The Management of Upper Respiratory Tract Infections

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Summary

Upper respiratory tract infections are the commonest reason for consultation in primary care. Group A ß-haemolytic Streptococcus (GABHS), the most important bacterial pathogen in this condition, can be cultured from about 30% of patients, more so in children than adults. Clinical features that are predictive of positive GABHS culture are *absence of cough*, fever, cervical adenopathy, tonsillar enlargement and tonsillar exudate. Use of a sore throat score can help in the detection of streptococcal throat infection. Symptomatic therapies which are useful include anticholinergic, antihistamine, decongestant, humified hot air and Vitamin C. Antibiotics are universally over-prescribed in this condition as a result of high patient expectation and faulty clinical decision making. Oral Penicillin V for 10 days is the drug of choice. Effective intervention to reduce inappropriate antibiotic prescription probably require a multi-faceted approach targeted at both the patients and the prescribers.

Key Words: Upper respiratory tract infection, Sore throat, Streptococcal infection, Antibiotic prescription

Introduction

Upper respiratory tract infections (URTIs) are the commonest reason for consultation in ambulatory care. Although in the majority of cases they are trivial and self-limiting, nonetheless they are major cause of morbidity in terms of work loss and school absenteeism. There is considerable over-prescription of antibiotics and symptomatic therapy for this group of illness.

In this review, URTIs refer to acute infections of nasal mucosa and throat (including larynx). Although sinuses and middle ear are conventionally considered as part of the upper respiratory tract, we have decided not to include these complications of URTIs in the review. In writing the article, we rely primarily on guidelines and systematic reviews published in the last five years.

Epidemiology

On average, preschool children have 4 - 8 episodes of URTI per year, school age children have 2 - 6 episodes per year while adults have 2 - 5 episodes per year[1]. The Second National Health and Morbidity Survey[2] conducted in 1996 reported that 35.8% of children under 5 had an URTI episode in the preceding two weeks. Almost three-quarter of these children sought treatment from doctors. URTIs are the commonest cause of consultation in hospital outpatient department and general practice[3,4].

Aetiology

Most URTIs are viral in origin. Viral URTIs are generally referred to as common colds (colloquially the word "flu" is frequently used). Clinically it is difficult to differentiate the various viral causes which include: adenovirus, parainfluenza virus, rhinovirus, herpes simplex virus, respiratory syncytial virus, Ebstein-Barr (EB) virus, influenza virus, Coxsackie A virus, coronavirus and cytomegalovirus[1]. Influenza virus tends to cause more severe constitutional symptoms and may lead to complications such as bronchitis and pneumonia. Viral URTI spread primarily by direct contact with respiratory secretions of infected individuals. In general, the incubation period is 2 - 4 days and the median duration of symptoms is 7 - 13 days.

Group A ß-haemolytic Streptococcus (GABHS) is the most important bacterial pathogen in URTI. Foong *et al*[5] reported a prevalence of 14.2% in a local university-based primary care clinic adults patients presenting with sore throat. The prevalence of GABHS in patients with sore throat in primary care setting is more common in children (Table I). Streptococcal pharyngitis resolved rapidly even if it is left untreated, 75% of the patients become afebrile within 3 days after the onset of a sore throat. Other bacteria that may cause URTI are non-group A streptococcus, *Corynebacterium diphtheriae, Corynebacterium haemolyticum, Neisseria gonorrhoea and Chlamydia trachomatis*[1].

Diagnosis

A typical patient with URTI may present with some or all of the following symptoms: fever, cough, runny nose, sore throat, body ache, headache, nausea and vomiting. The symptoms help to identify the area of upper airway that is infected: runny nose (rhinitis), facial pain and purulent nasal discharge (sinusitis), throat itchiness (postnasal drip), sore throat (pharyngitis, tonsillitis) and hoarseness of voice (laryngitis). It is not unusual for the patients to have symptoms referable to several area of the upper airway, hence the term rhinopharyngitis. For the unwary, the patients presenting predominantly with recurrent nasal symptoms may be having chronic rhinitis (vasomotor or allergic) rather than URTI. URTI is often a trigger of asthma in susceptible patients, especially in children.

Diagnosis of streptococcal pharyngo-tonsillitis

The main challenge in diagnosis lies in detecting the small proportion of GABHS infection. There is considerable overlap between the symptoms and signs of viral and bacterial causes of sore throat. Even experienced clinicians have been shown to fare poorly in detecting GABHS infection using

Table I
Prevalence of GABHS in Patients with Sore Throat

Setting	Children	Adults	Total
Dutch general practice, [6]n=598	57.5%*	28.6%	32.4%
United States primary care clinics, [7]n=657	40.7%#	22.4%	29.1%

*n=number of patients; *children aged < 15 years; # children aged < 12 years*

Table II
Sensitivity, Specificity and Positive Predictive Values of Five Characteristics Independently Associated with Positive GAS Throat Culture

Characteristics	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
Absence of cough	54.2	69.0	22.0
Temperature >38°C	52.8	71.9	23.2
Tender anterior cervical adenopathy	75.0	62.4	24.2
Tonsillar swelling	56.9	81.1	32.5
Tonsillar exudates	29.2	93.5	42.0

Children (age < 14) is also a positive predictor (data not shown).

