

ANTIBIOTIC TREATMENT IN CHILDHOOD COMMUNITY-ACQUIRED PNEUMONIA – CLINICAL PRACTICE VERSUS GUIDELINES: RESULTS FROM TWO UNIVERSITY HOSPITALS

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Abstract

Background and aims. Community-acquired pneumonia (CAP) is a both common and serious childhood infection. Antibiotic treatment guidelines help to reduce inadequate antibiotics prescriptions.

Methods. We conducted a retrospective study at the Clinical Emergency Hospital for Children, 3rd Pediatric Clinic, Cluj-Napoca and Dr. Gavril Curteanu Clinical City Hospital, in Oradea. All patients discharged with a diagnosis of CAP between December 1, 2014 and February 28, 2015, were included in the study.

Results. There were 146 cases discharged with pneumonia in Cluj-Napoca center (mean age 4 years; range: 1 month – 16 years), and 212 cases in Oradea center (mean age 0.9 years; range: 2 weeks – 8 years). All cases were analyzed. The analysis made in Clinical Emergency Hospital for Children, 3rd Pediatric Clinic, Cluj-Napoca, showed that the antibiotics used in children hospitalized with community-acquired CAP are cefuroxime (43%), ceftriaxone (23%), macrolides (16%), ampicillin in association with an aminoglycoside (6%) and other antibiotics. The same antibiotics were used in Dr. Gavril Curteanu Clinical City Hospital of Oradea, where ampicillin in association with aminoglycoside was utilized in younger children (mean age 1.3 years), while ceftriaxone in older children (5.7 years) and children with high inflammation markers (ESR, CRP). From 11 pleurisy cases, 9 received cefuroxime or ceftriaxone.

Conclusions. There was a wide variability in CAP antibiotic treatment across university hospitals, regarding antibiotic choice and dosing. Antibiotic selection was not always related to the clinical and laboratory characteristics of the patient. The national guideline was not followed, especially in children aged one to three months.

Keywords: community-acquired pneumonia, guideline, antibiotics, child

Background and aims

Globally, community-acquired pneumonia (CAP) is

a leading cause of mortality, representing 15% of under-five years mortality and accounting for almost one million deaths in 2013 [1]. CAP is also a major cause of morbidity in young children (120 million episodes worldwide in 2010 [2]), being one of the most common reasons for pediatric

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hospitalization [3-5]. CAP accounts for more antibiotic use than any other condition in children’s hospitals [6].

There are several published guidelines related to CAP diagnosis and treatment in children [7-12], including a Romanian one [13]. Despite existing guidelines, there is a substantial variability in the empiric antibiotic therapy of CAP across hospitals [6,14-16], the proportion of children receiving treatments as recommended ranging from less than 1% to more than 80% [6].

The goals of the present study were to assess the antibiotic treatment, evaluate factors involved in the antibiotic choice, and compare the prescriptions with national (Romanian) and USA CAP guidelines in university hospitals, namely children hospitalized with CAP.

Methods

We conducted a retrospective cohort study in two university hospitals located in two different cities: Clinical Emergency Hospital for Children, 3rd Pediatric Clinic, Cluj-Napoca, Romania and Dr. Gavril Curteanu Clinical City Hospital, Oradea, Romania. The study included all children hospitalized in the two centers with a diagnosis of radiologically confirmed CAP (alveolar and interstitial), between December 1, 2014 and February 28, 2015. Data extracted from medical charts included patient demographics, presence of respiratory distress (tachypnea and/or recessions), laboratory data (ESR, CRP, WBC), radiological signs of CAP (extended or interstitial opacities), pleural effusion, and antibiotic therapy (drug and dose in mg/kg/day). We compared antibiotic treatment to national [13] and USA [7] CAP guidelines. The data were expressed as means and standard deviations or percentages.

Results

There were 146 cases discharged with pneumonia in Cluj-Napoca center (mean age 4 years; range: 1 month – 16

years), and 212 cases in Oradea center (mean age 0.9 years; range: 2 weeks – 8 years). All prescriptions were analyzed. The most frequently used antibiotic in Cluj-Napoca was cefuroxime (43%), followed by ceftriaxone and macrolides (Table I). Patients treated with ceftriaxone were of older age, presented respiratory distress, pleural effusion, ESR and CRP (Table I). The most frequently used antibiotic in Oradea was also cefuroxime (41%), but followed by ampicillin or ampicillin associated with gentamicin (Table II). Ceftriaxone was the third most common choice, and macrolides were not used at all in Oradea (Table II). There were no significant differences between patients treated with cefuroxime vs. ceftriaxone.

