Letters

Antibiotic Prophylaxis and Anaphylaxis

Editor – In our article “Infective endocarditis: rationale for revised guidelines for antibiotic prophylaxis,”¹ we attempted to summarize the various points discussed among different guidelines for antibiotic prophylaxis with the aim of presenting an evidence-based approach in advocating a lesser role for antibiotics in infective endocarditis (IE) prophylaxis. As noted in our discussion, an antibiotic-related adverse effect like anaphylaxis is only one of the many factors influencing this change in recommendations. Also, we did specifically mention that the risk of adverse effects like anaphylaxis is very low. It is important to note that this was a summary of all the factors discussed in various guidelines, and the emphasis given among the guidelines for these factors was varied. It was clearly not our intent to show that all the guidelines discussed in our review gave the same weight to all the factors for basing their recommendations. However, three recent guidelines, British Society for Antimicrobial Chemotherapy (BSAC), American Heart Association (AHA) and National Institute for Health and Clinical Excellence (NICE), do specifically discuss anaphylaxis.

The British Society for Antimicrobial Chemotherapy (BSAC) guidelines discuss anaphylaxis as one of the reasons for their recommendation restricting antibiotic prophylaxis to high risk groups. It states in Appendix I:

The main reasons for this (restricting antibiotic prophylaxis before dental treatment to patients with healed IE, prosthetic heart valves and surgically constructed conduits) are the lack of any supporting evidence that dental treatment leads to IE and the increasing worry that administration of antibiotics may lead to other serious complications such as anaphylaxis (severe allergy) or antibiotic resistance.²

The American Heart Association (AHA) guidelines, while mentioning that use of a single dose of amoxicillin or ampicillin for IE prophylaxis in patients with no history of type I hypersensitivity reaction to a penicillin is safe, does discuss the risk of anaphylaxis with antibiotic use:

Fatal anaphylactic reactions were estimated to occur in 15 to 25 individuals per 1 million patients who receive a dose of penicillin.³⁻⁵ Among patients with a prior penicillin use, 36% of fatalities from anaphylaxis occurred in those with a known allergy to penicillin compared with

64% of fatalities among those with no history of penicillin allergy.^{3,4,6}

While the article mentions this could be an over estimation, it still does not rule out risk of anaphylaxis, albeit low. Also clear from the discussion is the fact that a lack of history of penicillin allergy, even in patients with prior penicillin exposure, does not rule out allergic responses including fatal anaphylactic reactions on re-exposure. In the case series referenced in AHA guidelines, a study of 151 reported fatal anaphylactic reactions from penicillin use, anaphylactic reactions were reported after the first dose in 123 of these 151 patients, and of these, three occurred after the first dose of oral penicillin. One-hundred and four of the 151 patients included in the review had known exposure to penicillin in the past.⁶

The National Institute for Health and Clinical Excellence (NICE) guidance summary states:

In summary, this guideline recommends that antibiotic prophylaxis solely to prevent IE should not be given to people at risk of IE undergoing dental and non-dental procedures. The basis to support this recommendation is: ...antibiotic prophylaxis against IE for dental procedures may lead to a greater number of deaths through fatal anaphylaxis than a strategy of no antibiotic prophylaxis, and is not cost effective.⁷

The NICE statement referred to by Dr. Friedlander⁸ – “The studies included in this review that considered antibiotic prophylaxis against IE did not adequately report rates of adverse events or identify any episodes of anaphylaxis”⁶ – also brings into question whether lack of reported anaphylactic episodes was due to non-occurrence or rather misidentification of anaphylactic episodes under a broader category (eg, allergic responses). Regardless, the NICE guidance discusses antibiotic-related anaphylactic reactions at several instances throughout the manuscript (reference 7, pages 60, 78, 79, 82, 83, etc), and in summary states:

The GDG [Guideline Development Group] discussed the possible adverse effects of taking antibiotic prophylaxis. They concluded that although antibiotic-related anaphylaxis is a rare event, it is potentially fatal and therefore the possibility of anaphylaxis needs consideration. The occurrence of other adverse effects of antibiotic usage, notably the risk of increasing

antibiotic resistance, was also acknowledged. ... The GDG therefore concluded that offering antibiotic prophylaxis before dental procedures is not clinically beneficial and was associated with a risk of harm (anaphylactic reaction to antibiotics, notably penicillins).⁷

As pointed out by Dr. Friedlander,⁸ and we agree, anaphylactic reactions are very rare, and both AHA guidelines and NICE guidance do recognize this fact. At the same time, the guidelines also acknowledge that there is a lack of evidence demonstrating clear benefit for antibiotic prophylaxis. With lack of a clear benefit, even theoretical or rare risks like anaphylactic reactions have to be factored in while making public health recommendations affecting large patient populations (as anaphylactic reactions could be fatal) as was discussed in the NICE guidance.

We feel our statements are accurate in the context of anaphylactic reactions, as our discussion of various arguments and reasons put forth by the different guidelines provides support for the diminishing role of antibiotics in IE prophylaxis. Some of the reasons we discussed in our review¹ are greater cumulative exposure to bacteremia from daily activities compared to dental procedures, paucity of evidence for clear association of dental procedures and infective endocarditis, paucity of evidence for efficacy of antibiotic prophylaxis in preventing bacteremia or endocarditis, contradictory evidence regarding cost benefit analysis of antibiotic prophylaxis, emergence of antibiotic resistant strains, concern for antibiotic-related adverse effects like *Clostridium difficile* colitis, and allergic reactions like anaphylaxis. We would also like to reemphasize that each of these factors were given different weights among different guidelines, as was the case with anaphylaxis. We understand that the new recommendations signify a dramatic shift from current practices. A healthy discussion among practitioners, as well as with their patients, is vital while implementing these recommendations.

References

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