Group A β Hemolytic Streptococci in rheumatic patients receiving long acting penicillin

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ABSTRACT

Objective: To detect group A β hemolytic streptococci (GABHS) in the throat of rheumatic patients receiving long acting penicillin (LAP) for 2yr prophylaxis using different schedules and to compare the results of ordinary throat culture versus latex agglutination for the rapid detection of streptococci.

Patients and methods: Setting. Pediatric cardiology and general pediatrics clinics, Ain Shams University, Cairo, Egypt. A prospective study on 200 rheumatic children and 100 controls; all cases complained of sore throat. Rheumatic groups were: GI (n = 60) receiving LAP (Benzathine penicillin) every 2 weeks, GII (n=60) receiving LAP every 4 weeks, GIII (n=40) on oral penicillin (Phenoxy methyl penicillin), GIV (n=40) in rheumatic activity. Two throat swabs were taken from each case one for ordinary culture and the other for latex agglutination.

Results: Latex agglutination test for rapid detection of group A streptococci had a 100% sensitivity and specificity. The biweekly LAP regimen significantly (P<0.01) eradicated throat streptococci than the 4 weeks and oral regimens A highly significant difference (P<0.001) was found between the biweekly regimen and the control group as regard the presence of GABHS. Streptococci were the cause of pharyngitis in 20% of controls.

Conclusion: The latex agglutination test is a rapid, sensitive and specific tool for the detection of GABHS. LAP is still the corner stone for 2yr prophylaxis in rheumatic fever. The biweekly schedule is superior to both the 4 weeks and the oral regimens in eradicating GABHS.

Keywords: Group A β hemolytic streptococci (GABHS), latex agglutination, rheumatic fever (RF), long acting penicillin (LAP).


streptococcal pharyngitis is a common infection occurring in one third of cases of pharyngitis in school aged children and teenagers. The relation between GABHS and acute RF has been established for many years. Inspite of being a common infection, the symptoms and signs of GABHS are usually non-specific and reliable clinical diagnosis is difficult.

The recommended treatment of GABHS pharyngitis for over 45 years has been 10 days penicillin. For the prevention of RF recurrences in patients with rheumatic history, the use of intramuscular LAP or oral penicillin have been used successfully. In developing countries, secondary prophylaxis using LAP has significantly decreased the mortality, prevalence hospital admission and severity of RF and rheumatic heart disease. In these countries the most cost-effective control strategy appears to be secondary prophylaxis.

The efficacy of penicillin against GABHS has been doubted lately due to the resurgence of RF in industrialized countries. Moreover, some authors...
reported the failure of penicillin to eradicate the streptococci from the throat of 20% of cases.10
In an attempt to evaluate penicillin, efficacy in the eradication of GABHS, this work was done to detect the presence of these streptococci in the throat of rheumatic patients suffering from a congested sore throat and receiving regular LAP prophylaxis. The results of ordinary culture were compared to those of rapid detection of streptococci by latex agglutination.

<table>
<thead>
<tr>
<th>Group</th>
<th>Throat +ve</th>
<th>Throat -ve</th>
<th>Latex agglutination +ve</th>
<th>Latex agglutination -ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI (n=60)</td>
<td>0</td>
<td>60</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>GII (n=60)</td>
<td>7</td>
<td>53</td>
<td>7</td>
<td>53</td>
</tr>
<tr>
<td>GIII (n=40)</td>
<td>5</td>
<td>35</td>
<td>6</td>
<td>34</td>
</tr>
<tr>
<td>GIV (n=40)</td>
<td>4</td>
<td>36</td>
<td>3</td>
<td>37</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>80</td>
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<td>80</td>
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The study was carried out on 200 rheumatic patients (110 females and 90 males) suffering from a congested sore throat with or without fever, during their attendance for follow up in the pediatric cardiology clinic. Their ages ranged between 6-18 years with a mean of 10 years.

