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Editorial

Why are we seeing an increasing incidence of infective endocarditis in the UK?

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Standfirst

The increasing incidence of infective endocarditis in England is real, and education is critical to ensure swift diagnosis and best clinical outcomes. Factors responsible remain speculative, but multiple explanations are likely.

Introduction

The question of why we are seeing an increasing incidence of infective endocarditis in the UK, while not limited to the UK, is perhaps most relevant to this country, considering the National Institute for Health and Care Excellence recommendations to cease all antibiotic prophylaxis for invasive dental and other procedures in March 2008, based on the absence of evidence from prospective, randomised, placebo-controlled trials that antibiotic prophylaxis prevents infective endocarditis. By comparison, guidelines from the USA in 2007 (Wilson et al, 2007) and Europe in 2009 (Habib et al, 2009) reduced (but did not eliminate) antibiotic prophylaxis for invasive dental procedures. However, these changes resulted in much-heralded concerns that the incidence of infective endocarditis caused by oral streptococci would markedly escalate as a result of a lack of antibiotic prophylaxis in the dental setting.

In response, over 20 investigations have examined the incidence of infective endocarditis 'before and after' amendment of these national and international guidelines. Overall, these have demonstrated mixed results – some demonstrating an increased incidence (Dayer et al, 2015) and others showing no change or a decline (Bikdeli et al, 2013; Thornhill et al, 2018). However, given the differing study methodologies, it is not surprising that their findings were disparate. Furthermore, microbiological data were unavailable in several studies, thereby limiting their ability to assess the impact of antibiotic prophylaxis on the incidence of oral streptococcal infective endocarditis in the dental setting. Further difficulties relate to the lack of specific ICD-9/ICD-10 coding for oral (viridans group) streptococci and substitution in some studies by a 'rule out' strategy to eliminate other streptococcal species (such as *Streptococcus pneumoniae*, *S. pyogenes*). Conversely, all streptococci were included in other studies, while erroneous ICD-9 coding (designating 'enterococcus' as 'streptococcus') may have resulted in overestimation of the incidence of oral streptococcal infective endocarditis in at least one investigation.

Changes in incidence over time

The authors' group has serially monitored the incidence of infective endocarditis using Hospital Episode Statistics admissions data for some years. The initial investigation between January 2000 and April 2010 (incorporating the 2 years immediately after publication of the National Institute for Health and Care Excellence guidelines in March 2008) identified a 78% reduction in use of antibiotic prophylaxis but no significant increase in the incidence of infective endocarditis. This evaluation was subsequently extended by 3 years and demonstrated a continued decline in use of antibiotic prophylaxis accompanied by an increasing incidence of cases of infective endocarditis (Dayer et al, 2015). However, there were insufficient data to demonstrate a causal relationship and inadequate microbiological information to investigate the specific use of antibiotic prophylaxis in association with dental procedures.

The findings of the most recent survey was published in 2020 (Thornhill et al, 2020) and analysed Hospital Episode Statistics admissions data between 1998 and 2019 to reveal an 86% increase in the incidence of infective endocarditis in England between 2009–10 and 2018–19. Almost simultaneously, other investigators (Quan et al, 2020) used Hospital Episode Statistics data from 1998–2017 to demonstrate a similar increase in overall incidence of infective endocarditis and Public Health England microbiological data to exclude a major role of oral streptococci (although data were only available for 0–50% of cases, making definitive conclusions difficult).

Risk factors for developing infective endocarditis

A further important change in the infective endocarditis guidelines merits emphasis. While indications for the use of antibiotic prophylaxis before dental procedures were removed or markedly reduced, they were eliminated completely for all other invasive procedures (including those involving the respiratory, gastrointestinal and genitourinary tract). However, in 2018 a Swedish national case-crossover study demonstrated an array of procedures that were performed more frequently in the 12 weeks before the diagnosis of infective endocarditis than at other time points (Janszky et al, 2018). These findings support the observation that a variety of bacteria (including staphylococci and enterococci) could account for an increase in the incidence of infective endocarditis after non-dental invasive procedures performed without antibiotic prophylaxis.

