

β -haemolytic streptococci in acute pharyngitis

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العقديات الحالة للدم بيتا والتهاب البلعوم

جلال بوقديدة، نعيمة بوقديدة، هشام بن سعيد، هدى المهرش، نائلة الحناشي، صلاح الراعي، كامل المنستيري

الخلاصة: من أجل تحديد دور وأهمية العقديات الحالة للدم بيتا في حالات التهاب البلعوم الحادة واستجابتها النسبية للمضادات الحيوية، فقد قمنا بزراعة عينات من 143 مريضاً (تتراوح أعمارهم ما بين 3 و72 عاماً) واجعوا ثلاثة مراكز للرعاية الصحية الأولية في سوسة بتونس على مدى خمسة أشهر عام 2001. وقد كشفت المزارع عن 80 من العقديات الحالة للدم بيتا (65 من الزمرة A و21 من غير الزمرة A). إلا أن كل الذراري أظهرت حساسيتها لبينزيل البنسلين والأموكسيسيلين والكلوRAMفنتكول والريفاميسين والبريستيناميسين. وقد تفاوتت درجة الحساسية للأريثروميسين والتيتراسيلين والفوسفوميسين والتيليثروميسين والليفوفلوكساسين. وقد تم تحديد الحد الأدنى من التركيز التثبيطي من خلال اختبارات E لبينسلين والأريثروميسين والليفوفلوكساسين. وقد أكدت النتائج التي حصلنا عليها أن البنسلين لا يزال العلاج المرجعي لالتهاب البلعوم الحاد. ولكن من أجل الحد من احتمالات المضاعفات الناتجة عن استخدامه، فلا بد من التيقظ المستمر.

ABSTRACT To determine the role and importance of β -haemolytic streptococci in acute pharyngitis and its relative susceptibility to antibiotics, we cultured samples from 143 patients (age range: 3–72 years) who presented over a 5-month period in 2001 at three primary health care centres in Sousse, Tunisia. The cultures yielded 80 β -haemolytic streptococci (59 group A streptococci and 21 non-group A streptococci). All strains were susceptible to benzylpenicillin, amoxicillin, chloramphenicol, rifampicin and pristinamycin. Susceptibility was variable in erythromycin, tetracycline, fosfomycin, telithromycin and levofloxacin. Minimum inhibitory concentrations were determined by E-test for penicillin, erythromycin and levofloxacin. Our results confirm that penicillin is still the reference treatment for acute pharyngitis. However, to minimize the potential for complications arising from its use, continued vigilance is required.

Les streptocoques β -hémolytiques dans la pharyngite aiguë

RESUME Afin de déterminer le rôle et l'importance des streptocoques β -hémolytiques dans la pharyngite aiguë et leur sensibilité relative aux antibiotiques, nous avons procédé à la culture de prélèvements de gorge de 143 patients (fourchette d'âge : 3-72 ans) qui se sont présentés dans trois centres de soins de santé de base à Sousse (Tunisie) pendant une période de cinq mois en 2001. La culture a mis en évidence 80 streptocoques β -hémolytiques (59 streptocoques du groupe A et 21 streptocoques n'appartenant pas au groupe A). Toutes les souches étaient sensibles à la benzylpénicilline, à l'amoxicilline, au chloramphénicol, à la rifampicine et à la pristinamycine. La sensibilité était variable pour l'érythromycine, la tétracycline, la fosfomycine, la télithromycine et la lévofloxacine. Les concentrations inhibitrices minimales ont été déterminées par E-Test pour la pénicilline, l'érythromycine et la lévofloxacine. Nos résultats confirment que la pénicilline demeure le traitement de référence de la pharyngite aiguë. Toutefois, il est nécessaire de maintenir une vigilance afin de réduire les possibilités de complications liées à son utilisation.

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Introduction

Acute pharyngitis is a frequently occurring illness with a global distribution and is one of the most common conditions for which antibiotics are prescribed. Most cases are of viral etiology, while others are mainly bacterial [1,2]. The most prevalent of the bacterial pharyngitids are due to β -haemolytic streptococci. *Streptococcus pyogenes*, or group A β -haemolytic streptococcus (SA), is the principal bacterial pathogen implicated in this illness and its potential complications [3]. Non-group A β -haemolytic streptococci (SNA) also cause infections that mimic group A streptococcal pharyngitis [1]. A lack of knowledge of these bacteria could result in ineffective treatment for patients [4]. Only streptococcal pharyngitis justifies the use of antibiotics. Antibiotic treatment of non-bacterial pharyngitids adds greatly to the potential for the emergence of resistant strains in oropharyngeal human flora [5].

We conducted a study in Sousse, Tunisia, to determine the prevalence of *S. pyogenes* and non-group A β -haemolytic streptococci in acute pharyngitis and the pattern of antibiotic susceptibility of β -haemolytic streptococci for the optimal treatment of streptococcal pharyngitis.

