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REVIEW ARTICLE

Recommendations on the use of antimicrobials in upper respiratory tract infections in pediatrics

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Abstract

Objective: The aim of this study was to update the topic by reviewing the literature and determining the most recent studies on the most common upper respiratory tract infections. **Method:** We searched on Medline, PubMed, Scielo, Lilacs and Cochrane platforms, using keywords on the topic. After selecting the main papers, we carried out the analysis. **Final remarks:** upper airway infections are part of the majority of outpatient consultations and ER visits, and it is imperative for professionals who care for children to be constant updating their knowledge and skills so that their work can be performed in the right way. One of the most worrying problems is the prescription of antimicrobials, which has been occurring indiscriminately. Therefore, it is necessary to revise the criteria for the correct conduct in the face of UAI and the indication of antimicrobials, in order to avoid this increased incidence of bacterial resistance, adverse effects and the unnecessary rise in treatment costs.

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INTRODUCTION

Upper airway infections (UAI) are one of the main health problems in children. In the Americas, UAI account for 40% to 60% of pediatric consultations and are the main reason for the use of antibiotics in children[1]. Despite advances in knowledge about the etiology and pathophysiology of diseases and the emergence of new drugs and vaccines, acute respiratory infections remain the most important cause of morbidity and mortality in children under five years of age[2].

In most countries, the three groups of drugs most commonly used in children - antibiotics, analgesics/antipyretics and respiratory medications - are indicated for the treatment of these problems. Many of these drugs are used inappropriately, especially concerning problems related to the use of antibiotics to treat infections of viral etiology[2].

Although most infections are viral, a large percentage are treated with antibiotics. Overuse of antibiotics may lead to resistance, increased cost, and increased incidence of adverse effects, including anaphylaxis[3].

Antimicrobial-resistant bacterial infections are reported to affect around 2 million people and are associated with 23,000 deaths annually in the United States, a major problem that underscores the importance of determining the correct use of such drugs to reduce these figures. However, the numbers concerning the inappropriate use of antibiotics and how likely they are to be reduced is still unknown. What is known is that between the years 2010 and 2011, half the prescriptions of antibiotics for acute respiratory diseases may have been unnecessary, which is an alarming figure[4].

Thus, the objective of this article is to present an updated literature review on the use of antimicrobials in the most common upper respiratory tract infections in daily practice, such as the common cold, rhinosinusitis, pharyngotonsillitis, acute otitis media and laryngitis. The diagnosis, propaedeutic and therapeutics indicated in the most current articles in the medical literature will be discussed, as will the indiscriminate use of these drugs.

MATERIALS AND METHODS

This paper is a review of the literature, aimed at determining, among the most current papers, the diagnosis, propaedeutics and therapeutics of upper respiratory tract infections in pediatrics, emphasizing the prevention of abusive use of antimicrobials, and criteria for the administration of such drugs.

The information was taken from papers found in databases such as Medline, PubMed, Scielo, Lilacs and Cochrane. The search was based on key words, such as antimicrobials in pediatrics; upper airway infections; acute otitis media; acute rhinosinusitis; acute pharyngotonsillitis; acute laryngitis. We selected review papers on the topic, most of them were published in the last 6 years.

COMMON COLD

The common cold is a disease that causes acute inflammation of the nasal or pharyngeal mucosa, but unrelated to other specific respiratory conditions[5]. It is a mild, self-limiting upper airway infection with running nose, sore throat, sneezing and nasal congestion[3]. Although it is a benign condition, the common cold causes a great economic burden, since it requires several visits to doctors and consumption of large numbers of medicines. Symptoms begin two days after virus inoculation in patients infected with rhinovirus or coronavirus and after five days in those infected by the respiratory syncytial virus. Symptoms persist for at least 5 days in 50% of the patients, but 5% to 10% of children may have persistent symptoms for up to 10 days[1].

The etiology of the common cold is diverse. Children, the elderly and other age groups with comorbidities such as prematurity, chronic lung disease, congenital heart disease and asthma are not more prone to having a common cold caused by respiratory syncytial virus, rhinovirus, parainfluenza, coronavirus, and adenovirus, with rhinovirus accounting for 50 to 80% of common colds. The main factors that contribute to the spread of this disease are poor hand hygiene, overpopulation, and attending nurseries and schools[6].

