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Original Article

An analysis of the rational application and characteristics of antibiotics in a pediatric outpatient department

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Abstract: Objective: To study the rational application and characteristics of antibiotics in pediatric outpatient departments. Methods: Information on the antimicrobial drug use in a pediatric outpatient department was retrieved from the information system through a retrospective study, and the information included the total number of prescriptions and total usage amounts among the pediatric outpatients, the number of antimicrobial prescriptions and the usage amount, the types of antimicrobial drugs, and the number of antimicrobial drugs used. Then we calculated the defined daily doses (DDDs), the defined daily cost (DDC), and the annual average rate of growth (AARG) of the antimicrobial drug prescriptions among the pediatric outpatients in the past three years. Results: From 2016 to 2018, the total number of prescriptions written for the pediatric outpatients showed an increasing trend, while the number of prescriptions for antibiotics and the proportion of antibiotics used decreased. In the past three years, children aged 1-5 years had the highest utilization rate. The total drug consumption of the pediatric outpatients showed an increasing trend, while the proportion of the total amount of antibacterial drug use showed a decreasing trend, among which the proportion of oral antibacterial drug use showed an increasing trend, and the proportion of injection drug use showed a decreasing trend. The top three antibacterial drugs used were third-generation cephalosporin, second-generation cephalosporin, and macrolides, among which the macrolides showed an increasing trend in their proportion of use, with a statistical difference ($P<0.001$). The antibiotic with the highest DDC value from 2016 to 2018 was latamoxef for injection, and the top three antibiotics ranked by DDDs among pediatric outpatients were all classified into macrolides and third-generation cephalosporins. The top antibiotic ranked by DDDs was cefixime particles for three consecutive years. The antibiotic with the highest DDC value from 2016 to 2018 was latamoxef for injection. In addition, the top five antibacterial drugs in the past three years were oral dosage forms. Conclusions: The utilization rate and usage amount of antibacterial drugs in the pediatric outpatient department of the Maternal and Child Health Hospital of Jiujiang City showed a declining trend, and the use of antibacterial drugs was basically reasonable. However, it is still necessary to control the use of antimicrobial agents, reduce the irrational use of drugs, and strengthen the monitoring of antimicrobial agents to reduce the occurrence of drug-resistant strains.

Keywords: Pediatric outpatients, antibacterial drugs, application and characteristics, rational use of drugs

Introduction

Due to children's underdeveloped immune systems and their weak resistance to exogenous pathogens, they are susceptible objects, and cross-infection occurs easily in them, which has an adverse impact on their prognoses [1]. Respiratory tract infections are the most common infectious disease in children [2]. Studies have reported that more than 1.5 million children under 14 years old suffer from acute respiratory tract infections every year in developing countries, and it is an important cause of death for children under 5 years old [3]. Although the prevalence of acute respiratory infections varies from season to season [4], antibiotics are the most commonly used drugs in pediatric outpatient clinics [5]. Antibacterial drugs are double-edged swords: on one hand, they have anti-infective effects, but on the other hand, the irrational use of them or drug abuse leads to an increase in the proportion of

multi-drug resistance [6]. The emergence of multi-drug resistance will increase the severity of diseases and increases the mortality rate, while it also increases the economic burdens of families and society [7]. The abuse of antibiotics is particularly serious in China [8]. Due to the unreasonable use of antibacterial drugs, the proportion of drug-resistant bacteria continues to rise [9, 10]. Studies have shown that antimicrobial resistance may cause the deaths of approximately 300 million people between 2014 and 2050 if we don't control antimicrobial abuse [11]. Regulating the management of antibacterial drugs can significantly reduce the number of prescriptions of antibacterial injections, and the total number of prescriptions for pediatric outpatients can be reduced to 12.01%, which is lower than the World Health Organization's standard for injectable use in developing countries, which is 13.4% to 20.1% [12]. Controlling antibacterial drugs can effectively reduce their irrational use, which is of important clinical significance. This study analyzed the application and characteristics of antibacterial drugs in the Pediatrics Department at the Maternal and Child Health Hospital of Jiujiang City, and provided a scientific basis for guiding the rational application of antibiotics moving forward.

