Original article

Oral Cephalosporin Cefodox for treatment of out patient pneumonia in children

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Abstract

Objectives: to evaluate the efficacy and tolerability of the oral third generation cephalosporin Cefodox in the treatment of community-acquired pneumonia in children.

Patients: the study was conducted in pediatric outpatient clinic at prince Rashid military hospital over six months from 1-09- 2013 to 28-02-2015. A total number of 270 children aged from1 to 14 year with diagnosis of chestinfections were included in the study. Patients who have any chronic illnesses, immunodeficiency or were taking any antibiotics within 5 days of diagnosis were excluded.

Methods: according to the age, patients were divided into three age groups: first group with age 1-4 years, second group from 4-8 years and the third group 8 to 14years. Males to females ratio was (1.7:1).All patients were started on oral Cefodox twice daily for 10 days.Follow up was done for all patients at day 5 and day 10 after treatment.Chestradiograph was performed to all patients on day 10.

Results: The efficacy of the drug Cefodox was evaluated by the change and improvement of the clinical symptoms, physical examination and chest radiograph.All children in all age groups and both sexes showed improvement in all parameters by day 10 without complications and significant drug reactions.

Conclusion: Cefodox is effective, well tolerated and safe in the treatment of children with community-acquired pneumonia.

Keywords: *Children, pneumonia, Cefodox.*

Introduction

Community-acquired pneumonia (CAP) is acommon and potentially serious infection affecting children throughout the world, especially those younger than 5 years of age. The age group in which the annual incidence reaches 34 to 40 cases per 1000 in Europe and North America (1). In the developing world CAP is more common and more severe and is the largest killer of children.Recent data have shown that the number of children with severe CAP is increasing worldwide (2).

According to the World Health Organization (WHO) report from 2006, over 2 million children die from pneumonia each year, accounting for almost one in five deaths worldwide (3) and the School of Public Health at Johns Hopkins University (Johns Hopkins Bloomberg School of Public Health) has found that today one third of

children less than 5 years die from acute respiratory infections and pneumonia (4).

Definitions of pneumonia vary widely. Some require only the presence of infiltrates on a chest radiograph (5) whereas others require only certain respiratory symptoms or signs (6). But as a rule, the presence of symptoms and signs consistent with acute lower respiratory tract infection, in association with new radiographic shadowing for which there is no alternative explanation, can be managed as pneumonia (7).A chest X ray (CXR) may be useful for confirming the presence of pneumonia and detecting complications such as lung abscess or empyema.(8).

Good and proper selection of antibiotics for the treatment of pneumonia in children is possible by knowing the etiological factor and identification of the pathogen. Currently, however, rapid tests are insufficiently reliable and not always available. Therefore, the antimicrobial drug is often selected empirically taking into account the most likely causative agent, the characteristic symptoms, the patient's age, time and location of the disease. Results of recent works indicate that the accuracy of the empirical choice of antimicrobial drugs can be very high (9).

Patients and methods:

A total number of 270 children with age range from 1 to 14years were included; the patients were divided into three age groups. First group from 1-4 years, second group from 4 - 8 years and third group was from 8 to 12 years.

The number of males was 170, while the females were 100 with a ratio of (1.7:1).

The study excluded patients with immunodeficiency, cardiac diseases, liver disease and kidney diseases. Patients who were taking any antibiotics within 5 days were also excluded.

The diagnostic criteria of acquired pneumonia for all patients was based on the: (1) clinical presentations and symptom **(**acute onset of fever, cough, increased respiratory rate), (2) physical finding (the shortening of percussion tones, and auscultative changes local finely rales, crepitation, decreased breath) and (3) radiological finding of pneumonic changes and infiltration on chest radiography.

All patients with the diagnosis of pneumonia were started on oral Cefodox with a dose of 10 mg / kg body weight per day in 2 divided doses after meals, for 10 days duration for all patients.

All patients completed their follow up on day 5 and 10 after treatment. Complete history and physical examination were performed with concern to complications and drug reactions. CXR was done on day 10 for all patients.

The efficacy of the drug Cefodox was evaluated by the change and improvement of the clinical symptoms (the disappearance of toxicity, normalization of body temperature ,change in the nature of cough, its cessation along with disappearance of respiratory distress in form of dyspnea and tachypnea) , besides normal physical examination data (percussion, auscultation) and normalization of CXR findings.

Results

All study patients showed predominance of toxicity symptoms (100%). Increased body temperature was seen in 250 (92.6%) patients, dyspnea at rest was observed in 220 (81, 5%) patients, while dyspnea on exercise was observed in 50 (18.5%) patients. Frequent coughing was detected in 230 (85%) patients, and 110 patients (40.7%) had dry cough, while 120 (44, 5%) patients showed wet non productive cough. dullness of percussion sound was seen in190 (70.4%) patients, decreased breath sounds by auscultation was observed in 200 (74.0%) patients, the presence of finely wheezing in 100 (37, 0%) patients, and crepitation in 50 (18, 5%) patients; table1.

The patient's improvement was noticed on day 3 and 4 post-treatment by a decrease in toxicity signs, changing the character of cough, with easier sputum discharge, and appetite and sleep improvement. by the 2nd day of treatment body temperature already started to decrease and returned back to normal on the third day in 150 (55.5%) patients and in 170 (62,9%) patients on the 4th day. Shortness of breath at rest disappeared on the second day in 20 (7.4%) patients, on the third day in 50 (18, 5%) patients and by the 4thday in 130 (48, 1%) patients.

