Review Article

Guide to Diagnosis and Treatment of Acute Pneumonia in Children

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Abstract

By definition, inflammation of the lung parenchyma is called pneumonitis, and if the cause of that inflammation is a microbial agent, it is called pneumonia. Microbial agents can be bacterial, viral, or even parasitic agents. According to the WHO definition, IMCI (Integrated Management of Children's Illness) project, clinically, pneumonia is an acute attack of cough with or without fever, which is accompanied by difficulty breathing or increased breathing rate (tachypnea). After the successful implementation of the control and treatment program for acute gastrointestinal infections and gastroenteritis caused by it, acute respiratory infections and especially pneumonia are considered the most important infectious cause of death of children in developing countries in recent years. Pneumonia diagnosis is mainly a clinical diagnosis that can be divided into three categories bacterial, viral, and acute pneumonia based on four criteria clinical, epidemiology, radiology, and routine laboratory findings. In each case, based on the characteristics of that pneumonia, a possible diagnosis is given and the corresponding treatment is carried out. The correct and accurate knowledge of doctors on how to diagnose and treat this important disease in children without spending extra costs can play a fundamental role in preventing and reducing its mortality and morbidity.

Keywords: Children, Acute pneumonia, Treatment, Diagnosis

Introduction

According to the 2000 statistics published by the WHO, 1.4 million deaths worldwide are caused by acute respiratory infections (ARI) annually, and about 90% of these cases are caused by acute pneumonia. According to the same statistics, 1.9 million of them are children under the age of 5 [1], most of which are related to developing countries due to the underlying factor of malnutrition [2, 3]. On the other hand, acute lower respiratory infection, especially pneumonia, accounts for about 20% of children's deaths. So, for every 1000 children born in developing countries, 12 to 20 children die before the age of 5 due to pneumonia [1, 4, 5]. Therefore, it seems that the burden of disease (burden of disease) of acute respiratory infections and especially pneumonia in children is high [6, 7].

By definition, inflammation of the lung parenchyma is called pneumonitis, and if the cause of that inflammation is a microbial agent, it is called pneumonia. Microbial agents can be bacterial, viral, or even parasitic agents. According to the WHO definition, IMCI (Integrated Management of Children's Illness) project, clinically, pneumonia is an acute attack of cough with or without fever, which is accompanied by difficulty breathing or increased breathing rate (tachypnea) [8]. Of course, this definition is not much different between the two important acute lower respiratory infections, i.e., pneumonia and bronchiolitis, which are not considered, and this is because the presence of tachypnea has a high sensitivity in diagnosing acute lower respiratory infections, especially pneumonia. In other words, fever and tachypnea have high sensitivity and low specificity. Listening to pulmonary rales or pleural pain has high specificity and low sensitivity in diagnosing pneumonia [9, 10].

Classification of Pneumonia

Pneumonia in children can be divided based on different criteria. These classifications are very useful for making decisions about the management and treatment of the disease. Pneumonia is divided into different types based on the origin of the infection, the microbial agent, the clinical process, the

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location of the involvement, the severity of the disease, and the presence or absence of accompanying complications.

Classification of Pneumonia According to the Anatomical Location of Involvement

The classification of pneumonia is divided into one of the following types based on the anatomical location of the involvement. Local pneumonia (lobar, segmental, and round) is limited to one part or one lobe of the lung; Interstitial pneumonia with pulmonary interstitial tissue involvement is usually diffuse and bilateral; And bronchopneumonia, which in this type of involvement, in addition to the alveoli, the involvement of the bronchi and especially the terminal bronchi is also seen.

Classification of Pneumonia Based on the Origin of Infection

Community-acquired pneumonia (CAP) is associated with less antibiotic resistance due to the origin of the disease; Hospital Acquired Pneumonia (HAP) is associated with more antibiotic resistance due to the hospital origin of the infection which is usually transferred to hospitalized patients due to the transfer of microbes colonized in the skin and mucous membranes of hospital personnel with high resistance, such as methicillin-resistant staphylococci (MRSA) colonized in the nasal mucosa [11, 12].

