Sore throat: Avoiding antibiotic prescription

Summary of 3 relevant articles

1. Sore throat in primary care project: a clinical score to diagnose viral sore throat

Sore throat is a common problem in general practice. The majority of sore throats are viral in origin and only symptomatic treatment is required. However, documented beta-haemolytic streptococci (GABHS) infection is found in 15%-30% of children and 10% of adults. Although these patients may require antibiotics, antibiotics are generally overprescribed in sore throat. In a survey of antibiotic prescribing in general practice in the UK, antibiotics were prescribed for half of all patients presenting with coughs, colds and viral sore throats. Antibiotic overprescribing is of concern, because it encourages worldwide emergence of resistant bacteria.

The clinical presentation of viral and bacterial sore throat is similar. There are simple clinical scores available to predict the probability of bacterial sore throat (e.g., Centor score). The purpose of this study was to determine the rate of bacterial and viral causes of sore throat and to form a new scoring system to diagnose viral sore throat that might reduce overuse of antibiotics.

Over the course of one year, throat culture for GABHS and a nasopharyngeal swab to detect 16 respiratory viruses were obtained from 624 patients with sore throat presenting to a family medicine center. Overall, 10% were preschool children, 43% were students and the remainder were adults.

Viral infections were found in 44% of patients and GABHS in 18%. Mixed viral and bacterial infections were present in 6%, so that 38% had viral infection only and 13% had bacterial infection only. An infectious cause was not identified in 43% of sore throats. Rhinovirus was the most commonly detected infectious agent, accounting for 25% of viruses. Coronavirus, parainfluenza and influenza A viruses were the next most common, accounting for 6.2%, 5.1% and 4.6% of viruses isolated.

The novel predictive score (Mistik score) for positive viral analysis included the following variables: absence of headache, stuffy nose, sneezing, temperature ≥37°C and the absence of tonsillar exudate and/or swelling. One point was assigned for each item if it was applicable, so that the total possible score was 5. The sensitivity of the score was 60% and specificity was 72%, positive predictive value was 63% and negative predictive value was 71%. The probability of a positive viral analysis for scores 0 to 5 were as follows:

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<tr>
<th>Number of positive criteria</th>
<th>Probability of positive viral analysis</th>
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<tbody>
<tr>
<td>0</td>
<td>8%</td>
</tr>
<tr>
<td>1</td>
<td>15% - 20%</td>
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<tr>
<td>2</td>
<td>25% – 36%</td>
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<tr>
<td>3</td>
<td>42% – 55%</td>
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<tr>
<td>4</td>
<td>62% - 71%</td>
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<tr>
<td>5</td>
<td>82%</td>
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No GABHS was present in patients with a score of 5.
Since a Mistik score of 5 was relatively reliable to predict the presence of viral infection, it may be useful in clinical practice in combination with a simple score, such as the Centor score or modified Centor score, which helps to predict presence of bacterial infection.


2. Spectrum of bactericidal action of amylmetacresol/2,4-dichlorobenzyl alcohol lozenges against oropharyngeal organisms implicated in pharyngitis

Even though patients with sore throat who consult their doctor are often primarily seeking reassurance and symptomatic relief, antibiotics are often inappropriately prescribed. Approximately 90% of acute pharyngitis cases are viral in origin. Antibiotics do not offer symptomatic relief and inappropriate prescribing contributes to the global rise in antibiotic resistance. Consequently there is a need for alternative non-antibiotic strategies that have broad anti-infective effects, while meeting the patients’ need for symptom relief.

Amylmetacresol (AMC) and 2,4-dichlorobenzyl alcohol (DCBA) is an antiseptic that has been shown to have antiviral effects and anaesthetic-like effects with established benefits in providing symptomatic relief from pain.

The most common bacterial cause of sore throat is Group A beta-haemolytic Streptococcus (GABHS, S. pyogenes), which accounts for approximately 30% of paediatric pharyngitis cases, but only 10% of episodes in adults. It rarely results in complications. Other bacteria are less commonly implicated and may present with a more complicated pathology, or represent either an opportunistic infection or an underlying medical condition. Examples include Fusobacterium necrophorum, which is a true pathogen rather than a coloniser of the oropharynx, and Streptococcus dysgalactiae, which can cause severe or recurrent pharyngitis. Moraxella catarrhalis may occur as a co-pathogen with S. pyogenes and can potentiate the adhesion of S. pyogenes to the nasopharyngeal epithelium. Others include Haemophilus influenzae, Arcanobacterium haemolyticum and Staphylococcus aureus. Organisms that may be important in tonsillitis are F. necrophorum and S. aureus, which was the most common pathogen isolated in patients undergoing tonsillectomy due to recurrent tonsillitis.

Nonantibiotic antimicrobial treatments may be beneficial to patients by sparing them exposure to an antibiotic and also by providing symptomatic relief. The purpose of this study was to investigate the in vitro bactericidal activity of AMC/DCBA lozenges against a broad range of potentially pathogenic oropharyngeal bacteria to evaluate the potential in vivo action of these lozenges against organisms associated with pharyngitis.

