Pathogens and antibiotic resistance of children with community-acquired pneumonia.

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Abstract

Objective: To investigate the pathogens and antibiotic resistance of Community-Acquired Pneumonia (CAP) in children under 5 y old in our hospital during the recent two years.

Methods: 759 CAP patients in our hospital from October 2015 to July 2017 were analysed. The sputum samples of CAP patients were collected. The pathogens and antibiotic resistance were detected.

Results: In the 759 cases, 296 specific pathogens were identified in 265 cases (34.91%), included 119 (40.2%) ones of gram-positive (G+) bacteria and 177 (59.8%) ones of gram-negative (G-) bacteria. The most main G+ bacteria were *Staphylococcus aureus* (17.23%) and *Streptococcus pneumoniae* (9.12%). The most main G- bacteria were *E. coli* (24.32%) and *Klebsiella pneumoniae* (9.46%). The antibiotic resistances of *Staphylococcus aureus* to penicillin, erythromycin, tetracycline, clindamycin were high. The antibiotic resistances of *Streptococcus pneumoniae* to erythromycin were high. The antibiotic resistances of *Staphylococcus haemolyticus* to penicillin and tetracycline were high. The antibiotic resistances of *E. coli* to ampicillin, gentamicin, piperacillin and ciprofloxacin were high. The antibiotic resistances of *Klebsiella pneumoniae* to ampicillin and gentamicin were high. The antibiotic resistances of *Enterobacter cloacae* to amoxicillin and cefazolin were high. The antibiotic resistances of *Pseudomonas aeruginosa* to ceftriaxone, levofloxacin and ciprofloxacin were high.

Conclusion: It's suggested that the isolating rate of G- bacteria could be higher than G+ bacteria in our hospital, which have the different resistance characteristics to general antibiotics.

Introduction

Community-Acquired Pneumonia (CAP) refers to the pulmonary parenchyma and/or interstitial acute inflammation of the patient with a definite incubation period in the hospital, which is one of the leading causes of death in children under five years old, and the high cost of treatment for children with family also bring heavy economic burden [1,2].

CAP belongs to dynamic disease, the epidemic characteristics of pathogenic bacteria and clinical manifestation and sign of children in relevant with season, climate, region, time, economic condition and medical level [3]. To master the distribution and antibiotic resistance is the prerequisite for effective antibiotic therapy.

The clinical data of children with CAP in our hospital are diversity. By analyzing the characteristics of pathogenic bacteria and the resistance of antibiotics of 759 CAP patients in our hospital from October 2015 to July 2017, we hope to provide a reference basis for empiric therapy and scientific and appropriate prevention and control measures of the children under 5 y old in our hospital.

Information and Method

General information

This study selected during August 2015 to July 2017 in our hospital internal CAP 759 cases of children in the hospital, with 423 cases male children, 336 cases of female, age of 6 months to 5 years, the average age was 2.31 ± 0.74.

Inclusion criteria: 1. All children are eligible for the diagnostic criteria of CPA. 2. The guardian or the family member should sign the informed consent form.

Exclusion criteria: 1. Children who do not meet the criteria of CAP diagnosis. 2. Children with aspiration pneumonitis, hypersensitivity pneumonitis and bronchial asthma. 3. During the first two weeks of the visit, there was a history of hospitalization, which could not conclude hospital acquired pneumonia. 4. Children with pulmonary diseases such as tuberculosis, pulmonary tumor, non-infection pulmonary disease, pulmonary edema, pulmonary embolism, etc. 5. Patients who have long-term use of drugs such as hormonal drugs, immunosuppressant or immune globulin, etc.

Research method

Sputum samples: All the children were admitted to the hospital the next morning, clean mouth, back to stimulate cough with low pressure aspirator connect disposable sterile sputum suction tube, after collecting sputum samples, the examination of the pathogen in 2 h.

Samples of sputum samples were collected: The number of squamous epithelial cells in the microscope<10, and multiple nuclear leukocyte counts>25.