Classification of Pneumonia Based on the Clinical Process

Typical pneumonia, which is usually seen with the sudden onset of high fever and local infiltration in the chest X-ray, is caused by common bacteria such as pneumococcus and Haemophilus influenzae and responds to treatment with beta-lactam antibiotics. Atypical pneumonia, which in this type of pneumonia usually has a gradual course, the fever is usually not high, and the lung lesions in the chest radiograph are diffuse and are caused by common non-bacterial factors such as viruses, mycobacteria, fungi, Mycoplasma, chlamydia, etc. are created and do not respond well to treatment with beta-lactam antibiotics.

Classification of Pneumonia Based on Disease Complications

Noncomplicated pneumonia is pneumonias that do not have specific complications and have a fast recovery process. Complicated pneumonia is pneumonia that is associated with complications such as pleurisy and empyema, pneumothorax, wide atelectasis, or abscesses, and the recovery process is usually slow in these cases.

Pneumonia Classification Based on WHO Proposal in MCI Plan

No pneumonia, which is defined by the presence of cough and other upper respiratory symptoms, without the presence of tachypnea and dysregulation of the child's regulation; mild pneumonia, which is characterized by the presence of respiratory symptoms with tachypnea without respiratory distress in a child; server pneumonia, which is characterized by the presence of respiratory symptoms along with tachypnea and the presence of respiratory distress in the form of retraction of the secondary respiratory muscles in a child. Very severe pneumonia, manifests itself despite the symptoms of severe pneumonia in a child, in addition to one of the symptoms of decreased level of consciousness, convulsions, or severe cyanosis.

Etiology

As mentioned, infectious factors such as bacterial, viral, protozoan, etc. are the factors that cause pneumonia. Of course, in about 25 to 33% of studies, the infectious agent causing pneumonia has not been identified [13-15], or in some cases, pneumonia infection with two microbes has been seen at the same time. So in about 41% of hospitalized patients, due to pneumonia, two or more microorganisms have been identified as their etiological factor [16].

Important Etiological Factors of Pneumonia in Children

Viruses

Viruses are the most common cause of pneumonia in younger children, and their prevalence decreases with age [17]. Important viruses that cause pneumonia in children include RSV, influenza, and rhinoviruses. Other factors such as adenoviruses, parainfluenza, enteroviruses, and coronaviruses are in the next degree. Recently, human metapneumovirus (HPV) has been identified as one of the important causes of viral pneumonia [18]. Of course, the important viral agent of measles, which is considered one of the most important and severe viral pneumonia, is being eradicated due to extensive vaccination coverage [19, 20].

Streptococcus Pneumoniae

Pneumococcus is the most common cause of bacterial pneumonia in all stages of human life, except for infancy [21]. Pneumococcus usually manifests as a typical local pneumonia, but it can be seen in other forms such as pneumonia with effusion, or interstitial pneumonias. Routine use of heptavalent pneumococcal vaccine in some developed countries has reduced pneumonia caused by it. In a large study, the prevalence of radiologically proven pneumonia was reduced by 35% [22].

Haemophilus Influenzae

Another of the two important causes is bacterial pneumonia, especially in children under 5 years of age, and its clinical manifestations are indistinguishable from pneumococcal so that its symptoms vary from mild to severe infection. Due to the use of the Haemophilus influenzae type B conjugate vaccine in developed countries, invasive infections caused by it, including pneumonia, have been significantly reduced [23]. Of course, nontypable Haemophilus influenzae is still an important cause of pneumonia in these countries, especially in developing countries. Unlike type B, which can involve the lungs following bacteremia, this agent usually

causes pneumonia following upper respiratory tract aspiration [24].

Staphylococcus Aureus

Pneumonia caused by it is usually caused in early infancy and usually after an initial viral infection, especially the influenza virus. Pneumonia is usually severe and has a sudden onset, and its progress is fast and accompanied by empyema, abscess formation, and scattered pneumatoceles in the lung. In older children, its clinical and radiological course may not be different from other bacterial causes. 75% of the initial cases of this type of pneumonia are caused by an underlying problem in the child, 65% of which are unilateral and mostly seen under one year of age. Its secondary type is usually bilateral and occurs due to the spread of infection from another place to the lung.

Group a Streptococcus

Pneumonia caused by this microbe is rare in children. One of its characteristics is extensive necrosis of respiratory tract mucosa with edema and bleeding, which prolongs the fever in these patients for days (sometimes even up to ten days despite proper treatment) [25]. Pleurisy and pneumatocele are also seen after this pneumonia.