Table III
Sensitivity, Specificity, Negative and Positive Predictive Values of Sore Throat Score

Score	Negative Predictive Value (%)	Positive Predictive Value (%)
0	97.5	2.5
1	94.9	5.1
2	88.8	11.2
3	72.2	27.8
4	47.2	52.8

clinical criteria alone[8]. The problem is compounded by the inability of throat swab in differentiating carriers from acute infection. Only 20 - 50% of patients with sore throat and positive throat culture were demonstrated to have objective evidence of infection (raised antistreptolysin O titre)[9]. Many rapid streptococcal antigen detection tests are now commercially available. Although these tests have a high degree of specificity, their sensitivity in clinical practice is unacceptably low[10].

Studies using throat culture as the gold standard of GABHS infections have consistently confirmed certain clinical feature as independent predictors of infection. Table II is recalculated from the data published by Mclsaac *et al*[11]. Since the predictive value of single symptom or sign is rather low, scoring methods that use a combination of the above clinical features are able to increase the identification of GABHS infection. In Mclsaac's study one point was assigned to the presence of each feature in Table II, from this a sore throat score is generated (Table III). For example, a child with fever, tonsillar swelling, sore throat without cough and cervical lymphadenopathy (score = 4) has about 50% chance of having GABHS infection. However, the chance of detecting streptococcal infection in an adult with cough, sore throat and fever (score = 1) is about 5% only. Thus a low sore throat score (0 - 1) is highly suggestive of non-GABHS (presumably viral) infection.

Most doctors are aware that runny nose is suggestive of viral infection. However, many doctors and patients erroneously gave undue emphasis to clinical features that are weakly associated with bacterial infection such as discoloured phlegm[12], severity of sore throat, red (inflamed) throat and duration of illness.

In view of the low sensitivity and specificity of clinical diagnosis of GABHS, guidelines from developed countries[10,13] recommend throat swab as a method of deciding antibiotic therapy. Mclsaac also suggested culturing those with sore throat score 2 - 3 and treat only if culture positive. Tsevat *et al*[14] showed that basing antibiotic therapy on the culture result in paediatric practice in the United States may be the most cost-effective approach. In this cost-effectiveness analysis, empirical therapy is considerably more expensive than culture because of the high cost of treating the acute rheumatic fever developed in patients treated with the later approach.

Management

Treatment for common colds

There are 103 items grouped under the category "Cough & Cold Remedies" in a recent issue of MIMS Malaysia[15]. The bewildering varieties of remedies attest to the huge market for such products. These over-the-counter remedies may contain one or more of the following drugs: antihistamines (e.g. diphenhydramine), narcotic (e.g. codeine), analgesic (e.g. paracetamol), anti-tussive (dextromethorphan) and sympathomimetic (e.g. pseudoephedrine) and mucolytic (e.g. guaiphenesin). A critical review of these over-the-counter remedies showed that there is some improvement in symptoms in the adults but little evidence for effectiveness in children[16].

An evidence-based summary of the treatment for viral URTI (common colds) is given in Table IV. Some of the treatments that have been shown to be effective are not yet part of routine clinical practice in Malaysia. Kaiser *et al*[20] has shown that a subgroup of viral URTI with nasopharyngeal colonisation of bacteria can improve with a course of antibiotic. However two recent systematic reviews[25,26] have shown that antibiotics do not confer benefits in childhood and adult viral URTI.

Antibiotic therapy for streptococcal pharyngo-tonsillitis

Most guidelines recommended the prescription of antibiotic for streptococcal pharyngo-tonsillitis[10,13,27]. There are four reasons for treating this condition:

1. Prevention of rheumatic fever (but not post-streptococcal glomerulonephritis).
2. Prevention of suppurative complications, e.g. peritonsillar abscess, suppurative otitis media.
3. Decreased spread to close contacts.
4. Prompt antibiotic therapy decreases the duration of symptoms.

In a systematic review by Del Mar *et al*[28] the impact of antibiotic therapy for acute sore throat is relatively modest (shortening of symptom duration of only about 8 hours). Little *et al*[29] had recently argued against antibiotic therapy citing the decreasing incidence of rheumatic fever as well as the likelihood of promoting antibiotic resistance and side effects of therapy. In a subsequent trial of prescribing strategies, they demonstrated that the prescribing of antibiotic encouraged future reattendance for sore throat[30]. In developing countries where rheumatic fever and suppurative complications are still relatively prevalent, antibiotic therapy is still appropriate for patients with streptococcal pharyngo-tonsillitis[27].

