

Evaluation of the drug effect and rational use of antiseptic drugs in outpatient and emergency department of hospital

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Abstract: With the popularization and application of antiseptic drugs, the abuse of antiseptic drugs and various unreasonable applications have also become a serious medical problem. The prescriptions of antibiotics in our hospital were randomly selected for statistical analysis. Further, we analyzed the various situations of the use of antibiotics in outpatient department, and calculated the DDDs of different drugs based on the defined daily dose (DDD). The results showed that there were 403 unreasonable prescriptions, accounting for 24.9% of the drug prescriptions. The main problems of irrational prescriptions were unsuitable drugs, non indications and improper frequency of administration, which accounted for 27.1%, 21.3% and 18.3%. It is suggested that the quality department of the hospital should strengthen the special training for rational use of antimicrobial agents, intervene in time and effectively, and gradually change post evaluation into prevention and intervention in advance.

Keywords: Antiseptic drugs, cephalosporin, drug-resistant strain, define daily dose.

INTRODUCTION

Antibacterial drugs are one of the most widely used drugs (Amin *et al.*, 2017). In recent years, with the continuous development and utilization of new varieties and forms, the use of antibiotics is becoming more and more widely used in clinics and its irrational use is also rising (Danir *et al.*, 2017). The consequences of irrational use, such as the increase of adverse reactions, the growth of drug resistant strains and the abuse of antibiotics caused by nosocomial infection, have brought many adverse effects to the patients and even the safety of life is threatened (Hu, 2013; Ji *et al.*, 2015). Since the isolation of penicillin by Alexander Fleming in the laboratory in 1928, the use of antibiotics has been used to effectively prevent and cure all kinds of bacterial infections and effectively reduce the mortality of severe bacterial infections (Cahill *et al.*, 2015; Bergmann *et al.*, 2016). At the same time, it also raised the climax of the development and wide application of antibacterial drugs, making the most important and most widely used drug in the hospital (Livia *et al.*, 2015; Jubie *et al.*, 2012). The high cost of antibiotics is a difficult problem in the current patients, hospitals, pharmaceutical companies and pharmaceutical enterprises, which restricts the further improvement of medical and health status in China (Cormier *et al.*, 2012). Rational use of antibiotics can reduce patient's medical burden, reduce adverse drug reactions and effectively cure bacterial infectious diseases.

With the popularization of antibacterial drugs and the increasing familiarity of ordinary people to such drugs,

the abuse of antibiotics and various irrational applications have also become a serious medical and social problem (Bartzatt *et al.*, 2010; Altorki *et al.*, 2016). China is a big country in the application of antibiotics. In the top 10 drugs in the hospital, the antibacterial drugs generally occupy the 2~6 position (Chen *et al.*, 2009; Karen *et al.*, 2017). Because of various kinds and different characteristics of antibiotics, the health departments and hospitals have weak guidance and supervision on rational drug use. The role of clinical pharmacists in rational drug use has not been paid much attention; also there are many problems in the application of clinical antibacterial drugs (Fardeau *et al.*, 2014). The irrational application of drugs is quite common, which leads to the growth of various bacteria resistance and drug origin disease (Ghoneum *et al.*, 2015). With the increasing number of diseases and the increased cost of treatment, the utilization of medical resources is not reasonable (Dindo *et al.*, 2004). At the same time, the adverse drug reactions and other hazards caused by the abuse of antibiotics have also been exposed more and more, which is recognized and valued by all walks of life. In recent years, the incidence and mortality of infectious diseases in China are no longer significantly reduced and the resistance of pathogenic bacteria is more and more strong. More and more refractory infections are coming. Clinically, many severe infections are mostly caused by drug-resistant bacteria and antibiotic treatment.

MATERIALS AND METHODS

According to the sampling method of clinical application monitoring network of the Ministry of health, through the

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HIS system (hospital information management system), the outpatient prescriptions of our hospital on the 25th of each month were extracted. The data was collected in 2016, 400 pieces were extracted each month randomly, of which there were 4800 prescriptions, including 2089 prescriptions for antibiotics. The relevant information contained in the prescription of antiseptic drugs was counted. Evaluation criteria for the application of antiseptic drugs in outpatients see table 1.

