Impact of susceptibility to antibiotics of streptococci & enterococci isolated from patients with infective endocarditis on antibiotic treatment

Liliana Mihaila-Amrouche, Laurent Schlegel, Anne Bouvet & the Association pour l’Étude et la Prévention de l’Endocardite Infectieuse (AEPEI) Study Group*

Centre National de Référence des Streptocoques - Service de Microbiologie, Hôtel Dieu, Assistance Publique-Hôpitaux de Paris, Université Paris VI, 1 place du Parvis Notre-Dame, F-75181 Paris Cedex 04 & *AEPEI: Service de Maladies Infectieuses et Tropicales, Hôpital Bichat-Claude Bernard, 75018 Paris, France

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Background & objectives: Streptococci and enterococci are the most frequent pathogens causing infective endocarditis. In order to update the recommendations for both curative and prophylaxis treatment, the susceptibility to antibiotics of the most prevalent species of Streptococcaceae isolated from the patients with infective endocarditis was determined.

Methods: Streptococcal and enterococcal isolates (n=133) isolated from confirmed cases of infective endocarditis during a one-year prospective survey conducted in 1999 in France were studied. The identification of 106 streptococci and 27 enterococci to the species level was carried out by conventional methods. Their susceptibility to ten antibiotics used in curative or prophylactic treatment was measured. Minimal inhibitory concentrations were determined by agar dilution method.

Results: All the streptococcal and enterococcal isolates were susceptible to 4 mg/l or less of penicillin or amoxicillin. High levels of resistance to aminoglycosides were observed in two species, Streptococcus gallolyticus subsp. gallolyticus and Enterococcus faecalis. All isolates were susceptible to glycopeptides. Resistance to erythromycin, clindamycin, and pristinamycin was restricted to some species.

Interpretation & conclusion: Curative treatments recommended for streptococcal or enterococcal endocarditis, including penicillin, amoxicillin or vancomycin in association with gentamicin were found to be appropriate for 98.5 per cent of cases. The emergence of erythromycin resistance in oral streptococci led to the use of pristinamycin in oral prophylactic treatment in patients allergic to β-lactams.

Key words Antimicrobial treatment - Enterococci - infective endocarditis - prophylaxis - Streptococci

Streptococcaceae represent 60 per cent of the microorganisms isolated from blood or cardiac vegetations of patients with infective endocarditis¹. The common condition found to be responsible for endocarditis streptococci was due to oral dental procedures. The bacteraemia due to group D streptococci or enterococci were mostly associated with intestinal diseases².

In order to update the recommendations for the treatment and the prophylaxis of endocarditis, the susceptibility to antibiotics of the most prevalent species of streptococci and enterococci was determined and compared with the results of the previous national survey³,⁴.
Material & Methods

Streptococcal and enterococcal isolates (n=133) were isolated from patients with endocarditis during a one-year prospective survey conducted in 1999 by the Association for Study and Prevention of Infective Endocarditis (AEPEI) study group in France. The diagnosis was confirmed according to the Duke University criteria.

The 106 streptococcal and 27 enterococcal isolates were identified by conventional methods on the basis of morphology, haemolysis, Lancefield’s group antigen, growth in NaCl 6.5 per cent (wt/vol) broth, and bile-esculin test. Biochemical characters of identification were obtained with the rapid ID 32 STREP and Api 20 Strep systems (BioMérieux, Marcy l’Etoile, France). Species terminology was adapted from the results of recent taxonomic studies.

Titrated powders of the ten antibiotics recommended for the curative or the prophylactic treatment of endocarditis were used: penicillin G, amoxicillin, ceftriaxone, gentamicin, tobramycin, vancomycin, teicoplanin, erythromycin, clindamycin, and pristinamycin. Minimal inhibitory concentrations (MICs) were determined by the agar dilution method in Mueller-Hinton agar for enterococci and Mueller-Hinton agar supplemented with 5 per cent horse blood for streptococci. Susceptibility, intermediate susceptibility, and resistance to antibiotics were interpreted according to the recommendations of the Comité de l’Antibiogramme de la Société de Microbiologie Française (CA-SFM). As an additional marker, high level of resistance to streptomycin was detected with the disk diffusion method using paper-load disk with 500 mg of streptomycin (Bio-Rad, Ivry sur Seine, France). In addition, the phenotypes of resistance to erythromycin, observed on the basis of a double diffusion disk test and E-test strips (AB Biodisk, Sweden) with both erythromycin and clindamycin, were indicative of their mechanism of resistance.

