Antibiotic therapy of acute upper respiratory tract infections and otitis media in adults

Antybiotykoterapia ostrych zakażeń górnych dróg oddechowych i ucha środkowego u dorosłych

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ABSTRACT: An estimated 50% of antibiotic prescriptions may be unjustified in the outpatient setting. Viruses are responsible for most acute respiratory tract infections. The viral infections are often self-limiting and only symptomatic treatment remains effective. Bacteria are involved in a small percentage of infections etiology in this area. In the case of a justified or documented suspicion of a bacterial infection, antibiotic therapy may be indicated. Based on the Polish „Recommendations for the management of non-hospital respiratory infections 2016”, the indications, the rules of choice, the appropriate dosing schedules and the therapy duration, in the most frequent upper respiratory tract infections in adults, have been presented. Implementation of the presented recommendations regarding our Polish epidemiological situation, will significantly reduce the tendency to abuse antibiotics, and thus will limit the spread of drug-resistant microorganisms.

KEYWORDS: antibiotics, drug resistance, acute rhinosinusitis, acute pharyngitis, acute laryngitis, acute otitis media

INTRODUCTION

The word infection makes doctors think of prescribing antibiotics to their patients. Because of an increasing microbial resistance to antibiotics, particularly in bacteria, doctors must use antibiotics prudently. Several important documents have set out the principles of rational antibiotic therapy for patients with infections of the respiratory tract. For instance, it is fundamental to use antibiotics for only bacterial infections of the respiratory tract, with an aim to eradicate the bacteria from the site of infection, which is also a measure of effectiveness. [1,2] In the USA, acute infections of the upper respiratory tract...
and bronchi are the most common reason for giving antibiotics, and antibiotics are prescribed for adult patients during 100 million outpatient visits per year. [3,4] Notably, although in 85% to 90% of patients acute pharyngitis is due to viral infections, over 70% of these patients receive antibiotics. Unofficial data indicate that more than a half of antibiotic prescriptions in the outpatient setting are unnecessary or wrong. [3,5] Such an unwarranted use of antibiotics for acute respiratory infections increases the prevalence of multidrug resistant bacteria. [5] In the USA, diseases related to antibiotic resistance cause 23,000 deaths per year. Antibiotics are also the most common cause of drug-induced adverse events; antibiotics cause adverse effects in 5% to 25% of patients. Diarrhea due to infections with Clostridium difficile is one of the most serious adverse effects of antibiotics. In the USA, infections with Clostridium due to antibiotics cause more than 29,000 deaths per year. [3] Thus, doctors should feel obliged to prescribe antibiotics rationally.

Each year we know more and more about microbial resistance in Poland. Data from the National Reference Center for Bacterial Susceptibility to Drugs (appointed by the Minister of Health in 1997), the National Center for Diagnosis of Bacterial Infections of the Central Nervous System, and other Polish centers were used to formulate guidelines for the treatment of respiratory infections (the document titled “Recommendations for the management of community-acquired respiratory infections in 2016”). [5] These guidelines take into account the Polish epidemiological situation and thus differ from the European and American guidelines.

Viruses cause most of acute respiratory infections. These viruses include rhinoviruses, adenoviruses, coronaviruses, influenza and parainfluenza viruses, the respiratory syncytial virus, and enteroviruses. By damaging the respiratory epithelium, viruses might pave the way for bacterial infections. Viruses cause most of acute inflammatory diseases of the nose, sinuses, throat, larynx, and middle ear. In the outpatient setting, acute bacterial infections of the respiratory tract are much less common than viral infections. Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes cause most of the bacterial infections of the respiratory tract. [5] Thus, when bacterial infections of the respiratory tract are suspected or diagnosed, penicillin, cephalexin, macrolides, lincosamides, and fluoroquinolones are the best antibiotics.