Methods

The study was carried out at 3 primary health care centres in Sousse, during 5 hot, dry months beginning in May 2001. All patients with acute pharyngitis aged ≥ 3 years were eligible for inclusion in the study. The throat of each patient was examined for bacteria. Patients with symptoms of viral infections or allergic responses (including conjunctivitis, lachrymation, hoarseness, anterior stomatitis, cough, diarrhoea, coryza and sneezing) were excluded as were

those who had been treated with antibiotics in the previous 3 days and those who declined swab sampling.

Throat swab (Portagerm-Amies agar swab, bioMérieux, France) samples were cultured on agar blood plates within a maximum of 3 hours of the swab being taken and incubated in an atmosphere containing 5% carbon dioxide at 37 °C for 24–48 hours. Samples with a count of > 20 β -haemolytic colonies were identified [4]. Pastorex STREP (Sanofi-Pasteur, Paris, France) was used to group the strains. Susceptibility patterns to various antibiotics were determined according to National Committee for Clinical Laboratory Standards norms [6]. The agents used were: benzylpenicillin, amoxicillin, erythromycin, tetracycline, fosfomycin, chloramphenicol, pristinamycin, rifampicin, telithromycin and levofloxacin. Minimum inhibitory concentrations (MIC) were determined by E-test for penicillin, erythromycin and levofloxacin. The control strain was *Streptococcus pneumoniae* ATCC 49619.

Results

Of the 143 patients studied (mean age: 13 years; range: 3–72 years), the incidence of sore throat was highest among children. We obtained 63 negative cultures and 80 positive cultures without redundancy, from which 59 clinical isolates of SA were recovered. The highest frequency of SA was among children (Figure 1). Of all throat cultures, 41.2% were SA and, of all β -haemolytic streptococci isolates, 73.8% were SA isolates. Additionally, 21 clinical isolates of SNA were recovered, i.e. 14.7% of all throat cultures and 26.3% of all β -haemolytic streptococci isolates. Among these SNA isolates, 11 strains (13.8% of all β -haemolytic streptococci) were group G

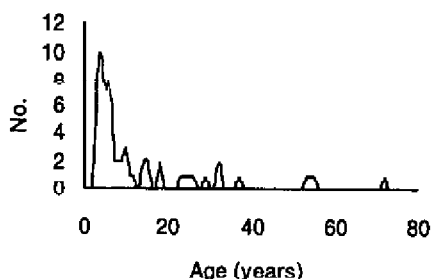


Figure 1 Number of isolates of group A streptococcus in acute pharyngitis by age

streptococci, 7 (8.8%) were group C streptococci and 3 (3.8%) were group F streptococci.

Susceptibility patterns of the isolates for SA to antibiotics were: benzylpenicillin 100% of SA, MIC 0.016–0.192 mg/L; levofloxacin 78%, MIC 0.016–3.000 mg/L (MIC range norms: 2–4 mg/L); telithromycin 100%; pristinamycin 100%; rifampicin

100%; erythromycin 59.3%, MIC 0.016–256+ mg/L; and chloramphenicol 100%. Susceptibility to other antibiotics was variable (Tables 1,2).

For all SNA, the concentration of penicillin required to inhibit all isolates was < 0.25 mg/L. In this study, the overall rate of erythromycin resistance in SNA strains was 100%, 85.7% and 66.7% for groups G, C and F respectively (Tables 1,2). The MIC of the macrolides was high, with susceptibility to erythromycin of all the group G streptococci studied ranging from intermediate to resistant. All strains of groups G and C were susceptible to levofloxacin (MIC for group G 0.380–1.000 mg/L; group C 0.032–0.750 mg/L; group F 0.250–0.750 mg/L). For group F streptococci, only 66.7% of the strains were susceptible to tetracycline (Tables 1,2). Susceptibility patterns for other antibiotics varied.

Table 1 Susceptibility* to antimicrobials tested for isolates of groups A, G, C and F streptococci

| Susceptible to: | Group A (n = 59) % | Group G (n = 11) % | Group C (n = 7) % | Group F (n = 3) % |
|------------------|--------------------------|--------------------------|-------------------------|-------------------------|
| Amoxicillin | 100.0 | 100.0 | 100.0 | 100.0 |
| Benzylpenicillin | 100.0 | 100.0 | 100.0 | 100.0 |
| Chloramphenicol | 100.0 | 100.0 | 100.0 | 100.0 |
| Erythromycin | 59.3 | 0.0 | 14.3 | 33.3 |
| Fosfomycin | 68.8 | 72.7 | 57.1 | 100.0 |
| Levofloxacin | 78.0 | 100.0 | 100.0 | 100.0 |
| Pristinamycin | 100.0 | 100.0 | 100.0 | 100.0 |
| Rifampicin | 100.0 | 100.0 | 100.0 | 100.0 |
| Telithromycin | 100.0 | 54.5 | 71.4 | 100.0 |
| Tetracycline | 67.9 | 10.0 | 71.4 | 66.7 |

*Susceptibility excludes resistant and intermediate responses.