Kenealy & Arroll[5] carried out a study evaluating randomized clinical trials from 1966 to 2009 comparing antibiotic therapy with placebo in people who had symptoms of acute UAI, of less than seven days of duration or acute purulent rhinitis of less than 10 days of duration. The authors concluded that antibiotics offer no benefit to the initial treatment of the common cold and acute purulent rhinitis.

Regarding prevention of the common cold, Simancas-Racines and collaborators[6] mention vaccination as an important measure, but the development of vaccines for the common cold has been challenging, given the existence of a multiple etiology and antigenic variability of the causative viruses.

Although the vaccines against rhinovirus, adenovirus and respiratory syncytial virus are still under intense study due to the described variability, there is already a vaccine against parainfluenza virus, which is safe and immunogenic in seronegative children in the age group of 6 and 18 months, which can still be demonstrated in randomized trials[6].

ACUTE RINOSINUSITIS

Acute rhinosinusitis is a common diagnosis in the outpatient setting. It is defined as inflammation of the nasal mucosa and paranasal sinuses. Rhinosinusitis is classified as acute when symptoms are present for less than 4 weeks, subacute from four to twelve weeks, and chronic for more than 12 weeks[3]. The most common bacterial agents are Streptococcus pneumoniae, non-typing Haemophilus influenzae and Moraxella catarrhalis[7].

Differentiation between viral and bacterial rhinosinusitis is important because the antimicrobial treatment of all cases would result in excessive prescription of antibiotics[3]. Therefore, before establishing the diagnosis of acute bacterial sinusitis, it is important for the physician to differentiate between subsequent episodes of uncomplicated viral UAI from the establishment of acute bacterial sinusitis with persistent symptoms; and decide on which symptoms are not clearly improving[7].

Chow et al.[8] carried out a study with recommendations on the diagnosis, propaedeutics and therapeutics of acute rhinosinusitis. His paper shows some ways to differentiate bacterial rhinosinusitis from its viral counterpart. As for viral infections of upper airways, they are characterized by the presence of nasal symptoms (congestion and obstruction) and/or cough, and may present with odynophagia.

The nasal secretion usually begins hyaline; however, in several cases it evolves into thicker secretion, until it becomes purulent, reverting to hyaline within days. In this case, due to the characteristic evolution of viral infections, there is the benefit of using antibiotics. Most of these patients do not develop a fever, but if there is a fever, it occurs at the onset of the disease and is accompanied by constitutional symptoms, such as headache and myalgia. Typically, fever and constitutional symptoms disappear within the first 24-48 hours, when the respiratory tract symptoms become more prominent. In most cases of uncomplicated respiratory infections of the upper respiratory tract, respiratory symptoms last 5-10 days, peaking from 3 to 6 days, with improvements thereafter[8].

Already considering the diagnosis of acute bacterial rhinosinusitis, one should be aware of the unfavorable evolution of the common cold, such as persistent purulent rhinorrhea, persistent nocturnal cough, face pain, halitosis, lasting more than or equal to ten days without signs of improvement. Another aspect is the appearance of severe symptoms or signs such as high fever (> 39ºC), purulent nasal discharge or facial pain lasting for up to 3-4 consecutive days at the onset of illness; or appearance of symptoms or signs of worsening, characterized by a new onset of fever, headache or increased nasal secretion after an upper airway viral infection that lasted 5-6 days and initially improved (biphasic evolution)[8].

Wald et al.[7] published a review of the literature on the subject, where they proposed evidence-based behavior. According to their publication, the physician may prescribe antibiotic therapy for acute bacterial sinusitis in children with severe or worsening conditions, since: a) Children who present with a more severe condition presumably have a bacterial infection, because the axillary temperature of at least 39°C/102.2°F along with at least 3 consecutive days of purulent nasal secretion is not consistent with the already well-documented viral UAVI; b) Children with worsening of the UA infection have an evolution that is not compatible with the pattern of uncomplicated viral UAI[7].

In the case of persistent progression of UAI, the doctor can either prescribe antibiotic therapy, or offer the family the option to observe the evolution of the condition for 3 days. Such a decision should be made jointly with those responsible for the patient in question[7].

