

The drug use to treat community-acquired pneumonia in children

A cross-sectional study in China

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Abstract

To evaluate the rationality of drug use to treat community-acquired pneumonia (CAP) in children of a Chinese hospital using a set of developed indicators.

We performed a retrospective cross-sectional study in West China Second University Hospital. Hospitalized children (0–18 years old) diagnosed with CAP from October 2015 to January 2016 were included. A set of developed indicators for assessing rational drug use (RDU) to treat CAP in children were used to evaluate the rationality of drug use. The data of the indicators were compared with the recommendations of the available guidelines, analyzing the situation of drug use in the children diagnosed with CAP.

Eight hundred ninety-four children were included, 99.4% of them received antibiotics and 87.4% received more than 1 antibiotic. Antibiotics were administered intravenously in 880 (99.0%) children. About 20 (2.2%) children received antiviral agents and 19 (2.1%) children received antiviral drugs combined with antibiotics. About 208 (23.3%) children received traditional Chinese medicines and the injection of traditional Chinese medicines was given in 20 (2.2%) children.

This study illustrated that drug use was partly not consistent with the recommendations of current guidelines, especially antibiotics. The drug use of CAP in children needs to pay more attention to.

Abbreviation: CAP = community-acquired pneumonia.

Keywords: antibiotics, children, china, community-acquired pneumonia, drug use

1. Introduction

Community-acquired pneumonia (CAP) is one of common infectious disease in children, which is responsible for high rate of hospital admission.^[1] More than 2 million 0 to 5 years old children die from pneumonia each year, accounting for almost 1 in 5 under-5 deaths in the world.^[2] In China, pneumonia was one of the leading causes of under-5 deaths and 14.8% of the 6.3 million children who died from pneumonia under the age of 5 years.^[3,4]

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Rational drug use (RDU) would contribute to ensure best use of medical resources, minimizing potential side-effects and reducing of the disease burden.^[5] In 1986, RDU was firstly defined as “the patient should receive medicines appropriate to their health care conditions, at optimum doses and sufficient time, as well as at the cost that the individual can afford” by the World Health Assembly (WHA).^[6] WHO reported that more than 50% medicines were prescribed, dispensed, or sold inappropriately while 50% of patients fail to take them correctly in the world.^[7] In children, the particular process of drug absorption, distribution, metabolism, excretion, and the lacking in specialized medicines for children, makes it to be one of the high-risk population of using drugs.^[8] Meanwhile, drug therapy is the main treatment for CAP in children.^[4] However, present study rarely assesses the drug use to treat CAP in children.^[9] In 2018, our research group developed a set of indicators to assess RDU for the treatment of CAP in children, which were applied to hospital departments and clinics to evaluate the rationality of drug use during a given period of time.^[10] Therefore, the aim of this study was to assess the rationality of drug use to treat CAP in children using a set of developed indicators and to provide reference for clinical drug use by performing a retrospective cross-sectional study in a Chinese University Hospital.

2. Methods

2.1. Study setting and patients

A retrospective, cross-sectional study was conducted in West China Second University Hospital (WCSUH). Hospitalized children (0–18 years old) diagnosed with CAP from October 2015 to January 2016 were included. CAP was defined as the

presence of signs and symptoms of pneumonia (fever and respiratory symptoms) and pulmonary condensation on chest radiography in a previously healthy child caused by an infection that was acquired in the community who has not been hospitalized within 14 days prior to onset of symptoms or has been hospitalized <4 days prior to the onset of symptoms.^[11] We excluded children that suffered from an underlying chronic respiratory disease, congenital diseases, such as congenital heart disease and congenital immunodeficiency disease, tuberculosis infection, immune abnormalities, such as acquired immune deficiency syndrome, tumor.^[12]

This study was approved by the Institutional Review Board of West China Second University Hospital.

2.2. Monitoring indicators

Seventeen indicators (a set of indicators to assess RDU to treat CAP in children developed by our research group using modified Delphi method) which were used to monitor the drug use of CAP in children on the hospital level.^[10] The indicators were based on “Drug selection,” “Drug Usage and Dosage,” and “Duration of Drug Therapy,” and covered antibiotics, antiviral agents, traditional Chinese medicines, and adjuvant drugs.

2.3. Data collection and analysis

The information of patient, medication, and microbiologic examination, including register number, age, sex, diagnosis, admission time, discharge time, drug generic name or drug trade name, drug usage and dosage, microbial test information, all of these were collected from West China Second University Hospital Information System (HIS) by clinical pharmacists.

