Preventive strategies against infective endocarditis: Are these worthless?

Jagdish C. Mohan, MD, DM; Vishwas Mohan, Resident

Department of Cardiac Sciences, Fortis Hospital, Shalimar Bagh, Delhi, India

Abstract

In the past, we have expended considerable effort and resources in devising strategies for antibiotic prophylaxis against infective endocarditis. There has been several sets of guidelines and strategies enunciated in this regard without any hard evidence, since 1955. Antibiotic prophylaxis given before invasive dental and non-dental interventional procedures have been the focus for infective endocarditis prevention for more than 50 years and remains the standard of care for patients at high risk in most parts of the world. Anesthetists, dentists, cosmetologists, urologists, and gynecologists are the ones who have to implement these guidelines primarily. In the past half a century, a tendency can be seen towards shorter duration and lower dose of antibiotics, and that fewer patients are considered to be at risk of infective endocarditis (IE). There has never been a randomised study into the use of antibiotic prophylaxis in this context. The American Heart Association published updated guidelines for IE prevention in 2007 that markedly restricted the use of antibiotic prophylaxis in certain at-risk patients undergoing dental and other invasive procedures. The French had begun this 2002 onward. National Institute of Health and Clinical Excellence (NICE) in United Kingdom took a drastic step in 2008 in recommending a policy of "no antibiotic prophylaxis". There has been support and criticism for this policy. This minimalistic approach has found good support in Europe. However, newer research presented at end-2014 has shown that implementation of these guidelines may have resulted into 25% greater increased number of infective endocarditis in the United Kingdom. Safety of the 2008 NICE guidelines is under review. In this short write-up, the whole gamut of antibiotic prophylaxis of infective endocarditis is revisited with special regard to developing countries.

Key Words

• Trans fats/trans-fatty acids
• Partially hydrogenated vegetable oils

Introduction

Infective endocarditis (IE) is an uncommon but deadly disease with an in-hospital mortality of 20% and 1-year mortality approaching 40%. The incidence is about 5/100,000 population. Incidence of IE in India is hard to guess in view of lack of population studies. Applying worldwide data to Indian population would yield an incidence of about 50,000 to 100,000 cases per year. About 5% of the entire population is abnormally

Received: 30-11-14; Revised: 06-07-15; Accepted: 07-07-15

Disclosures: This article has not received any funding and has no vested commercial interest

Acknowledgments: None
IE as of now, about 50% of staph infections are
villages, certainly contribute to our share of right-sided
developing countries, reuse of syringes by unqualified
intravenous drug abusers may not be a big problem in the
changed microbial profile of the disease. Although,
accounts for more than one-third of all IE and this has
immunosuppressive therapy, hemodialysis, etc.
Coagulase-negative staph is getting implicated more
embolic complications, greater need for surgery,
even in the population-based studies. Staph infections
Viridans group streptococci are part of the normal skin,
demonstrated for this strategy. Can we rely only on good
to adverse events including anaphylaxis. Hence, definite
based on expert opinion. Antibiotics not only entail cost
regimen in humans has never been properly investigated
dental interventional procedures. The efficacy of this
antibiotic prophylaxis before dental and certain non-
dentalsurgical procedures. The exact microbiology remains under cloud.10,11 Portal of
entry of infection is not clear in vast majority of patients and hence prophylaxis can never be very effective.

Patients at risk
Following categories are at special risk of developing IE:
1. Patients with congenital structural heart diseases (excluding atrial septal defects, closed ductus arteriosus, and devices for closures)
2. Patients with acquired valvular heart disease
3. Patients with prosthetic heart valves
4. Previous IE
5. Hypertrophic cardiomyopathy
6. Patients with implanted cardiac rhythm devices
7. Patients with percutaneous intravenously inserted long-term use catheters and ports

Both the American and European guidelines initially suggested dividing patients into high risk and moderate risk.12,13

IE epidemiology
Epidemiology of IE has changed over last half a century.1 IE caused by Streptococcus viridans is decreasing and
that caused by Staphylococcus aureus is increasing.1 Viridans group streptococci are part of the normal skin,
oral, respiratory, and GI tract flora, and they are either caused at least 50% of cases of community-acquired native
IE are associated with intravenous drug use. However, streptococcal IE is decreasing in frequency even in the population-based studies.1 Staph infections are associated with longer hospital stay, more frequent embolic complications, greater need for surgery, increased cost, and higher in-hospital mortality.1 Coagulase-negative staph is getting implicated more because of healthcare-associated infections.1 Entercoccal infection is rising due to increasing age, immunosuppressive therapy, hemodialysis, etc. Entercocci are notorious for multidrug resistance. Reuse of disposable material in catheterisation laboratories in the developing world is fuelling IE caused by gram-negative bacilli. Healthcare-associated IE now accounts for more than one-third of all IE and this has changed microbial profile of the disease. Although, intravenous drug abusers may not be a big problem in the developing countries, reuse of syringes by unqualified personnel in the remote areas, and unsafe deliveries in villages, certainly contribute to our share of right-sided IE. As of now, about 50% of staph infections are methicillin-sensitive and this number is declining. In India, culture-positive IE is only about 50% and, hence, the exact microbiology remains under cloud.10,11