Results

The 106 streptococcal isolates belonged to 13 different species (Table I). They were distributed between three major groups: the pyogenic group (n=7), the oral group (n=38), and the S. bovis / S. equinus complex (group D streptococci) (n=61). The 27 enterococcal isolates were Enterococcus faecalis. The level of susceptibility to antibiotics differed according to the groups and the species (Table II). Most of the streptococcal isolates, 102 of 106 (96%) were susceptible to penicillin G (MICs < 0.25 mg/l). Four out of 38 oral streptococci had an intermediate susceptibility (0.5 mg/l < MIC < 16 mg/l); of these, three were S. sanguinis and one S. oralis. All enterococcal strains were also of intermediate susceptibility. No strain was resistant to penicillin G. Among streptococcal isolates, 103 of 106 (97%) were categorized as susceptible to amoxicillin (MICs < 0.5 mg/l) and three S. sanguinis as intermediate (1 mg/l < MIC < 16 mg/l). No streptococcal isolates was found to be resistant to amoxicillin. All enterococcal isolates were susceptible to amoxicillin (MICs < 4 mg/l). All streptococcal isolates were susceptible to ceftriaxone (MICs < 0.5 mg/l) and all enterococcal isolates were resistant (MICs > 32 mg/l).
High-level of resistance to streptomycin was observed in two species: S. gallolyticus subsp. gallolyticus (20 of 51 strains) and E. faecalis (7 of 27). All streptococci had a low level of resistance to gentamicin and tobramycin. Only two of the 27 E. faecalis had high level of resistance to gentamicin and tobramycin (MICs > 1024 mg/l). All isolates were susceptible to glycopeptides.

The intermediate susceptibility or resistance to erythromycin and clindamycin was restricted to some species: S. mitis (4 and 2 of 14, respectively), S. sanguinis (3 of 7), S. anginosus (1 of 3), S. dysgalactiae subsp. equisimilis (1 of 2), S. gallolyticus subsp. gallolyticus (41 of 51) and E. faecalis (12 of 27). Both the phenotype of resistance to erythromycin and the high level of MICs of erythromycin and clindamycin indicated a constitutive mechanism of methylation for all isolates except two S. mitis. These two isolates were resistant to erythromycin and susceptible to clindamycin due to an inducible phenotype of methylation mechanism of resistance in one isolate and a phenotype of an efflux mechanism in another. In addition, two isolates of S. sanguinis among the 38 oral streptococci and 11 of S. gallolyticus subsp. gallolyticus among the 61 group D streptococci showed intermediate susceptibility (MICs = 2mg/l) or resistance (MICs > 4mg/l) to pristinamycin. All isolates studied were susceptible to penicillin or amoxicillin levels reached in the serum during the treatment. All isolates were susceptible to vancomycin and teicoplanin. Only two isolates of E. faecalis had a high level of resistance to gentamicin.

**Discussion**

Both curative and prophylactic treatment of endocarditis depends on the causative organisms and their antibiotic susceptibilities. The curative treatment recommended for endocarditis combines penicillin or amoxicillin with gentamicin. In allergic patients, vancomycin or teicoplanin replaces β-lactams. Our results indicated that these recommendations were appropriate in 98.5 per cent of the cases. The choice of antibiotics to prevent endocarditis in at risk patients depends on the streptococcal and enterococcal species present on the portal of entry of the bacteria. For the oral prophylaxis during dental procedures, erythromycin (or other 14- and 15 C membered macrolides), clindamycin, and pristinamycin are the alternatives to amoxicillin in allergic patients. In the present study, 21 per cent of the oral streptococci were resistant or of intermediate susceptibility to erythromycin. This emergence of macrolide resistance led to the use of pristinamycin (5% of resistant strains).

Among group D streptococci, S. gallolyticus subsp. gallolyticus was the predominant species. It is associated with colonic cancer and endocarditis. Although most of the isolates were resistant to several antibiotics, they were susceptible to the antibiotics recommended for prophylaxis during intestinal procedures which included penicillin, amoxicillin, gentamicin and vancomycin. Less than 10 per cent of isolates of E. faecalis associated with endocarditis of intestinal or urogenital origin, had a high level of resistance to gentamicin which is recommended in combination with amoxicillin or vancomycin in prophylaxis.

<table>
<thead>
<tr>
<th>Penicillin G</th>
<th>Amoxicillin</th>
<th>Erythromycin</th>
<th>Clindamycin</th>
<th>Pristinamycin</th>
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<tr>
<td>S I</td>
<td>S I</td>
<td>S I R</td>
<td>S R</td>
<td>S I R</td>
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<tr>
<td>Oral streptococci</td>
<td>34 4</td>
<td>35 3</td>
<td>30 2 6</td>
<td>32 6</td>
</tr>
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<td>(n=38) (I+R%)</td>
<td>(11)</td>
<td>(8)</td>
<td>(21)</td>
<td>(16)</td>
</tr>
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<td>Group D streptococci</td>
<td>61 20</td>
<td>41</td>
<td>20 41</td>
<td>50 8</td>
</tr>
<tr>
<td>(n=61) (I+R%)</td>
<td>(67)</td>
<td>(67)</td>
<td>(18)</td>
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S, susceptible; I, intermediate susceptibility; R, resistant
The association observed between different species and their susceptibility to various antibiotics confirmed the need of accurate identification of causative microorganism for appropriate treatment of endocarditis.

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References