Data were typed into an excel spreadsheet and categorical data were described by proportion.

3. Results

3.1. Baseline patient characteristics

From October 2015 to January 2016, 894 CAP children (under 18 years old) among who 553 (61.8%) were male, and 341 (38.2%) were female, were included in the retrospective cross-sectional study to assess the drug use. The average age of these children was 1.8 years (SD 2.9 years). Table 1 shows the characteristics of included children.

3.2. Use of antibiotics

Among the total of 894 children, 889 (99.4%) children received antibiotics and more than one antibiotic was administered in 781 (87.4%) children. Among the children with antibiotics therapy, 278 (48.3%) children received β -lactam antibiotics for the first choice at the age of 4 months to 5 years, 631 (71.0%) children received 3rd-generation cephalosporin antibiotics, 53 (21.8%) children received macrolide antibiotics at the age of 0 to 3 years or 5 to 18 years, and 66 (7.4%) children received sequential therapy. Among the 781 children with antibiotics combination therapy, 218 (27.9%) children were given macrolide antibiotics combined with β -lactam antibiotics.

Among the 889 children who received antibiotics, microbiologic examination was taken in 771 (86.7%) children. About 291 (82.2%) children accepted broad-spectrum antibiotics after the identification of pathogens, and 13 (31.7%) children used vancomycin or clindamycin when the pathogen is *Staphylococcus*

Table 1

Characteristics of patients.

Children (n)	894
Age, y (mean \pm SD)	1.8 \pm 2.9
Gender	
Female, n (%)	341 (38.2%)
Male, n (%)	553 (61.8%)
Other diseases	
Diabetes, n (%)	4 (0.4%)
Epilepsy, n (%)	66 (7.4%)
Kawasaki syndrome, n (%)	32 (3.6%)
Hypertension, n (%)	12 (1.3%)
Urticaria, n (%)	8 (0.9%)
Metabolic syndrome, n (%)	20 (2.2%)
Drug use	
Antibiotics, n (%)	889 (99.4%)
Antiviral agents, n (%)	20 (2.2%)
Traditional Chinese medicines, n (%)	284 (31.8%)
Antipyretics, n (%)	221 (24.7%)
Systemic corticosteroids, n (%)	205 (22.9%)
Glucocorticoids, n (%)	407 (45.5%)

n = the number of patients.

aureus. Intravenously of antibiotic was administered in 880 (99.0%) children and the average days of antibiotics treatment were about 8.0 days.

3.3. Use of antiviral agents

Twenty (2.2%) children received antiviral agents and 19 (2.1%) children received antibiotics combined with antiviral drugs. Among the 20 children, antiviral drugs were administered intravenously in 19 (95.0%) children and the average days of using antiviral drugs were 12.0 days.

3.4. Use of traditional Chinese medicines

Among 208 children used traditional Chinese medicines, 20 (7.0%) children were given the injection of medicines.

3.5. Use of adjuvant drugs

Among the 221 children taken antipyretics, 149 (67.4%) children were given acetaminophen or ibuprofen. And of the 407 children taken glucocorticoids, 322 (79.1%) used inhaled corticosteroids and 205 children accepted systemic corticosteroids therapy, the average days of systemic glucocorticoids's treatment was about 7.5. Seventeen (8.3%) children taken systemic glucocorticoid therapy combined with β -agonist.

Table 2 shows the characteristics of drugs use.

4. Discussion

This study evaluates the drug use in treating the children who suffered from CAP by using a set of developed indicators in China.^[10] About 894 children were included to assess the rationality of drug use and the majority of them are male (61.8%). The results demonstrate that antibiotics, antiviral agents, traditional Chinese medicines, and adjuvant drugs are the principal drugs to treat CAP in children. The widespread use of antibiotics is particular concern. The guideline of Infectious Diseases Society of America 2011 (IDSA 2011) recommended that antibacterial therapy is not essential for children, no matter