Materials and methods

Methods

This study was approved by the ethics committee of the Maternal and Child Health Hospital of Jiujiang City. We used the retrospective study method to review the use of antimicrobial drugs recorded in the information system in the pediatric outpatient department of the Maternal and Child Health Hospital of Jiujiang City from 2016 to 2018, which included the total number of prescriptions and the total usage amount among the pediatric outpatients, the number of antimicrobial prescriptions written and the usage amounts, the types of antimicrobial drugs and the number of antimicrobial drugs used. Then we calculated the defined daily doses (DDDs). DDDs are calculated by dividing the limited daily dose of the drug (DDD) by the total annual use of a drug (g), where DDD is calculated as the average daily dose set for adults with the main indications of treatment, and for minors as the average daily dose of adults. Defined daily cost (DDC) is calculated as dividing the DDDs by the annual consumption amount of the drug. The annual average rate of growth (AARG) is calculated as follows: AARG = [(end year expense or dosage)/(start year expense or dosage)$^{(1/(\text{end year - start year}))}$-1] × 100%. The above indicators refer to the monitoring indicators in the guiding principles for the clinical applications of antibacterial drugs.

Statistical methods

All analyses were performed using SPSS 25.0. The continuous variables were expressed as ($\bar{x}$ ± S), and a one-way analysis of variance was used when it conformed to the normal distribution and homogeneity of variance, otherwise homogeneity of variance was used. The counting data were expressed as a percentage (%) and analyzed using Pearson chi-square tests and the Fisher exact probability method. $P< 0.05$ was considered statistically significant.

Results

The use of antimicrobial agents in the pediatric outpatient department showed a declining trend

From 2016 to 2018, the total number of prescriptions for pediatric outpatients showed an increasing trend, and the number of prescriptions for antibiotics and the proportion of antibiotics used decreased (**Table 1**).

The use of antimicrobial drugs at different ages

The utilization rate of children aged 1-5 years was higher than it was in the other age groups during the 3 years, as shown in **Table 2**.

Comparison of the total expenditures on antibacterial drugs in the pediatric outpatient department

From 2016 to 2018, the total expenditures of the pediatric outpatient department showed an increasing trend, and the proportion of the total expenditure of antibacterial drugs showed a decreasing trend, among which the proportion of oral antibacterial drugs showed an increasing trend, while injection drugs showed a downward trend, as shown in **Table 3** and **Figure 1**.

Table 1. Comparison of antibiotic use in the pediatric outpatient department

Project	2016	2017	2018	AARG (%)
Total number of prescriptions for pediatric outpatients (10,000)	10.78	11.21	12.79	8.92
Number of prescriptions of antimicrobial drug used in the pediatric outpatient department (10,000)	2.34	2.12	2.02	-7.09
Proportion of the antimicrobial prescriptions to the total number of prescriptions (%)	21.71	18.91	15.79	-14.72

Table 2. Use of antimicrobial drugs at different ages

Proportion of antimicrobial drugs used in different age groups (%)	2016	2017	2018	AARG (%)
<1 (month)	0.08	0.07	0.06	-13.40
1-12 (month)	9.12	10.21	9.65	2.86
1-5 (year)	57.81*	54.12*	55.23*	-2.26
5-10 (year)	20.12	19.19	18.98	-2.87
10-14 (year)	12.81	16.34	16.03	11.86
≥14 (year)	0.06	0.07	0.05	-8.71

Note: compared with the other groups, *P<0.05.

