [10,11]. And adverse reactions are easy to occur during special periods of the female (such as menstrual period, gestation period, and suckling period) [12]. Besides, as the age grows, old patients have decreased organ functions, lower liver blood flow, weaker activity of liver enzyme, and reduced tissue and organ functions, which influence the drug metabolism [13-15].

Intravenous injection had more ADRs than other routes of administration, which was in light of most of the results of literature reports [16]. With quick working mechanism, intravenous injection is often used to treat infectious diseases, which can explain why clinical intravenous injection is much more popular than other ways when it comes to antibacterial drug administration [17]. Cephalosporins caused the most adverse reactions, followed by β-lactams, β-lactamase inhibitors, fluoroquinolones, nitroimidazoles, macrolides, glycopeptides, and penicillins and so on [18,19].

ADRs of the antibacterials mainly involve skin and its appendages, clinically manifested as maculopapule, urticaria, pruritus, inflammation, skin ulcer, and rubeosis [20,21]. As most antibacterials have antigenicity, they are prone to immunoreactions, while the skin and its appendage can be observed easily, and the manifestations can be clearly stated to the doctor.

## Conclusion

All in all, ADRs of antibacterial drugs are relevant with many factors. The application management on the antibacterials of medical institutes should be strengthened, an efficient ADR monitoring system should be established, more attention should be paid to ADR monitoring, and the administration of clinical antibacterials should be standardized, then ADRs can be effectively controlled and also serve as references for rational clinical administration of drugs.

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