# Antibiotics use and drug resistance analysis of neurology patients' infection

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**Abstract**: Recent studies have shown that nosocomial infection is an important factor affecting the quality and service level of neurology. Based on the characteristics of neurology patients, the application of antibacterial drugs has certain particular characteristic. In this paper, we analyzed the distribution of pathogenic bacteria in neurology patients in 2016-2017 year, and made statistics on the utilization of antibiotics. The results showed that 84 strains of pathogenic bacteria were isolated from the neurology department, including Gram-negative bacteria (44 strains, 52.38%), Gram-positive bacteria (31, 36.9%), and fungi (9, 10.71%). At the same time, as for the use of antibiotics, the drug category is most cephalosporins and the top 5 antiseptic drugs are cephalosporins, beta lactamase inhibitors, quinolones, aminosides and penicillins. The highest DUI (drug utilization index) value was for cefoperazone tazobactam (1.33), followed by ceftriaxone Mino (1.20) and ciprofloxacin (1.18). Clinicians should guide the selection of antimicrobial agents based on the results of etiological examination, and formulate a reasonable treatment plan based on the characteristics of patients, common pathogens and drug resistance.

**Keywords**: Antibiotics, neurology, drug-resistant strains, adverse reactions, cephalosporin.

## INTRODUCTION

The patients receiving neurology treat are mainly patients with cerebral hemorrhage, cerebral infarction, intracranial space occupying lesions, craniocerebral injury and so on, which require internal medical treatment, surgical treatment and intensive care (Balmadrid *et al*., 2015). After acute stroke and craniocerebral injury, most of the patients are in serious condition, requiring long-term hospitalization, or even part of the performance of stress. The patient is a high-risk group of nosocomial infections. Studies have shown that nosocomial infection is an important factor affecting the quality and service level of neurology (Chen *et al*., 2015). Antibiotics refer to antibacterials and antifungal agents, including antibiotics and chemical synthetic drugs, such as sulfonamides, quinolones, nitroimidazole and so on (Inzucchi *et al*., 2015; Hou *et al*., 2015). Based on the characteristics of neurology patients, the application of antibacterial drugs has particular characteristic. When infectious diseases occur, doctors should consider the patient's physical fitness, infection site, common pathogens and drug resistance, consider the pharmacokinetics and adverse reactions of antibiotics, and select antibiotics reasonably (Chen *et al*., 2009).

Patients with cerebral hemorrhage and craniocerebral trauma are treated with craniotomy or focus drainage, which are easy to secondary to central nervous system infection or wound infection (Dai *et al*., 2010). In addition, the infection of other parts of the brain can also be caused by the dissemination of blood in the central nervous system. The incidence of postoperative infection is closely related to surgical cleanliness, such as the incidence of surgical infection is 30% to 80% and cleaning operation is less than 5% (Jean *et al*., 2017). The most common bacteria causing infection after surgery are Gram-positive cocci, with *Staphylococcus aureus* in the first place, followed by *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, Gram-negative bacilli, and mixed infections caused by a variety of bacteria (Cahill *et al*., 2015). Among them, most of the meningitis caused by open craniocerebral trauma or craniotomy are caused by Staphylococcus and Streptococcus and in the Enterobacteriaceae and *Pseudomonas aeruginosa*; closed craniocerebral trauma or craniocerebral fractures and cerebrospinal rhinorrhea, more common with *S. pneumoniae* and *Haemophilus influenzae* infection (Hou *et al*., 2015). Most of the postoperative infections were caused by *Staphylococcus epidermidis* and Enterobacteriaceae. The infection in other parts of the department of neurology is mostly nosocomial infection, the incidence is 5%~8%, which is the forefront of infection in the same period (Inzucchi *et al*., 2015). The neurology intensive care unit (NICU) is a high incidence area of nosocomial infection. The common infection sites include respiratory tract, urinary tract, gastrointestinal tract, skin and blood flow. This article analyzes the prevalence rate of nosocomial infection in neurology department in recent two years, aiming at providing evidence for target monitoring and reducing nosocomial infection rate in neurology department.

