Prophylaxis against infective endocarditis in obstetrics: new NICE guidance: a commentary

C Tower, S Nallapeta, S Vause

Department of Obstetrics, St Mary’s Hospital, Manchester, UK

Correspondence: Dr C Tower, Maternal and Fetal Health Research Group, St Mary’s Hospital, Whitworth Park, Manchester M13 0JH, UK.

Email clare.tower@manchester.ac.uk

Accepted 10 August 2008.

In March 2008, the National Institute for Health and Clinical Excellence (NICE) in the UK published a clinical guideline for prophylaxis against infective endocarditis.¹ It is now recommended that women at risk of infective endocarditis undergoing gynaecological and obstetric procedures do not require antibiotic prophylaxis, regardless of cardiac lesion. This represents a significant change from current practice and is based on the lack of evidence of efficacy and cost. However, this requires careful scrutiny and consideration before it is adopted into widespread clinical practice.

Fortunately, infective endocarditis is a rare event, with an incidence in developed countries of around 24 cases per million, a rate that has remained static from the early 1970s until the 1990s.² Although accurate data on the incidence in developing countries are unavailable, the incidence is reportedly higher, with different epidemiological patterns and a higher mortality.³ Data from pre-1970 have suggested an incidence in pregnancy of 1:8000.⁴ Although rare, the consequences are catastrophic, with a maternal mortality of 29% and a fetal mortality of 23%.⁵ Indeed, the most recent Confidential Enquiries into Maternal and Child Health report has highlighted cardiac disease as the leading cause of indirect deaths.⁶ Infective endocarditis was implicated in two indirect deaths (4% of all indirect cardiac deaths) and two late deaths (6% of all late deaths) reported to the assessors.

Current practice in most UK units is to administer intravenous antibiotic prophylaxis to women with high-risk cardiac lesions during labour and delivery, especially to those with artificial valves or with a previous episode of endocarditis.⁷ NICE has recommended that this is not necessary based on the data from a single paper, discussed in more detail below.⁸

Pathogenesis

The normal heart is relatively resistant to infection. Development of endocarditis requires both a predisposing abnormality of the endocardium and microorganisms in the bloodstream (bacteraemia). The bacteraemia can be transient, thus up to 14% (much higher in developing countries) of cases of infective endocarditis are associated with negative blood cultures.³ The three most common causative organisms are *Streptococcus viridans*, staphylococci and enterococci.¹³ *Streptococcus viridans* is part of the normal skin, oral, respiratory and gastrointestinal tract flora and causes at least 50% of cases of community-acquired native valve infective endocarditis not associated with intravenous drug use. Enterococci are part of the normal gastrointestinal and genitourinary tract flora. *Staphylococcus aureus*, a common skin organism, is increasing in incidence.³

Traditionally, infective endocarditis has been classified into acute and subacute. Subacute bacterial endocarditis (SBE) usually develops insidiously and progresses slowly. Often, no source of infection or portal of entry is evident. SBE is caused most commonly by *S. viridans* and enterococci and less commonly by *S. aureus*. Subacute infective endocarditis often develops on abnormal valves after asymptomatic bacteraemia due to periodontal, gastrointestinal and genitourinary infections. In contrast, acute bacterial endocarditis develops abruptly and progresses rapidly, with a source of infection evident. It is usually caused by *S. aureus*, group A haemolytic streptococci, pneumococci or gonococci.

Evidence for bacteraemia in obstetric procedures

Bacteraemia is considered a prerequisite for the development of infective endocarditis. While a large body of evidence exists pertaining to bacteraemia following dental procedures, the same is not true for obstetric procedures. The NICE guidelines cite a single paper, reporting an absence of bacteraemia in 26 women undergoing elective caesarean section.⁸ This paper compared 26 women undergoing elective caesarean
section with 93 women undergoing a caesarean section after a minimum of a 4-hour labour or 4 hours of ruptured membranes. None of the 26 women undergoing elective caesarean section had bacteraemia compared with 14% of women undergoing an emergency caesarean section performed in labour. This 14% is likely to be an underestimate as the study design excluded women at high risk of infection, such as those with intrapartum fever or those delivering out of hours. However, there are no good data to support this. Women undergoing a vaginal delivery were not studied.

There is a paucity of evidence relating to the frequency of bacteraemia following vaginal delivery. The available data are from publications from 1959 to 1989, and rates of 0.5–8% were reported. The frequency of bacteraemia following an instrumental delivery is unknown. Extrapolating from the paper cited by NICE, a conservative estimate for vaginal delivery may be much higher than this at 14%. Higher rates of bacteraemia have been reported following dental procedures (approximately 25%), although the cultured organisms are very different. Following dental extraction, 58% of organisms were S. viridans, whereas the most common organisms cultured in women postpartum were group B streptococci (Streptococcus agalactiae) (38%) or Gardnerella vaginalis (46%). This study demonstrated S. viridans in only one case (8%). While S. viridans is the most common cause of endocarditis, all other organisms, except G. vaginalis have been reported to cause endocarditis. However, other anaerobes are capable of causing endocarditis. Hence, extrapolation between dental and obstetric studies may not be appropriate.

**Evidence for antibiotics to prevent endocarditis in obstetric women**

Endocarditis has been reported in relation to vaginal delivery, caesarean section, termination of pregnancy and intra-uterine contraceptive device (IUCD) insertion. However, there have been no prospective studies of the use of antibiotics to prevent endocarditis in obstetric women. Indeed, no such study has been conducted in any patient group deemed to be at risk of endocarditis. To obtain sufficient power, such a study would require randomisation of at least 6000 women. The incidence of valvular lesions in pregnant women in the UK is unknown but has been reported as 0.5% in Saudi Arabia. It is therefore extremely unlikely that such a study will ever be undertaken. Therefore, evidence for the success of antibiotics to prevent endocarditis has been taken from animal studies, retrospective case series and case-control studies. None of these were conducted in pregnant individuals. There are also case series in which failures of antibiotic prophylaxis have been reported.