The mean dose for ampicillin was at the lower limit compared to the Romanian guideline recommendations [7], and well below compared to the American guideline [8] (Table III). In a significant proportion of patients, ampicillin was below the minimum recommended dose (100 mg/kg/day), in both centers. Regarding cefuroxime, the doses were above the minimum recommended dose by the Romanian guideline (Table III). The average dose of ceftriaxone was above the recommended dose by the Romanian guideline, but there were patients in Cluj-Napoca receiving doses well below the recommended one (Table III).

In infants aged 1 to 3 months, the preferred antibiotics were ampicillin (associated or not with gentamicin) in Cluj-Napoca and ampicillin or cephalosporins (2nd or 3rd generation) in Oradea, while the Romanian guideline is recommending a 3rd generation cephalosporin (Table IV). In the 4 months to 4 years age group in Cluj-Napoca and Oradea cefuroxime and ceftriaxone were preferred, and this was according to the Romanian guideline (Table IV). In children 5 years or above, cefuroxime, ceftriaxone or macrolides were used in Cluj-Napoca; ceftriaxone, but no macrolides, was used in Oradea (Table IV).

Table I. Antibiotics used in the 3rd Pediatric Clinic, Cluj-Napoca.

n = 146	Ampicillin and gentamicin	Cefuroxime	Ceftriaxone	Macrolides	Others
% (from n)	6	43	23	16	12
Age (years)	1.3	3.4	5.7	4.4	3.0
Respiratory distress (%)	37	27	35	22	44
Chest X-ray	Extended opacities	Extended opacities	Extended opacities	Interstitial opacities	Interstitial opacities
Pleural effusion (%)	0	8	12	4	6
ESR (mm/h)	11	20	30	19	16
CRP (mg/dL)	0.8	1.7	4.7	0.9	2.3
Leukocytes (x103/μL)	10.3	12.0	11.4	9.0	10.4

Values represent means, if not otherwise specified.

Table II. Antibiotics used in Oradea Municipal Hospital.

n = 212	Ampicillin ± Gentamicin	Cefuroxime	Ceftriaxone	Macrolides	Others
% (from n)	30	41	18	0	12
Age (years)	0.6	0.8	1.33	-	1.87
Respiratory distress (%)	28	40	31	-	36
Chest X-ray	Interstitial opacities	Interstitial opacities	Interstitial opacities	-	Interstitial opacities
CRP (mg/dL)	0.66	0.69	0.86	-	0.05
Leukocytes (x103/ μ L)	13.6	13.3	14.3	-	17.2

Values represent means, if not otherwise specified.

Table III. Antibiotics dosage - comparison between guidelines and dosage used in Cluj-Napoca and Oradea.

Antibiotic (mg/kg/day)	Cluj-Napoca	Oradea	Romanian guideline, 2007[7]	USA guideline,2011 [8]
Ampicillin				
Mean	107	127	100-200	150-200 ¹
Mean \pm 2SD	70-145	69-185		300-400 ²
Cefuroxime				
Mean	78	96	30-75	NA
Mean \pm 2SD	47-110	63-124		
Ceftriaxone				
Mean	75	88	50	50-100 ¹
Mean \pm 2SD	30-121	57-120		100 2

¹Sensitive *Streptococcus pneumoniae*; ²Resistant *Streptococcus pneumoniae*; NA - not available

Table IV. Comparison between practice and guidelines.

Cluj-Napoca ¹		Oradea ¹	Romanian guideline [7]	USA guideline [8]
Extended or disseminated opacities or pleurisy or sepsis on CXR				Presumed bacterial
1 - 3 months	Ampicillin \pm gentamicin	Ampicillin Cephalosporins	Cephalosporins 3 ^o	Not immunized for Hib and <i>S. pneumoniae</i> ; local resistance of <i>S. pneumoniae</i> is significant: ceftriaxone
4 months - 4 years	Cefuroxime Ceftriaxone	Cefuroxime Ceftriaxone	Cephalosporins 2 ^o or 3 ^o	
\geq 5 years	Cefuroxime Ceftriaxone OR Macrolide	Ceftriaxone	Cephalosporins 2 ^o or 3 ^o \pm Macrolides	
No extended or disseminated opacities, no pleurisy on CXR				Presumed atypical
1 - 3 months	Macrolides \pm ampicillin	Ampicillin Cephalosporins	Macrolides \pm cephalosporins 2 ^o or 3 ^o	Macrolides
4 months - 4 years	Macrolides or cephalosporins 2 ^o or 3 ^o	Cephalosporins 3 ^o	Ampicillin or amoxicillin/clavulanate	
\geq 5 years	Macrolide s	Cephalosporins 3 ^o	Macrolides	