We first screened out the prescriptions containing antibacterial drugs, counted the total number of prescriptions, and analyzed the selection of antibiotics, the usage and dosage, the course of treatment, the combination of drugs and the classification management, and found out the irrational drug use and analyzed it. Further, we analyze the situation of all kinds of outpatient antimicrobial drug use, and defined daily dose (DDD) as the standard to calculate DDDs. The DDD value of the drug is determined by the recommended daily dose recommended by WHO(World Health Organization), referring to the Ministry of health's clinical application monitoring network drug dictionary and DDD value. The total amount of DDDs= drug sales / the DDD value of the drug, the addition of different specifications of the same drug to the DDDs, is the total DDDs of the drug. The greater the value of the drug shows, the more the use times and the higher the frequency of use; the DDDc reflects the overall price level of the drug, indicating the use of the average daily cost of the drug, which directly indicates the use of the patient. The higher the average cost of the drug, the higher the cost of the drug and the heavier the economic burden of the patient.

STATISTICAL ANALYSIS

SPSS19.0 software was used to analyze the data. Measurement data were expressed as $\bar{x} \pm s$, were compared with paired t test, comparison between groups using independent sample t test; count data in%, using a test. The difference was statistically significant in $P < 0.05$.

RESULTS

Basic situation of prescription statistics and review

In the 4800 statistics, 2089 prescriptions have used antibiotics, and the proportion of the prescription was 43.6%. It was obviously higher than the standard of not more than 40% of the prescription of the emergency antibiotics required by the Ministry of health. Through the special comment on 2089 prescriptions for the use of antibiotics, the total number of irrational prescriptions totaled 403, accounting for 24.9% of the total prescriptions for antimicrobial agents. The main problems of irrational prescriptions were unsuitable drugs, non indications and improper frequency of administration,

which accounted for 27.1%, 21.3% and 18.3% of the irrational prescriptions. For details, see table 2.

Investigation of combined use of antibiotics

73.7% of them were single drugs, including cephalosporins, fluoroquinolones and macrolides, and cephalosporins were the first, accounting for 28.7%. The details were table 3, table 4.

Antiseptic drugs using the first 10 sites of frequency

The results showed that the top 10 antibiotics in the emergency department ranked first in Cefodizime Sodium for Injection, and injection accounted for 7. For details, see table 5. Among them, the lowest DDDc was Cefprozil Capsules, as 15.414. And the highest of DDDc is Azithromycin Lactobionate for Injection, as 22.013. The oral dosage form of DDDc is far lower than the DDDc of injection type antibiotics, and the consumption of injection type antibiotics is more than that of the outpatient antibiotics.

DISCUSSION

There are many reasons for the high use of antibacterial drugs (Li *et al.*, 2013). The main reasons are as follows: first, the clinicians' idea of rational use of antibiotics is not strong, and some symptoms such as fever, minor skin trauma, and the upper respiratory tract infection caused by the virus are used as antibiotics (Liu *et al.*, 2013). Second, there is fewer bacteria culture and drug sensitivity tests in the outpatient clinic, mainly by experience, a considerable number of doctors are afraid of patients' infection and are too much to prevent drug use, such as the habit of applying antibiotics to patients with viral diseases (Nguyen *et al.*, 2011). The misuse of antiseptic drugs for unexplained fever covers the symptoms and causes the disease, and a mild skin injury can achieve the purpose of controlling the infection by aseptic treatment, but it is also given to antibiotics (Patel *et al.*, 2009; Purkayastha *et al.*, 2015). Some obvious viral infections, such as hand foot mouth disease and chickenpox, are all given antimicrobial treatment (Patel *et al.*, 2010; Lu, 2014). The irrational use of these antibiotics will not only affect the effect of treatment, increase the economic burden of the patients, but also cause serious adverse reactions, resulting in the production of resistant strains (Qin *et al.*, 2015).