Bacterial culture and drug susceptibility testing: Using the French merry Emmanuel Company produces the VITEK® 2 COMPACT automatic microbe instrument to identify the bacteria identification and drug susceptibility.

Positive criteria: Detection of any pathogen can be determined as positive, including single infection (detection of only one pathogen) and mixed infection (detection of more than 2 pathogens).

Quality control strains: *Escherichia coli* ATCC25922, *Staphylococcus aureus* ATCC29213, *Pseudomonas aeruginosa* ATCC27853.

Statistical processing

Using SPSS22.0 statistical software for processing the data, set up the database, the detailed input survey data, measurement data with mean ± standard deviation ($\bar{x} \pm s$), using t-test data comparison between the two groups. The count data was expressed as a percentage (%), and the chi-square test was adopted. $P<0.05$ indicates that the difference was statistically significant.

Results

Detection of the pathogen of CAP

Of the 759 samples tested by CAP pathogens, 265 positive samples were tested and accounted for 34.91%. In 31 cases (4.08%), 2 pathogenic bacteria were isolated and 296 strains were detected. Among them, 119 were gram-positive bacteria (G$^+$ bacteria), G$^+$ bacterial positive detection rate was 40.2%, and *Staphylococcus aureus* (17.23%) and *Streptococcus pneumoniae* (9.12%) were the most common. 177 strains were gram-negative bacteria (G$^-$ bacteria), and the positive detection rate of G$^-$ bacteria was 59.8%, with *Escherichia coli* (24.32%) and *Klebsiella pneumoniae* (9.46%) as the most common (Table 1).

Table 1. Distribution of pathogenic bacteria of sputum samples of children with CAP (n, %).

	Pathogenic bacteria	Strains	Positive rate (%)
Gram-positive bacterium	*Staphylococcus aureus*	51	17.23
	Streptococcus pneumoniae	27	9.12
	Staphylococcus haemolyticus	14	4.73
	Staphylococcus epidermidis	13	4.39
	Staphylococcu lugdunensis	6	2.03
	Staphylococcus hominiis	2	0.68
	Corynebacterium diphtheroides	2	0.68
	Others	4	1.35
	Total	119	40.20
Gram-negative bacterium	*Escherichia coli*	72	24.32
	Klebsiella pneumoniae	28	9.46
	Enterobacter cloacae	25	8.45
	Pseudomonas aeruginosa	25	8.45
	Klebsiella oxytoca	11	3.72
	Haemophilus	9	3.04
	Baumann hemolysis	2	0.68
	Enterobacter aerogenes	1	0.34
	Others	4	1.35
	Total	177	59.80

The drug sensitivity analysis

The pathogenic bacteria detected by the children of CAP included penicillin, ampicillin, erythromycin, amilinine, amikacin, ciprofloxacin, levofloxacin, etc.

Main G$^+$ bacteria drug resistance to commonly used antibiotics detection results

51 strains of *Staphylococcus aureus* to penicillin, erythromycin, tetracycline, clindamycin resistance was the highest, 66.67%, 52.94%, 47.06% and 41.18% respectively, the imipenem, cefazolin and amoxicillin resistance times. The sensitivity to linezolid was highest, about 100%, and the sensitivity to azithromycin, gentamycin and peracillin was second.

27 strains of *Streptococcus pneumoniae* were the most resistant to erythromycin, up to 81.48%, azithromycin and clindamycin resistance times, amoxicillin, gentamicin and rina thiazole amine sensitivity can reach 100%.

14 strains of haemolytic *Staphylococcus*, the highest resistance to tetracycline and penicillin, were 85.71% and 71.43% respectively, and there was little resistance to azithromycin, cefazolin and gentamycin (Table 2).