Table 3. Comparison of the total expenditure of antibacterial drugs in pediatric outpatient departments

Project	2016	2017	2018	AARG (%)
Total amount of consumption in pediatric outpatient departments (ten thousand yuan)	862.21	914.22	1165.65	16.27
Consumption of antibiotics in pediatric outpatient departments (ten thousand yuan)	132.65	103.65	114.22	-7.21
The proportion of oral antibacterial drugs (%)	68.23	74.28	77.18	6.36
The proportion of antibacterial drugs for injection (%)	31.77	25.72	22.82	-15.25
The proportion of the amount of antibiotics used in the total amount (%)	15.38	11.34	9.80	-20.18

Note: AARG, annual average rate of growth.

Distribution ratio of the antibacterial drugs used

Of all the types of antibacterial drugs used from 2016 to 2018, the top three were the third-generation cephalosporins, the second-generation cephalosporins, and the macrolides. Among them, the proportion of macrolides showed an increasing trend, with a statistically significant difference (P<0.001), as shown in **Table 4**.

Comparisons of DDDs and DDCs in the top ten drugs among the pediatric outpatients

From 2016 to 2018, the top three antibiotics ranked by DDDs among pediatric outpatients were all classified into macrolides and third-generation cephalosporins. The top one antibiotic ranked by DDDs was cefixime particles in the three consecutive years. The antibiotic with highest DDC value from 2016 to 2018 was latamoxef for injection. The top five antimicrobial agents used in the three years were all the oral dosage forms, as shown in **Table 5**.

Discussion

Because the immune function of children has not been fully established and the body's defense against foreign bacteria is poor, the incidences of infection in children aged 1 to 10 years are the highest [13, 14]. Most of these are preschool children, and the high incidence of infection may be related to cross-infection and influenza epidemics in schools [15]. The present study found that the use of antibiotics was highest at the ages of 1-5 years and 5-10 years, and the usage rate was 57.81% and 20.12%, respectively. The usage rate of antibiotics indicated that the incidence of infection was highest in these two age groups, which was consistent with the above studies. Antibacterial drugs have a positive effect on infectious diseases, but antibacterial drugs are mainly for bacterial infections. For those with viral infections, although they have similar symptoms to bacterial infections, the use of antibiotics is ineffective [16, 17]. Studies have shown that the use of antimicrobial agents in

