THE LINKAGE BETWEEN UPPER RESPIRATORY TRACT INFECTIONS AND OTITIS MEDIA: EVIDENCE OF THE 'UNITED AIRWAYS CONCEPT'

DANIELA BENTIVEGNA[1], PIETRO SALVAGO[1], MONICA AGRIFOGLIO[2], ANTONELLA BALLACCHINO[2], SERGIO FERRARA[1], MARIANNA MUCIA[2], FEDERICO SIRECI[1], FRANCESCO MARTINES[1]

[1]University of Palermo, BioNeC Department, Section of Otolaryngology, [2]University of Palermo, Di.Bi.Me.F. Department, Audiology Section

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ABSTRACT

Upper respiratory tract infection (URTI) is a nonspecific term used to describe acute infections involving the nose, paranasal sinuses, pharynx and larynx and resulting from interplay between microbial load (viral and bacterial) and immune response. Infant and young children are prone to developing upper respiratory tract infections, which often result in bacterial complications especially acute otitis media because of the passage of bacteria (colonizing the nasopharynx) in the middle ear via Eustachian tube.

Key words: Upper respiratory tract infections, rhinosinusitis, otitis media.

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The impact of urti

Upper respiratory tract infection (URTI) is a nonspecific term used to describe acute infections involving the nose, paranasal sinuses, pharynx and larynx which serve as gateways to the trachea, bronchi, and pulmonary alveolar spaces; of them rhinitis and sinusitis usually coexist and are concurrent in most individuals; thus, the correct terminology is now rhinosinusitis[(1)]. Literature data reported that 29% to 50% of all URTI develop into otitis media (OM) (2,3,4).

The clinical syndrome of URTI comprises a variety of symptoms. Cough is usually the main symptom. Other symptoms are nasal blockage/obstruction/congestion, discoloured nasal discharge, fever and headache. Symptoms typically peak after 2-3 days, and then gradually clear. However, the cough may persist after the infection has gone. This is because inflammation in the airways, caused by the infection, can take a while to settle. It may take 2-3 weeks, after other symptoms have gone, for a cough to clear completely[(5)].

Factors contributing to urti

URTI are mainly infectious diseases resulting from interplay between microbial load (viral and bacterial) and immune response.

First of all, the host needs to recognize the presence of microorganism through pattern recognition initiating the host defense mechanisms through activation of multiple signal pathways. Host defense mechanisms consist of both cellular immune responses and release of soluble chemical factors, which operate in the body through a complex interaction with cytochines and other mediators[(6)].

Literature data showed that in children submitted to serial nasal lavages, in order to assess nasal cytokine expression during acute upper respiratory infections, interleukin 1, IL-8, IL-6, and tumor

necrosis factor-a (TNF-α) were markedly elevated in nasal lavage fluid during acute URTI compared to baseline, and all except TNF-α decreased significantly by 2-4 weeks later. Thus, cytokines are likely to participate in regulation of respiratory virus-induced inflammation[7].

Based on references and reports, the most common causes of URTI are viruses. The most common viruses isolated are rhinovirus, parainfluenza virus, coronavirus, adenovirus, respiratory syncytial virus, coxsackievirus and influenza virus.

Fewer than 10% of cases is associated with bacterial infection. The most common bacteria in URTI are those belonging to the "infernal trio" (Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis) and staphylococcus aureus[8,9,10,11].

URTI is the third most common reason for a primary care provider consultation, with approximately a third of these attributed to acute rhinosinusitis. Prevalence rate vary from 6-15% depending on the methods used and population characteristics.

Prevalence varies with season (higher in the winter months) and climatic variations and increasing with damp environment and air pollution. Exposure to cigarette smoke increased susceptibility to rhinosinusitis.

Anatomical factors including Haller cells, concha bullosa, septal deviation, choanal atresia, nasal polyps and hypoplasia of sinuses have all been associated with rhinosinusitis[6].

The role of allergy in rhinosinusitis is the subject of much debate. Literature data support the role of allergy in predisposing for rhinosinusitis. In 1989 Savolainen reported that 25% of 224 patients with sinusitis had allergy[12]. In 1993, Ciprandi et al. demonstrated that expression of the inflammatory adhesion molecule, ICAM-1, which is a receptor for rhinovirus, is elevated in allergic children[13]; in 2006 they also conducted a cohort study that showed that children with allergies have more frequent and severe respiratory infections than children without allergies[14].

In contrast to the above literature, Pant et al in 2009 concluded that insufficient evidence exist to confirm seasonal or perennial allergy as a significant predisposing factor for rhinosinusitis. In contrast to this review, Lin recently reported that children with atopy were more likely to develop rhinosinusits[16].

From urti to otitis media

Infant and young children are prone to developing upper respiratory tract infections, especially those who attend day care centers, which often result in bacterial complications expecially acute otitis media.