Main G$^-$ bacteria drug resistance to commonly used antibiotics results

72 strains of *E. coli*, detection of ampicillin, gentamicin, piperacillin, ciprofloxacin resistance was the highest, 44.44%, 43.06%, 38.89% and 34.72% respectively, levofloxacin, cefazolin and cefepime times. The sensitivity of Imipenem was highest, 100%, and the sensitivity of ceftriaxone was second.

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The 28 strains of *Klebsiella pneumoniae*, with the highest resistance to gentamycin and ampicillin, were 57.14% and 46.43% respectively, followed by resistance to piperacillin and ciprofloxacin. The sensitivity to ceftriaxone and Imipenem was 100% and almost without resistance.

25 strains of *Enterobacterium*, which were almost completely resistant to amoxicillin and cefazolin, were resistant to ampicillin, up to 96%, and were almost no resistance to levofloxacin.

25 strains of *Pseudomonas aeruginosa* detection of ceftriaxone, levofloxacin, ciprofloxacin, tobramycin and gentamicin have certain resistance, between 20% and 44%, to piperacillin, cefepime and imipenem almost without resistance (Table 3).

Table 2. *The drug resistance of Staphylococcus aureus, Streptococcus pneumoniae and hemolytic Staphylococcus aureus in common antibiotics (n, %).*

	Stapphylococcus aureus (n=51)		Streptococcus pneumoniae (n=27)		Shaemolytic staphylococcus (n=14)	
	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity
Penicillin	34 (66.67)	17 (33.33)	10 (37.04)	17 (62.96)	10 (71.43)	4 (28.57)
Tetracycline	24 (47.06)	27 (52.94)	11 (40.74)	16 (59.26)	12 (85.71)	2 (14.29)
Erythromycin	27 (52.94)	24 (47.06)	22 (81.48)	5 (18.52)	8 (57.14)	6 (42.86)
clindamycin	21 (41.18)	30 (58.82)	18 (66.67)	8 (29.63)	5 (35.71)	9 (64.29)
Azithromycin	2 (3.92)	49 (96.08)	20 (74.07)	7 (25.93)	0	14 (100.0)
Amoxicillin	8 (15.67)	42 (82.35)	0	27 (100.0)	1 (7.14)	13 (92.86)
Imipenem	9 (17.65)	42 (82.35)	1 (3.70)	26 (96.30)	3 (21.43)	11 (78.57)
Cefazolin	9 (17.65)	43 (84.31)	3 (11.11)	24 (88.89)	0	14 (100.0)
Peracillin	4 (7.83)	47 (92.16)	2 (7.41)	25 (92.59)	2 (14.29)	12 (85.71)
Gentamycin	3 (5.88)	48 (94.12)	0	27 (100.0)	0	14 (100.0)
Rina thiazole amine	0	51 (100.0)	0	27 (100.0)	1 (7.14)	12 (85.71)

Table 3. *The results of the resistance of Enterobacterium, Klebsiella pneumoniae, gutter enterobacter and Pseudomonas aeruginosa on common antibiotics (n, %).*