Numerous risk factors are associated with the development of infective endocarditis and it seems unlikely that a single explanation is responsible for its increasing incidence in the UK. Indeed, greater disease recognition and use of diagnostic tools are likely to have had significant impact. Blood culture sampling has increased and positive results in multiple sets are often the initial clue to the diagnosis of infective endocarditis in a febrile patient with no obvious source of infection. In one nationwide investigation (Ostergaard et al, 2019), infective endocarditis was frequent in patients with positive blood cultures for *Enterococcus faecalis*, *S. aureus* or streptococci (1:6, 1:10 and 1:14 respectively). Given that infective endocarditis is a life-threatening condition, systematic echocardiography to investigate the possibility of infective endocarditis is appropriate in patients with bacteraemia caused by these organisms.

Echocardiography is a critical diagnostic tool in infective endocarditis and Hospital Episode Statistics data from England using OPCS-4 procedure codes (not specifically focused on infective endocarditis) have shown an enormous increase in its use between 2008 and 2011 (transthoracic echocardiography >300%, transoesophageal echocardiography ~22%). Other more novel imaging techniques (multislice computed tomography with angiography, positron emission tomography/computed tomography, and single-photon emission computed tomography) are also important to secure the diagnosis of infective endocarditis in selected cases. All three modalities are particularly useful in suspected prosthetic valve endocarditis when echocardiography is normal. Increased use of advanced diagnostic procedures may augment the number of definite infective endocarditis cases that were previously considered uncertain.

Injection drug use accompanying the opioid epidemic has dramatically impacted upon the medical and surgical management of infective endocarditis in the USA. England, like the USA and other developed countries, witnessed an increasing rate of hospital admissions for infectious complications of injection drug use (including infective endocarditis) between 2012–13 and 2015–16 (Lewer et al, 2017). Although this may not have been a predominant factor predisposing to development of infective endocarditis in England, injection drug use could certainly have played a contributory role (Quan et al, 2020).

England's aging population may have also contributed to the increasing incidence of infective endocarditis. Aging has long been recognised as a predisposing condition, with the highest rates of infective endocarditis in patients aged >60 years. This is particularly true in high income countries where rheumatic fever is now exceedingly rare (with the exception of immigrant or migrant populations).

Increasing use of cardiovascular devices is a likely final contributor, as demonstrated by the increasing rates of valve replacement, cardiac implantable electronic devices, and use of prosthetic material in congenital heart disease in England, all of which harbour risk of infective endocarditis (Dayer et al, 2015). Consistent with these observations, a recent large multinational European infective endocarditis registry (*n*=3116) including UK cases demonstrated prosthetic valve endocarditis in 30% and cardiac implantable electronic device-related infective endocarditis in 10%.

Conclusions

The increasing incidence of infective endocarditis in England is real and wider education is critical to ensure swift diagnosis and best clinical outcomes. Factors responsible remain speculative, but multiple explanations are likely.

Key points

- The incidence of infective endocarditis has increased in England.
- Factors responsible have yet to be defined, but multiple explanations are likely.
- Changes in guidelines for the prevention of infective endocarditis may or may not have played a role but are unlikely to be entirely responsible.
- Wider use of advanced cardiac imaging may have increased the diagnosis of infective endocarditis (and reduced the number of uncertain cases).
- Injection drug use accompanying the opioid epidemic has increased the incidence of infective endocarditis in some areas of the USA and other countries but is unlikely to explain all of the increase in England. *Staphylococcus aureus* is the predominant pathogen in injection drug use-related infective endocarditis.
- The incidence of infective endocarditis caused by *S. aureus* and enterococci has increased as a result of healthcare-related interventions (including cardiovascular device implantation).

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