

Evidence-based problem solving: What is the efficacy of pneumococcal vaccination in people with asthma?

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SUMMARY

Aims: To determine the efficacy of pneumococcal vaccination in asthmatic patients using a pragmatic evidence-based approach to solve therapeutic problems.

Methods: Use of local information, expert-opinion guidelines, evidence-based guidelines and a systematic literature search of the Medline database to identify clinical trials designed to assess vaccine efficacy among asthmatics.

Results: Expert-opinion guidelines advocating the use of pneumococcal vaccine among asthmatics were found, but there was no evidence-based assessment of vaccine efficacy among asthmatics. The Medline database described no clinical trials that specifically addressed our question, although a number of studies assessing the broader question of overall vaccine efficacy were identified, with conflicting results.

Conclusions: Current UK expert opinion recommends that people with asthma receive pneumococcal vaccination, but there is little high-quality evidence to support this. The search strategy used may be adapted to address other therapeutic questions that may arise in primary care consultations.

THE CASE

Having recently seen a poster highlighting the importance of pneumococcal vaccination in those with lung disease, ML, a 29-year-old middle-class professional, consulted her medical practitioner for his opinion. Her asthma was mild and well controlled with the occasional use of salbutamol, and she was otherwise well, with no significant past medical history. ML was taking no other medication and had no known drug allergies. She was a non-smoker.

As her practitioner, I was aware of recommendations to vaccinate 'high-risk' patients, a category including those with asthma, but was unaware of the evidence on which this recommendation was based. At the time of consultation, I felt that I was not able to adequately answer the question and informed ML that I would contact her after making further enquiries.

IN SEARCH OF THE ANSWER

I started my enquiry with the *British national formulary (BNF)*, my first port of call for most UK therapeutic enquiries, which advised that the pneumococcal vaccine is recommended for use in persons aged over two years with certain medical conditions, one category included those with chronic lung disease.¹ No evidence was cited in support of this recommendation. The *Monthly index of medical specialities* provided no additional information,² so I turned to the Department of Health (DoH) guidelines³ on immunisation, also easily available within the practice. The DoH supported the *BNF*, stating that vaccination 'is recommended for all those aged two years or over in whom pneumococcal infection is likely to be more common and/or

dangerous.' The overall efficacy of the vaccine in preventing pneumococcal pneumonia was estimated to be between 60–70%. Although no specific guidance was provided for asthmatics, it was suggested that those with chronic lung disorders were among those most likely to benefit. No mention was made of the methods used in appraising evidence to arrive at this conclusion.

The expert-opinion pronouncements consulted thus far were very much in keeping with what I already knew of the subject. While acknowledging their importance, they did little to help with quantifying the benefits and risks with respect to my patient. I turned next to the Cochrane library,⁴ hoping to find a systematic review on the subject of pneumococcal vaccination in asthmatics. A review protocol addressing the broader question of the efficacy of the vaccine in preventing pneumococcal infection was identified.⁵ Contacting the lead reviewer confirmed that there was no specific subgroup analysis of asthmatics planned with respect to vaccination (Holden J, personal communication, 1999). Searches on other important evidence-based databases, namely, Bandolier⁶ and The University of York NHS Centre for Reviews and Dissemination,⁷ failed to yield the desired information.

Having failed to locate a specific evidence-based review of the subject, I decided to search for primary research evidence on the subject myself. Clinical trials constitute the highest level of evidence for therapeutic decision-making, so I focused my search on this particular type of evidence. Despite using the comprehensive search strategy described by Greenhalgh,⁸ I was unable to identify any randomised trials (with or without blinding) focused on asthmatics. These results explained both why I had failed to locate any systematic reviews on the subject and the rather unconvincing expert pronouncements on the subject.

In view of the limited information obtained, I decided not to search any other databases as I doubted whether the additional time spent would be rewarded. However, in the course of my searches, I had identified a number of abstracts and references that were of possible relevance, and which I wished to pursue. Full text copies were obtained of all papers that were of interest and easily accessible from my local medical school library.^{9–17}

These papers yielded useful background information to the subject. A retrospective study, for instance, looking at risk factors for adverse outcomes in patients with pneumococcal pneumonia, revealed the importance of preexisting lung disorders, the presence of which resulted in an adjusted odds-ratio of 4.1 (95% CI 1.3, 13.0).⁹ A recent multi-author quasi-systematic review of the vaccine showed that, whereas mild side-effects comprising local swelling, pain or erythema were common, systemic side-effects were rare.¹⁰

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Of particular relevance was a high-quality meta-analysis of nine randomised controlled trials, involving a total of 40,341 adults,¹¹ which has subsequently been assessed and commented on by the NHS Centre for Reviews and Dissemination.¹² The latter concluded that the vaccine was effective in reducing bacteraemic pneumococcal pneumonia in low-risk adults, but was of no benefit in the heterogeneous group of patients labelled as high-risk. Although the data did not permit individual disease-based conclusions of vaccine efficacy to be drawn, the reviewers postulated that these surprising results may have been due to the current definition of high-risk, which includes many patient groups for whom the vaccine is either not, or only minimally, effective. The explanation offered is in keeping with the results of case-control studies that have demonstrated vaccine efficacy in groups such as those with chronic lung disease,^{13,14} but failed to demonstrate this benefit in other high-risk groups.¹⁵ A recently reported single-blind, randomised, controlled trial in the elderly has added further plausibility to this explanation by demonstrating efficacy of the vaccine in preventing pneumococcal pneumonia) in particular subgroups of patients, including those with bronchial asthma.¹⁶

THE OUTCOME

I explained the results of my enquiries to ML with emphasis that, in view of the paucity of high-quality research on the subject, it was difficult to arrive at any firm conclusions regarding the effectiveness of the vaccine. I then outlined the epidemiology of pneumococcal pneumonia, explaining that its incidence increases sharply in the elderly.¹⁷ I also explained that it was licensed for use in those with asthma aged over two years and that the UK expert opinion was that those with chronic lung diseases should be vaccinated. This was based on the observation that, if patients with pre-existing lung disease developed pneumonia, this was associated with a significantly increased risk of severe adverse outcomes. This led to a discussion regarding the promising, though limited, data supporting vaccine use in asthmatics. Finally, we discussed the strong and consistent data showing the good safety profile of the vaccine. In the light of our discussions, ML opted not to have the vaccine, stating that she would review her decision over the next few years in the hopes that, by then, the evidence would be clearer.

Personally, I found the research process stimulating and rewarding, although rather time-

consuming. This particular enquiry served to highlight the limited evidence on which many of our day-to-day decisions are based. Aware of the limitations of my searches, the possibility of bias as a consequence of the somewhat haphazard search strategy used and the need for a comprehensive review in this field, I have decided to complete my enquiries with a systematic review of the subject and have registered the title of *Efficacy of pneumococcal vaccine in asthmatics* with the Cochrane Airways Group. ■

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