The factors that will influence this decision are the degree of severity of symptoms, patient quality of life, recent antimicrobial use, concern of those responsible with possible side effects of antibiotics, previous experiences with similar conditions, the cost of antibiotics and its ease of administration, the persistence of respiratory symptoms or the development of complications[7].

Children with acute bacterial sinusitis who have received antibiotic treatment within the past four weeks or who have another associated bacterial infection, or who have at least signs or symptoms of suspected acute sinusitis complications, or patients with underlying conditions are usually managed with antibiotic therapy[7].

Such guidelines help in deciding what course of action should be taken in view of the fact that the limitation in the use of antibiotics in children with persistent conditions decreases the adverse effects related to their use, such as diarrhea, diaper rash and skin rash, as well as decreased growth of bacterial resistance[7].

Regarding the choice of antimicrobial, for children 2 years of age and older, with uncomplicated mild to moderate, acute bacterial sinusitis who do not attend daycare centers and has not used antibiotics in the last 4 weeks, amoxicillin in the initial dose of 45mg/kg/day bid[7].

In the case of communities with a high prevalence of non-susceptible Streptococcus pneumoniae, treatment should be started at 80-90 mg/kg/day bid, at a maximum dose of 2 grams per dose. In the case of patients with moderate to severe disease, as young as < 2 years of age, who attend day care or who have used antibiotics in the last 4 weeks, should receive amoxicillin with clavulanic acid (80-90 mg/kg/day and amoxicillin and 6.4 mg/kg/day of clavulanic acid). If the patient is allergic to amoxicillin, a recommended option would be a cephalosporin[7].

Zoorob et al.[3] reported that short-term (five-day mean) antibiotic therapy was as effective as long-term treatment (mean of 10 days) in patients with uncomplicated acute bacterial rhinosinusitis.

ACUTE PHARYNGOTONSILLITIS

Pharyngotonsillitis is defined by inflammation of the pharyngeal structures with the onset of erythema, edema, pharyngeal exudate, ulcers and vesicles. Most cases of pharyngotonsillitis are of viral etiology before three years of age, and parainfluenza, influenza and coronavirus infections are characterized by a mild condition associated with symptoms such as cough and coryza. Adenovirus infections can generate

exudative pharyngotonsillitis with adenomegaly lasting up to 7 days, often associated with conjunctivitis. The viral-related symptoms are of spontaneous resolution[1].

In the case of bacterial plaques, group A beta-hemolytic Streptococcus is the bacterium that most commonly causes acute pharyngotonsillitis, accounting for 20-30% of odynophagia in children. Accurate diagnosis of streptococcal pharyngotonsillitis associated with an appropriate antimicrobial treatment is important for the prevention of rheumatic fever; for the prevention of suppurative complications (such as peritonsillar abscess, cervical lymphadenitis, mastoiditis, and possibly other invasive infections); for the relief of signs and symptoms; for the rapid decrease in transmission of Group A beta-hemolytic Streptococcus to family members, classmates and other contactors; to allow a quick return to normal activities; and to minimize the potential adverse effects due to inappropriate antibiotic therapy[9].

Shulman et al.[9], state that upon diagnosis, the signs and symptoms of streptococcal pharyngotonsillitis are so easily confused with those of non-streptococcal pharyngotonsillitis that it is impossible to make a clinical-based diagnosis, except when there are viral characteristics such as rhinorrhea, oral ulcers, and/or hoarseness. Therefore, for an accurate diagnosis, an oropharynx swab should be performed for a rapid antigen detection for Group A beta-hemolytic Streptococcus, and/or culture.

In children and adolescents, the rapid strep test should be confirmed with a culture, but if the rapid test is positive, there is no need for it because of its high specificity. The aforementioned rapid tests should not be done in patients with clinical signs that strongly suggest viral infection and in children younger than 3 years, because rheumatic fever is rare in this age group and so is streptococcal pharyngotonsillitis[9].

Post-antibiotic monitoring with culture or rapid test is not recommended, but should be considered in special cases. ASLO (Anti Streptococcal Antibody) dosage is not recommended as it reflects past, not current, events. Regarding diagnostic tests and empirical treatment of close contacts of patients with acute streptococcal pharyngotonsillitis, it is not routinely recommended[9].