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## MATERIALS AND METHODS

***Main materials and reagents***

The data of the prevalence rate of hospital infection in hospital neurology department in 2016-2017 were investigated. Hospitalized patients included patients who were discharged, transferred and died on the day, but did not include the new hospitalized patients on the same day. All patients were approved by ethics committee of our hospital, ethical approval number as 15SDCPHD2 and all patients signed on the informed consent. The hospital infection management staff and the clinical department of hospital infection monitoring doctor team, two people per group are responsible for the investigation of a sick area, according to the current rate of investigation method of hospital patients on the same day to take bedside inquiries, physical examination and access to the medical records of the survey. The questionnaire included general information of patients, nosocomial infection related information, drug sensitivity test and antibacterial drug use. All the investigations were completed on the day and the questionnaire was reunified into the infection management office. Through the audit of the full-time staff, the qualified case data were recorded into the computer summary statistics.

***The diagnostic criteria of nosocomial infection***

According to the diagnostic standard for nosocomial infection issued by China Health Planning Commission in 2001, the diagnosis and determination of hospital infection sites were carried out. All patients in the hospital infection state were counted as hospital infection cases on the day of investigation, including the new cases of nosocomial infection on the day of investigation and the case of hospital infection in the past on the day of investigation patients or parts of the infection has not yet recovered, but does not include the investigation on patients and the site of infection and community-acquired infection patients and infection has been cured in hospital.

***Drug sensitivity test***

Strain in the Department of Neurology, Department of Neurosurgery inpatient clinical isolated bacterial infection bacterial culture. In 2016, 45 strains were isolated from bacteria, 57 strains were isolated in 2016 were continuously isolated and non-repetitive strains. Using the GHF agar diffusion method, according to the standard operation issued by the American clinical laboratory standardization committee, the quality control of the quality control standard strain ATCC25923 *Staphylococcus aureus*, ATCC25922 *Escherichia coli* and ATCC27853 *Pseudomonas aeruginosa* was taken every week.

## STATISTICAL ANALYSIS

The SPSS16.0 statistical software was used to describe and compare the rate of hospital infection, the rate of infection, the proportion of infection sites, the ratio of pathogenic bacteria detection and the application of antibiotics and the count data were tested by the Chi 2 test.

## RESULTS

***Infection rates***

The incidence of nosocomial infection in the Department of Neurology in 2016 was 12.14%, while 7.58% in 2017 (Jean *et al*., 2017). It has a significant decrease in 2017 compared with 2016. The difference was statistically significant ($x2 = 3.174$, $P<0.05$), as shown in table 1.

***Distribution of pathogenic bacteria***

In the Department of Neurology, 874 strains of pathogenic bacteria were isolated in the Department of Neurology, mainly from the sputum and urine specimens, among which 44 were Gram-negative bacteria, 52.38% were gram-negative, 31 were Gram-positive and 10.71% were fungi and 4 strains of *Acinetobacter baumannii* sensitive only to polymyxin, as shown in table 2.

***Distribution of nosocomial infection sites***

The main infection sites were respiratory infection and urinary tract infection, of which lower respiratory tract infection accounted for 51.35%, upper respiratory tract infection accounted for 32.43%, urinary tract infection accounted for 16.21%. The incidence of infection was slightly different in each year, as shown in table 3. The application rate of neurology antibiotics was controlled in 26%-35%, two years of neurology department. There was no significant difference in the application rate of antibiotics. The application of antibacterial drugs is mainly therapeutic drugs and a combination of drugs, as shown in table 4. The resistance rates of main bacteria to commonly used antimicrobials are compared with those shown in table 5.