They were divided into the following groups: GI (n = 60) rheumatic patients who received LAP injections every 2 weeks. GII (n = 60) rheumatic patients who received LAP injections every 4 weeks. GIII (n = 40) rheumatic patients who received oral penicillin prophylaxis. GIV (n = 40) patients in rheumatic activity (10 in arthritis and 30 had carditis alone or with arthritis). The same brand of LAP was used to all patients in groups I & II.

The rheumatic patients in groups I, II and III were suffering from either valvular heart disease or had a rheumatic history of arthritis and or carditis that recovered without residual heart disease. The diagnosis of RF was based on the revised Jones’ criteria.11

A control group of 100 children suffering from congested sore throat with or without fever were included. They were otherwise healthy and didn’t receive any antibiotic treatment for 2 weeks prior to examination. (The study was carried out from May 1994 to May 1996). For every child, a pair of throat swabs were taken. They were taken 2 weeks after LAP in groups I & III and after 4 weeks in group II, by rubbing a sterile cotton tipped swab on a wooden applicator over the tonsillar area without touching the tongue or the lips. The first swab was rolled on an agar plate containing sheep blood. The inoculum was further distributed by streaking with a loop to obtain isolated colonies. The plates were then incubated at 35°C under anaerobic conditions for 24 -48 hours. These plates were observed for the presence of b hemolytic streptococci. All the organisms isolated from the throat swab gave significant pure heavy growth in culture. GABHS colonies were identified as white grey colonies surrounded by a clear zone of complete b-hemolysis. They were also sensitive to Bacitracin test which was done as follows: disks containing 0.04 units of Bacitracin were added to the primary culture plates. Streptococci of Lancefield group A were sensitive to Bacitracin i.e. gave a large zone of inhibition around disk (> 15 mm inhibition in diameter), while most other streptococci were resistant i.e. gave no inhibition or only a very small zone. Serotyping was not done to the strains that were difficult to eradicate.

The other swab was used for rapid antigen detection using the “Reveal color strept A” latex agglutination test from “Murex Company”. It detects group A streptococcal antigen in pharyngeal swabs. The results of the test were obtained in 10-15 minutes and were read as : positive, negative or non-specific.

The results of culture were used to assess penicillin efficacy but penicillin level was not done at the time of culture.

Statistical methods. Statistical analysis were done using Fisher exact and Chi square according to Epi Info Ver 6-0 1994. Both sensitivity and specificity were done for the evaluation of the latex agglutination test.

The results of throat culture and latex agglutination are shown in Table 1.

Statistical analysis using Fischer exact revealed a highly significant decrease (p<0.01) in GABHS in the throat of patients receiving LAP every 2 weeks than those receiving it every 4 weeks or on oral penicillin.

<table>
<thead>
<tr>
<th>Throat culture</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>0</td>
</tr>
<tr>
<td>GII</td>
<td>7</td>
</tr>
<tr>
<td>GI</td>
<td>0</td>
</tr>
<tr>
<td>GIII</td>
<td>5</td>
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<tr>
<td>GI</td>
<td>0</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
</tr>
<tr>
<td>GI &amp; II</td>
<td>7</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
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</table>

p<0.01 = highly significant  p<0.001 = highly significant
A highly significant difference was also noted between those receiving LAP/2 weeks and the control group. The intake of penicillin (either every 2 or 4 weeks) decreased GABHS than the control group.

The overall sensitivity of latex agglutination was 100% and its specificity 100%. The culture (in all cases and controls) revealed the presence of the following organisms: GABHS (13%), normal flora i.e. strept. viridans and neisseria catarrhalis (28%), staph. aureus (28%), others as strept pneumonias, klebsiella and diphtheroids in 22% while no growth was found in 9% of cases (Fig. 1).

R.F. relapse occurred in 1 patient from group II and 1 patient in group III. Thus affecting 14% and 25% of rheumatic patients with documented streptococcal infection and receiving LAP/4 weeks or oral penicillin respectively.