These authors discuss extensively about the inadequate use of antimicrobials in cases of UAI, especially in pharyngotonsillitis. They state that despite the decrease in the prescription of unnecessary antimicrobials, there are still a large number of patients being treated with such drugs, which has contributed to the emergence of bacterial resistance to common antimicrobials. However, if the bacterial infection is confirmed, treatment with penicillin or amoxicillin should be initiated and, in the case of allergy to them, first-generation cephalosporin (for patients whose allergy does not generate anaphylactic shock) can be treated with 10 days, clindamycin or clarithromycin for 10 days, or azithromycin for 5 days[9].

ACUTE OTITIS MEDIA

Acute otitis media is an infection of the middle ear characterized by rapid onset of signs and symptoms of inflammation. Otalgia, fever, irritability and difficulty sleeping are frequently present, and symptoms of infection of the upper airways preceding otitis are common[10,11].

The most common pathogens are H. influenzae, S. pneumoniae, and M. catarrhalis. Viruses are among the causes of acute otitis media, and may be responsible for several cases of antibiotic treatment failure. In infants less than 8 weeks of age, one should think of Group B Streptococcus, gram-negative enterobacteria and Chlamydia trachomatis[3].

The following are risk factors for acute otitis media: the increase of respiratory infections due to the attendance of day care centers; exposure to cigarette smoke and other irritants and allergens that may interfere with Eustachian tube function; absence of breast milk supply; decubitus feeding; use of pacifiers in infants and older children; family history of recurrent acute otitis media; craniofacial abnormalities; immunodeficiency; and gastroesophageal reflux.

This same study provides recommendations for the diagnosis of AOM (acute otitis media) in children. For this, they should present moderate to severe tympanic bulge or new appearance of otorrhea not related to acute external otitis; light bulging of the tympanic membrane and recent onset (less than 48 hours) of otalgia (or the act of holding, rubbing or pointing for those children who do not speak) or intense hyperemia of the tympanic membrane.

Another recommendation to be aware of is not to diagnose AOM in children who do not have fluid in the middle ear, based on pneumatic otoscopy and/or tympanometry.

Regarding treatment, the physician should always prescribe antibiotic therapy for uni/bilateral AOM in children aged 6 months or less. In children older than 24 months with bilateral AOM with no signs or severe symptoms (e.g., moderate to severe otalgia for at least 48 hours or a temperature higher than or equal to 39°C), there is no indication of an initial prescription of antibiotics but only analgesic medication and observation (expectant behavior). If the condition develops with severe signs and symptoms, then antimicrobial treatment is prescribed. There is also the alternative of prescribing antimicrobial or making observation, based on mutual decision between medical staff and family members, for children between 6 and 23 months of age without signs or severe symptoms[12].

If there is a recommendation for the use of antibiotics, the first choice is amoxicillin at the dose of 50 to 90mg/kg/day for 10 days. For the higher dose of amoxicillin, consider recent exposure to antibiotics (≤ 3 months), attendance at day care/early childhood education, resistance profile of S. pneumoniae in the community, and vaccination status. For the second option, amoxicillin-clavulanic acid (50mg/kg/day)

is recommended for 10 days. If the child is allergic to penicillin with anaphylaxis, rash, angioedema, IgE-mediated, azithromycin at the dose of 10mg/kg/day on the first day and 5mg/kg/day in the next 4 days or clarithromycin at a dose of 15mg/kg/day for 10 days.

For those children allergic to non-anaphylactic and non-IgE-mediated penicillin, use cefuroxime at a dose of 30mg/kg/day for 10 days. In children over two years of age, the recommended antibiotics are the same for children under 2 years of age, but the duration of treatment is 5 to 10 days. For children over two years of age with AOM and general condition compromised it is recommended the immediate treatment with antibiotic therapy for 5 to 10 days. It is recommended for children with recurrent AOM at less than 1 month of the first episode or who used antibiotics for other reasons in the last month and who has AOM, an antibiotic alternative to amoxicillin. The first choice would be amoxicillin-clavulanic acid (90mg/kg/day amoxicillin and 6.4mg/kg/day clavulanic acid for 10 days). There is no evidence to prolong or use prophylactic antibiotics in recurrent AOM[13].