The antibiotic of choice for streptococcal pharyngo-tonsillitis is oral Penicillin V[10] because of the lack of antibiotic resistance, fewer adverse effects and lower cost. It should ideally be given for 10 days to achieve satisfactory eradication of the bacteria from the throat (82% in Schwartz's study[31]). Recently Zwart[32] showed that 7-day therapy with Penicillin V has an acceptable eradication rate (72%). Intramuscular Benzathine Penicillin 0.6 - 1.2 mega units as a single dose is recommended when compliance is doubtful[10]. The alternative antibiotics are cephalosporins and macrolides, particularly for patients who are allergic to penicillins.

Promoting appropriate prescription for URTI

Studies in the United States had shown that about 50% of both children and adults with URTIs are prescribed antibiotics[33,34]. Aljunid[35], in a survey of primary care doctors in a rural district, demonstrated that private physicians prescribed more antibiotics for URTI than government clinic doctors (76% vs 46%). Excessive use of antibiotics has been identified as the most important cause of the emergence of antibiotic resistance[36]. Furthermore it also exposes patients to needless side effects. Some doctors and patients mistakenly believed that antibiotic is indicated when patients have fever, severe sore throat or discoloured phlegm[11]. Many doctors probably succumb to

Table IV
Treatment for Common Colds

Treatment	Comment
Nasal decongestants/α-adrenergic agonist (e.g. pseudoephedrine)[16,17]	May improve sleep. Excessive use causes rebound effect (rhinitis medicamentosa)
Anticholinergics (e.g. intranasal ipratropium bromide*)[18]	Reduced rhinorrhoea and decreased sneezing, especially if initiated early.
Analgesics (e.g. paracetamol and NSAIDs)	Symptomatic relief
First generation antihistamines (e.g. chlorpheniramine)[19]	Reduced sneezing and rhinorrhoea. Sedative effect may help sleep at night but causes daytime sleepiness
Antibiotics (e.g. co-amoxiclav)[20]	Possible benefit if there is colonisation by bacteria
Vitamin C21	Does not prevent colds. Modest reduction of duration of nasal symptoms (about half a day) when taken at the onset of colds.
Zinc gluconate lozenges*[22]	Some trials showed reduced severity and duration of nasal symptoms. Leave a bitter taste.
Humidified hot air[23]	Reduced nasal symptoms.
Extract of Ecchinaceae*[24]	Most trials demonstrated symptom relief

** Not available in Malaysia*

patient's expectation of an antibiotic easily for fear of damaging the rapport; educating the patients otherwise is perceived to be difficult and time consuming. The financial gain from the prescription and dispensing of an antibiotic may also be operating in private general practice.

Educating the public regarding URTI through the mass media alone had been shown to have little or no impact[37]. Changing doctors' behaviour by means of guidelines alone is less likely to be effective[38]. Trials succeeded at reducing antibiotic prescription for URTI in primary care[39-42] have used a combination of education strategies including guidelines, opinion leaders, outreach visit (academic detailing), reminders and feedback to the high prescribers. Thus effective intervention probably require a multi-faceted approach targeted at both the patients and the prescribers.

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MCQs For The Management of Upper Respiratory Tract Infections

1. The following statements regarding streptococcal pharyngo-tonsillitis are correct:

A. It is more common in children than adults.
B. If untreated, it leads to rheumatic fever in the majority of patients.
C. Rapid streptococcal antigen testing is a highly sensitive diagnostic method.
D. A positive throat culture of Group A beta-haemolytic streptococcus does not prove the presence of this infection.
E. It can be accurately diagnosed from clinical criteria alone.

2. Clinical features that are independently associated with a positive throat culture of Group A beta- haemolytic streptococcus are:

A. Cough
B. Tonsillar enlargement
C. Redness of throat
D. Cervical adenopathy
E. Yellowish phlegm

3. Appropriate choice of antibiotic for streptococcal pharyngo-tonsillitis are:

A. Erythromycin
B. Cloxacillin
C. Penicillin V
D. Co-trimoxazole
E. Benzathine penicillin

4. Treatments that have been shown to reduce or shorten nasal symptoms in common colds are

A. Antihistamine
B. Humidified hot air
C. Cephalosporin
D. Vitamin C
E. Dextromethorphan

5. The following statements regarding antibiotic use in upper respiratory tract infections are correct.

A. Over-prescription of antibiotics is a universal phenomenon.
B. Excessive use of antibiotic contributes to the emergence of antibiotic resistance.
C. Changing patient expectation for antibiotic through mass media campaign is effective.
D. Feedback to high prescribing doctors about their prescribing behaviour is a useful approach.
E. Wide dissemination of guideline effectively reduced over-prescription of antibiotics.