

UPPER RESPIRATORY TRACT INFECTIONS IN CHILDREN: FROM CASE HISTORY TO MANAGEMENT

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ABSTRACT

Respiratory tract infections are the most common diseases in childhood. The respiratory tract, widely branched system of ducts, is particularly exposed to the action of microorganisms transmitted by air from here the high frequency of infections they face especially in the first years of life. It is usual distinguish: upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI). In particular, in infections of the upper airways, the inflammatory process, result of the interaction between microbes and the immune response, can be localized to the mucosa of the nose or sinuses (common cold and sinusitis), or the pharynx or larynx (pharyngotonsillitis and laryngitis) and it has predominantly a viral etiology although occasionally it may be followed by bacterial complications such as otitis media. The aim of the following article is the description of these different clinical pictures, highlighting the clinical and epidemiological features and current management guidelines.

Key words: Upper respiratory tract infections, sinusitis, pharyngotonsillitis, laryngitis and otitis media, management.

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Introduction

The respiratory tract is a widely branched system of ducts, which start from the nostrils (from the mouth in the case of mouth breathing) and include: the nasal cavities, the pharynx and larynx up to the lower edge of the cricoid cartilage (upper airways), the trachea and the various orders of bronchi to the terminal bronchioles (lower airways). Going through these ducts, the inhaled air is changed and conveyed to the alveolar structures, home of the respiratory exchange with the blood.

They are therefore particularly exposed to the action of pathogenic microorganisms transmitted by air and not surprisingly the high frequency of infections they face especially in the first years of life;

respiratory tract infections in fact represent the 50% of all diseases in pre-school children and 30% of those between 5 and 12 years. Moreover it is widely-documented how in the first three years of life all children without statistically difference among sex, experience at least eight episodes of respiratory infections per year, a rate that decreases then to six in the range of age between 3 and 7^(1,2).

Commonly it is usual to distinguish: upper respiratory tract infections (URTI) from lower respiratory tract infections (LRTI). The pathogens involved are basically the same, considered the anatomical and physiological commonality between upper and lower respiratory tracts deriving from the common embryological origin (subsequent budgings of the primitive foregut endodermal tube

between the second and the fourth bronchial pocket). The most frequently viruses responsible for respiratory diseases are: the respiratory syncytial virus, influenza viruses A, B and C, and the parainfluenza, adenoviruses, rhinoviruses and enteroviruses occasionally in the summer months (both belonging to the family of picornaviruses), coronavirus and the newly identify bocavirus⁽³⁾. To these viruses proper we must add some mycoplasmas and bacteria (such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, and others)^(4,5,6).

The inflammatory process always occurs with the same features: inflammation and edema of the mucosa, vascular congestion, hypersecretion of mucus and alteration of transport and mucus ciliary clearance.

From what has been affirmed it can be stated that different infectious agents are responsible for respiratory ailments like and therefore one of the most effective criteria to define them results to be the anatomy clinical localization of the infection, from the nose to the lung parenchyma.

In particular, in infections of the upper airway, the inflammatory process, result of the interaction between microbes and the immune response⁽⁷⁾, can be localized to the mucosa of the nose or sinuses, or the pharynx or larynx, and it has predominantly a viral etiology although occasionally it may be followed by bacterial complications such as sinusitis and otitis media. We can distinguish in this way, according to the prevailing location and the intensity of symptoms, different clinical pictures such as the common cold or rhinitis, the sinusitis and the rhinosinusitis, the pharyngotonsillitis, laryngitis and finally the otitis media.

Materials and methods

The author's search targeted evidence-based guidelines, evidence-based summaries, systematic reviews, and controlled trials of interventions for rhinosinusitis, pharyngitis, and otitis media.

The keywords used were "rhinitis" or "common cold" or "rhinosinusitis" or "pharyngitis" or "tonsillitis" or "otitis" and (practice guideline or systematic or clinical evidence or clinical trial).

Even this simple strategy identified more than 6500 sources using PubMed alone. Inclusion as an evidence-based guideline, summary, or systematic review required an explicit search strategy and criteria for study inclusion.

Inclusion as a clinical trial required randomization. The author used three primary sources to identify relevant information: Clinical Evidence (<http://clinicalevidence.bmj.com>); the Cochrane library (<http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME>); Medline and SCOPUS (last accessed via PubMed and SCOPUS on October 16, 2014).

Discussion

Common cold or rhinitis

Among the diseases of the upper respiratory tract during the winter and spring, which make up 50% of all diseases in pre-school children and 30% of those between 5 and 12 years, rhinitis or common cold is undoubtedly the most frequent⁽⁴⁾.

This inflammatory process of the nasal mucosa in most cases tends to heal spontaneously. The symptoms (stuffy nose, sneezing, runny nose, and in more severe infections fever, illness, and muscle aches) usually resolve within a few days, but may persist for up to one to two weeks. The pathogens responsible are for 90% viral agents (rhinovirus, adenovirus, respiratory syncytial virus, influenza and parainfluenza virus) and only occasionally bacterial pathogens *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*⁽⁷⁾.