	E. coli (n=72)		Klebsiella pneumoniae (n=28)		Enterobacterium (n=25)		Pseudomonas aeruginosa (n=25)	
	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity	Resistance	Sensitivity
Ampicillin	32 (44.44)	40 (55.56)	13 (46.43)	15 (53.57)	24 (96.0)	1 (4.0)	-	-
Gentamicin	31 (43.06)	40 (55.56)	16 (57.14)	12 (42.86)	4 (16.0)	21 (84.0)	5 (20.0)	20 (80.0)
Piperacillin	28 (38.89)	44 (61.11)	10 (35.71)	18 (64.29)	5 (20.0)	20 (80.0)	0	25 (100.0)
Amoxicillin	3 (4.17)	69 (95.83)	2 (7.14)	26 (92.86)	25 (100.0)	0	-	-
Ciprofloxacin	25 (34.72)	47 (65.28)	8 (28.57)	20 (71.43)	3 (12.0)	22 (88.0)	8 (32.0)	17 (68.0)
Levofloxacin	21 (29.17)	51 (70.83)	4 (14.29)	23 (82.14)	0	25 (100.0)	9 (36.0)	16 (64.0)
Tobramycin	19 (6.39)	53 (73.61)	4 (14.29)	24 (85.71)	5 (20.0)	20 (80.0)	7 (28.0)	18 (72.0)
Cefazolin	15 (20.83)	57 (79.17)	5 (17.86)	23 (82.14)	25 (100.0)	0	-	-
Cefepime	14 (19.44)	57 (79.17)	5 (17.86)	23 (82.14)	7 (28.0)	18 (72.0)	0	25 (100.0)
Cefataxime	4 (5.56)	68 (94.44)	2 (7.14)	25 (89.29)	16 (64.0)	9 (36.0)	4 (16.0)	21 (84.0)
Ceftriaxone	1 (1.39)	71 (98.61)	0	28 (100.0)	14 (56.0)	11 (44.0)	11 (44.0)	14 (56.0)
Imipenem	0	72 (100.0)	0	28 (100.0)	1 (7.14)	24 (96.0)	0	25 (100.0)

Discussion

Due to the children's respiratory tract anatomy and the immune system is not fully development, the adults are more likely to be infected with respiratory tract inflammation caused by pathogenic microorganisms, especially under the age of five. The incidence and fatality rate of CAP in our country has been high. For a long time, infantile CAP has been one of the leading causes of hospitalized children [4], often accompanied by obvious clinical symptoms such as fever, cough, respiratory failure, and even poisoning symptoms of infection, not only affects the health and development level of children immediate and long-term, but also bring a heavy burden to families. Especially infant pneumonia in children, characterized by acute onset, quickly development, multiple complications and cause systemic infection easily. If not timely, reasonably and effectively gives anti-infection treatment, children with high mortality [5]. How to effectively reduce the incidence of CAP in children and the detection rate of pathogenic bacteria has become an urgent problem. Because CAP belongs to dynamic disease and influenced by different seasons, regions, ages, climatic conditions, economic conditions, medical level, etc., the pathogen distribution of CAP is different [3,6]. The study on the basis of monitoring in our hospital, through the detection of sputum samples composing spectrum and drug susceptibility of pathogenic bacteria, hoping to have a preliminary understanding in the region of present children with CAP pathogenic bacteria distribution and drug resistance, and to provide reference frame for monitoring, management, prevention and treatment of children with CAP in our hospital.

Because of some small children age, sputum samples collected not easily, which need to use equipment or a professional to collect. This study adopts method of sputum suction negative pressure try to avoid injury in children with respiratory tract mucous membrane. We examined the sputum of children under 5 y of age in our hospital in the past years and tested positive samples in 265 cases (34.91%). In 31 cases (4.08%), 2 pathogenic bacteria were isolated and 296 strains were detected. Among them, 119 (40.2%) were gram-positive and were most common with *Staphylococcus aureus* (17.23%) and *Streptococcus pneumoniae* (9.12%). 177 strains (59.8%) were gram-negative, with *Escherichia coli* (24.32%) and *Klebsiella pneumoniae* (9.46%) as the most common. There are major differences in the major pathogenic bacteria of CAP with children, and there have been reports from abroad that *Streptococcus pneumoniae* and *Haemophilus influenzae* are the main pathogenic bacteria of CAP in children [7]. There were also reports in China that the main pathogenic bacteria of CAP were *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and others [8]. According to the results of the study from August 2015 to July 2017, hospitalized in pediatric medicine in children with CAP, *E. coli* and *Staphylococcus aureus* were the main pathogenic bacteria, followed by *Streptococcus pneumoniae*. There are also significant differences in bacterial spectra in different regions.