**ACUTE RHINOSINUSITIS**

Acute rhinosinusitis is an inflammatory condition involving the mucous membrane of the nose and paranasal sinuses; it has an abrupt onset and lasts no longer than 12 weeks. Symptoms with diagnostic importance for rhinosinusitis include impaired nasal patency, rhinorrhea (serous-mucous, mucopurulent, purulent), mucus drip on the back wall of the pharynx, pain or fullness in the face, and impaired olfaction. The European guidelines (EPOS 2012) define the following types of rhinosinusitis:

- acute viral rhinosinusitis (common cold), in which the symptoms are self-limiting and last no longer than 10 days,
- acute post-viral rhinosinusitis, in which the symptoms persist for more than 10 days but no longer than 12 weeks; the symptoms may worsen after 5 days,
- bacterial rhinosinusitis, which is characterized by the presence of at least three of the following symptoms: purulent rhinorrhea (mainly unilateral) or purulent secretion in the nasal passages, severe localized pain (more severe on one side), fever (>38 °C), increased erythrocyte sedimentation rate or an increased concentration of c-reactive protein, and worsening of symptoms after an initial mild disease. The European guidelines stress that bacterial rhinosinusitis may develop at any stage described above. [6]

Typically, rhinosinusitis is caused by viruses (rhinoviruses, coronaviruses, the respiratory syncytial virus, influenza and parainfluenza viruses, adenoviruses), and bacterial infection might follow, but only in 0.5% to 2% of cases. *S. pneumoniae* and *H. influenzae* are responsible for nearly 80% of bacterial rhinosinusitis cases. Other bacteria that can cause rhinosinusitis are *M. catarrhalis*, *Staphylococcus aureus*, and *S. pyogenes*. Based on studies than analyzed various symptoms and ancillary findings (computed tomography and aspiration of sinus material) in patients with acute rhinosinusitis, the symptoms that might indicate bacterial rhinosinusitis are unilateral facial pain, dental pain in the jaw, unilateral sinus tenderness, and mucopurulent rhinorrhea. However, none of these symptoms is sensitive enough to diagnose bacterial rhinosinusitis. The type of rhinorrhea, particularly if purulent, can differentiate between viral and bacterial infections. Because obtaining material for reliable microbiological tests is invasive, it is not recommended in everyday clinical practice. However, it should be considered in patients with an atypical course of rhinosinusitis or complications, as well as in patients with immunodeficiency. [5] According to the American recommendations, bacterial rhinosinusitis might be characterized by symptoms persisting for more than 10 days, severe symptoms, high fever (>39 °C), purulent rhinorrhea, facial pain for at least 3 consecutive days, clinical deterioration after initial improvement, and symptoms of a viral disease for at least 5 days. [3]

Only symptomatic treatment is recommended for viral rhinosi-
nusitis. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment for viral rhinosinusitis when there are no contraindications. Other treatments can be used as well, such as analgesics (paracetamol), nasal rinsing with saline solutions, nasal decongestants (up to 7 days), intranasal preparations with ipratropium bromide, and plant-derived secretolytic agents. In post-viral rhinosinusitis, as in all chronic respiratory infections, the mucous secretions become thicker, which promotes bacterial infections. Therefore, adequate drainage of the nasal cavities and paranasal sinuses by proper hydration and humidification of inhaled air is important. The European and Polish guidelines recommend nasal glucocorticoids for post-viral rhinosinusitis; glucocorticoids can reduce inflammation and nasal edema, and they can improve the drainage of mucus. In bacterial rhinosinusitis, nasal glucocorticoids are recommended in addition to systemic antibiotic therapy, which considerably shortens the treatment. Antibiotics are recommended for acute bacterial rhinosinusitis only. [5,6] Antibiotics for bacterial rhinosinusitis should be active against S. pneumoniae and H. influenzae. According to the Polish recommendations, which take into account the resistance of local bacteria, amoxicillin is the drug of choice for the treatment of bacterial rhinosinusitis. Amoxicillin was chosen as the first-line drug because it has a high activity against pneumococci, including strains with a reduced sensitivity to penicillin (provided that a sufficiently high dose is used). Amoxicillin has a similar effectiveness as other antibiotics with a broader spectrum; moreover, H. influenzae strains producing beta-lactamases are rare in Poland. Because the prevalence of pneumococci with reduced sensitivity to penicillin has risen considerably in Poland, amoxicillin should be used at a dose of 1.5 g to 2 g every 12 hours for 10 days (in adults). If no improvement is seen after using amoxicillin for 48 hours, a different antibiotic should be given, and the patient should be referred to a specialist. [5]