High risk
1. Previous IE
2. Prosthetic heart valves
3. Unoperated congenital cyanotic heart disease or complex congenital heart disease with residual lesions or with prosthetic material used during repair
4. Valvulopathy post cardiac transplantation

Moderate risk
1. Valvular heart disease
2. Hypertrophic cardiomyopathy
3. Previous rheumatic fever
4. Heart murmur
5. Uncomplicated ventricular septal defects, etc.

Propylaxis against IE
The AHA made radical changes in their IE prevention guidelines in 200717 that recommended use of antibiotic prophylaxis for invasive dental procedures to only four groups of patients who would be at higher risk from complications and mortality if they developed endocarditis. A single dose of amoxicillin or ampicillin was considered safe and the preferred prophylactic agent for individuals who did not have a history of type I hypersensitivity reaction to penicillin, such as anaphylaxis, urticaria, or angioedema. The major changes in the updated recommendations included the following:
1. Only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis for dental procedures even if such prophylactic therapy were 100% effective.
2. Infective endocarditis prophylaxis for dental procedures is reasonable only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from infective endocarditis (previous IE), unoperated cyanotic congenital heart disease, complex congenital heart disease with residual lesions or with prosthetic material having been used in repair, prosthetic heart valves, valvular heart disease in post-transplant patients.
3. For patients with these underlying cardiac conditions, prophylaxis is reasonable for all dental procedures that involve manipulation of gingival tissue or the peripheral region of teeth or perforation of the oral mucosa.
4. Prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of infective endocarditis.
5. Administration of antibiotics solely to prevent endocarditis is not recommended for patients who undergo a genitourinary or gastrointestinal tract procedure.

NICE guidelines 2008
In March 2008, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom produced controversial new guidance recommending the cessation of antibiotic prophylaxis for all patients at risk of infective endocarditis undergoing dental and a wide range of other invasive procedures.18 Summary of these guidelines is shown below:

1. Good oral hygiene for all including susceptible subjects
2. Discourage chlorhexidine mouthwash before dental procedures
3. Proper asepsis before body piercing and tattooing
4. No routine antibiotic use
5. Antibiotic prophylaxis only if instrumentation of an infected area
6. Suspected IE should be vigorously investigated at the earliest.

Why “no antibiotic prophylaxis”?19
Active or potential infection treatment needs antibiotics. Premise of antibiotic prophylaxis is that invasive procedures on teeth, gums, respiratory tract, and genitourinary system lead to bacteremia. This bacteremia may be the underlying mechanism of IE in susceptible individuals. However, bacteremia occurs in many daily activities like tooth brushing or massage of the gums, etc. and also routine diagnostic procedures like endoscopy, bronchoscopy, transesophageal echocardiography, urinary catheterisation, vaginal examination, etc. One can’t be prescribing antibiotics in every scenario which can cause transient bacteremia. There are no published prospective, randomized, placebo-controlled trials to evaluate either the risk of IE attributable to dental or non-dental procedures or the efficacy of antibiotic prophylaxis in these setting.19

Consequence of “no antibiotic policy”20
Given the lack of demonstrated efficacy of IE antibiotic prophylaxis, it is of paramount importance to identify any increase in viridans group streptococcal IE that would and could result from the restricted/no use of antibiotic prophylaxis.

Twelve months before the NICE guidelines were introduced, dentists accounted for 91.9% of prescriptions for antibiotic prophylaxis, whereas 14 to 25 months after the introduction of the guidelines, the number of prescriptions written by dentists decreased significantly by 79.9%.19 For the first two years, there was no increase in incidence of IE. However, after that the incidence showed a trend and, overall, the incidence of infective endocarditis in England has increased significantly by 25% between 2008 and 2013.19 This increase in incidence has affected both high-risk and lower-risk individuals. Infective endocarditis-associated in-hospital mortality also increased, although this increase was not significant, possibly because of the lower mortality associated with infective endocarditis caused by oral streptococci. Although, there is temporal relationship between cessation of antibiotic prophylaxis and increase in incidence of IE, it is difficult to establish a causative relationship.