***Utilization of antibacterial drugs***

The antibiotics for inpatients were administered intravenously and orally, totally 10 kinds of 18 kinds of antibiotics. The number of antibiotics used was (10.2±6.4) days, the longest 27 days and the shortest 2 days. Cephalosporins are the most antibacterials, and the top 5 antibiotics are cephalosporins, β-lactamase inhibitors, quinolones, aminosides, penicillins. The highest DUI value was cefoperazone tazobactam (1.33), followed by ceftriaxone (1.20) and ciprofloxacin (1.18). The antiseptic drugs with DUI value less than 1 were cefpimo (0.86), levofloxacin (0.97), ceftriazone (0.95), gentamicin (0.98), cefuroxime (0.94), vancomycin (0.87), azithromycin (0.67), as shown in table 6.

## DISCUSSION

Drug use evaluation (DUE) is one of the important branches of drug epidemiology and also one of the

**Table 1**: Nosocomial infection rate in neurology department

| Year | Investigation cases | Infection cases | Infection rate |
|---|---|---|---|
| 2016 | 2800 | 341 | 12.14% |
| 2017 | 2800 | 225 | 7.85% |

**Table 2**: Distribution and constituent ratio of pathogenic bacteria

| Pathogenic bacteria | 2016 | | 2017 | | Total | |
|---|---|---|---|---|---|---|
| | Plants | Constituent ratio | Plants | Constituent ratio | Plants | Constituent ratio |
| Gram-negative bacteria | 253 | | 195 | | 459 | |
| *Escherichia coli* | 112 | 44.0% | 81 | 42.10% | 193 | 43.18% |
| *Pseudomonas aeruginosa* | 67 | 24.0% | 72 | 36.84% | 139 | 29.54% |
| *Acinetobacter baumannii* | 52 | 20.0% | 20 | 10.52% | 72 | 15.90% |
| *Enterobacter cloacae* | 15 | 4.0% | 0 | 0% | 15 | 2.27% |
| *Klebsiella pneumoniae* | 20 | 8.0% | 20 | 10.52% | 40 | 9.09% |
| Gram-positive bacteria | 180 | | 135 | | 322 | |
| *Staphylococcus aureus* | 51 | 27.78% | 62 | 46.15% | 113 | 35.48% |
| *Coagulase negative Staphylococcus* | 73 | 38.89% | 41 | 30.76% | 114 | 35.48% |
| *Acinetobacter Baumanii* | 32 | 16.66% | 20 | 15.38% | 52 | 16.12% |
| *Hemolytic Staphylococcus* | 21 | 11.11% | 12 | 7.69% | 33 | 9.67% |
| *Enterococcus faecalis* | 10 | 5.55% | 0 | 0 | 10 | 3.22% |
| Fungus | 51 | | 42 | | 93 | |
| *Candida albicans* | 41 | 80.0% | 30 | 75.0% | 71 | 77.8% |
| *Candida glabrata* | 10 | 20.0% | 12 | 25.0% | 22 | 22.8% |

**Table 3**: Distribution and constituent ratio of infection sites

| Infection site | 2016 | | 2017 | | Total | |
|---|---|---|---|---|---|---|
| | Cases | Constituent ratio | Cases | Constituent ratio | Cases | Constituent ratio |
| Upper respiratory tract | 71 | 38.88% | 52 | 26.31% | 125 | 32.43% |
| Lower respiratory tract | 92 | 50.0% | 101 | 52.63% | 191 | 51.35% |
| Urinary tract | 20 | 11.11% | 43 | 21.05% | 64 | 16.21% |

**Table 4**: Antibiotic use rate

| Year | Investigation cases | Cases of drug use | Usage rate | Combined use of drugs | | |
|---|---|---|---|---|---|---|
| | | | | Single drug | Two combined drugs | Triple drug use |
| 2016 | 2800 | 741 | 26.42 | 461 | 162 | 128 |
| 2017 | 2800 | 962 | 34.28 | 525 | 214 | 233 |

