EDITORIAL COMMENT

Antibiotic Prophylaxis Guidelines and Infective Endocarditis
Cause for Concern?*

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In 1923, Lewis and Grant (1) were the first to suggest that bacteria released into the circulation as a consequence of a dental procedure might cause infective endocarditis (IE). In 1955, the American Heart Association (AHA) published the first guidelines that recommended antibiotic prophylaxis to reduce the risk of IE following invasive procedures (2). Since that time, there has been a gradual reduction in the intensity and duration of antibiotic prophylaxis, and the number of patients for whom it is recommended has been reduced.

In April 2007, the latest iteration of the AHA guidelines (3) provided an update on the previous guidelines from 1997 (4). The authors of the most recent guidelines felt that the benefits of antibiotic prophylaxis were likely to be small, and that only patients at the highest risk of an adverse outcome should be offered prophylaxis for invasive dental procedures. Prophylaxis for those at moderate risk of an adverse outcome, and/or for those having genitourinary or gastrointestinal tract procedures was no longer recommended. In the final paragraph of the document, the AHA urged that studies to document the impact be instituted promptly, “so that any change in incidence may be detected sooner rather than later.”

Since 2007, a number of studies have been published that have examined the impact of the AHA guidelines. Rogers et al. (5), who reported on their experience in a San Francisco medical center in 2008, demonstrated no increase in the number of admissions 9 months after the guideline change. A study by Bor et al. (6), which used National Inpatient Sample Data to assess a broad sample of patients from 1998 to 2009, did not show any inflection in the rise of IE after the guideline change, nor was there an increase in the number of cases secondary to streptococcal infections; however, these investigators only looked out to 2 years after the change. DeSimone et al. (7), who looked at data from the start of 1999 to the end of 2010, used very detailed data from the Rochester Epidemiology Project. They concluded that there was no perceivable increase in the incidence of viridans group streptococci (VGS) in their sample; however, the small sample size must be considered. There were only 3 documented cases of VGS-IE in their sample between 2007 and 2010. Pasquali et al. (8), who looked specifically at IE in children in 37 hospitals between 2003 and 2010, found no significant change in the absolute numbers of cases before and after the guideline change. Finally, Bikdeli et al. (9) looked at admissions of patients older than 65 years by using Medicare inpatient Standard Analytic Files. They recorded a reduction in the absolute numbers, but no correction was made for the absolute numbers of patients enrolled in Medicare eligible for treatment. They commented, “our analysis, however, was not meant to be a comparative effectiveness study to prove the non-inferiority of more restrictive use of antibiotics for endocarditis prophylaxis.”

The latest study to look at the impact of the 2007 guidelines is published in this issue of the Journal (10). The data were extracted from the National Inpatient Sample, as in the Bor et al. study (6). The investigators examined the data between 2000 and 2011, extending the follow-up time after the change in guidelines to 4 years. The data confirmed a steady rise in the number of cases of IE. Importantly, there was no acceleration in this rise, unlike in the United...
The reasons for the rise are, almost certainly, multifactorial. They probably reflect a lowered diagnostic threshold, an aging population, and an increase in the number of procedures that can predispose patients to the development of IE. There might also be some artefact in this rise, because of changes in hospital coding practice, with double (or more) counting of patients, because of transfer between hospitals, or because patients are discharged and brought back on a daily basis for outpatient-based antimicrobial therapy. In the aforementioned Rochester Epidemiology Project, the incidence of IE decreased (7).

As in the Bor et al. (6) study, the investigators attempted to look at the microbiology of IE. This was difficult for 2 reasons: 1) because the proportions of patients coded as having a causative organism changed over time; and 2) the organism coded was not necessarily the organism that caused IE. Nonetheless, what is disconcerting is that the number of streptococcal cases appears to be rising significantly, raising the possibility that the change in guidelines has resulted in an increase in the number of streptococcal cases.

Examination of a longer time frame is potentially important. In the United Kingdom, in March 2008, the National Institute for Health and Care Excellence recommended that antibiotic prophylaxis should no longer be used for anyone. Dental protection societies rapidly withdrew insurance coverage for reactions to prophylactic antibiotics, and there was a dramatic fall in their prescription. In 2011, we published a study looking at 2 years of follow-up, and we found no difference in the incidence of IE (12). However, a subsequent study that looked at 5 years after the guideline change demonstrated a significant increase in the number of cases above the baseline trend (12).

The problems with the trials that enroll large numbers of patients and that rely on coding data are that there are likely to be inaccuracies in the database, which may affect the results, although the numbers, and hopefully, the lack of systematic bias, minimizes this effect. There are data to suggest that the coding of IE in similar databases is quite accurate (13). Also, there is no estimation in the paper of the impact of the 2007 AHA guidelines on the prescribing of antibiotic prophylaxis. It remains unclear how practice has changed, if at all, and who continues to get antibiotic prophylaxis, although there is a suggestion that there has been some shift, at least among dentists (14). Furthermore, correlation does not equal causation, and there is no proof that the effect seen is the result of the guideline change.

This is an important study that raises important questions about the impact of the AHA guidelines and underlines the need for ongoing monitoring of both antibiotic prophylaxis prescribing practices and the incidence of IE. However, as the investigators point out, the fundamental problem is that there has never been a randomized controlled clinical trial into the efficacy of antibiotic prophylaxis, and so there is no reliable evidence to support its use. The time for this to change is long overdue.

REFERENCES


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