Table 2**The characteristics of drug use.**

Indicators	Calculation formula	Outcomes
The characteristics of antibiotics use		
Proportion of antibiotics use (n/N, %)	Number of children used antibiotics/total number of children	889/894, 99.4
Proportion of preference for β -lactam antibiotics (4 mo to 5 y old, n/N, %)	Number of children used β -lactam antibiotics for the first choice/number of children used antibiotics	278/575, 48.3
Proportion of the 3rd-generation cephalosporin antibiotics use (n/N, %)	Number of children used 3rd-generation cephalosporin antibiotics/number of children used antibiotics	631/889, 71.0
Proportion of macrolide antibiotics use (0–3 and 5–18 ys old, n/N, %)	Number of children used macrolide antibiotics/number of children used antibiotics	53/243, 21.8
Proportion of antibiotics combination therapy (n/N, %)	Number of children with antibiotics combination therapy/number of children used antibiotics	781/889, 87.4
Proportion of combined use of macrolide and β -lactam antibiotics (n/N, %)	Number of children used macrolide antibiotics combined with β -lactam antibiotics/number of children with antibiotics combination therapy	218/781, 27.9
Proportion of sequential therapy (n/N, %)	Number of children received sequential therapy/number of children used antibiotics	66/889, 7.4
Microbiologic examination rate of children with CAP using antibiotics (n/N, %)	Number of children taking microbiologic examination before antibiotics therapy/number of children used antibiotics	771/889, 86.7
Proportion of broad-spectrum antibiotics use after the identification of pathogens (n/N, %)	Number of children used broad-spectrum antibiotics after the identification of pathogens/number of children identified the pathogens	291/354, 82.2
Proportion of using vancomycin or clindamycin when the pathogen is <i>Staphylococcus aureus</i> (n/N, %)	Number of children used vancomycin or clindamycin when the pathogen is <i>Staphylococcus aureus</i> /number of children infected with <i>Staphylococcus aureus</i>	13/41, 31.7
Proportion of antibiotics administered intravenously (n/N, %)	Number of children received antibiotics administered intravenously/number of children used antibiotics	880/889, 99.0
The average number of days of antibiotics treatment, d	The total number of days of antibiotics treatment/number of children used antibiotics	7129/889, 8.0
The characteristics of antivirals agents use		
Proportion of antivirals agents use (n/N, %)	Number of children used antivirals agents/total number of children	20/894, 2.2
Proportion of antibiotics combined with antiviral drugs (n/N, %)	Number of children used antibiotics combined with antiviral drugs/total number of children	19/894, 2.1
Proportion of antiviral drugs administered intravenously (n/N, %)	Number of children used antiviral drugs administered intravenously/number of children used antivirals agents	19/20, 95
The average number of days using antiviral drugs (day)	The total number of days using antiviral drugs/number of children used antivirals agents	240/20, 12
The characteristics of traditional Chinese medicines use		
Proportion of injection used among the children who took traditional Chinese medicines (n/N, %)	Number of children used injection of traditional Chinese medicines/number of children used traditional Chinese medicines	20/284, 7.0
The characteristics of adjuvant drugs use		
Proportion of acetaminophen or ibuprofen used among the children who used antipyretics (n/N, %)	Number of children with fever used acetaminophen or ibuprofen/number of children used antipyretics	149/221, 67.4
Proportion of systemic corticosteroids therapy combined with β -agonist (n/N, %)	Number of children with systemic corticosteroids therapy combined with β -agonist/number of children with systemic corticosteroids therapy	17/205, 8.3
Proportion of the inhaled corticosteroids among the children who took glucocorticoids (n/N, %)	Number of children used inhaled corticosteroids/number of children used glucocorticoids	322/407, 79.1
The average duration of systemic glucocorticoids use, d	The total number of days taking systemic glucocorticoids/number of children receive systemic corticosteroids therapy	1541/205, 7.5

who are outpatients or inpatients, or who are with a positive test result for influenza virus while in the absence of clinical, laboratory, or radiographic findings to suggest bacterial co-infection.^[4] However, this study finding that only 5 children did not take antibiotics while most of the children took microbiologic examination. Moreover, up to 87.4% children received more than one kind of antibiotics. Such a high rate of antibiotics use is not consistent with the recommendations of the guideline, which illustrates the antibiotics use may be unreasonable in clinical. Rational drug selection is crucial in effective therapy. Most guidelines recommended β -lactam antibiotics for 4 months to 5 years old children and macrolide antibiotics for 0 to 3 years and 5 to 18 years old.^[13–16] The present study finding that the proportion of use was about 50%, respectively. In addition, drug selection, usage, and dosage also play an important role in