Gram-Negative Intestinal Bacilli

Pneumonia with these microbial agents is usually seen in infancy or due to underlying immunodeficiency in children, although it is rarely seen in normal children. Pneumonia with Klebsiella pneumoniae is accompanied by severe pneumonia with fever and chills as necrotizing pneumonia or severe tissue destruction. Pneumonia with Pseudomonas aerogenosa or, to a lesser extent, Burkhardria cepacia is an important problem in children with cystic fibrosis (CF).

Anaerobic Bacteria

This group of bacteria is usually seen following aspiration pneumonia in the age after teething, which usually has a slow clinical course and leads to lung abscess if not treated.

Mycoplasma Pneumoniae

It is probably the most common cause of acute pneumonia, especially in children after 5 years [26]. It is usually seen in the photo of the lung in the form of diffuse infiltration, which is sometimes bilateral interstitial pneumonia. Rarely, pneumonia is seen together. Extrapulmonary manifestations are commonly seen as skin, nerve, heart, and blood manifestations so 25% of hospitalized patients with Mycoplasma infection find extrapulmonary symptoms during the disease [27].

Chlamydial Infections

All three types of chlamydia are among the important causes of acute pneumonia. Chlamydia trachomatis is the common cause of pneumonia without fever and is usually bilateral in infants under 4 months, which is mainly the transmission route of the infected mother's vaginal secretions. Chlamydia pneumonia is also an important cause of acute pneumonia in school and adolescent age. Its epidemiology is very similar to Mycoplasma pneumoniae and in most cases, it is asymptomatic [28]. And finally, Chlamydia psittaci, which is usually transmitted by contact with birds and can cause high fever, tonsillitis, and severe headache. An increase in liver enzymes and alkaline phosphatase is one of the characteristics of this rare pneumonia in children.

Clinical Findings

The signs and symptoms of pneumonia vary according to the type of pathogen, the age of the patient, and the severity of the disease. So in small infants, symptoms may be non-specific, and clinical findings may be few. The signs and symptoms of pneumonia in children can be divided into five categories: non-specific symptoms, general symptoms of lower respiratory tract involvement, specific symptoms of pneumonia, symptoms of pleural involvement, and extrapulmonary symptoms.

Nonspecific symptoms include fever, chills, headache, lethargy, restlessness, and anorexia. Common symptoms of lower respiratory tract involvement include cough (which usually starts without sputum and then becomes sputum), tachypnea (which is a sensitive and specific clinical finding in the diagnosis of pneumonia in children), and symptoms of respiratory distress which include grant or Respiratory whine (which is due to the vocal cords coming together and creating a loud breath when exhaling), the use of the secondary respiratory muscles in the form of retraction of the intercostal, subcostal and supracostal muscles, the contraction of the nasal lobes. The specific symptoms of pneumonia are among the important auscultatory symptoms of the lung, which may be in the form of decreased breathing sounds, bronchophony (increasing the intensity of the sound transmitted from the bronchus in the consolidation area), and listening to a fine crackle, especially at the end of the tail. Small audio signals are not reliable. Other important symptoms are chest pain that causes the child to breathe shallower and the child may want to press on the affected lung. Wheezing in auscultation is usually against the diagnosis of pneumonia, but sometimes it is heard in acute pneumonia [29]. Abdominal distention, especially in younger children, due to air swallowing or ileus may also be seen. Chest pain and auscultation friction rub in the early stages of pleurisy cause dyspnea and reduce auditory symptoms in its severe stages, pleural irritation in the lower parts accompanied by abdominal pain and sometimes acute abdomen and pleural irritation in the upper parts with symptoms of meningeal irritation. They are symptoms of pleural involvement. The presence of pleural effusion with pneumonia increases the probability of bacterial infection up to 6 times [17].