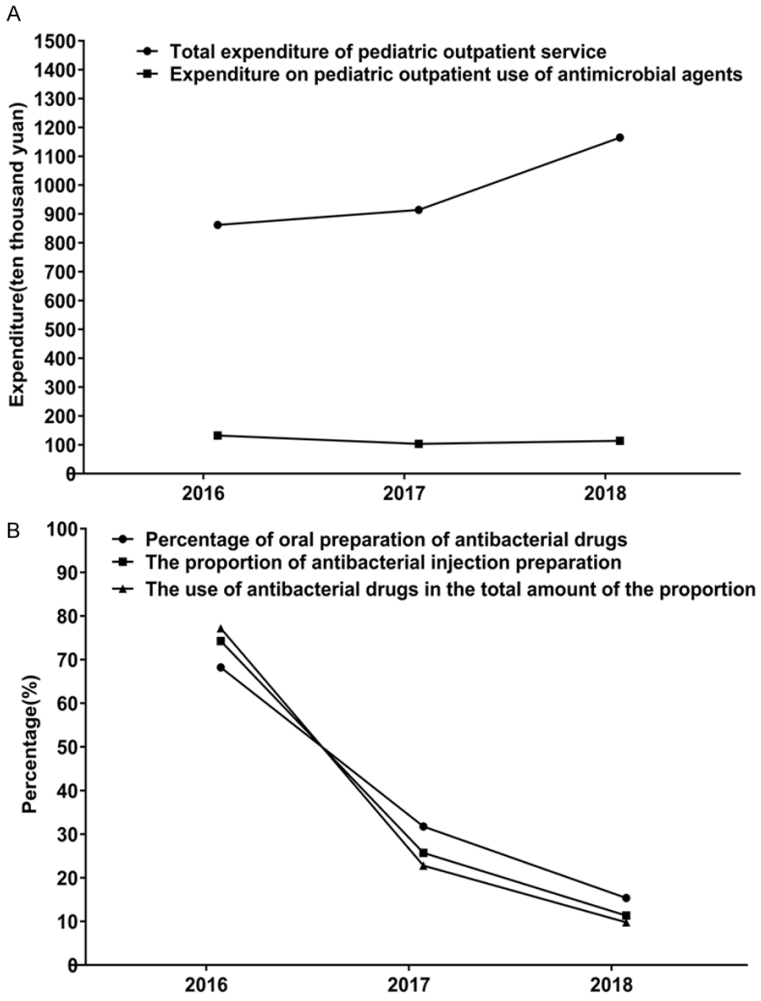

Figure 1. Comparisons of the amounts of antimicrobial agents used in the pediatric outpatient department. A. The trend of total drug costs and total antibacterial costs in the pediatric outpatient department from 2016 to 2018; B. The percentage trend of the amount of oral antibacterial drugs, the amount of injection antibacterial drugs, and the amount of antibiotics used as a proportion of the total amount.

many countries is unreasonable and abusive, especially in China [18-21]. The abuse of antibiotics has led to an increase in the incidence of multi-drug resistance [6], so the control of antibiotics is urgent. In 2015, China published *Guiding Principles for the Clinical Application of Antimicrobial Drugs* and the *National Guidelines for Antimicrobial Therapy* (Second Edition) to guide the use of antibacterial drugs [16]. We actively implemented the use of antibacterial drugs according to the requirements of the guidelines. This managed to reduce the irrational use of antibiotics and the proportion of expenditures of antibiotics in the three years from 2016 to 2018.

In 2016, China's investigation into the rational use of all antimicrobial drugs in pediatrics found that the top three were azithromycin, ceftriaxone, and amoxicillin potassium clavulanate [22]. Among them, azithromycin is a macrolide, ceftriaxone is a third-generation cephalosporin, and amoxicillin-clavulanate potassium is a compound preparation containing a penicillinase inhibitor. In this study, the top three antimicrobial agents in our hospital were third-generation cephalosporins, second-generation cephalosporins, and macrolides. The top three most frequently used antibacterial drugs in 2018 were azithromycin dry suspension, cyclic erythromycin tablets, and cefixime granules, which were basically consistent with the use of antimicrobial agents investigated in 2016.

Respiratory infections are most common in children, and mycoplasma pneumoniae is the most common pathogen. Antimicrobial agents for the treatment of mycoplasma pneumoniae include tetracycline, aminoglycosides, quinolones, and macrolides. Due to the particularity of children, the first three kinds of drugs often have side effects when used in children, so macrolides become the first choice for the treatment of respiratory tract infections caused by mycoplasma pneumoniae, and the DDDs and DDC of macrolides are relatively low [23, 24]. However, some studies have found that drug-resistant strains of mycoplasma pneumoniae have been reported in various countries due to the increased use of macrolides [10, 25, 26]. The incidence of macrolide-resistant strains of mycoplasma pneumoniae in China from 2008 to 2012 also increased from 68.9% to 90.0% [27]. Studies have shown that mycoplasma pneumoniae resistance to macrolides is also on the rise in other countries [28-

Table 4. Distribution ratio of the antibacterial drugs used

Project	2016	2017	2018	χ^2	P
The total number of prescriptions	23400	21200	20200		
First generation cephalosporin (%)	737 (3.15)	653 (3.08)	642 (3.18)	0.350	0.839
Second generation cephalosporin (%)	6346 (27.12)	5620 (26.51)	5350 (26.49)	2.958	0.228
Third generation cephalosporin (%)	11441 (48.89)	10332 (48.74)	9736 (48.20)	2.252	0.342
Macrolides (%)	4453 (19.03)	4232 (19.96)	4165 (20.62)	19.561	<0.001*
Penicillin (%)	105 (0.45)	87 (0.41)	74 (0.37)	1.800	0.407*
Linkamide (%)	96 (0.41)	81 (0.38)	72 (0.36)	0.824	0.662
Nitroimidazole (%)	70 (0.30)	66 (0.31)	61 (0.30)	0.058	0.971
Antifungal agents (%)	152 (0.65)	129 (0.61)	100 (0.50)	4.656	0.097

Note: *P<0.05.