Amoxicillin is a beta-lactam antibiotic, and all beta-lactam antibiotics have a beta-lactam ring; other beta-lactams available in Poland include penicillin, cephalosporins, carbenapens, and beta-lactamase inhibitors. The beta-lactam antibiotics inhibit the synthesis of the cell wall in susceptible bacteria, which kills the bacteria. The antibacterial effectiveness of beta-lactam antibiotics is the higher, the longer their concentrations remain above the minimum inhibitory concentration for a given bacterial strain. Amoxicillin is a penicillin with a wide range of actions; it kills most streptococci (including S. pneumoniae), staphylococci (including S. aureus, but only MSSA - methicillin-sensitive), anaerobes, and many Gram-negative bacilli, including H. influenzae. Unfortunately, amoxicillin is deactivated by beta-lactamases produced by various bacteria. For instance, beta-lactamases that hydrolyze natural penicillins, aminopenicillins, and ureidopenicillins, provide antibiotic resistance to certain H. influenzae strains. In Poland, the percentage of these beta-lactamase-producing H. influenzae strains remains small in the respiratory tracts of people in the community. Adding a beta-lactamase inhibitor, such as clavulanic acid, to amoxicillin makes H. influenzae sensitive to treatment. [7]

If the first-line treatment is ineffective, the Polish guidelines recommend to use amoxicillin with clavulanic acid at a dose (calculated for amoxicillin) of 1.5 g to 2 g every 12 hours for 10 days. If the patient is allergic to penicillin, oral cefuroxime axetil is recommended at a dose of 0.5 g every 12 hours for 10 days. If the patient is allergic to all beta-lactam antibiotics, clarithromycin at a dose of 0.25 g to 0.5 g every 12 hours, levofloxacin at a dose of 0.5 g once a day, or moxifloxacin at a dose of 0.4 g once a day for 5-10 days can be used. [5]

**ACUTE PHARYNGITIS**

In adults, 90% to 95% of acute pharyngitis cases are caused by viruses. Most commonly, these are rhinoviruses, coronaviruses, adenoviruses, the Epstein-Barr virus, the Coxsackie virus, herpes simplex viruses, and influenza and parainfluenza viruses. The remaining 5% to 10% are caused by bacteria, most often by S. pyogenes (group B beta-hemolytic streptococci), less often by group C and G streptococci, and extremely rarely (<1% of cases) by Mycoplasma and Chlamydia pneumoniae, Neisseria gonorrhoeae, Corynebacterium diphtheriae, Arcanobacterium haemolyticum, and anaerobic bacteria, such as Fusobacterium necrophorum). [3,5]

Because most patients with acute pharyngitis have viral infections, analgesics and antipyretics are sufficient. In the USA, pharyngitis is the reason for 12 million outpatient visits per year, and more than 60% of patients with sore throat receive antibiotics, which, clearly, is too much. [3] However, patients with bacterial infections must be treated with antibiotics. Both medical and physical examination have low specificity and sensitivity in the differentiation between viral and bacterial pharyngitis. First, the clinician should assess the likelihood of a streptococcal infection. If viral pharyngitis is diagnosed, no further workup is necessary; however, if bacterial pharyngitis is suspected, microbiological tests can confirm or exclude this diagnosis. It is necessary to identify patients with group A streptococcal infections. The clinical score developed by Centers and modified by be can be used to assess the likelihood of infection with S. pyogenes

Give one point each for a fever (>38° C), lack of cough, enlarged cervical lymph nodes, fibrin exudate on tonsils or tonsil swelling, and age 3-14 years. Subtract one point for age >
Acute laryngitis is an inflammation of the vocal folds and the surrounding tissues, and it lasts up to 3 weeks. In adults, acute laryngitis is usually caused by infections, irritants (cigarette smoke, air pollution), or voice strain. The disease is usually self-limiting. Acute laryngitis is usually viral. Therefore, hydration, humidification, and voice saving are the mainstay of treatment. Antibiotics are rarely needed in patients with acute laryngitis. A systematic review showed that patients with acute laryngitis do not require antibiotics unless there is a clear evidence of co-existing bacterial pharyngitis. Improper use of antibiotics in patients with acute laryngitis increases the risk of antimicrobial resistance.