The clinical diagnosis of GABHS throat infection is a difficult one in most cases. Viruses are a frequent cause of sore throat. In this work, 9% of patients had no growth by culture and 28% had normal flora. These 37% of cases are probably viral in etiology. The patient with viral sore throat might be seen early before the development of rhinitis or conjunctivitis thus making the diagnosis difficult. Typically, GABHS throat infection leads to high fever, follicular tonsillitis and enlarged lymph nodes. Nowadays, the clinical picture is not so typical and many patients simply complain of a sore throat. The study was carried out on patients with congested sore throat because they are the most common finding that lead the pediatrician to prescribe an antibiotic in developing countries.

If we consider the early diagnosis and treatment of GABHS important to avoid RF, the diagnosis becomes of paramount importance in patients with past history of RF and RHD. Laboratory tests are helpful in the diagnosis of GABHS. Throat cultures identify GABHS and patients with negative cultures don't receive antibiotics. Their drawback is that 24-48 hours elapse before the organism is identified. In some areas, the patient can not be reached 48 hours later.

In this work, the comparison of culture and latex agglutination revealed a high sensitivity (100%) and specificity (100%). A previous study (16) found a sensitivity of 95% and specificity of 100% while another (15) reported a sensitivity of 84% and a specificity of 99%. The higher percentages found in this work may be due to the use of a different recent brand.

The results of the rapid antigen detection test are promising because of its easy technique and rapid data that make it possible to prescribe an antibiotic (if needed) for the patient in the same visit. Another main advantage is that a patient with a positive result will have to continue treatment for ten days. It is also cost-effective to treat patients with positive results only than to treat all cases with sore throat. Moreover, early diagnosis and therapy may reduce the period of infectivity and morbidity allowing the patient to return to normal activity soon. The main drawbacks of the test are being expensive and the false negative results.

The problem of penicillin failure to treat GABHS throat infection poses a more serious problem when it comes to 2yr prophylaxis against RF. Other antibiotics have been suggested to be effective in the treatment of GABHS.13,15 Yet, for 2yr prophylaxis these antibiotics are expensive for long term usage, their side effects after years of intake haven't been studied and in general compliance to oral prophylaxis is difficult to assess. It was found11 that RF recurrences were doubled in patients on oral penicillin prophylaxis than in those receiving LAP injection. This was explained by the lack of compliance to oral intake.

In this work, bi-weekly LAP was highly effective in eradicating streptococci from the throat. It was superior to LAP/4 weeks and oral penicillin. The difference between these groups and the control is significant denoting the efficacy of penicillin in general in treating GABHS. RF relapse occurred only in patients on LAP taken every 4 weeks and in those receiving oral penicillin. Yet, none of the patients on LAP/2 weeks developed rheumatic fever relapse. The biweekly regimen was adopted based on the clinical experience about the number of recurrences of RF on this regimen compared to the 3 and 4 weeks regimens. The biweekly schedule is also adopted by
other workers\textsuperscript{10,17} who found it more effective in preventing rheumatic recurrences than the 3 weeks or 4 weeks regimens.

The efficacy of penicillin in treating GABHS has been strengthened by the work\textsuperscript{4} that found streptococcal isolates from acute pharyngitis patients to be exclusively susceptible to penicillin. Moreover, available data indicate that the minimal inhibitory concentrations of penicillin to GABHS have not changed in the past four decades.\textsuperscript{9}

Only, 10% of our patients with RF activity had GABHS denoting that streptococci are difficult to retrieve from the throat once activity started.

The results of this work indicate that LAP is still the cornerstone for the treatment of GABHS. The bi-weekly schedule is superior to other schedules whether the 4 weekly or oral regimens. The latex agglutination test is both sensitive and specific, its a break through in microbiological diagnosis. It helps in the rapid detection of GABHS in the throat and thus facilitates early treatment and prevention of RF.

References