important contents of clinical pharmacy (Kargulewicz *et al*., 2016). The qualitative research on the evaluation of drug use mainly focuses on the rationality of the clinical medication (Dindo *et al*., 2004). The proportion of the elderly in the inpatients of neurology is very high and the patient's age is high. Lower and often accompanied by disturbance of consciousness, patients have a high probability of nosocomial infection, especially lower respiratory tract infection (Ghoneum *et al*., 2015). The results of this study suggest that the DUI value of antibiotics in hospitalized patients is relatively concentrated, but there is still room for improvement in rational application (Gunaldi *et al*., 2015). The central nervous system often involves the lower respiratory tract infection in neurology patients. The reason may be: The patient's gas exchange is involved, resulting in insufficient oxygen supply to the brain (Hou *et al*., 2015). Lower respiratory tract infection increases the body temperature, increases metabolism and increases oxygen consumption. The cerebral anoxia is aggravated, Nervous system disease and lower respiratory tract infection form a vicious circle, which aggravates the patient's condition. The Gram-negative bacteria in the lower respiratory tract of the inpatients in the neurology department were mainly *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and Escherichia coli and Gram-positive bacteria were mainly *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Streptococcus pneumonia* (Larsen *et al*., 2013). The results of this study suggest that cephalosporins are the most effective antibiotics, and the first 3 categories of antibiotics are cephalosporins, beta lactamase inhibitors and quinolones, which suggest that the selection of drug categories is basically reasonable (Liu *et al*., 2013). In the process of application, the more reasonable antibiotics are ciprofloxacin, amoxicin, vancomycin, zinoxime, cefuroxime, cefotaxime and cefoperazone - sulbactam,

**Table 5**: Antibiotic resistance rate

| Antibiotic | *Escherichia coli* (n=193) | | *Pseudomonas aeruginosa* (n=130) | | *Staphylococcus aureus* (n=113) | | Coagulase negative staphylococcus (n=114) | |
|---|---|---|---|---|---|---|---|---|
| | Cases | Rate (%) | Cases | Rate (%) | Cases | Rate (%) | Cases | Rate (%) |
| Vancomycin | 51 | 26.31 | 31 | 23.07 | 20 | 18.18 | 22 | 18.18181818 |
| Oxacillin | 23 | 10.52 | 42 | 30.76 | 32 | 27.27 | 14 | 9.09 |
| Tetracycline | 10 | 5.26 | 20 | 15.38 | 20 | 18.18 | 14 | 9.09 |
| Gentamicin | 21 | 10.52 | 0 | 0 | 14 | 9.09 | 22 | 18.18 |
| Teicoplanin | 45 | 21.058 | 20 | 15.38 | 32 | 27.27 | 14 | 9.09 |
| Clindamycin | 12 | 5.26 | 0 | 0 | 0 | 0 | 14 | 9.09 |
| Ciprofloxacin | 12 | 5.26 | 12 | 5.26 | 11 | 9.09 | 14 | 9.09 |