The child should be re-evaluated if those responsible say that the symptoms have worsened or if there was no initial response to treatment within 48 to 72 hours, since in this case, another concomitant disease or viral infection should be considered, or the causative bacteria must be resistant to therapy. In children with severe and persistent symptoms of AOM and otological findings without improvement after initial treatment, the physician should consider changing to another antimicrobial agent; if the child was initially treated with amoxicillin and there was no improvement, amoxicillin should be used with clavulanic acid; if it was initially treated with amoxicillin with clavulanic acid or 2nd generation cephalosporin, an alternative would be intramuscular ceftriaxone.

In children with recurrent AOM, consider consulting with pediatric subspecialties in order to optimize treatment and diagnosis, especially in the treatment of infections caused by multiresistant Pneumococcus[12].

Pneumococcus is probably the most common agent of acute otitis media (AOM) and a frequent cause of pneumonia, sinusitis and meningitis in children. Several factors, such as age and the patient's baseline health status, topography, extent and severity of infection and adequacy of treatment influence the clinical evolution of the pneumococcal infection. There are, therefore, some risk factors that lead to the appearance of pneumococcus resistant to penicillin, namely: children under two years of age; who attend daycare centers and who receive antimicrobials frequently; who have refractory or recurrent acute otitis media and are submitted to series of antibiotic treatments or prophylaxis; those who have immunosuppressive base disease, predisposing to pneumococcal infection. Other factors that lead to an increased resistance index, as already mentioned, are the indiscriminate use of antimicrobials[14].

Although there are studies concerning resistant Pneumococcus and H influenzae in day care centers and children with siblings younger than 5 years of age, further studies are needed to determine which of these and other risk factors should indicate the need for a different initial treatment[12].

ACUTE LARYNGITIS

Laryngitis is an inflammation of the subglottic portion of the larynx, which occurs during a respiratory virus infection. Congestion and edema of this region result in a variable degree of airway obstruction[15]. Anatomical features, such as the more elongated and less rigid epiglottis, the more anterior larynx, the smaller internal diameter of the trachea, and a proportionally larger head than the adult, increase susceptibility to obstruction caused by edema[16].

Viral etiology is the most common, with parainfluenza viruses (types 1, 2 and 3), influenza A and B and respiratory syncytial virus being the main agents. Mycoplasma pneumoniae is etiologically important in children older than 5 years of age. When the child with croup has recurrent disease, other etiologies should be ruled out, such as gastroesophageal reflux, recurrent laryngeal papillomatosis, laryngotracheal stenosis, and congenital abnormalities[17].

It affects children from 1 to 6 years of age, with a peak incidence at 18 months, predominantly in the male gender. Although most cases occur in autumn and winter, the disease manifests itself throughout the entire year[17].

The evolution can be a bit slow, with onset of coryza, feverishness and cough. In 24-48 hours, the involvement of the subglottic region is increased, with obstruction of mild to severe degree and proportional respiratory difficulty. The natural evolution, in most cases, is the persistence of the obstructive airway for 2-3 days and regression at the end of five days. The prodromes consist of coryza, nasal obstruction, dry cough and low fever, evolving to hoarse cough, dysphonia, hoarseness, and inspiratory stridor. In cases of more severe obstruction, there is more intense stridor, chest in-drawing, nasal alar beats, expiratory stridor and agitation. In extreme cases, in addition to intense dyspnea and agitation, pallor, cyanosis, numbness, convulsions, apnea and death appear[15].

The goal of treatment is to maintain patent airways, keeping the patient as calm as possible, avoiding unnecessary manipulation and exams. The use of nebulization with saline solution, or humidified air, has no proven efficacy. Corticosteroids have been shown to reduce the severity of symptoms, the need for and duration of hospitalization, the need for ICU admission, and the need to associate other drugs for treatment. The use of dexamethasone has been recommended because it is a potent glucocorticoid and has a long period of action (greater than 48 hours).

As for epinephrine, its inhalation decreases almost instantly the stridor and symptoms of respiratory failure, but

since the effect of the medication is brief (2 hours), the patient can return to the state of initial respiratory discomfort after the end of the action of this drug. Indications of epinephrine include moderate or severe condition and children with previous upper airway procedure or manipulation[17].

According to a review of the literature conducted by Zoorob. et al, 2012, it has been shown that the use of antibiotics in acute laryngitis does not reduce the duration of symptoms nor leads to an improvement in voice pattern. Laryngitis is therefore a self-limiting viral infection that does not respond to antibiotic therapy.