The treatment is mainly symptomatic and considering the prevailing viral nature of affection, administration of antibiotics is not recommended by the main guidelines⁽⁶⁾. Among the drugs paracetamol is the most employed (it is the drug of first choice in paediatrics, after more than 40 years of use), used as antipyretic and analgesic, with few side effects (liver and renal toxicity), mostly related to overdose^(8,9,10). To relieve nasal congestion and restore normal mucosa, especially in infancy and early childhood, with topical nasal decongestants are preferred nasal washes with saline or hypertonic saline, to be carried out several times during the day. These washes remove secretions, moisturize and relieve congestion of the mucous membranes, facilitate the elimination of airborne particles such as allergens and dust environment and foster the reactivation of mucociliary clearance^(11,12). For all these reasons, they are not only indicated in the treatment and prevention of colds but also in other related diseases such as sinusitis, otitis and pharyngolaryngitis as well as in allergies^(13,14).

Rhinosinusitis

When the inflammation in the nasal mucosa lasts for more than ten days and/or is particularly intense, the edema which results may determine, with the interaction of predisposing factors, the obstruction of one or more of the hosts that physiologically ensure the normal drainage of the paranasal sinuses. The obstruction, which could be origin of the onset of migraine⁽¹⁵⁾, leads to the formation of a closed sinus space, separated from the corresponding nasal cavity and characterized by a decrease in oxygen tension and endosinusal pH, ciliary dysfunction and stagnation of secretions, conditions that favour the engraftment and proliferation of pathogenic bacteria⁽¹⁶⁾.

A simple rhinitis, usually of viral origin, thus evolving into a more serious bacterial infection of the nose and paranasal sinuses for which we talk about rhinosinusitis, reserving the terms of rhinitis and sinusitis to self limited and short lived infections. In many individuals, however, rhinitis and sinusitis are often coexist and for this reason we prefer the unique term rhinosinusitis⁽¹⁷⁾.

The acute rhinosinusitis has symptoms that may persist for 10 to 30 days and may occur in mild form (with nasal obstruction, rhinorrhea catarrhal moderate facial pain, absent or moderate fever) and in severe form (with strong nasal congestion, mucopurulent rhinorrhea, facial pain from moderate to severe pain, high fever, cough and headache)⁽¹⁵⁾. The diagnosis is usually based on clinical signs and nasal endoscopy using optic fibres, reserving the radiological examinations for children with severe complicated cases that do not respond to drug therapies⁽¹⁸⁾. These, as recommended by the American Academy of Otolaryngology Head and Neck Surgery Foundation, vary according to the severity of the clinical picture: in mild forms is preferable to delay antibiotic treatment for a few days and in the meantime using anti-inflammatory drugs, nasal decongestants (to be used for limited periods of time to avoid mucosal abnormalities and possible rebound effect and complications or systemic infection) without forgetting the already mentioned nasal washes with hypertonic saline.

When the symptomatology lasts for more than 15 days, to the treatment already mentioned, should be associated an antibiotic treatment to ensure healing, prevent complications and/or chronicity. According to current guidelines in mild acute rhinosinusitis, bearing in mind that the most responsible germs are *Streptococcus pneumoniae*,

Haemophilus influenzae and *Moraxella catarrhalis*, the first line antibiotic is oral amoxicillin (50 mg/kg/day in three divided doses for 10 days), considering its action on these germs. In case of intolerance, treatment failure, emergence of resistance or other different pathogens, according to each case, it is possible to resort to the association amoxicillin/clavulanic acid (80-90 mg/kg/day in three doses) or to a second or third generation cephalosporin, to a macrolide or, in the case of allergy, to B-lactam antibiotics. In severe complicated cases you may approach the administration by injection of ceftriaxone (100 mg/kg/day in a single dose) or cefotaxime (100 mg/kg/day in three divided doses) or ampicillin-sulbactam (100-200mg/kg/day in three doses). In these cases, antibiotic treatment may vary from 14 to 28 days, even though the optimal duration of antibiotic therapy in various forms of rhinosinusitis is not well defined up today^(18, 19, 20, 21, 22).

