INVITED ARTICLE

UPPER RESPIRATORY TRACT INFECTIONS – OTITIS MEDIA, SINUSITIS AND PHARYNGITIS

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ABSTRACT

Management of the patient with otitis media, sinusitis or pharyngotonsillitis is based on information about the host, the organism and the antimicrobial agent.

Otitis media (OM) is a common infection in children but selected children have recurrent and chronic OM. The predominant organisms responsible for OM are Streptococcus pneumonia, Haemophilus influenzae and Moraxella catarrhalis. Changes in the antimicrobial susceptibility govern the choice of antimicrobial agents. Surgical treatment should be considered if the child has persistent hearing loss in both ears.

Sinusitis shares with OM similar pathogenesis, microbiology and choices of antimicrobial therapy. Endoscopic surgery is the treatment of choice for chronic sinusitis.

Pharyngitis may be either viral or bacterial in origin. Penicillin remains the treatment of choice for bacterial pharyngotonsillitis. In patients with recurrent infection, the emergence of B-lactamase producing strains has to be considered and erythromycin or oral cephalosporins might be indicated.

Keywords: *B-lactamase, recurrent, antibiotic, surgery.*

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Upper respiratory tract infections (URTIs) are the most common human infections. Management of patients with otitis media, sinusitis or pharyngitis is based on information about the host, the organism and the antimicrobial agent.

OTITIS MEDIA (OM)

Otitis media is a bacterial infection of the middle ear cleft. Acute Otitis Media is one of the most frequently diagnosed infectious diseases of childhood, but becomes less frequent with advancing age. The annual OM incidence ranges between 14% and 62%[1].

Acute OM usually follows a viral URTI which results in congestion of the respiratory mucosa throughout the respiratory tract. Congestion of the eustachian tube leads to accumulation of middle ear secretions. Microbial pathogens proliferate in the secretions and result in a suppurative and symptomatic otitis media[2]. Effusion persists in the middle ear for weeks to months after every episode of acute otitis media. Some children are subject to recurrent OM and chronic OM with effusion. Longitudinal studies have provided information regarding the characteristics of children who have recurrent OM (Table I)[3].

The diagnosis of acute OM is made based on clinical findings of inflammatory changes of the tympanic membrane and acute purulent effusion in the middle ear plus associated symptoms such as earache and fever. The tympanic membrane appears erythematous in the early stage and appears opaque, full or bulging with diminished mobility due to accumulations of purulent effusion in the middle ear as the infection progresses. The membrane may rupture allowing the effusion to drain. There is conductive hearing loss with the middle ear effusion.

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Table I – Risk factors associated with recurrent otitis media

- Male gender
- Native American or Alaskan or Canadian Eskimo
- Sibling or parent history of recurrent ear infections
- Early onset at time of initial episode of acute otitis media
- Not breast fed
- In group day care
- Altered host defence: anatomical, physiologic or immunologic
- Exposure to environmental antigens (allergy) or pollutants (tobacco smoke)

Bacteria can be isolated from the middle ear fluid in 50-70% of cases with acute OM. The predominant pathogens in children are *Streptococcus pneumoniae* (20-40%), *Haemophilus influenzae* (10-30%) and *Moraxella catarrhalis* (5-15%)[4,5]. In a recent study on acute OM in adults, *H. influenzae* and *S. pneumoniae* were the two most common organisms isolated with only 9% of the isolates producing β-lactamase[6]. During the past 10 years, there has been an increase in the prevalence of penicillin-resistant *S. pneumoniae* in acute OM and a progressive rise in the percentage of β-lactamase producing *H. influenzae* and *M. catarrhalis*[5]. Microbiological efficacy should be defined for each bacterial pathogen by the cultures of pretreatment middle ear aspirates.

Adults and children with acute OM should be treated with antibiotics. The antimicrobial of choice for initial empiric therapy is amoxicillin for 10 days since it is inexpensive and provides coverage for the majority of the relevant organisms.

Second-line therapeutic agents should be used in patients who are responding poorly to treatment with amoxicillin and

include cefuroxime axetil, amoxicillin-clavulanate, cefixime and trimethoprim-sulphamethoxazole. Second-line agents should also be used in patients with penicillin hypersensitivity, in patients at high risk of complications (such as diabetic or immunocompromised individuals) or if the organisms are resistant to amoxicillin. Recent studies have shown that a shorter duration of treatment may be effective[8,9].

A significant improvement should occur within 48-72 hours. If such a response is not observed, the patient should be evaluated for the possibility of complications (Table II). Some patients may develop persistent otitis media with middle ear effusion despite 2 courses of antibiotics and a minority may develop chronic OM.