FINAL REMARKS

Upper airway infections are part of most outpatient and emergency room visits, requiring correct diagnosis and treatment. This brings a demand for trained, up-to-date professionals to do the job properly, thus avoiding misconduct.

Such infections have been responsible for the vast majority of antimicrobial prescriptions in the pediatric range. In addition to these drugs, it is also possible to prescribe analgesics, antipyretics and other medications indicated for respiratory diseases, but there are many of these medications prescribed unnecessarily or inadequately.

Thus, there is a great need for more and more current studies on the subject, so that professionals have access to the protocols. Such studies can guide professionals in the field, improving clinical care and having more correct, evidence-based behavior.

Overuse and misuse of antimicrobials, for example, can lead to bacterial resistance, increased cost, and increased incidence of adverse effects, including anaphylaxis, and abusive use of other drugs that may cause unwanted effects such as drug intoxication. For this reason, the most up-to-date approaches in upper airway infections have been addressed in this paper, and this topic is always lacking in updates.

REFERENCES

1. Berezin EN. Infecções de vias aéreas superiores. In: Campos Júnior D, Burns DAR, Lopez FA, eds. Tratado de Pediatria. São Paulo: Manole; 2014. p. 1477-81.
2. Bricks LF. Uso judicioso de medicamentos em crianças. J Pediatr (Rio J). 2003;79(Supl 1):S107-14.
3. Zoorob R, Sidani MA, Fremont RD, Kihlberg C. Antibiotic use in acute upper respiratory tract infections. Am Fam Physician. 2012;86(9):817-22.
4. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM Jr, et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits. JAMA. 2016;315(17):1864-73.
5. Kenealy T, Arroll B. Antibiotics for the common cold and acute purulent rhinitis. Cochrane Database Syst Rev. 2013;(6):CD000247.
6. Simancas-Racines D, Franco JV, Guerra CV, Felix ML, Hidalgo R, Martinez-Zapata MJ. Vaccines for the common cold Cochrane Database Syst Rev. 2017;5:CD002190.
7. Wald ER, Applegate KE, Bordley C, Darrow DH, Glode MP, Marcy SM, et al.; American Academy of Pediatrics. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. Pediatrics. 2013;132(1):e262-80.
8. Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJ, Hicks LA, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clin Infect Dis. 2012;54(8):e72-e112.
9. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012;55(10):1279-82.
10. Lieberthal AS, Carroll AE, Chonmaitree T, Ganiats TG, Hoberman A, Jackson MA, et al. The diagnosis and management of acute otitis media. Pediatrics. 2013;131(3):e964-99.
11. Schilder AG, Chonmaitree T, Cripps AW, Rosenfeld RM, Casselbrant ML, Haggard MP, et al. Otitis media. Nat Rev Dis Primers. 2016;2:16063.
12. Harmes KM, Blackwood RA, Burrows HL, Cooke JM, Harrison RV, Passamani PP. Otitis media: diagnosis and treatment. Am Fam Physician. 2013;88(7):435-40.
13. Diretriz Assistencial. Otite média aguda em crianças e adolescentes - Diretrizes para o diagnóstico e tratamento [Internet]. São Paulo: Sociedade Beneficente Israelita Brasileira, Departamento de Ensino e Pesquisa; 2017 [acesso 2017 Ago 27]. Disponível em: https://pubdiretrizes.einstein.br/download.aspx?ID=%7BFD5AB051-3E19-48CD-8949-D5F9694E1344%7D
14. Mantese OC. Pneumococo resistente à penicilina: implicações práticas. J Pediatr (Rio J). 1999;75(Supl.1):S74-90.
15. Pitrez PMC, Pitrez JLB. Infecções agudas das vias aéreas superiores: diagnóstico e tratamento ambulatorial. J Pediatr (Rio J). 2003;79(Suppl.1):S77-86.
16. Amantéa SL, Silva APP. Manejo clínico da obstrução de via aérea superior: epiglotite e laringotraqueobronquite. J Pediatr (Rio J). 1999;75(Supl 2):S177-84.
17. Crupe Viral e Bacteriano. Rio de Janeiro: Sociedade Brasileira de Pediatria - Departamento de Emergências; 2017. 9 p.