The combination of antibacterials should have a clear indication. The infection that can be effectively treated by a single drug does not require a combination of drugs (Tsiaras *et al.*, 2016). Unnecessary combination of drugs will not only waste medical resources, but also increase the risk of adverse drug reactions (Sultana *et al.*, 2011). such as: 1) the clinical diagnosis of urinary tract infection, the prescription antibacterial drugs for aztreonam for injection 2 g, once a day, intravenous drip; Levofloxacin lactate and sodium chloride injection 0.3 g, once a day,

Table 1: Evaluation criteria for application of antimicrobial agents

Index	Reasonable	Unreasonable
Indications of drug use	has	none
Time of drug use	≤ 7days	> 7days
Combined use of drugs	none	has
Usage rate	≤ 20%	>20%

Table 2: The type of irrational prescription of antibiotics

Category	Prescriptions	Composition/%
Unsuitable drug use	109	27.1
Non indication drug use	86	21.3
Improper frequency of administration	74	18.3
Unsuitable dosage	51	12.6
The selected drugs are not suitable	45	11.2
Drug dosage forms and drug delivery are unsuitable	38	9.4
Total	403	100

Table 3: Combined application of antimicrobial agents

Drug use	Prescription of antiseptic drugs (n=2089)		Proportion of total prescription (%)
	Prescription	Ratio (%)	
Single drug	1540	73.7	32.1
Two-drugs	446	21.3	9.2
Three-drugs or more	103	4.9	2.1
General prescription	2089	100	43.5

Table 4: The use of various kinds of antibiotics

Category	Times of drug use	Proportion (%)	sort
Cephalosporins	759	28.7	1
Fluoroquinolone	421	15.9	2
Macrolide	305	11.5	3
Cephamicins	288	10.9	4
Nitromidazoles	240	9.1	5
Lincomycin	236	8.9	6
Penicillins	204	7.7	7
Other	185	7.0	8
Total	2638		

Table 5: Top 10 frequency of use for antiseptic drugs

S. No.	Drug name	Frequency	DDD/g	DDDs	DDDc
1	cefodizime sodium for injection	701	2.50	2314.5	28.452
2	Cefprozil capsules	958	1.30	2514.6	15.414
3	Cefixime dispersible tablets	646	0.50	450.2	29.547
4	Levofloxacin lactate and sodium cholride injection	594	0.60	480.5	32.124
5	Aztreonam for injection	464	3.60	506.5	29.246
6	Etimicin sulfate and sodium chloride injection	423	0.20	465.3	30.891
7	Cefmetazole sodium for injection	304	3.80	354.2	24.354
8	Cefprozil dispersible tablets	213	1.10	387.3	18.642
9	Azithromycin latobionate for injection	256	0.50	180.5	22.013
10	Ceftizoxime sodium for injection	242	4.00	132.1	34.264

intravenous drip. Levofloxacin is a fluoroquinolone, which has the characteristics of broad antibacterial spectrum and strong antibacterial effect. It is used for respiratory infection and urinary tract infection caused by sensitive bacteria, and aztreonam for Injection can also be used in urinary tract infection and lower respiratory tract infection caused by sensitive Gram-negative bacteria. 2) for patients diagnosed with upper respiratory tract infection or pharyngitis, using cefodizime sodium for injection 2g, two times a day, intravenous drip; levofloxacin lactate and sodium chloride injection 0.3 g, once a day, intravenous drip, this prescription is not suitable for combination, drug selection and drug delivery.

Non indication drug use means give antibiotics to those who lack the evidence of bacterial and pathogenic microorganism infection and virus infection (Xuan, 2015). In the special review of the prescription of the antibacterials, it was found that the proportion of the prescriptions of non indications in the emergency department of our hospital accounted for 21.3% of all the irrational prescriptions, mainly in the clinical diagnosis of upper respiratory tract infection and acute gastroenteritis. Such as: 1) the clinical diagnosis is upper respiratory tract infection, giving cefodizime sodium for Injection 2 g, two times daily, intravenous drip. More than 90% of the upper respiratory tract infection is caused by the virus infection. The initial treatment is mainly with rest, symptomatic and antiviral treatment. It is not suitable for the use of antibacterials, except for the use of antibiotics in the case of bacterial infection. 2) clinical diagnosis of diarrhea, given aztreonam for Injection 2 g, once a day, intravenous drip; etimicin sulfate injection 0.15 g, once a day, intravenous drip. According to the guiding principles of clinical application of antibacterial drugs, the diarrhea caused by virus or bacterial toxin is generally not required. The treatment can be made by supplementing liquids and electrolytes in a timely manner. Even for bacterial infectious diarrhea, we should follow the principle of light oral medication and heavy intravenous administration, without bacterial treatment. Under the condition of unclear indication of bacterial infection, it is obviously unreasonable to choose etimicin sulfate injection combined with aztreonam for injection (Zhu *et al.*, 2015).

