

Interactive clinical case: to give, or not to give, infective endocarditis prophylaxis

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ABSTRACT

The practice of prophylactic use of antibiotics before certain procedures for preventing infective endocarditis (IE) is not based on rigorous scientific data. It seems reasonable, however, to offer prophylactic antibiotics before dental procedures to patients who would have the highest risk of adverse events if they were to develop IE. The current recommendations do not include patients with rheumatic heart disease (RHD) in such a category. In the real world, however, patients with underlying RHD suffer high morbidity and mortality with IE due to several reasons. Consequently, prophylactic antibiotics should be used judiciously in patients with RHD. Further, other patient related factors might influence the decision to use antibiotics.

Infective endocarditis (IE) remains a serious illness. The incidence of IE has not declined in the last five decades.¹ Mortality rates from IE, even in the current era, vary from 8–30% in different reports, and morbidity remains high.^{2–14} Consequently, prevention of IE remains a priority for physicians caring for patients predisposed to IE.

Ideas for preventing IE have undergone significant changes over time. The evolution of these ideas makes for instructive reading.¹⁵ The basic tenets for the use of IE prophylaxis include: (1) bacteria cause IE; (2) common bacteria that cause IE are found in the oral, gastrointestinal and urinary tract regions of the human body; (3) bacteraemia results from procedures undertaken at these sites involving manipulation of the mucosae; (4) in animal experiments, preprocedural antibiotics have reduced the incidence of IE. Therefore preprocedural antibiotics could reduce the occurrence of IE in humans.

The disease was uniformly fatal before antibiotics were discovered. Even with treatment, the rates of mortality and morbidity resulting from IE were very high. The fear of the disease was legitimately great, and soon after antibiotics were discovered, recommendations were suggested to prevent IE by using antibiotics before procedures that could cause IE in predisposed individuals. As our understanding about IE grew, and better information became available, the predisposed population was divided into low, medium and high risk categories, and the procedures that could cause IE were also stratified. The American Heart Association (AHA) recommendations were revised nine times from 1955 to 2007.^{16–25}

The empirical nature of the recommendations was repeatedly emphasised, but in practice the recommendations were followed enthusiastically like commandments. However, in 2007, after

nearly five decades of using preprocedural antibiotics, the AHA recommendations underwent a major overhaul necessitated by the increasing realisation of a lack of evidence for the efficacy of previous practices.²⁵ It became apparent that bacteraemia from daily activities far outweighs the bacteraemia resulting from procedures. Further, prophylactic antibiotics reduce a very small number of IE cases, if at all, even if it were 100% effective. In addition, costs and other implications associated with the widespread use of preprocedural antibiotics are not small. Therefore, antibiotic prophylaxis is now recommended only for patients at greatest risk of adverse events in the event of IE.²⁵

Meanwhile, the epidemiology of IE has changed significantly, more so in the western world. The emergence of nosocomial IE, the increasing population of older patients, the emergence of *Staphylococcus* species as a causal agent, and the decline of RHD in the western world are significant noteworthy changes,¹ which impact the practice of IE prophylaxis. Also, the prevailing medico-legal climate has led to demands for increasingly evidence-based recommendations.²⁵ The AHA recommended prophylaxis for patients with prosthetic heart valves, cyanotic congenital heart disease, previous IE, or cardiac transplant valvulopathy undergoing invasive dental procedures. No prophylaxis was recommended for patients undergoing gastrointestinal or genitourinary procedures. Other western societies endorsed these guidelines, and some recommended completely abolishing the practice of prophylaxis before any procedures.^{26–28} All these guidelines do not recommend prophylaxis for patients with rheumatic heart disease (RHD).

IS RHD NOT A HIGH RISK CONDITION?

Patients with RHD were advised to receive prophylaxis in the 1990 recommendations, were considered at ‘moderate risk’ in the 1997 recommendations, and were not advised prophylaxis in the 2007 recommendations based on their moderate risk lesion status in the previous recommendations. The decline of RHD in the western world seems to have influenced the decision, since the rates of morbidity and mortality in RHD patients with IE in many other parts of the world remain disturbingly high—high enough to classify RHD under the ‘highest risks of adverse events’ category currently. The value judgement of ‘highest risk of adverse events’ in the event of IE remains arbitrary and difficult to standardise, but the large number of contemporary reports of IE from many parts of the world including India, Pakistan, South America and other regions in the current era show



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inordinately high rates of morbidity and mortality.^{2–14} Although not specifically analysed, RHD remains a dominant predisposing condition in these reports. The incidence of IE in RHD (380–440 cases/100 000 person years) is not very different from that in patients with prosthetic heart valves (308–630/100 000 person years) or with previous IE (300–740/100 000 person years).²⁹ However, it is recognised that IE prophylaxis is based on the risks of adverse events following IE and not on the risks of incurring IE; but the risks from IE in RHD are not small as evident by the current literature.