Table 5. Comparisons of the DDDs and DDCs in the top ten drugs among pediatric outpatients

Year and Name of drug	DDDs	DDD (g)	Annual use of drug (g)	Annual consumption amount (ten thousand yuan)	DDC (yuan)
2016					
Cefixime granules	3256.11	0.10	3256.11	97.22	40.23
Azithromycin dry suspension	24166.04	0.10	24166.04	26.11	8.02
Cefdinir dispersible tablets	18698.08	0.30	5609.424	107.14	57.30
Azithromycin syrup	15808.08	0.50	7904.04	12.52	7.92
Cyclic ester erythromycin tablets	12838.41	0.30	3851.523	27.41	21.35
Cefaclor dry suspension	11697.97	0.75	8773.4775	14.95	12.78
Cyclic ester erythromycin dry suspension	10848.69	0.50	5424.345	38.86	35.82
Azithromycin lactate for Injection	5580.86	0.50	2790.43	49.24	88.23
Cefuroxime ester	1002.23	0.50	2004.46	0.59	5.82
Lavocef for injection	781.24	2.00	1562.48	49.54	634.12
2017					
Cefixime granules	27456.36	0.10	27456.36	73.85	40.21
Azithromycin dry suspension	1836.595	0.10	1836.595	22.02	8.02
Cefdinir dispersible tablets	17622.46	0.30	5286.738	93.54	53.08
Cyclic ester erythromycin tablets	15407.66	0.30	4622.298	31.37	20.36
Cyclic ester erythromycin dry suspension	13257.24	0.50	6628.620	47.62	35.92
Azithromycin syrup	9133.76	0.50	4566.880	7.17	7.85
Cefaclor dry suspension	5812.69	0.75	4359.518	7.51	12.92
Azithromycin lactate for injection	3452.60	0.50	1726.300	30.01	86.92
Lavocef for injection	1306.54	2.00	2613.080	39.46	302.02
Cefuroxime ester	635.74	0.50	317.870	0.37	5.82
2018					
Cefixime granules	33665.84	0.10	33665.84	81.86	40.14
Azithromycin dry suspension	31827.84	0.10	31827.84	27.00	8.02
Cyclic ester erythromycin tablets	2039.362	0.30	6108.086	89.85	28.23
Cefdinir dispersible tablets	18819.18	0.30	5645.754	99.29	52.76
Cyclic ester erythromycin dry suspension	17691.86	0.50	8845.930	61.78	34.92
Azithromycin Lactate for injection	5760.30	0.50	2880.150	52.58	91.28
Cefaclor dry suspension	4901.32	0.75	3675.990	5.96	12.16
Lavocef for injection	1046.04	2.00	2092.08	31.83	304.30
Azithromycin syrup	501.28	0.50	250.640	0.39	7.78
Cefuroxime ester	281.69	0.50	140.845	0.16	5.68

30], and azithromycin resistance rate is the highest among macrolides [31]. In our hospital, the usage rate of erythromycin tablets was increased while macrolide was controlled, which

could reduce the incidence of drug resistance. For children with mycoplasma pneumoniae who are ineffective in macrolides and have a severe condition, many countries have reported the successful use of tetracyclines or quinolones, and no significant adverse reactions have been found. Based on this study, we have strengthened the use of tetracycline or quinolones to reduce the utilization rate of macrolide and thus reduce the occurrence of drug resistance.

