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

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Previous guidelines¹² 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 USA³⁴, Europe⁵, and Australia⁶, have narrowed these recommendations radically, but still recommend prophylaxis for certain dental procedures in high risk cardiac patients (Table 1). NICE⁶ 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 committee³ 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 (IE). Regular toothbrushing almost certainly represents a greater risk of IE than a single dental procedure;

(2) the clinical effectiveness of antibiotic prophylaxis is not proven;

(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 study⁷ of 273 patients with IE found no association with dental work in general, but extractions occurred in 6 patients with IE and in no case-controls (p=0.03). However, only about a third had IE 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 IE of 4.91⁸. A French case-controlled study⁹ showed a significant association between IE and repeated scaling and canal treatment although not for all dentistry. Other studies¹⁰-¹¹ have also found an association between IE and extraction or, less frequently, with root canal work. Animal models¹² suggest an inconsistent relationship between bacterial load and the likelihood of IE depending on the strain of alpha-haemolytic streptococcus. There may also be genetic differences in susceptibility¹³. These possibilities may help to explain variations in the human literature.

The NICE committee correctly stated that, in the absence of a prospective randomised clinical trial, the clinical effectiveness of antibiotic prophylaxis is not proven. However a number of studies suggest a benefit. A Dutch case-controlled study⁹, which was also the only study found eligible for a Cochrane review¹⁴, 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 valves¹⁵ there were 6 cases of IE in 304 who were unprotected by antibiotics, but no cases in 229 protected patients. A French study¹⁶ estimated an incidence of IE 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%¹⁷, 70%¹⁸ and 91%¹⁹. These clinical observations suggest that animal work showing the effectiveness of a single dose of amoxicillin in preventing streptococcal endocarditis¹⁶,²¹ may be relevant to humans.

The NICE 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 5-fold higher risk of developing IE than those with native valve disease⁷. The mortality is substantially higher, about 25% during the acute event²², and up to 41% at 30 days²³. Long-term survival rates are only 55% at 5 years and 38% at 10 years²⁴. This is largely because 10-35% of survivors need further cardiac surgery which is at markedly increased risk²⁵. International guideline groups¹³-¹⁷, clinical studies¹¹,¹², and a study modelling cost-effectiveness²⁶ 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 dying received parenteral penicillin\(^2\), 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 over estimate\(^2\). 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 IE 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, International guidelines that continue to recommend antibiotic prophylaxis for high risk cardiac patients, particularly those with prosthetic heart valves, remain preferable to NICE.

References