Systemic glucocorticoids do not bring clear benefit to patients with acute laryngitis and should be used only in patients who cannot refrain from using their voice. Although clinical practice shows that glucocorticoids might be effective in acute laryngitis, there is no evidence from randomized trials. Nebulization with glucocorticoids can be an alternative to oral glucocorticoids in acute laryngitis. [10]

**ACUTE OTITIS MEDIA**

Acute otitis media is characterized by a sudden occurrence of symptoms due to inflammation or infection within the middle ear. It occurs most often in children. It is estimated that 80% of children experience at least one episode of acute otitis media until the age of 6. After the age of 7, the incidence of otitis media decreases. There are no reliable data on the incidence of acute otitis media in adults, with most studies focusing on children. In adults, treatment guidelines for acute otitis media are de-
riological tests of samples from the throat or nasopharynx are not necessary for choosing treatment. [5]

In patients with acute otitis media, antibiotics should be active against \textit{S. pneumoniae} and \textit{H. influenzae}. For similar reasons as in acute pharyngitis, amoxicillin, administered orally at a dose of 1.5g to 2 g every 12 hours, is effective for acute otitis media. The best duration of antibiotic therapy in patients with acute otitis media is being discussed. The Polish guidelines recommend a 5-day course of antibiotics for uncomplicated acute otitis media. Cephalosporins and clarithromycin (a macrolide) are alternatives to amoxicillin. If the patient is allergic to amoxicillin (delayed hypersensitivity), cefuroxime axetil can be given orally at a dose of 0.5 g twice a day for 5 days (in adults). In more severe cases, third-generation cephalosporins can be given (ceftriaxone, 1-2 g once daily, intravenously or intramuscularly for 3 days). If the patient is allergic to beta-lactam antibiotics (delayed hypersensitivity to all beta-lactams or immediate hypersensitivity to any beta-lactam), clarithromycin can be given orally (0.25 g to 0.5 g every 12 hours for 10 days). It is accepted that clarithromycin is the only macrolide effective in the treatment of acute otitis media. Azithromycin should not be used in patients with acute otitis media because it was proven effective only at a large dose (2 g, not registered in Poland) and only in children. [5,13]

Tab. 1. Centor and Molsaak’s score

<table>
<thead>
<tr>
<th>SYMPTOM / FEATURE</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body temperature &gt; 38°C</td>
<td>1</td>
</tr>
<tr>
<td>There is no cough</td>
<td>1</td>
</tr>
<tr>
<td>Enlarged cervical lymph nodes</td>
<td>1</td>
</tr>
<tr>
<td>Exudate on and swelling of the tonsils</td>
<td>1</td>
</tr>
<tr>
<td>Age 3-14 years</td>
<td>1</td>
</tr>
<tr>
<td>Age 15-44 years</td>
<td>0</td>
</tr>
<tr>
<td>Age &gt; 45 years</td>
<td>-1</td>
</tr>
</tbody>
</table>

Management depends on the total score

<table>
<thead>
<tr>
<th>TOTAL SCORE</th>
<th>LIKELIHOOD OF STREPTOCOCCAL INFECTION</th>
<th>RECOMMENDED MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>&lt;10%</td>
<td>Symptomatic treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacteriological workup is unnecessary</td>
</tr>
<tr>
<td>2–3</td>
<td>2 points: 11 - 17%</td>
<td>3 points: 28 - 35%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Give treatment depending on the result</td>
</tr>
<tr>
<td>4–5</td>
<td>38–63%</td>
<td>- severe symptoms - prescribe an antibiotic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- mild symptoms - perform a quick streptococcal antigen test; if not available, a throat swab culture is recommended; Give treatment depending on the result.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Give antibiotics when the bacteriological workup is pending; Discontinue antibiotics if the bacteriological workup is negative</td>
</tr>
</tbody>
</table>

Antibiotics are the mainstay of treatment in adults with uncomplicated purulent acute otitis media because they accelerate the resolution of symptoms, eradicate bacteria from the middle ear, and prevent purulent complications. Bacteriological examinations of the exudate from the middle ear is not routinely needed in children and adults with acute otitis media, and antibiotics are chosen based on epidemiological data. Bacteriological tests of samples from the throat or nasopharynx are not necessary for choosing treatment. [5]

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(calculated for amoxicillin) of 1.5 g to 2 g every 12 hours. In patients with septic symptoms or persistently recurring otitis media, ceftriaxone is the drug of choice. [5 – 12]

CONCLUSION

Viruses are responsible for about 80% of all acute infections of the respiratory tract. These diseases are often self-limiting, and symptomatic treatment is usually sufficient. In patients with infections of the respiratory tract, it is fundamental to use antibiotics only when there is evidence of bacterial infection.

References