Pharyngosillitis and Laryngitis

The pharyngitis and tonsillitis diseases are very frequent between 4 and 10 years, in these cases the inflammatory process involves the oropharynx and/or the tonsils and in the majority of cases has viral etiology with a clinical outcome (characterized by sore throat, cough, fever, rhinorrhea, general malaise) that resolve within three to five days with a predominantly symptomatic treatment. However, in 37% of cases of acute pharyngitis the germ responsible results to be B-hemolytic *Streptococcus* group A (SBEGA)⁽²³⁾. The streptococcal infection, rare in the first three years of life, is characterized by the following signs and symptoms: high fever with sore throat, pharyngeal exudate and/or tonsils, headache, gastrointestinal symptoms, anterior cervical lymph edema and increased in volume, presence of petechiae at the level of the soft palate. If not treated properly with antibiotics, it can undergo suppurate complications (cervical lymphadenitis, peritonsillar abscess and/or back of throat, ear infections and sinusitis), and not suppurate as acute rheumatic fever, glomerulonephritis, and reactive arthritis. Penicillin V (45mg/kg/die in three doses) is the first line antibiotic according to the main guidelines, although recent trials have highlighted a greater effectiveness of amoxicillin (50mg/kg/die in two divided doses) both used for a period of at least ten days.

In case of allergies to these molecules you may resort to the use of macrolides such as clar-

ithromycin (15mg/kg/die in two doses) for ten days or azithromycin (10mg/kg/die) for three days^(24,25).

Even for laryngitis, inflammatory processes of the larynx, the most common cause are viruses, although it is not to exclude the presence of bacterial agents when the laryngeal disease is due to a bacterial pharyngitis. Considering then the prevalent viral nature antibiotic treatment is not suitable and in the presence of more severe forms can be used an oral anti-inflammatory. What is important, in the presence of laryngeal affection, is to exclude the presence of a medical emergency such as epiglottitis for which it is urgent hospitalization to ensure a regular respiratory tracts functions and initiate antibiotic therapy with a third-generation cephalosporin (ceftriaxone or cefotaxime)⁽²⁶⁾.

Otitis Media

As reported in literature from 29% to 50% of URTI evolves in otitis media (OM) (7,27), an inflammatory process of the middle ear generally associated to fluid accumulation in the tympanic cavity (the latter detected by the presence of swelling, presence of air-fluid levels limited or absent mobility of the tympanic membrane and/or otorrhea). In general, there are two forms of otitis media: an acute (AOM) with rapid onset, characterized by signs and symptoms of inflammation of the middle ear (tympanic membrane erythema, otalgia, otorrhea, fever, and/or irritability especially in younger children)⁽²⁸⁾ associated with effusion, and a form of otitis media with effusion (OME) in which there aren't any signs and symptoms of acute inflammation. This latter can occur de novo or as a sequel to an acute form then, the two forms can be considered different stages of a unique process of the middle ear⁽²⁹⁾. The pathogens are mainly responsible, in both cases, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*^(30,31).

In the treatment of AOM the goal is to achieve the resolution of symptoms and the prevention of relapse. In children younger than 6 months, the guidelines of the American Academy of Pediatrics suggest an attitude of watchful waiting that immediately takes into account pain symptoms with the possible administration of analgesics (paracetamol, ibuprofen) and postpones to 48-72 hours treatment with antibiotics. The Antibiotic therapy is however indicated in all children younger than 6 months, those aged between 6 months and two years in diagnosis and for children older than 2 years with

severe infection (all subjects are at high risk of experiencing recurrent episodes, and septic complications in chronic forms. The drug of first choice is amoxicillin associated with clavulanic acid to be administered at intervals of 8 hours, choice shared by the main international guidelines but do not agree dosage to be used: 40-45 mg/kg/day (standard dose) for some, 90 mg/kg/day for others. The duration of treatment may vary, depending on the severity of the case and the age of the young patient, from 5-7 days to 10 days. In patients allergic to penicillin, the choice may fall on azithromycin or clarithromycin^(31,32).

In the case of OME, as a recent study by Martines and others confirms the literature data, it is shown how children with a history of upper respiratory tract infections (URTI) are more likely to develop this form of otitis^(33,34). Hence the necessity of observing these young patients integrating with the medical history and clinical examination with audiometry and tympanometry to settle a diagnostic suspicion and establish adequate therapy. Particularly in the management of these pathological conditions it is necessary to achieve two important goals: first, to heal the inflammatory process interesting the upper airway (restoring the ventilation of the 'middle ear through the Eustachian tube and reducing the bacterial load), and second, prevent new episodes of URTI and OME, maintaining the normal physiology of the mucosa of the upper airways and strengthening the immune system, avoiding middle-ear surgery^(7,34,35,36).

Conclusion

URTI can be neutralized with antibiotic therapy (limiting the use of aminoglycosides and macrolides for their ototoxic effect)⁽³⁷⁾, associated with the administration of steroids for nasal route (to reduce eosinophil infiltration) and/or antihistamines (in particular for allergic forms), all supported by irrigations nasal saline solutions (to help to release allergens and mucus from the nose). For the prevention it may be used the administration of bacterial lysates orally, such as OM-85, a bacterial lysate of *Streptococcus pneumoniae*, *Haemophilus influenzae* and other bacteria particularly involved in URTI and otitis media, which is effective in reducing the number and intensity of infections^(31,38).

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