The use of antibacterial drugs in our hospital during the 3-year period was characterized by the high utilization rates of second-generation cephalosporin and the third-generation cephalosporin. Among the single drug, cefdinil and cefixime ranked in the top three in the 3-year period, and they both belong to the third-generation cephalosporin. Because of the their wide antibacterial spectrum, their strong effect, low toxicity, and low incidence of allergies, the second and third generation cephalosporins are suitable for all ages, but the higher DDDs and DDCs of cephalosporin increase the economic burden [13]. In view of this situation, we plan to strengthen the use of alternative cephalosporins (such as penicillin, tetracycline or aminoglycoside) in the next step. In 2015, the guiding principles for the clinical application of antimicrobial agents recommended the use of penicillin for children infected with antibiotics. A study from abroad found that the highest use rate of penicillin was found in pediatric outpatient departments in developing countries [32]. The usage rate of penicillin was relatively low in our outpatient department, which might be related to the limited use of penicillin due to the need for skin tests. Therefore, further management should be strengthened to increase the usage rate of penicillin. And we did not use aminoglycoside antibiotics in the pediatric clinic, which might be related to the long-term nephrotoxicity, ototoxicity, and neuromuscular side effects of aminoglycoside antibiotics. Although the drugs are narrow-spectrum antibiotics, they can be used safely if the blood concentration monitoring is done well. In the selection of antimicrobial agents in pediatric department, the oral dosage forms were mainly used by us, whose DDC were lower than the costs of injection dosage, indicating that we did not blindly use high-grade antimicrobial agents in our use of antimicrobial agents. In response to the above problems, these corrective measures are proposed: the application of antibacterial drugs may lead to the emergence of drug-resistant bacteria. Therefore, in order to promote a more rational application of antibacterial drugs in pediatrics, the following corrective measures are proposed. First, we should establish a multi-disciplinary team (MDT) to manage the use of antimicrobials. The MDT consists of the infection department, the medical department, and the clinical pharmacy room and laboratory. Experts from other hospitals are invited to participate in the MDT regularly. Second, key training in the use of antibiotics for children should be given to the pediatric medical staff. For the frequent use of the third-generation cephalosporins, the clinicians should raise attention. If the results of the bacterial culture and drug susceptibility test are not known, we should predict possible pathogens based on the infection site, infection degree, underlying disease, previous history of antimicrobial use, and treatment response, and select effective narrow-spectrum antibiotics preferentially. After the results of bacterial culture and drug sensitivity test are clear, the antimicrobial agents should be selected reasonably to avoid the blind and high starting point use of the drugs. Third, we should increase the strength of the pharmacist's prescription review and do well in "four checks and ten pairs." Finally, the annual "World Health Organization antimicrobial resistance week" should be used to implement educational activities. We can publicize the rational application of antimicrobial drugs by pasting posters in our hospitals, making full use of the media, inviting experts and government officials to conduct interviews and discussions, and engaging with the community.

This study has some limitations. On one hand, this study was a retrospective study and the patients were outpatient infected children. Because the outpatient electronic medical record system had not been established, it was impossible to judge the severity of the disease, the necessity of using antibacterial drugs, and the relevant auxiliary examination based on the medical records such as symptoms and signs. On the other hand, the detection of pathogens was weak in outpatients, so we should strengthen the management of pathogen detection in outpatients and reduce the number of cases treated with antibiotics due to the viral infections by targeted medication. It can be im-

proved by taking the following measures: First, control mode such as PDCA management mode, and MDT mode should be further used to strengthen the control of antibacterial drugs and improve the quality of antibacterial drugs; second, we should improve the electronic medical record system, an improvement which will be more beneficial for the rational use of antibacterial drugs.

In summary, the use rate and usage amount of antibiotics in pediatric outpatient clinics in the Maternal and Child Health Hospital of Jiujiang City have a downward trend and the application is basically reasonable. However, it is still necessary to control the use of antimicrobial agents, reduce the irrational use of drugs and strengthen the monitoring of antimicrobial agents, which is helpful in reducing the occurrence of drug-resistant strains.

Disclosure of conflict of interest

None.

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