On the other hand, after a highly restrictive policy regarding antibiotic prophylaxis, there has been no

J. Preventive Cardiology • Vol. 4 • No. 4 • May 2015

727
susceptible if bicuspid aortic valve, mitral valve prolapse, and degenerative valvular heart disease alone are included as criteria of susceptibility. It is apparent that one in 1000 susceptible subjects develops IE every year (with a risk multiple of 50). Bacteremia secondary to an interventional procedure in a susceptible subject (with a pre-existing cardiac lesion) is the underlying risk factor. In an attempt to prevent this disease, over the past 50 years, at-risk patients have been empirically given antibiotic prophylaxis before dental and certain non-dental interventional procedures. The efficacy of this regimen in humans has never been properly investigated and clinical practice has been dictated by guidelines based on expert opinion. Antibiotics not only entail cost and the spectrum of developing resistance, but may lead to adverse events including anaphylaxis. Hence, definite evidence and cost-effectiveness needs to be demonstrated for this strategy. Can we rely only on good oral hygiene and cleanliness during medical (catheter insertion, dialysis, etc.) and non-medical procedures like tattooing, piercing, etc., for preventing IE?

### IE epidemiology

Epidemiology of IE has changed over last half a century.1 IE caused by *Streptococcal viridans* is decreasing and that caused by *Staphylococcus aureus* is increasing.2 Viridans group streptococci are part of the normal skin, oral, respiratory, and GI tract flora, and they are generally associated at least 50% of cases of community-acquired native IE and are associated with intravenous drug use. However, streptococcal IE is decreasing in frequency even in the population-based studies.3 Staph infections are associated with longer hospital stay, more frequent embolic complications, greater need for surgery, increased cost, and higher in-hospital mortality.4 Coagulase-negative staph is getting implicated more because of healthcare-associated infections.5 Entercoccal infection is rising due to increasing age, immunosuppressive therapy, hemodialysis, etc. Entecococci are notorious for multidrug resistance. Reuse of disposable material in catheterisation and hence prophylaxis can never be very effective.

### Patients at risk

**Following categories are at special risk of developing IE:**

1. Patients with congenital structural heart diseases (excluding atrial septal defects, closed ductus arteriosus, and devices for closures)
2. Patients with acquired valvaral heart disease
3. Patients with prosthetic heart valves
4. Previous IE
5. Hypertrophic cardiomyopathy
6. Patients with implanted cardiac rhythm devices
7. Patients with percutaneous intravenously inserted long-term use catheters and ports
8. Pregnancy

Both the American and European guidelines initially suggested dividing patients into high risk and moderate risk.6-9

### High risk

1. Previous IE
2. Prosthetic heart valves
3. Unoperated congenital cyanotic heart disease or complex congenital heart disease with residual lesions or with prosthetic material used during repair
4. Valvulopathy post cardiac transplantation

### Moderate risk

1. Valvular heart disease
2. Hypertrophic cardiomyopathy
3. Previous rheumatic fever
4. Heart murmur
5. Uncomplicated ventricular septal defects, etc.

### Prophylaxis against IE

**The AHA made radical changes in their IE prevention guidelines in 2007** that recommended use of antibiotic prophylaxis for invasive dental procedures to only four groups of patients who would be at higher risk from complications and mortality if they developed endocarditis. A single dose of amoxicillin or ampicillin was considered safe and the preferred prophylactic agent for individuals who did not have a history of type I hypersensitivity reaction to penicillin, such as anaphylaxis, urticaria, or angioedema. The major changes in the updated recommendations included the following:

1. Only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis for dental procedures even if such prophylactic therapy were 100% effective.
2. Infective endocarditis prophylaxis for dental procedures is reasonable only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from infective endocarditis (previous IE), unoperated cyanotic congenital heart disease, complex congenital heart disease with residual lesions or with prosthetic material having been used in repair, prosthetic heart valves, valvular heart disease in post-transplant patients.
3. For patients with these underlying cardiac conditions, prophylaxis is reasonable for all dental procedures that involve manipulation of gingival tissue or the peripheral region of teeth or perforation of the oral mucosa.
4. Prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of infective endocarditis.
5. Administration of antibiotics solely to prevent endocarditis is not recommended for patients who undergo a genitourinary or gastrointestinal tract procedure.

### NICE guidelines 2008

In March 2008, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom produced controversial new guidance recommending the cessation of antibiotic prophylaxis for all patients at risk of infective endocarditis undergoing dental and a wide range of other invasive procedures.10 Summary of these guidelines is shown below.