The results showed that irrational prescriptions accounted for 32.30% due to inadequate or large dose of single dose or inappropriate frequency of administration. Such as: 1) the clinical diagnosis of pulmonary infection, the prescription drug is piperacillin sodium and tazobactam Sodium for injection 3.375g, once a day, intravenous drip, the typical frequency of drug delivery is not reasonable. The half-life of piperacillin sodium and tazobactam sodium for injection's plasma is 0.7 ~ 1.2 hour, so the adult is recommended for 3.375g, once a day, intravenous drip, and 1 times a day in the above prescription not only can not maintain the effective bactericidal concentration,

but also easily lead to the production of bacterial resistance. 2) The clinical diagnosis of bronchitis was given to cefodizime sodium for injection 3.0g, once a day, intravenous drip and cefodizime sodium for injection as a time dependent antibacterials. The antibacterial effect is closely related to the contact time with the bacteria, but the relationship with the peak concentration is small. The prescription does not consider the pharmacokinetic characteristics of the drug itself (Zhang *et al.*, 2015). By adding a single dose, the one day dosage form can not only reach the expected antibacterial effect, but also increases the probability of the adverse drug reaction.

CONCLUSION

In this paper, the use of antibiotics in hospitals was studied. The results showed that cephalosporins were the most frequently used antibiotics. This is mainly because the cephalosporins have the advantages of broad antibacterial spectrum, strong antibacterial effect, less allergic reaction and suitable price, which are very popular with the clinicians and are similar to other medical institutions. Among them, cefodizime sodium for Injection ranks the first in the frequency of use and it is widely used for upper respiratory tract infection and single dose. Most of the pathogenic bacteria of upper respiratory tract infection are mainly gram-positive bacteria. One or two generation cephalosporins can cover the bacterial spectrum and achieve effective treatment. The first three generation cephalosporin cefodizime sodium for injection is first used for upper respiratory tract infection, with high starting point, unsuitable selection and excessive use of drug use. Levofloxacin lactate and sodium chloride injection, aztreonam for injection and etimicin sulfate and sodium chloride Injection are also in the forefront of the use of the Department, in the prescription review found that the above 3 kinds of drugs are often combined with the upper respiratory tract infection, trauma, diarrhea and so on, and there is an excessive use of the tendency. Rational use of antibiotics is a key indicator of rational drug use in hospitals, and also an important part of medical quality. The efficacy of antibacterial agents depends not only on the biological activity of antibacterial agents, but also on the indications and dosing regimens.

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REFERENCES

Amin O and Patricia N (2017). Review: Antimicrobial efficacy validation using in vitro and in vivo testing methods. *Adva. Dru. Deli. Revi.*, **112**: 61-68.