Extrapulmonary symptoms, which are mainly seen in optic pneumonia, can be sore throat, headache, skin symptoms (skin rashes such as erythema multiforme, erythema nodosum, urticaria, and Steven Johnson), ear symptoms (otitis media), neurological symptoms (such as aseptic

meningitis, encephalitis, ataxia, and transverse myelitis), blood symptoms (hemolytic anemia and thrombocytopenia), digestive symptoms (increased liver enzymes, diarrhea, and vomiting), cardiac symptoms (myocarditis and pericarditis), rheumatological symptoms (myalgia and polyarthritis) with pulmonary symptoms. Increased respiratory rate (tachypnea) in children is a sensitive and specific finding in the diagnosis of pneumonia in children. The number of breaths should be taken in a full minute while the child is calm.

Diagnosis

In most cases of community-acquired pneumonia (CAP), finding the responsible organism is not necessary, and the diagnosis of pneumonia is clinical, and only in certain cases, such as some cases of hospital-acquired pneumonia (HAP), severe and fulminant pneumonia, and complicated pneumonia. In cases of empyema or pulmonary abscess, cases of progressive pneumonia that do not respond adequately to initial therapy, and patients with underlying disease (such as children with primary immunodeficiency or CF patients), determination of the microorganism involved is essential [30].

It is usually difficult to prepare sputum in children, especially those under 6 years of age, although occasionally hypertonic saline nebulizers are used to obtain sputum in children. The sputum sample is suitable when the number of white blood cells (PMN) is more than 10 and the number of epithelial cells is less than 25 in each microscopic field with a magnification of 10 (LPF) [31].

Preparation of samples from nasopharyngeal secretions for antigen evaluation or microorganism culture is not reliable due to the possibility of natural colonization in that area and is only used in special cases such as some viral infections (RSV and influenza). Taking samples from the throat and oropharynx is usually not useful in determining the etiological agent of pneumonia [32]. The use of invasive methods such as bronchoscopy and preparation of bronchoalveolar lavage (BAL) or closed or open lung biopsy in special cases as gold standard tests are sometimes necessary for definitive diagnosis and appropriate treatment. Blood or pleural fluid culture is also helpful in case of pleurisy. Finding germs in the blood is one of the findings with high specificity, but its sensitivity is low so only about 15% of bacterial pneumonia have a positive blood culture. Therefore, a blood culture is recommended for every child with a possible diagnosis of bacterial pneumonia. Serological tests are used to detect some microorganisms such as Mycoplasma pneumoniae and Chlamydia pneumoniae, and usually, a delayed test is required to evaluate the increase in antibody titer, so the diagnosis is retrospective, and on the other hand, serological tests in children under 6 months of age Low immunological response and transmission of antibodies from the mother is less reliable. A simple immunochromatographic strip test to find bacterial polysaccharides in urine, especially Streptococcus pneumoniae in adults, is an acceptable and quick test to diagnose pneumonia. This test is not reliable due to false positive cases caused by the colonization of the pharynx and nasopharynx in children, especially in developing countries where up to 60 to 90% of children carry pneumococcus in their throat [33].

Basically, after the diagnosis of pneumonia in children, it is usually divided into three categories bacterial, viral, and acute pneumonia based on the sum of the four findings below. 1- Clinical findings, 2- Epidemiological findings, 3- Radiological findings, 4- Primary laboratory findings such as ESR, CBC, and CRP.

Treatment of Patients

Based on the MCI method, the treatment of patients in four groups is as follows: 1- No Pneumonia: does not require antibiotic treatment; 2- Mild Pneumonia: patients are treated with oral antibiotics including amoxicillin or cotrimoxazole (amoxicillin is preferred over cotrimoxazole due to existing resistances) [34]) for a period of 3 to 5 days; 3: Severe Pneumonia: the patient is hospitalized and treated with intravenous antibiotics; 4: Very severe Pneumonia: the patient is hospitalized in the intensive care unit and is treated with antibiotics. Following the use of this method in developing countries, a decrease in mortality due to pneumonia has been seen by about 40% in children under 5 years of age [35].

According to the four findings including epidemiology findings, clinical findings, radiology findings, and routine laboratory findings, one of the three types of bacterial, anti-peak, or viral pneumonia is considered for the patient. The increasing resistance of penicillin-resistant pneumococci is a very important point, but the more important point is that if the infection is limited to the lungs and the patient only has pneumonia, still penicillins are the primary drugs of choice, and only increasing their dose will cause them to break. resistance to penicillin [36]. Intravenous cephalosporins of the 3rd generation are the drugs of choice, and vancomycin is added to the treatment in cases where there is no initial response and the pneumococcal MIC to penicillin is higher than 4 μg/dl.