**Table 6**: Antibiotics utilization parameters in hospitalized patients

| Antibiotic name | Category | Patients | Defined daily dose (DDD) | Time of drug use (d) | Dosage (g) | Frequency of drug use (DDDs) | Drug utilization index (DUI) |
|---|---|---|---|---|---|---|---|
| Cefepine | IV generation cephalosporins | 714 | 4.00 | 9828 | 34125 | 8531.25 | 0.86 |
| Ceftazidime | III generation cephalosporins | 638 | 4.00 | 7014 | 32084 | 8021 | 1.14 |
| Cephalosporin | Cephamicins | 546 | 2.00 | 6218 | 15017 | 7508.5 | 1.20 |
| Cefazolin | III generation cephalosporins | 430 | 4.00 | 5305 | 23408 | 5852 | 1.10 |
| Levofloxacin | Quinolones | 389 | 0.60 | 4579 | 2670 | 4450 | 0.97 |
| Clozo | I generation cephalosporins | 364 | 6.00 | 4231 | 24126 | 4021 | 0.95 |
| Ceftaetan | Cephamicins | 317 | 4.00 | 3547 | 15107 | 3776.75 | 1.06 |
| Gentamicin | Aminosides | 291 | 0.50 | 3508 | 1727 | 3454 | 0.98 |
| Cefuroxime | I generation cephalosporins | 275 | 3.00 | 3370 | 9534 | 3178 | 0.94 |
| Ampicillin-salbactam | Compound β-lactam compatibility | 213 | 3.00 | 2518 | 8817 | 2939 | 1.16 |
| Cefoxitin | Cephamicins | 184 | 6.00 | 2204 | 15032 | 2505.33 | 1.13 |
| Cefoperazone - tazobactam | III generation cephalosporins | 152 | 6.00 | 1852 | 14821 | 2470.16 | 1.33 |
| Ciprofloxacin | Quinolones | 106 | 0.50 | 1694 | 1345 | 2690 | 1.18 |
| Vancomycin | Glycopeptide | 71 | 2.00 | 859 | 1502 | 751 | 0.87 |
| Azithromycin | Macrolide | 48 | 0.50 | 542 | 184 | 368 | 0.67 |
| Picacillin | Penicillin | 35 | 14.00 | 431 | 6142 | 357 | 0.89 |
| Ceftazine | I generation cephalosporins | 27 | 3.00 | 282 | 847 | 281 | 1.02 |
| Linezolid | Oxazole | 18 | 1.50 | 257 | 273 | 252 | 1.13 |

ceftathan, cefoperazone tazobactam and cefoperazone, head and cefoperazotaxime and cefoperazotaxime, head and cefoperazotaxime ceftazidime and ceftriaxone. The antiseptic drugs that may have insufficient dose and lack of treatment are cefprine, rifampicin, Amikacin, cefuroxime, and takacillin clavulanic acid (Lu, 2014; Okuyama *et al*., 2015). The excessive use of antimicrobial agents can cause side effects and increase the probability of adverse reactions, and the use of antibiotics is easy to increase the production of resistant strains and reduce the efficacy of antimicrobial agents.

In the survey, 1 patient received 27 days of piperacillin sodium and Sulbactam Sodium for respiratory tract infections. The use of antibiotics was too long. When doctors choose antibiotics, they generally do not choose the appropriate antibiotics according to the antimicrobial spectrum, but tend to choose broad-spectrum antibiotics and new special drugs, such as the tongue bite caused by epileptic seizures and the use of ceftazen to prevent infection (Muraki *et al*., 1985). According to the grading table of antibiotics, cefotaxime is a limiting drug, and it is unreasonable to prevent infection. In addition, the neurology department of our hospital generally used the second, third generation cephalosporins for general infections, and the starting point of drug selection was too high. Some doctors ignore the bacteria culture before drug use and choose antibiotics instead of antibiotics according

to the results of drug sensitivity test (Souich *et al*., 2013). When the effect of anti-infection treatment is not good, other antibiotics are replaced, which cause frequent replacement of drugs. In addition, the lack of medicine in the sick area pharmacy is also one of the reasons for frequent clinical change. Frequent dressing change during anti infection therapy will not only affect the therapeutic effect, but also make the bacteria resistant to some extent.