1. Good oral hygiene for all including susceptible subjects
2. Discourage chlorhexidine mouthwash before dental procedures
3. Proper asepsis before body piercing and tattooing
4. No routine antibiotic use
5. Antibiotic prophylaxis only if instrumentation of an infected area
6. Suspected IE should be vigorously investigated at the earliest

### Why “no antibiotic prophylaxis”?

Active or potential infection treatment needs antibiotics. Premise of antibiotic prophylaxis is that invasive procedures on teeth, gums, respiratory tract, and genitourinary system lead to bacteremia. This bacteremia may be the underlying mechanism of IE in susceptible individuals. However, bacteremia occurs in many daily activities like tooth brushing or massage of the gums, etc. and also routine diagnostic procedures like endoscopy, bronchoscopy, transesophageal echocardiography, urinary catheterisation, vaginal examination, etc.11 One can’t be prescribing antibiotics in every scenario which can cause transient bacteremia. There are no published prospective, randomized, placebo-controlled trials to evaluate either the risk of IE attributable to dental or non-dental procedures or the efficacy of antibiotic prophylaxis in these settings.12

### Consequence of “no antibiotic policy”

Given the lack of demonstrated efficacy of IE antibiotic prophylaxis, it is of paramount importance to identify any increase in viridans group streptococcal IE that would and could result from the restricted/no use of antibiotic prophylaxis. Twelve months before the NICE guidelines were introduced, dentists accounted for 91.9% of prescriptions for antibiotic prophylaxis, whereas 14 to 25 months after the introduction of the guidelines, the number of prescriptions written by dentists decreased significantly by 79.9%.13 For the first two years, there was no increase in incidence of IE. However, after that the incidence showed a steady trend and, overall, the incidence of infective endocarditis in England has increased significantly by 25% between 2008 and 2013.14 This increase in incidence has affected both high-risk and lower-risk individuals. Infective endocarditis-associated inhospital mortality also increased, although this increase was not significant, possibly because of the lower mortality associated with infective endocarditis caused by oral streptococci. Although, there is temporal relationship between cessation of antibiotic prophylaxis and increase in incidence of IE, it is difficult to establish a causative relationship.

On the other hand, after a highly restrictive policy regarding antibiotic prophylaxis, there has been no
definite increase in IE in France, the United States, and India. Duval and colleagues reported a follow-up study in three French regions (with a total adult population of about 11 million) where a guideline change in 2002 restricted antibiotic prophylaxis to patients at high risk of infective endocarditis (roughly 10% of the total cases). They identified no significant increase in the incidence of oral streptococcal infective endocarditis in 2008 compared with their findings from 1991 and 1999. However, there was an increase in staphylococcal infections (36% of all IE vs 12% streptococcal in 2008), mostly in those subjects with no pre-existing valvular heart disease.

What to do in India?
In India, we cannot ignore rheumatic valvular heart disease, with its peculiar structural and immunological characteristics, nor the poor oral health of the general Indian population, which has not improved significantly over the past decades. Therefore, it is not wise to ignore our epidemiological peculiarity of valvular heart disease and general level of hygiene.

In India, it may be still reasonable to recommend antibiotic prophylaxis before starting dental interventional procedures that bear a high probability of significant bacteremia to patients who have either valvular or congenital heart diseases that represent a risk for IE, regardless of assumptions on differences of disease course. In addition, there is the need for prospective and controlled studies to support the probability of the effect of antibiotic prophylaxis.

References
definite increase in IE in France, and the United States. Duval and colleagues reported a follow-up study in three French regions (with a total adult population of about 11 million) where a guideline change in 2002 restricted antibiotic prophylaxis to patients at high risk of infective endocarditis (roughly 10% of the total cases). They identified no significant increase in the incidence of oral streptococcal infective endocarditis in 2008 compared with their findings from 1991 and 1999. However, there was an increase in staphylococcal infections (36% of all IE vs 12% streptococcal in 2008), mostly in those subjects with no pre-existing valvular heart disease.

What to do in India?

In India, we cannot ignore rheumatic valvular heart disease, with its peculiar structural and immunological characteristics, nor the poor oral health of the general Indian population, which has not improved significantly over the past decades. Therefore, it is not wise to ignore our epidemiological peculiarity of valvular heart disease and general level of hygiene.

In India, it may be still reasonable to recommend antibiotic prophylaxis before starting dental interventional procedures that bear a high probability of significant bacteremia to patients who have either valvular or congenital heart diseases that represent a risk for IE, regardless of assumptions on differences of disease course. In addition, there is the need for prospective and controlled studies to support the probability of the effect of antibiotic prophylaxis.

References