An alternative to a randomised controlled trial may be a decision tree analysis as this method combines medical probabilities and human values to guide decision-making. However, such an analysis would be hampered by the absence of good data, such as the proportion of bacteraemia in pregnancy that would cause endocarditis. It is notable that NICE did not attempt such an analysis.

Despite the rarity of the condition, and a lack of evidence for the efficacy of antibiotic therapy to prevent endocarditis in obstetrics, it has long been considered good medical practice to prescribe preventative antibiotics, particularly in women with high-risk lesions. Current guidelines produced by American Heart Association have suggested that prophylaxis is not required for vaginal delivery in women with most cardiac lesions. In contrast to NICE, prophylaxis is recommended for those with a prosthetic valve, a history of infective endocarditis, cyanotic congenital heart disease and cardiac transplant recipients with valvulopathy. European guidelines also suggest prophylaxis for those with high-risk lesions for ‘gynaecological procedures in the presence of infection’. Others consider the risk significant enough to recommend prophylaxis to those with lower risk cardiac lesions, even undergoing vaginal delivery.

**Risk of anaphylaxis**

A further reason from NICE for not using prophylaxis is the risk of anaphylaxis due to antibiotics. The risk of fatal anaphylaxis from intravenous antibiotics is estimated to be between 15 and 20 per million. There have been several studies suggesting that the risk of anaphylaxis from antibiotics may be greater than the number of cases of endocarditis prevented. However, these studies considered dental procedures. The risk of infective endocarditis following obstetric procedures is unknown, but women with a prosthetic valve have a lifetime risk of developing infective endocarditis of 308–383 per 100 000 patient years compared with 5 per 100 000 patient years in the general population without a cardiac risk factor. The risk of fatal anaphylaxis following treatment with intravenous penicillin in labour has been estimated at 1:100 000 women treated. Mortality in pregnant women with infective endocarditis is estimated at 29%, almost 50% higher than the 20% mortality estimated for the nonpregnant population. Although a direct comparison is difficult, risks to a pregnant woman with a high-risk valvular lesion are significant compared with the very small risk of anaphylaxis.

Antibiotic resistance is a further issue that was given little consideration in the recent NICE document. Widespread antibiotic use promotes the emergence of resistant organisms, such as S. viridans and enterococci. However, resistance tends to be associated with poor compliance; issues that are less relevant when single doses are given intravenously for prophylaxis. Furthermore, since valvular heart disease in the pregnant population is relatively rare, the impact of prophylactic antibiotics on resistance is likely to be minimal.
Cost

Cost-effectiveness is complex and depends on many factors including the prevalence of the infection to be prevented, the seriousness of the infection, the cost of treating the infection and the cost of adverse events. The paucity of data relating to infective endocarditis means that the majority of these factors are unknown. There have been no studies of cost-effectiveness for antibiotic prophylaxis to prevent infective endocarditis in obstetrics. The studies cited by NICE are contradictory and apply largely to dental procedures. Studies relating to dental procedures are unlikely to be relevant to obstetrics since the number of procedures is likely to be greater and different organisms are involved. In addition, the cardiovascular and immunological changes associated with childbirth are huge, which may influence morbidity and mortality. It should be remembered that the costs of intensive care associated with cardiac morbidity around delivery are significant compared with the small cost of a single intravenous dose of antibiotics.

Patient’s choice

Involvement of women in the clinical decision-making process is important, a fact acknowledged by the Guideline Development Group in the recent guidance. In order for women to make informed decisions about their care, the issues outlined in the commentary should be discussed with affected women. Many women with high-risk cardiac lesions will be used to receiving antibiotics for dental procedures. In view of the lack of evidence, it is probable that such women will want to continue receiving antibiotics for obstetric procedures.

Summary

Antibiotic prophylaxis is prescribed on labour wards in the UK for numerous risk factors and procedures, including prolonged rupture of membranes, repair of third-degree tears and during caesarean section. Current practice in the substantial majority of UK units is to give antibiotic prophylaxis to women with cardiac lesions to prevent infective endocarditis. NICE has recommended a substantial change in clinical practice based on one paper describing rates of bacteraemia at caesarean section.

NICE has suggested that antibiotic prophylaxis is unnecessary because there is a lack of evidence to support its use. Absence of evidence does not equate to absence of effectiveness when the studies required have not been conducted. Indeed, this is the case for a substantial portion of obstetric management. The American Heart Association guidelines have taken a more measured approach and recommended that women with high-risk cardiac conditions receive prophylaxis, as opposed to a blanket policy of no prophylaxis. Furthermore, good quality data in this area are urgently needed to allow the current dogma of ‘antibiotics for all’ to be challenged. The International Collaboration on Endocarditis was established in 2002 to facilitate this and to allow a global perspective to be developed. Reporting through a system such as the UK Obstetric Surveillance System would allow reliable UK data to be collected. Risks should continue to be considered on an individual patient basis, and antibiotics prescribed when the clinician and the patient deem this appropriate.

Disclosure of interests

No conflicts of interests.

Contribution to authorship

Commentary was written by C.T. and S.N., following the idea by S.V.

Details of ethics approval

None.

Funding

None.

References