The prevalence rate of nosocomial infection in the Department of neurology was controlled in 7.85%-12.14% for two years. The infection rate in hospital decreased significantly in 2017. It may be related to the severity of the disease, the time of hospitalization, resistance and so on (Szewczyk *et al*., 2015). The hospital has set up a special laminar ICU for the treatment of severe neurology patients and strengthened the hand hygiene equipment. The configuration and management of hand hygiene compliance have certain effects (Yoshio *et al*., 2013). The main area of nosocomial infection in the neurology department is respiratory infection and urinary tract infection, of which the lower respiratory tract infection accounts for 50%. The open airway, the use of ventilator assisted respiration and the dehydration of mannitol in the neurology department may lead to the dry mucous membrane of the patients and the sticky sputum not easy to cough, and make the infection spread to the lungs. 11.11% of the tract infection is because the patients in the neurology department have body movement or sensory dysfunction, as well as different degrees of deity dysfunction, which require long-term bed rest and indwelling catheterization (Tang *et al*., 2014). It is reported that 65% to 70% of the catheter related blood flow infection and urethral infection can be prevented through the current infection prevention strategy. Therefore, it is important to actively implement the guidelines for the prevention and control of urinary tract infection related to urinary tract infection issued by the National Health Planning Commission, which is important to reduce hospital infection. The most common bacteria causing infection after surgery are gram-positive cocci, with Staphylococcus aureus in the first place, followed by *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, gram-negative *bacilli*, and mixed infections caused by a variety of bacteria (Zhu *et al*., 2015). Among them, most of the meningitis caused by open craniocerebral trauma or craniotomy are caused by Staphylococcus and Streptococcus, and also in the Enterobacteriaceae and *Pseudomonas aeruginosa*; closed craniocerebral trauma or craniocerebral fractures and cerebrospinal rhinorrhea, more common with *Streptococcus pneumoniae* and *H. influenzae* infection; Most of the postoperative infections were caused by *Staphylococcus epidermidis* and Enterobacteriaceae (Shim *et al*., 2010). Overall, fungal infection cases have poor curative effect and high mortality. More than 70% of the patients with fungal infection are opportunistic infections of immunodeficiency, such as human immunodeficiency virus (HIV) infection, hematopoietic stem cell transplantation, lymphoma, granulocytic deficiency, congenital immune deficiency and immunosuppressant application (Rosenthal *et al*., 2015). The most common pathogenic fungi are *Aspergillus*, *mucormycosis* and *Cryptococcus*, among which, *Aspergillus* infection mainly occurs in the patients with granulocytic deficiency, and the infection of Trichoderma is mostly in those with low immune function and abnormal metabolic function, such as diabetic ketoacidosis, iron overload, malnutrition and so on. The new *Cryptococcus* is the most common HIV infection. The pathogenic Gram-negative bacteria accounted for about 70%. The isolation rate of Gram-positive bacteria was slightly higher than that of fungi, and most of them were multidrug-resistant bacteria, most of them were multidrug resistant bacteria (Schneider *et al*., 2011). The selection of antibacterials in neurology should not only consider the results of antimicrobial spectrum and drug sensitivity test, but also the selection of antibiotics to treat the infection of the central nervous system according to the capacity of the cerebrospinal fluid barrier (CSF) through blood (Xuan, 2015). According to the ability of antibacterials to penetrate cerebrospinal fluid barrier, they can be divided into 3 groups: (1) drugs that can pass through the normal blood and cerebrospinal fluid barrier, such as chloramphenicol, sulfadiazine, metronidazole, compound sulfamethazol, isoniazid, rifampicin, ethambutol, pyrazinamide, fluconazole and 5 - fluorine cytosine; (2) in large doses, it can be partially permeable by blood and cerebrospinal fluid barriers or drugs that can pass through the inflammatory meninges, such as penicillin, cephalosporins, fosfomycin, carbapenems, fluoroquinolones, vancomycin, voriconazole; (3) there are aminoglycosides, macrolides, tetracycline, polymyxin, clindamycin and amphotericin B which are not able to penetrate the cerebrospinal fluid barrier.

## CONCLUSION

This study provides reference for clinicians to provide empirical treatment. Meanwhile, it suggests that clinicians should guide the selection of antimicrobial agents based on the results of etiological examination. The excessive use of antimicrobial agents can cause side effects and increase the probability of adverse reactions, and the use of antibiotics is easy to increase the production of resistant strains and reduce the efficacy of antimicrobial agents. The patients in neurology department were mainly opportunistic pathogens. Respiratory tract infection is the main infection site and is highly susceptible to nosocomial infection. The application of antibiotics in the neurology department has many characteristics. The clinicians should synthesize the patient's age, the characteristic of infectious diseases, the common pathogenic bacteria and drug resistance, the concentration

of the drug to the local tissue, the basic disease, the liver and kidney function, the result of the pathogenic bacteria culture and the drug sensitivity test, to make a reasonable, effective treatment plan.

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