Table II - Complications of otitis media

Intratemporal
Mastoiditis
Petrositis
Facial palsy
Labyrinthitis
Intracranial
Extradural abscess
Subdural abscess
Sigmoid sinus thrombophlebitis
Meningitis
Cerebral abscess
Otitis hydrocephalus

Current recommendations for paediatric otitis media with effusion persisting for ≥ 3 months include a 2-3 week course of antibiotics with or without 7-day regimen of prednisolone. If the child fails to improve and especially so if there is persistence of conductive hearing loss of 30dB or more in both ears, then surgical treatment should be considered. This includes myringotomy with tympanostomy tube insertion and adenoidectomy[10]. Before embarking on surgical treatment, a search for an underlying cause like paranasal sinusitis should be made. Ear drops (antibiotic/steroid) are sometimes used in persons with chronic suppurative OM, but ear drops have the potential to cause complications and ototoxicity.

Chemoprophylaxis with a sulphonamide or amoxicillin has been effective in children with recurrent otitis media, reducing new episodes by 40% to 90%[10].

SINUSITIS

Approximately 0.5% of common colds are complicated by the development of paranasal sinusitis. Sinusitis is one of the most common infectious diseases seen in outpatient clinics. Normal sinus function is related to 3 factors:

1. patency of the sinus ostia
2. function of epithelial cilia, and
3. quality of secretions which are required for the normal functions of cilia. Ostial obstruction leads to negative intrasinal pressure resulting in bacterial invasion of a normally sterile sinus cavity. The most commonly involved sinus is the maxillary sinus.

Patients with sinusitis usually complain of headache in the area of the involved sinus, nasal congestion, purulent rhinorrhoea, postnasal drip, productive cough and pharyngitis. Pertinent historical features include recent upper respiratory tract infections, trauma, allergy, swimming, flying, dental repair and recent work in a poorly ventilated area with volatile or noxious material.

Physical examination may yield signs of recent upper respiratory tract infection or chronic nasal allergy ie nasal polyps and large "blue" inferior turbinates. The presence of yellow or green discharge in the middle or superior meatus with oedematous and erythematous mucosa is diagnostic. Palpation and percussion of the acutely involved sinuses may reveal tenderness. Ophthalmologic examination is essential in patients with sinus disease and orbital or intracranial complications (Table III).

Table III - Complications of sinusitis

1. Mucoceles - chronic cystic lesion of the paranasal sinuses
2. Orbital complications - result from direct extension through neurovascular foramina or through bone
   - Inflammatory edema - lid edema
   - Orbital cellulitis
   - Subperiostial abscess - globe displaced downwards and laterally
   - Orbital abscess - exophthalmos and chemosis, complete ophthalmoplegia
   - Cavernous sinus thrombosis - bilateral eye findings
   - Osteomyelitis
3. Intracranial complications - result from direct extension, septic thrombophlebitis and haematogenous spread
   - Meningitis
   - Epidural abscess
   - Subdural empyema
   - Venous sinus thrombosis
   - Cerebral abscess

The presence of sinus inflammation with fluid can be confirmed by:

1. transillumination in patients older than 10 years
2. radiographic findings (such as complete or partial opacification, mucosal swelling of at least 5mm or an air-fluid level), or
3. needle aspiration of the sinus cavity yielding bacteria in high density (colony count of at least 10^4 bacteria/ml)[11].

Conventional CT scanning is helpful in evaluating the anatomy and extent of disease in patients with chronic sinusitis and in patients requiring surgical intervention. CT scans are excellent for defining bony anatomy. However magnetic resonance imaging (MRI) and CT scans tend to overexaggerate the extent of soft tissue involvement in sinusitis. MRI is worse in this respect.

Most acute sinus infections in adults and children are caused by *Streptococcus pneumoniae,* non-typable *Haemophilus influenzae, Moraxella catarrhalis* and Group A beta-haemolytic streptococci[12,13]. Staphylococci and respiratory anaerobes are usually present in chronic sinusitis[14].

Medical treatment of acute sinusitis is generally indicated. Occasionally antral washout under antibiotic cover is necessary to relieve the congestion and pain and to prevent complications. In the presence of intraorbital or intracranial complications, open or endoscopic drainage[15,16] combined with antimicrobial treatment are required. Several antimicrobial agents or drug combinations are licensed internationally with approved indication for sinusitis treatment (Table IV). In uncomplicated cases, amoxicillin is appropriate as it is active in the majority of uncomplicated acute sinusitis

with an overall cure rate of 80% in one study[17]. Trimethoprim-sulphamethoxazole is efficacious in adults with acute maxillary sinusitis as well as paediatric acute bacterial sinusitis. This antimicrobial agent may, however, be ineffective in patients with Group A streptococcal pharyngitis[18].