The test results for drug resistance detection of G+ bacteria showed that *Staphylococcus aureus* had the highest resistance to penicillin, erythromycin, tetracycline, clinicycin, and the highest sensitivity to linezolid. *Streptococcus pneumoniae* is the most resistant to erythromycin, and the sensitivity to amoxicillin, gentamycin and linezolid can be reach 100%. Hemolytic *Staphylococcus* has the highest resistance to tetracycline and penicillin, and there is little resistance to azithromycin, cefazolin and gentamycin. *Staphylococcus aureus* is the main pathogenic bacteria of the suppurative infection, which can be produced by the production of β-lactamase, and resistant to the antibacterial drugs of penicillin easily [9]. In addition, in recent years, due to the antibiotic management is not standard, not rational drug use, as a result, *Staphylococcus aureus* also gradually to large ring lactone class antibiotic resistance, may be due to the presence of resistant genes *ErmC*, making in the 50 s subunit of 23 s rRNA methylation and cause resistance [10]. In many areas, *Streptococcus pneumoniae* is the main CAP pathogenic G+ bacteria, due to the membrane surface of penicillin binding protein, easily combined with penicillin or other β-lactam antimicrobial agents, interfere with the synthesis of bacterial cell walls, but in case of related gene mutations, binding protein structure variation, caused by penicillin will develop resistance [11]. The resistance mechanism of *Streptococcus pneumoniae* to the macrolide antibiotic is basically the same as that of *Staphylococcus aureus*, which is related to the target change of the ribosome. The sensitivity of G+ bacteria to rina thiazole amine is high, which belongs to antibiotics pbo alkane ketones, mainly inhibiting bacterial protein translation process, and a widely antimicrobial spectrum, suggested that clinical can be as the main treatment of G+ bacterial infection.

The test results for drug resistance detection of G- bacteria showed that *Escherichia coli* had the highest resistance to ampicillin, gentamycin, peracillin and ciprofloxacin, and the highest sensitivity to Imipenem. *Klebsiella pneumoniae* is the most resistant to gentamycin and ampicillin, and almost no resistance to ceftriaxone and amines. The *Bacilli* is almost completely resistant to amoxicillin and cefazolin, and the resistance to ampicillin is as high as 96%, and the levofloxacin is almost non-resistant [12]. *Pseudomonas aeruginosa* to ceftriaxone, levofloxacin, ciprofloxacin, tobramycin and gentamicin has certain resistance, between 20% and 44%, to piperacillin, cefepime and imipenem almost no resistance. *E. coli* and *Klebsiella pneumoniae* are common conditions for pathogenic bacteria, and the production of β-lactamase is still the main reason for the resistance to antibiotic resistance of β-lactamide [13]. The sensitivity to quinolones is relatively high, possibly due to the low dosage of children. Although the sensitivity of ciprofloxacin and levofloxacin to g-bacteria is high, the application plan is still to be discussed because of safety problems. The drug resistance rate of the bacteria is high, mainly because of its associated with the ampase and ultra-wide spectrum β-lactamase (ESBLs) [14]. The virulence of *Pseudomonas aeruginosa* is extremely strong. In recent years, resistance to antimicrobial agents has been gradually improving. Imipenem belongs to penicillium carbon alkene antimicrobial agents, high sensitivity of G- bacteria, may be related to its special structure, stability and rapidly in

combination with penicillin binding protein, leading to inactivation and play a role of antibacterial [15-18]. It has a wide antibacterial activity, not only for G⁻ bacteria, but also for G⁺ bacteria and anaerobes. It can be used as the third line of children's CAP. However, it is important to note that imipenem easily lead to *Pseudomonas aeruginosa* resistant, therefore in the CAP of *Pseudomonas aeruginosa* infection children treated with drug susceptibility results when the choice needs careful consideration.

To sum up, from August 2015 to July 2017 children with community-acquired pneumonia pathogen distribution has its own characteristics, by analyzing the composition of pathogens in detail rule, and the characteristics of the drug susceptibility to provide the basis for the reasonable selection of clinical regimen.

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