effective treatment. The guideline of British Thoracic Society 2011 (BTS 2011) recommended that antibiotics administered orally were safe and effective for children presenting with even severe CAP.^[13] In 2004, a study published in *Lancet* compared oral amoxicillin with injectable penicillin in the treatment of severe pneumonia in children, the study revealed that antibiotics administered orally and intravenously were equivalent for the treatment and oral treatment was even safer and more economical.^[17] In our study, we find that the majority of children received antibiotics administered intravenously rather than orally. Such a high proportion reminds us to pay more attention to the way of antibiotics use. As for duration of drug therapy, IDSA 2011 recommended that treatment courses of 10 days would have been best, although shorter courses may be effective, especially for some more mild disease which managed

on an outpatient basis.^[4] We find the average days of antibiotics treatment was 8.0 that is somewhat consistent with the recommendation of the guideline.

In addition, the rational use of other drugs also need pay attention to. The guideline of Chinese Medical Association 2013 (CMA 2013) recommended that the treatment of specific viral etiology is lagging behind for viral pneumonia, and the effective antiviral drugs are lacking.^[18] However, IDSA 2011 recommended that Influenza antiviral therapy should be administered as soon as possible to children with moderate to severe CAP consistent with influenza virus infection during widespread local circulation of influenza viruses, particularly for those with clinically worsening disease documented at the time of an outpatient visit.^[4] Thus, whether to use or not antiviral drugs should be combined with clinical practice and the results of microbiologic examination. This finding is consistent with the guideline that rare children used antiviral drugs. A guideline of State Administration of Traditional Chinese Medicine of People's Republic of China recommended that use oral Chinese medicine rather than injection as far as possible.^[19] This finding is consistent with the guideline as well.

The RDU was concerned in many studies.^[20–22] In this study, the high rate of antibiotic use is particularly concerned. Antibiotic misuse and abuse would contribute to several negative consequences. The incidence of drug-related adverse events is significantly increased in such instances.^[23,24] In addition, the emergence of multidrug-resistant bacterial pathogens is heavily favored in instances of improper antibiotic use, leading to longer hospital stays, increased healthcare costs, and increased patient mortality.^[23,24] Therefore, we should take some measures on the solution of the current issues. The implementation of antimicrobial stewardship is one of approach to preserve the activity of existing antimicrobial agents, including reviews and approvals of antibiotic prescriptions prior to the initiation of therapy, and reviews of prescriptions with feedback on antibiotics used are performed after the antibiotics have been prescribed.^[25] Moreover, additional possibilities to supplement core strategies or to improve antibiotic prescribing methods include education of pediatricians, creating a multidisciplinary inter-professional antimicrobial stewardship team to prepare guidelines, streamlining/de-escalation therapy, intravenous-oral conversion, and dose optimization.^[25,26] Whatever, all efforts must be made to ensure the rationality of antibiotic use to treat CAP in children.

4.1. Limitations

Although a standardized method was performed in this study, it still has limitations. First, CAP has no specific ICD-10 coding which make us could not include children through ICD-10 coding directly. To ensure the accuracy of included patients and improve the feasibility of indicators, data were collected by experienced pharmacists independently and cross checked data extraction. In instances of disagreement, pharmacists resolved their difference of opinion by discussion and consensus. Second, the character of the cross-sectional design precluded the ascertainment of causality; more research on explore the reason of irrational antibiotics use in the treatment of CAP in children in China is needed.

4.2. Future directions

Children comprise one of the highest risk populations that require monitoring for RDU. This cross-sectional study is first using set of indicators^[10] to evaluate the rationality of drug use to

treat CAP in children. The result reflects the current treatment situation objectively and guides people toward the promotion of RDU in the absence of drug monitoring indicators for CAP. In addition, we verified the scientific of indicators^[10] and provide a method for other hospitals to evaluate RDU for the treatment of CAP in children.

5. Conclusion

Eight hundred ninety-four children were included to evaluate RDU for CAP. The result illustrates that 99.4% of them received antibiotics and 87.4% received more than 1 antibiotic, which demonstrates drug therapy to some extent in the hospital is not consistent with the recommendations of current guidelines in children with CAP. The drug use of CAP in children, especially antibiotics, needs to pay more attention to.

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Author contributions

Xue Mi, Wenrui Li, Linan Zeng and Lingli Zhang performed research design.

Xue Mi, Wenrui Li and Jialian Li performed research execution. Mi Xue, Jialian Li, Lina Chen and Liang Huang performed data analysis

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