Table IV – Antimicrobial drugs licensed internationally with indications for treatment of sinusitis

Beta-lactams	Cephalosporins	Macrolides and sulphonamides
Amoxicillin	Cefaclor	Trimethoprim + sulphamethoxazole
Amoxicillin + Clavulanate	Cefuroxime Cefixime Cefprozil Cefpodoxime	Erythromycin + sulphisoxazole

Clinical improvement is expected in 48 to 72 hours after initiating treatment with the appropriate antimicrobial agent. In general, antibiotics are continued for 2 to 3 weeks. Broader spectrum beta-lactam and cephalosporins are available to treat amoxicillin nonresponders and chronic sinusitis. Further treatment should be guided by bacterial culture and sensitivity results.

Adjuvant treatment with saline nose drops, decongestants (oral and nose drops) and mucolytics have not been properly evaluated in subjects with acute bacterial sinusitis. Current indications for antral aspiration and lavage include:

1. sinusitis in an immunocompromised or chronically debilitated host,
2. failure of resolution of symptoms after 24 to 48 hours of empiric antibiotic therapy,
3. progression of symptoms while on antibiotics,
4. an orbital or intracranial complication of maxillary sinusitis,
5. refractory chronic sinusitis.

The treatment for chronic sinusitis is surgery. Endoscopic sinus surgery is generally accepted as the treatment of choice.

PHARYNGITIS (PHARYNGOTONSILLITIS)

Tonsillitis is defined as inflammation of the tonsils and pharyngitis. Pharyngitis may be either viral of bacterial in origin. Viruses that commonly cause pharyngitis include rhinovirus, herpes simplex, Coxsackie A viruses, Epstein-Barr virus (EBV) and cytomegalovirus (CMV). Bacterial pharyngitis is almost always caused by Group A beta-haemolytic *streptococcus* (*Streptococcus* pyogenes). Other causative bacteria include Group C and G *streptococci*, and beta-lactamase-producing *Moraxella catarrhalis*[19].

Streptococcal pharyngitis uncommonly occurs below the age of two and beyond age 50. By school age, 15% to 20% of children apparently harbour group A *streptococci* in the throat. The peak incidence of streptococcal pharyngitis is 5-8 and 11-13 years of age. It usually results from contact with individuals who have active or convalescent disease. It is spread by droplets of saliva or nasal secretion[20]. Viral pharyngitis can occur at any age but it seems less common with increasing age.

The patient with pharyngitis usually complains of a severe sore throat, malaise and sometimes headache, fever, chills and myalgia. The diagnosis of streptococcal pharyngitis can be made by direct antigen tests (DAT) and throat cultures. A small but highly significant fraction of patients with acute streptococcal pharyngitis/tonsillitis progress to develop complications (Table V).

Table V - Complications of streptococcal pharyngotonsillitis

1. Suppurative
   - peritonsillar abscess
   - retropharyngeal abscess
   - suppurative cervical lymphadenitis
   - otitis media
   - sinusitis
   - mastoiditis
2. Toxin mediated
   - scarlet fever
   - streptococcal toxic shock-like syndrome (TSLS)
     - hypotension and multisystem (organ) failure
3. Nonsuppurative (presumably immune-mediated)
   - post-streptococcal glomerulonephritis
   - rheumatic fever

The treatment of viral pharyngitis is rest, an analgesic such as acetaminophen or aspirin, plus plenty of liquids, including intravenous fluids, if necessary. Penicillin V has long been regarded as the treatment of choice in bacterial pharyngotonsillitis. In Sweden, the recommended dosage in the treatment of streptococcal pharyngotonsillitis in an adult is 12.5 mg/kg body weight twice a day for 10 days[21]. *Streptococci* are not easily eliminated as they are able to "hide" within the tonsillar crypts which are not easily accessible to antibiotics. In the penicillin-sensitive patients, one may consider erythromycin 500mg qid for 10 days or one of the newer macrolides or newer cephalosporins.

After treatment with penicillin, approximately 10% of patients will have recurrence within 2 weeks and as many as 25% of patients will have recurrence within 2 months. Recurrent pharyngitis is a multifaceted problems. Patient compliance, inadequate length of treatment, bacterial tolerance to penicillin, emergence of beta-lactamase producing bacteria and erythromycin resistant beta-*streptococci* have been cited as reasons for recurrence.

Certain alpha-*streptococci* have shown the ability to emit a bacteriocin with the capability to influence the growth of certain beta-*streptococci*. Reimplantation of alpha-*streptococci* with high interference capacity were recently shown to have some protective effect in patients with recurrent streptococcal tonsillitis[22].

The objective of treatment of recurrent pharyngotonsillitis is to lower frequency of recurrences and to avoid a tonsillectomy. Tonsillectomy is performed for recurrent infection confined to the tonsils. Erythromycin or oral cephalosporins might be considered antibiotics of choice for patients with recurrent pharyngitis. Studies by Paradise et al have pointed out the importance of using strict criteria for tonsillectomy[23]. However, because the indications for tonsillectomy remain controversial, each patient must be considered on a case-by-case basis.

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