Maintenance Treatments

In addition to antibiotic treatment, maintenance treatments play a very important role in the treatment of pneumonia in children. These treatments include:

Oxygen

Following hypoxia in pneumonia, the main mechanism of which is the imbalance between ventilation and perfusion, retraction of the intercostal muscles occurs due to a compensatory mechanism due to the soft sternum, more horizontal ribs, and weaker intercostal muscles in children. This compensatory mechanism to prevent the lungs from sleeping on top of each other cannot work for a long time, and therefore preventing hypoxia and resulting acidosis plays an

important role in the treatment of severe pneumonia, especially in children [37]. According to the WHO recommendation, it is recommended to give oxygen preferably with a nasal probe to every child with one of the symptoms of cyanosis, inability to eat, and breathing rate of more than 60 per minute [38].

Proper Nutrition and Hydration of the Child

Malnutrition is one of the important risk factors in the morbidity and mortality of children with pneumonia. In addition, starting oral nutrition and proper hydration of a child with severe pneumonia as soon as possible plays an important role in accelerating the child's recovery. Vitamin A deficiency doubles the risk of respiratory infection and mortality from pneumonia [39]. Therefore, malnutrition and lack of vitamin A, play an important role in the prognosis of patients. On the other hand, administration of sulfate at the same time reduces the prevalence of pneumonia by 40% and the duration of hospitalization by 25% [40].

Bed Rest and Positioning of the Patient

Sufficient rest, reducing the child's stress, and raising the patient's head to 30-45 degrees is a suitable position for the patient. An important point that should be mentioned here is the role of chest physiotherapy in the treatment of acute pneumonia, based on studies conducted in adults, in patients who do not have a specific underlying disease, chest physiotherapy is very beneficial for the patient and improves the prognosis [41].

Duration of Antibiotic Treatment

According to the IMCI plan, if oral treatment is chosen, a treatment period of 3 to 5 days is sufficient. However, it seems that oral treatment is different according to the type of crime. So, in cases of mild bacterial pneumonia, the treatment period is 5 to 7 days, and in future cases, the treatment period is 10 to 14 days. If hospitalization is required and injection treatment is started, if clinical symptoms improve and fever ceases for 48-72 hours and ESR decreases by 20%, as well as CRP decreases, intravenous treatment can be changed to oral treatment. The duration of treatment depends on the possible cause of pneumonia (for example, in staph aureus pneumonia, the duration of treatment can be about 3 to 6 weeks), the speed of the initial clinical response to treatment, and the presence or absence of complications of pneumonia (such as pleurisy, etc.).

Prevention

The use of the seven-valent pneumococcal vaccine (Heptavalan) in developing countries since 2000 and the Hemophilus influenza type B vaccine since 1990 has caused a significant reduction in the rate of invasive infections, including pneumonia, with these two microorganisms [42, 43]. Of course, today there is a study on the injection of 14-valent pneumococcal vaccine in pregnant mothers in the last months of pregnancy to prevent pneumococcal infection in small infants [44].

According to statistics, following the injection of the Heptavalan vaccine, there has been a 20-88% reduction in invasive pneumococcal infections. In a study in Belgium, the use of a 9-valent pneumococcal vaccine instead of a 7-valent vaccine was associated with a decrease in invasive pneumococcal infections from 45% to 73%. Influenza vaccine injection in children older than 6 months in recommended cases can reduce the risk of this infection and bacterial infections added to it [41, 45, 46].

Conclusion

After the successful implementation of the control and treatment program for acute gastrointestinal infections and gastroenteritis caused by it, acute respiratory infections and especially pneumonia are considered the most important infectious cause of death of children in developing countries in recent years. Pneumonia diagnosis is mainly a clinical diagnosis that can be divided into three categories bacterial, viral, and acute pneumonia based on four criteria clinical, epidemiology, radiology, and routine laboratory findings. In each case, based on the characteristics of that pneumonia, a possible diagnosis is given and the corresponding treatment is carried out. The correct and accurate knowledge of doctors on how to diagnose and treat this important disease in children without spending extra costs can play a fundamental role in preventing and reducing its mortality and morbidity.

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