¹Most used treatment(s); CXR - chest X-ray; Hib - *Haemophilus influenzae* type b; 2^o - second generation; 3^o - third generation

Discussion

The present retrospective cohort study showed a substantial variability of antibiotic treatment in the two hospitals, despite cefuroxime being preferred in both centers. In Cluj-Napoca, the second choice was ceftriaxone, while macrolides were used in 16% of the patients, whereas in Oradea the second choice was ampicillin (associated or not with gentamicin), and macrolides were not used at all. Cefuroxime, the preferred choice in the two centers, is still recommended for treatment of CAP by the Romanian guideline [13], but not by the USA guideline [7]. In the UK guideline, it is recommended for severe CAP, but the statement has the lowest grade, i.e. D [8]. Gentamicin was used in both centers (more often in Oradea), mainly in 1-3 months aged infants. The Romanian guideline recommends aminoglycoside only in neonates (0-3 months old) [13], and the USA and the UK guideline are not recommending aminoglycosides (including gentamicin) [7,8]. The antibiotic choice was not always related to the clinical and laboratory characteristics of the patient. The guidelines were not followed especially in children aged one to three months.

Significant variability in antibiotic treatment of CAP was observed in other studies [14-18]. In one study the prescription rate of 3rd generation cephalosporins varied across hospitals from 10.5% to 81.5% [16]. There are significant differences in the choice of antibiotics in community hospitals vs. children's hospitals [16]. Even after adjustments for patient demographics (e.g., age) and severity of disease substantial variability was observed in the use of first-line recommended antibiotics for children with CAP [6,15]. In the USA, cephalosporins were the most common used antibiotics in children with CAP before the publication of American guideline in 2011 [15]. Penicillin G or aminopenicillins were rarely used [15]. After guideline publication, the use of cephalosporins decreased significantly, and the use of penicillin G and aminopenicillins increased [19, 20]. The publication of the British CAP guideline led to the increase of amoxicillin prescriptions and shortening hospitalization period [21].

The strengths of the present study were that it was performed on a significant number of cases in two university centers, both having students and residents in training. The academic setting may be the major driver of differences between these practice locations, because teaching sites may be more likely to follow guidelines, and requires additional study [17].

There are several limitations of the present study. First, it was a retrospective cohort analysis, and, therefore, unmeasured confounding factors may be present that affect the choice of treatment prescribed. Second, additional characteristics that can influence antibiotic choice were not measured such as the baseline knowledge of each physician [17]. Thirdly, there may be differences in the radiological definition of CAP between centers, and because of this, it is

difficult to compare results.

Clinical practice guidelines are designated to enhance the quality of medical care by assisting prescribing practice that reflects the best evidence available [22-24]. The main results obtained with the implementation of guidelines were the improvement of medical care and a decrease in using resources [23-25]. Guidelines targeting antimicrobial prescribing can be an important tool for reducing unnecessary and inappropriate antibiotic use in the effort to enhance clinical outcomes while decreasing the development of antimicrobial resistance [19]. Multiple studies have shown that adherence to guidelines for treatment of community-acquired CAP in adults is associated with improved clinical outcomes and reduced costs [26-29]. However, elaboration and publication of guidelines alone do not ensure adherence of physicians to recommendations [30,31]. There are several explanations for not following the guidelines: (1) lack of information about guideline publication; (2) inertia of previous medical practice; (3) negative attitudes of doctors toward standardization; (4) disagreements with guidelines recommendations; (5) false perception that the guidelines are not effective [23]; (6) some of the guideline recommendations are not based on solid evidence; and [7] lack of financing and dedicated personnel to implement the guideline [32]. Writing guidelines in close collaboration with the specialists involved, representing a consensus view, making guidelines available online, active dissemination and promotion will improve compliance with guideline recommendations [33,34]. Also, local implementation efforts have enhanced guideline adoption [20,35].

Conclusions

In conclusion, there is a wide variability in CAP antibiotic treatment across university hospitals, regarding antibiotic choice and dosing. Antibiotic selection was not always related to the clinical and laboratory characteristics of the patient. The national guideline was not observed, especially in children aged one to three months. Updating the CAP national guideline and active dissemination will increase the guideline adoption.

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