At the 7-8th day of treatment the signs of toxicity were absent in 260 (96, 2%) patients and by the end of treatment thetoxicity signsresolved in (100%) of patients. Control chest radiographs was

performed to all patients on day 10 aftertreatment and showed significant improvement of the pneumonic infiltration of the lungs.

Follow up showed that 255 children (94.4%) tolerate the drug easily and in 189(70%) cases, the twice-daily administration was strongly agreed by care givers.

Fortunately no complications or significant drug side effects were observed during or afterCefodox therapy

Table1: Signs and symptoms of patients on presentation.

Signs and symptoms	Number of patient	Percentage %
High temperature	250	92.6%
Dyspnea on rest	220	81.5%
Dyspnea on exercise	50	18.5%
Frequent cough	230	85.2%
Dry cough	110	40.7%
Wet cough	120	44.5%
Dullness on percussion	190	70.4%
Breath sound on auscultation ↓	200	74%
Wheezes	100	37%
Crepitation	50	18.5%

Table 2: Cephalosporins and resistance to B-lactamase.

Cephalosporin groups	Activity Gram+v	Activity	Resistance to B-
I generation	+++	+\-	++ -
II generation	++	+	++ +\-
III generation	+	+++	+ +
IV generation	++	+++	++ ++

Discussion

Acute acquired chest infections in children were most often associated with Gram- positive (staphylococci and streptococci), intracellular pathogens (mycoplasma, Chlamydia) and viruses (10). Recent researches in pulmonology, showed that the main pathogens of upper and lower respiratory tract infection are Streptococcus pneumonia, Haemophilus influenza and Moraxella catarrhalisand most of Gram-negative microorganisms *as* (Klebsiella pneumonia, Pseudomonas aeruginosa, Acinetobacter *spp.*, Escherichia coli), are often resistant to most of antibiotics (11).

Recently the experts have noted (12) that un professional approach to antibiotic therapy, irrational, uncontrollable drug intake often leads to microbial resistance, and to conduct an adequate antibiotic therapy requires knowledge of the etiologic agents of infectious diseases and to determine their susceptibility to antimicrobial agents. Only if this is possible to select the most effective drugs with fewer side effects.

Among the antibiotics currently used in clinical practice, one of the leading positions was cephalosporins. It is connected to many properties of drugs in this group: a broad spectrum bactericidal antimicrobial activity, low frequency of microbial resistance, resistance to many beta-lactamases, good tolerability and low incidence of side effects, ease and convenience of dosing.Cephalosporins have a broad range of antimicrobial activity, concentration-independent bactericidal activity, and excellent tolerance in children, with almost no dose-related toxicity (13).

Cephalosporins were divided into 4 generation in accordance with the spectrum of antimicrobial activity; table 2.

First (I) generation cephalosporins are highly active against gram-positive cocci, including Staphylococcus aureus, pneumococcus, beta-hemolytic streptococcus, but with limited activity against Gram-negative cocciand not active against atypical organisms. Second (II) generation cephalosporins have a higher activity against Gram-negative bacteria, especially Haemophilus influenza, and also more resistant to beta-lactamases, While maintaining high activity against Gram-positive bacteria. Third (III) generation cephalosporins have a much greater spectrum of activity compared with previous generations of drugs, especially for Gram-negative bacteria, including nosocomial (hospital), with

some decrease in activity against gram-positive bacteria.Fourth (IV) generation cephalosporins compared with the three previous generations have a balanced antimicrobial spectrum; the union activity of cephalosporins I-II generation to the Gram-positive bacteria, and some anaerobes.

Knowledge of the activity of an antibacterial agent against the likely causative pathogens and of the local patterns of bacterial resistance is of key importance when selecting a suitable drug. The increased prevalence of β-lactamase producing *H. influenzae* and drug-resistant *S. pneumonia* worldwide are important issues to consider (12-15). Other factors influencing the choice of treatment include evidence of clinical efficacy and tolerability of the antibacterial drug, ease of administration, palatability, cost and the prescriber's clinical experience with the drug.

Cefpodoxime proxetil (Cefodox) is a third generation cephalosporin with a broad spectrum of antibacterial activity and a favorable pharmacokinetic profile, which allows twice-daily administration. Cefpodoxime has good *in vitro* activity against the bacterial pathogens that are responsible for common respiratory tract infections such as acute otitis media (AOM), acute sinusitis and tonsillopharyngitis.Cefpodoxime is active against penicillin-susceptible *S. pneumoniae* as well as against penicillin-intermediate strains of *S. pneumoniae.* It also shows good activity against *H. influenzae* (including β-lactamase producing strains). In a study conducted in the USA, cefpodoxime exhibited greater *in vitro* activity against *S. pneumoniae* than did cefaclor, cefuroxime, cefprozil or cefixime. Based on these characteristics, cefpodoxime proxetil is a suitable option for the treatment of pediatric patients with various common bacterial infections (16-19).

In the treatment of lower respiratory tract infections (e.g. pneumonia, bronchitis) in children, cefpodoxime has demonstrated significant efficacy in a number of controlled trials. In comparative trials, cefpodoxime 8 mg/kg/day for 10 days produced rates of clinical cure or improvement (93 and 95%) that were similar to those obtained after 10 days of therapy with cefuroxime axetil 30 mg/kg/day (93%) or amoxicillin/clavulanic acid 40/10 mg/kg/day (97%)(20, 21).

Conclusion: this study demonstrated that theuse of oral third generation cephalosporin Cefodox in children with pneumonia is highly effective, safe and well tolerated. Sowe recommendCefodoxto be considered as an appropriate choice for the empirical treatment of community-acquired pneumonia in children.

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