- Altorki N, Takiguchi S and Mori M (2016). An analysis of the extension system of drug patents in the United States the Enlightenment of Hatch-Waxman act on China's pharmaceutical industry. *Chi. Med. Ind.*, **2**(4): 215-224.
- Bartzatt R, Cirillo S and Cirillo J (2010). Design of ciprofloxacin derivatives that inhibit growth of methicillin resistant *Staphylococcus aureus* (MRSA) and methicillin susceptible *Staphylococcus aureus* (MSSA). *Med. Chem.*, **6**(2): 51-56.
- Bergmann A, Thuler LC, Moore MA and Nam BH (2016). The protection of test and other data required by article 39.3 of the TRIPS agreement. *Northwestern J. Int. Law Business*, **2**(4): 203-214.
- Cormier R, Burda W, Harrington L, Edlinger J and Kodigepalli K (2012). Studies on the antimicrobial properties of N-acylated ciprofloxacin. *Bioorg. Med. Chem. Lett.*, **22**(2): 6513-6520.
- Cahill G, Tran L, Huang YC and Ou CW (2015). Research on TRIPS protocol data protection of traditional Chinese Medicine. *Bus. Res.*, **1**(1): 27-38.
- Ceylan S, Bayrak H, Ozdemir S and Uygun Y (2016). Microwave-assisted and conventional synthesis of novel antimicrobial 1,2,4-triazole derivatives containing nalidixic acid skeleton. *Heterocycl. Commun.*, **22**(2): 229-237.
- Chen J, Liu S, Pan J, Zheng X, Zhu K, Zhu J, Xiao J and Ying M (2009). The relationship between patent protection and administrative protection. *Com. Engg.*, **36**(3): 80-486.
- Danir F and Jennifer A (2017). Beyond conventional antibiotics - New directions for combination products to combat biofilm. *Adva. Dru. Deli. Revi.*, **112**: 48-60.
- Dindo D, Demartines N and Clavien PA (2004). Marketing strategy and mode selection of pharmaceutical enterprises. *Disc. Modern Eco.*, **240**(2): 205-213.
- Fardeau S, Dassonville-Klimpt A, Audic N and Sasaki A (2014). Synthesis and antibacterial activity of catecholate-ciprofloxacin conjugates. *Bioorg. Med. Chem.*, **22**(2): 4049-4060.
- Ghoneum M, Felo N, Nwaogu OM, Fayanju IY, Jeffe JA and Margenthaler DB (2015). A comparative study of Chinese and Japanese innovative drug monitoring system. *Chin. J. New Drugs*, **1**(2): 73-82.
- Hu J (2013). The patent protection of medical law and its reference to China. *Chi. Phar.*, **6**: 25-30.
- Jubie S and Kalirajan R (2012). Design, synthesis and docking studies of a novel ciprofloxacin analogue as an antimicrobial agent. *EJ. Chem.*, **9**(2): 980-987.
- Ji C, Miller P and Miller M (2015). Syntheses and antibacterial activity of N-Acyated ciprofloxacin derivatives based on the trimethyl lock. *ACS Med. Chem. Lett.*, **6**: 707-710.
- Karen S, Candace R, Adam M and Michael J (2017). Anti-thrombotic technologies for medical devices. *Advan. Drug Deli. Rev.*, **112**: 2-11.
- Livia SR, Leonardo SB, Lys AB, André L and Marcia R (2015). Protease and phospholipase activities of *Candidasp.* isolated from cutaneous candidiasis. *Revi. Ibero. de Mic.*, **32**(2): 122-125.
- Li F, Zhang Y and Plattner J (2013). Synthesis and antibacterial evaluation of a novel tricyclic oxaborole-fused fluoroquinolone. *Bioorg. Med. Chem. Lett.*, **23**: 963-966.
- Liu G and Guo S (2013). Practice and experience of hospital drug supply chain optimization. *Chi. Drug App. and Mon.*, **4**: 15-16.
- Lu G (2014). Dose characteristics can have a limiting effect on pharmaceutical use claims. *J. Phar. Pra.*, **3**: 79-84.
- Nguyen S, Ding X and Butler M (2011). Preparation and antibacterial evaluation of decarboxylated fluoroquinolones. *Bioorg. Med. Chem. Lett.*, **21** (1): 5961-5963.
- Purkayastha N, Capone S and Beck A (2015). Antibacterial activity of enrofloxacin and ciprofloxacin derivatives of β -octaarginine. *Chem. Biodivers.*, **12**(5): 179-193.
- Patel N and Patel S (2009). Synthesis and antimicrobial studies of some 4-Thiazolidinone containing Fluoroquinolones analogous. *Der. Pharma. Chem.*, **9**(1): 199-209.
- Patel N and Patel S (2010). Synthesis and antimicrobial study of fluoroquinolone based 4-thiazolidinones. *Med. Chem. Res.*, **19**(2): 757-770.
- Qin T and Hou Y (2015). Drug supply chain information flow and its application. *Pharm. Deve.*, **2**: 13-16.
- Sultana N, Arayne M, Rizvi S and Haroon U (2011). Synthesis, characterization and biological evaluations of ciprofloxacin carboxamide analogues. *Bull. Kor. Chem. Soc.*, **32**(2): 483-488.
- Tsiaras N, Nishi T and Takahashi T (2016). Legitimacy of patent compulsory license. *Asian Pac. J. Surg. Oncol.*, **2**(4): 225-236.
- Xuan Z (2015). Study of optimal control of drug stock in hospital. *Chi. Phar.*, **1**: 59-66.
- Zhang L, Kumar K and Rasheed S (2015). Design, synthesis, antibacterial evaluation of novel azolythioether quinolones as MRSA DNA intercalators. *Med. Chem. Comm.*, **6**(2): 1303-1310.
- Zhu Y and Chen W (2015). Global public health crisis, international protection of intellectual property rights and the Doha declaration of WTO. *Medi. Wor.*, **20**(6): 1585-1591.