While native valve community-acquired viridans endocarditis is treatable with reasonable success in the current era, the realities of IE treatment in many parts of the world portray a different picture. There is a long delay in access to health care in these regions of the world. Inadequate diagnostic facilities, and inadequate treatment due to many socioeconomic factors, conspire to result in unfavourable outcomes from IE in these regions, and this should be duly recognised. RHD, a disease associated with poor socioeconomic status, occurs in these regions only. The contemporary multicentred Global Rheumatic Heart Disease Study (REMEDY) of 3343 RHD patients reveals a high risk of adverse events even without IE. In this study, 16.9% of patients died within 2 years follow-up. There was a gradient in mortality rates, ranging from 12.8% in upper middle income countries to 20.8% in low income countries.³⁰ Although it was a study based on tertiary care settings, it clearly shows the difficulties in accessing medical management and the severe disease status of patients with RHD in many regions of the world.

The impact of IE on such RHD patients as currently seen in major parts of the world is not difficult to imagine.

It might be reasonable to offer different sets of recommendations based on the regional outcomes of IE, but the patient with RHD clearly seems to be at high risk of adverse events in the event of IE. It is satisfying to note that Australian guidelines for IE prophylaxis suggest that indigenous Australians are advised prophylaxis before dental procedures (though others are not recommended) based on the similar reasoning as above.^{31–32} Even Brazilian guidelines concur with these sentiments and recommend prophylaxis for patients with RHD.^{33–34}

MAIN AREAS OF FOCUS FOR PREVENTING IE

It has long been apparent that ensuring optimum oral health would prevent far more episodes of IE than antibiotic prophylaxis. Similarly, appropriate infection control strategies would prevent far more nosocomial IE than any preprocedural antibiotics. The importance of such practices cannot be over-emphasised. But implementing these practices requires robust medical care facilities, and in the real world their implementation faces the same gradient of challenges as discussed above for RHD. The dearth of resources for dental care parallels that of the general medical care facilities,³⁵ and routine dental care is not a norm in most parts of the world where RHD still remains. Consequently, it is possible that the standard of oral hygiene in these patients could be worse than that seen in western societies, although this has not been systematically studied. Whether this could have a bearing on the prophylaxis question is not known, but is plausible.

DOES IE PROPHYLAXIS WORK?

The use of IE prophylaxis is a contentious issue. It is axiomatic nowadays to suggest that bacteraemia from daily activities far outweighs bacteraemia arising from procedures. But if that is the case, why is IE not more common? Obviously, there are

numerous other factors that are not clearly understood in the pathogenesis of IE. One of many such issues might relate to the quality and quantity of bacteraemia. Although, in general, the magnitude of bacteraemia from a dental procedure is relatively low (<10⁴ colony forming units (CFU)/mL, similar to that resulting from daily activities), and is less than that required to cause experimental IE in animals (10⁵–10⁸ CFU/mL), the infective dose or duration causing IE in humans is unknown.²⁵ The bacteraemia following daily activities like tooth brushing is certainly more intense in people with poor oral hygiene;³⁶ and the bacteraemia following tooth extraction is more severe and more often contains viridans streptococci than that which occurs during tooth brushing.³⁷ Obviously, such factors are difficult to study and difficult to standardise in recommendations. Further, although bacteraemia from daily activities is clearly a more important threat for IE, this does not mean that large episodes of bacteraemia from dental procedures are of no concern.³⁸ There are reports of small increases in the incidence of IE since the change in recommendations both from the USA and the UK, but the causality cannot be definitely established.^{39–40} There was an increase of 0.11 cases of IE/10 million patients/month in the UK report.³⁹ This was accompanied by a major decrease in the use of antibiotics, hence the cost effectiveness of the recommendations might favour the current recommendations. The estimated absolute risks of IE from a dental procedure are astonishingly small (eg, 1/1.1 million procedures for patients with mitral valve prolapse), but are similar for patients with RHD, prosthetic valves or previous IE (1/142 000, 1/114 000, and 1/95 000, respectively).⁴¹ Nevertheless, one study recently suggested that antibiotic prophylaxis might be cost effective, particularly in individuals at high risk.⁴² There are no similar systematic studies regarding the incidence of IE from parts of the world with RHD, nor is the adherence to changed guidelines known in these areas.

SHOULD IE PROPHYLAXIS BE INDIVIDUALISED?

Guidelines have acquired a statutory status despite reiterations that these are only guidelines to help physicians make appropriate clinical decisions. The situation is more complex in modern times with medico-legal implications. In an area such as prophylaxis of IE where individual risk assessments are almost impossible, a sledge hammer approach has been in vogue for a few decades, even if based on empirical half-truths. But that should not discourage clinicians from thinking rationally. In fact, the AHA committee on valve disease did suggest prophylaxis in selected circumstances based on the physician's or patient's choice, although they did not suggest it for RHD.⁴³ Even the 2007 AHA recommendation opts for antibiotic prophylaxis for invasive and incisional respiratory procedures, or genitourinary procedures in patients with infection, although routinely no prophylaxis is recommended for respiratory, gastrointestinal or genitourinary procedures. Similarly, would it not be prudent to offer prophylactic antibiotics before dental extraction in those patients with particularly poor oro-dental status? Similarly, would it not be reasonable to offer antibiotic prophylaxis to a patient with RHD and severe pulmonary hypertension requiring a dental procedure before double valve replacement, such as in this case?

Guideline based decisions should be tempered with clinical reasoning in an individual patient.

Based on the above reasoning, I would propose preprocedural antibiotics in the index case.

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