Otitis media (OM) describes an inflammatory process within the middle ear space that is generally associated with accumulation of fluid and that may lead to hearing loss, learning difficulties, and delays in language development. The pathogenesis of OM is multifactorial, involving the adaptive and native immune system, Eustachian tube dysfunction, viral and bacterial load, and genetic and environmental factors[16].

Two forms are recognized: acute otitis media (AOM) and otitis media with effusion (OME). AOM is defined as the presence of middle ear effusion (MEE) in conjunction

with the rapid onset of one or more signs or symptoms of inflammation in the middle ear, such as otalgia, otorrhea, fever, or irritability. OME is defined as MEE without signs or symptoms of an acute infection; it may occur de novo or as a sequel to AOM. Therefore, AOM and OME represent different stages of the OM continuum[17].

Otitis media is a common disease in children, with an incidence range from 6% to 64%.The peak age of incidence of AOM is at about 2 years of age, probably leading to immaturity of function of the immune system and to anatomic and functional diversity of the eustachian tube (ie, nearly horizontal orientation), and the other at about 5 years of age, probably for because children attend the same classes at school, with consequent increased susceptibility to infectious and allergic agents[18,19,20,21]. The pathogenesis of OME is clearly related to the dysfunction of the Eustachian tube that is generally related to upper respiratory tracts infections, adenoid hypertrophy, and craniofacial malformations, such as cleft palate deformities and Down syndrome[22].

As stated above literature data reported that 29% to 50% of all URTI develop into otitis media[2,3,4]. Recently, a study conducted by Martines et al confirms data literature showing that children who had previous URTI and ear infections were significantly more likely to suffer from OME[23,24].

For otitis media to occur, bacteria colonized in the nasopharynx mast enter the middle ear via Eustachian tube.

Normally, bacteria are prevented from entering the middle ear by ciliated epithelium that lines the Eustachian tube. Respiratory virus infection disrupts the mucociliary system and impairs the ear's primary mechanical defense from bacterial invasion. In addition, Eustachian tube dysfunction can lead to reduced middle ear pressure, which forces mucus, nasopharyngeal secretions, and bacteria into the middle ear.

The disease is primarily caused by: Streptococcus pneumaniae, Haemophils influenzae and Moraxella catarralis[25]. Viruses most commonly detected during URI were different. Henderson et al. used viral culture and reported that respiratory syncytial virus, adenovirus, and influenza virus were closely associated with AOM; the incidence of AOM associated with rhinovirus URI was the lowest. Ruuskanen et al. reported similar results. Vesa et al. found that URI associated with respiratory syncytial virus and rhinovirus had a higher rate of AOM than did URI associated with adenovirus. Pitkaranta et al. reported that rhinovirus (35%) was the most common virus found in cases of nasopharyngeal secretions and/or middle ear effusion in children with AOM[6].

Management

A child with suspect URTI and OME has to be assessed through clinical history, clinical examination, audiometry and timpanometry to confirm the suspected diagnosis and proceed with the suitable therapeutic strategy. Particularly the management of these pathologic conditions should reach two important objectives: first, to heal the inflammatory process interesting the upper airways (restoring the ventilation of the middle ears through Eustachian tubes and reducing the bacterial load); second, to prevent new episodes of URTI and OME maintaining the normal physiology of the upper airways mucosa and reinforcing immunitary system.

So the presence of an URTI can be countered with the administration of antibiotics (especially macrolides), intranasal steroids (to reduce airway eosinophil infiltration by preventing their increased viability and activation) and/or anthistaminics (in particular for allergic rhinitis) associated with nasal saline solution irrigations (to help to rid the nose of allergens and mucus). The latter treatment, used to fight the acute inflammatory process, can also reduce the probability to develop sinus infections and allergic rhinitis.

Furthermore, the prevention of URTI can be reached by the administration of oral bacterial lysates, obtaining the reduction of number and intensity of infective episodes. Specifically, OM-85 is a bacterial lysate of Streptococcus pneumoniae, Haemophilus influenzae and other bacteria mainly involved in URTI and in otitis media. It can prevent recurrent infective flogosis of these districts and, as shown by Heintz, it can be considered as an adjunct to standard medical treatment in adults with chronic rhinosinusitis without nasal polyps[26].

Children with persistent OME documented over a period of 3 months with a hearing level in the better ear of 25–30 dB HL or worse averaged at 0.5, 1, 2 and 4 kHz should be considered for surgical intervention (insertion of ventilation tubes). Children who have undergone insertion of ventilation tubes for OME should be followed up and their hearing should be re-assessed.

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Request reprints from:
Dr. FRANCESCO MARTINES
Via Autonomia Siciliana, 70
90143 Palermo
(Italy)