Antibiotic prophylaxis of endocarditis: the rest of the world and NICE

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Previous guidelines[1,2] recommended antibiotic prophylaxis for the majority of patients with congenital and heart valve disease. Almost all current national or international guidelines, including those from the USA,[3,4] Europe[5] and Australia,[6,7] have narrowed these recommendations radically, but still recommend prophylaxis for certain dental procedures in high-risk cardiac patients (Table 1). NICE[8] is alone in recommending no antibiotic prophylaxis for any cardiac patients undergoing dental or non-dental procedures except for manipulations at an infected non-dental site. Most cardiologists and cardiac surgeons still follow international guidelines rather than NICE. Is this justified?

The NICE committee[8] based their advice on the assertions that: (1) there is no consistent association between having an interventional procedure, dental or non-dental, and the development of infective endocarditis – regular tooth-brushing almost certainly represents a greater risk of IE than a single dental procedure; (2) the clinical effectiveness of antibiotic prophylaxis is not proven; and (3) antibiotic prophylaxis for dental procedures may lead to a greater number of deaths through fatal anaphylaxis than a strategy of no antibiotic prophylaxis and is not cost-effective.

Although NICE dismissed an association between a dental procedure and the development of endocarditis, many of the studies cited (para 2.3.2) suggest a link. A case-matched study[9] of 273 patients with infective endocarditis found no association with dental work in general, but extractions occurred in six patients with infective endocarditis and in no case-controls ($p = 0.03$). However, only about one-third had infective endocarditis as a result of mouth organisms and the extractions were not performed in patients with valve disease. A Dutch study showed that a combination of a heart lesion, natural dentition and a dental procedure gave a relative risk for infective endocarditis of 4.9.[10] A French case-controlled study[11] showed a significant association between infective endocarditis and repeated scaling and canal treatment although not for all dentistry. Other studies[12–14] have also found an association between infective endocarditis and extraction or, less frequently, with root canal work. Animal models[15] suggest an inconsistent relationship between bacterial load and the likelihood of infective endocarditis depending on the strain of alpha-haemolytic streptococcus. There may also be genetic differences in susceptibility.[16] These possibilities may help to explain variations in the human literature.

The NICE committee correctly stated that, in the absence of a prospective randomized clinical trial, the clinical effectiveness of antibiotic prophylaxis is not proven. However a number of studies suggest a benefit. A Dutch case-controlled study,[13] which was also the only study found eligible for a Cochrane review,[17] suggested a reduction in risk of only 49%. This was based on 48 cases with endocarditis after a dental or non-dental procedure, but, importantly, excluded high-risk patients with prosthetic valves. In a study specifically of prosthetic valves[12] there

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Table 1

Cardiac conditions requiring antibiotic prophylaxis for high-risk dental procedures included in International guidelines[3–7], but excluded by NICE[8]

Replacement heart valves or prosthetic material used for cardiac valve repair

Previous infective endocarditis

Congenital heart disease:

- Unrepaired cyanotic congenital heart disease including palliative shunts and conduits
- Completely repaired using prosthetic material or device during the first 6 months after the procedure (surgical or percutaneous)
- Repaired with residual defect at the site or adjacent to the site of a prosthetic patch or device

Cardiac transplantation with valve regurgitation due to structurally abnormal valve[3,4]

were six cases of infective endocarditis in 304 who were unprotected by antibiotics, but no cases in 229 protected patients. A French study[18] estimated an incidence of infective endocarditis in patients with valve disease of 1 case per 46,000 unprotected dental procedures compared with 1 case per 149,000 protected procedures. The protective effect of antibiotics has been estimated at 46%,[11] 49%,[13] 70%,[18] and 91%.[19] These clinical observations suggest that animal work showing the effectiveness of a single dose of amoxicillin in preventing streptococcal endocarditis[20,21] may be relevant to humans.

The NICE[8] committee considered, but decided against, defining a high-risk group, to include patients with prosthetic valves, because it felt that this would be confusing. Patients with prosthetic valves have a five-fold higher risk of developing infective endocarditis than those with native valve disease.[17] The mortality is substantially higher, about 25% during the acute event,[22] and up to 41% at 30 days.[23] Long-term survival rates are only 55% at 5 years and 38% at 10 years.[24] This is largely because 10–35% of survivors need further cardiac surgery which is at markedly increased risk.[24,25] International guideline groups,[3–7] clinical studies[11,18] and a study modelling cost-effectiveness[26] conclude, differently from NICE, that antibiotic prophylaxis, while no longer generally advisable, should be focused on such high-risk groups.

The NICE committee quoted a risk of fatal anaphylaxis of approximately 20 per million administrations of penicillin. This figure is based mainly on data published in the 1960s when most of the subjects who died had received parenteral penicillin,[27] often to treat syphilis. There is little published information on the risks of oral amoxicillin, but yellow card returns in the UK suggest that fatal anaphylaxis is extremely rare and the figures quoted by NICE may be an overestimate.[28] In the world literature there have been no reports of fatal anaphylaxis after oral amoxicillin prophylaxis for endocarditis. Patients with prosthetic valves who have received amoxicillin prophylaxis in the past without any problems are unlikely to develop anaphylaxis. Testing for hypersensitivity is now available.

All guidelines agree that the main measure for preventing infective endocarditis is the maintenance of excellent oral hygiene. There are few patients at high risk of endocarditis (Table 1) compared to those with native valve disease. The cost saved by adopting the NICE guidelines would therefore be relatively small. We suspect it would be offset by unnecessary deaths since there is good reason to think that antibiotic prophylaxis may be effective in high-risk groups before high-risk procedures like dental extractions.

There is no national surveillance programme for endocarditis to alert us to any potential increase in the incidence of prosthetic endocarditis as a result of the NICE guidelines. In our current state of knowledge, we advise our high-risk patients (Table 1) to take antibiotic prophylaxis before high-risk dental procedures such as extractions. This is in keeping with international guidelines.[3–7,29]

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