AMC 0.6 mg and DCBA 1.2 mg lozenges (Strepsils Honey and Lemon) were dissolved in 5 ml artificial saliva medium and applied to inoculum cultures of the following test organisms: S. aureus, S. pyogenes, M. catarrhalis, H. influenzae, F. necrophorum, A. haemolyticum and S. dysgalactiae. The solution was tested after 1, 5 and 10 minutes of contact, consistent with the time a lozenge takes to dissolve in the mouth.
For all organisms, evidence of bactericidal activity was recorded at the 1 minute time point, exceeding 99.9% decrease in colony forming units (CFU)/ml for *S. pyogenes*, *H. influenzae*, *A. haemolyticum* and *F. necrophorum*, whereas a similar decrease was observed at 5 minutes for *S. dysgalactiae* and *M. catarrhalis* and at 10 minutes for *S. aureus*. The results demonstrate that the AMC/DCBA lozenge exhibits rapid bactericidal activity against a wide range of pathogens relevant to pharyngitis in a time that is consistent with that required for the lozenge to dissolve in the mouth.

Previous studies have demonstrated that the AMC/DCBA lozenge exhibits *in vitro* virucidal activity against parainfluenza virus type 3, cytomegalovirus, respiratory syncytial virus, influenza A and severe acute respiratory syndrome coronavirus. Furthermore through its anaesthetic-like action against voltage-gated sodium channels, the lozenge has also been proven to provide relief from symptoms, particularly sore throat.

Therefore patients with uncomplicated bacterial and viral pharyngitis, especially those in low risk populations without additional risk factors, may benefit from the antiseptic action of the lozenge. Most cases of pharyngitis are typically self-limiting and often of viral origin and should not require antibiotics. By addressing symptoms and managing patient expectations, the lozenge may help to reduce the number of inappropriate antibiotic prescriptions for viral pharyngitis.


3. Efficacy of AMC/DCBA lozenges for sore throat: A systematic review and meta-analysis

Approximately 30% of the general population will experience at least one episode of sore throat during a year. Perceived patient pressure is an important factor for antibiotic prescriptions. However, doctors tend to overestimate patients' preferences for antibiotic treatment, whereas patients ask for antibiotics because they want pain relief. Lozenges containing AMC/DCBA are sold worldwide over-the-counter for relief of sore throat. They have virucidal and anaesthetic properties and may be a useful option for symptom relief, thereby reducing requests for antibiotic prescription for sore throat.

The purpose of this systematic review and meta-analysis of randomised controlled trials (RCTs) was to assess the safety and efficacy of AMC/DCBA lozenges for the treatment of acute uncomplicated sore throat in ambulatory patients. Eight publications were included, including 3 RCTs (N=661) comparing AMC/DCBA lozenges to placebo lozenges without AMC/DCBA.

Differences between the AMC/DCBA lozenges and placebo for various endpoints are listed in the table below.
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<thead>
<tr>
<th>Outcome</th>
<th>Measurements</th>
<th>Outcome</th>
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| **Sore throat pain intensity** (primary outcome) | Sore throat after 2 hours measured with an 11-point scale (0=no sore throat; 10=maximum sore throat)\(^a\) Mean score at baseline: 7.15 | Weighted mean sore throat pain reduction at 120 minutes:  
AMC/DCBA: -1.92  
Placebo: -0.95  
SMD: -0.6 (95%CI -0.75 to -0.45; \(P<0.00001\))                                      |
| **Sore throat relief**                 | Sore throat relief measured after 2 hours on a 7-point scale (0=no relief; 6=complete relief) | Mean absolute sore throat relief scores at 120 minutes:  
AMC/DCBA: 1.9  
Placebo: 0.87  
SMD: 0.89 (95%CI 1.04 to 0.73; \(P<0.00001\)) |
| **Difficulty swallowing**             | Difficulty swallowing after 2 hours measured with visual analogue scale [VAS] (0=swallowing not difficult; 100=very difficult)\(^b\) Baseline VAS: 67.1-66. | Mean decrease in VAS at 120 minutes:  
AMC/DCBA: -16.2  
Placebo: -6.1  
SMD: -0.9 (95%CI -1.06 to -0.75; \(P<0.00001\)) |
| **Throat numbness**                   | 5 point categorical scale (1=none; 5=complete numbness)                        | Mean increase in throat numbness after 120 minutes:  
AMC/DCBA: 2.05  
Placebo: 1.59  
SMD: -0.59 (95%CI -0.39 to -0.78; \(P<0.00001\)) |

\(\text{SMD: standardised mean difference; 95\%CI: 95\% confidence interval}\)
\(\text{a. Clinically important improvement = -2; b. Clinically important difference in postoperative pain = -33\%}\)

Additional results reported in one or more of the publications were as follows:

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<tr>
<th>Outcome</th>
<th>AMC/DCBA lozenge</th>
<th>Placebo lozenge</th>
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<tr>
<td>Free from symptoms at 48 hours</td>
<td>16%</td>
<td>6%</td>
</tr>
<tr>
<td>72 hours</td>
<td>35% Significant improvement vs. placebo</td>
<td>10%</td>
</tr>
<tr>
<td>Eating and speaking</td>
<td>Significant improvement vs. placebo</td>
<td></td>
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<tr>
<td>Emotional benefit</td>
<td>52% to 58%</td>
<td>19% (P&lt;0.00001)</td>
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The incidence of adverse events ranged from 2% to 16% and did not differ between the AMC/DCBA lozenge and placebo lozenge groups in any of the studies. Most of the reported adverse effects were mild and could be attributed to the upper respiratory tract infection.

The investigators conclude that AMC/DCBA lozenges can be a safe treatment option to relieve pain in patients with uncomplicated sore throat. They offer a modest additional effect compared to nonmedicated lozenges.