Table 2 Minimum inhibitory concentrations (MIC) of 3 antimicrobials for isolates of Groups A, G, C and F β -haemolytic streptococci

| Antimicrobial | MIC (mg/L) | | | |
|------------------|---------------|---------------|-------------|---------------|
| | Group A | Group G | Group C | Group F |
| Benzylpenicillin | 0.016–0.192 | 0.016–0.190 | 0.032–0.190 | 0.023–0.094 |
| Erythromycin | 0.016–256.000 | 0.047–256.000 | 0.016–4.000 | 0.010–256.000 |
| Levofloxacin | 0.016–3.000 | 0.380–1.000 | 0.032–0.750 | 0.250–0.750 |

Discussion

Acute pharyngitis is one of the most frequently occurring illnesses and one of the most common conditions for which antibiotics are prescribed [1,4,5,7–9]. Viruses are its most common cause [5]. The presence of clinical features such as conjunctivitis, cough, hoarseness, coryza, anterior stomatitis, discrete ulceration lesions and diarrhoea suggest a viral rather than bacterial etiology. Because patients with symptoms of viral infection were excluded from our study, positivity for bacteria was high, and yet β -haemolytic streptococci were absent from 44% of cases. SA was more frequently implicated in acute pharyngitis in our study (41.2%) than in several other studies [1,4,8–10] and justified the use of penicillin [1,5,7,10]. SNA, i.e. groups G, C and F streptococci, were less common but appeared to be associated with exudative pharyngitis [5,8]. In our study, almost 15% of clinical isolates were SNA, compared to 10%–12% in other studies [8,11].

A few studies have asserted that group B streptococci are capable of producing acute pharyngitis [8,11,12]. In our study, group B streptococci were not identified in any of the isolates. Nearly 15% of SNA isolates were positive for group F streptococci. While a review of current literature suggests that group F streptococci are not agents of streptococcal pharyngitis, the question remains whether group F strepto-

cocci are implicated in the etiology of acute pharyngitis or are simply a part of the normal oropharyngeal flora.

Recent studies have reported that clinical screening could be an effective supplement to rapid SA antigen tests to decrease the unnecessary use of antibiotics [2]. Double screening can contribute to the accurate management of acute pharyngitis and minimize the emergence of resistant strains of common bacteria, particularly *S. pneumoniae* and *Neisseria meningitidis* [13].

In our study, as in numerous other studies, all 80 isolates were susceptible to penicillin. *S. pyogenes* was still remarkably susceptible to most antibiotics [14]. The MIC of benzylpenicillin had not changed and remained < 0.2 mg/L. A clinical isolate of SA resistant to penicillin has never been documented anywhere [5]. All SNA strains were susceptible to benzylpenicillin, amoxicillin, chloramphenicol and pristinamycin. They were also susceptible to levofloxacin and rifampicin but although some of the newer antibiotics (particularly levofloxacin and telithromycin) have been efficacious in respiratory tract infections [15], these drugs should not replace benzylpenicillin or amoxicillin in the treatment of bacterial pharyngitis [14]. For patients allergic to penicillin [7,10,16], erythromycin and other macrolides have been recommended as alternative treatments.

Resistance to erythromycin and related drugs has become widespread [7,10,14,17] with 40% of the SA described in our study exhibiting such resistance. The overall rate of erythromycin resistance and intermediate susceptibility in SNA strains was high, ranging from 66.7% to 100%, compared with the rates reported elsewhere of between 10% and 55% [11,12,14,17–20]. These results call into question the role of erythromycin as a suitable alternative for patients allergic to penicillin. These patients require continuous surveillance and a carefully considered antibiotic approach [7]. Pristinamycin, telithromycin and levofloxacin can be used instead for erythromycin-resistant strains.

Available evidence suggests that penicillin and amoxicillin remain the reference treatments for acute pharyngitis despite the introduction of new antibiotics. The antimicro-

bial agents used to treat SA would be appropriate for SNA; however, the duration of treatment should be shorter, since SNA have never been shown to cause acute rheumatic fever [1].

SA is the main bacteria implicated in acute pharyngitis and justifies the continued use of penicillin. Our results confirm benzylpenicillin as the treatment of choice in acute pharyngitis because of its efficiency, safety, narrow spectrum and low cost [1,5]. The control of SA pathogenesis demands only the availability of primary care and appropriate treatment [1]. SNA are common agents of acute pharyngitis and are still susceptible to penicillin. Optimal management of acute pharyngitis is necessary to minimize the antibiotic pressure on oropharyngeal flora without increasing the risk of post-streptococcal complications.

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