Real world evidence of long-term benefits from allergen-specific immunotherapy (AIT)

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Clinicians often underestimate the adverse impacts of severe allergic rhinitis on quality of life and on the ability to perform well at school and work. Pharmacological treatments fail to relieve symptoms adequately in a significant minority of sufferers.[1] Even with the arrival of monoclonal antibody drugs, the most treasured treatment in the allergist's cabinet remains allergen-specific immunotherapy (AIT), with its unique promise of 'disease-modification': lasting allergen-specific tolerance, equating to a persistent effect even after completion (and washout) of treatment. This has been conclusively demonstrated for grass pollen immunotherapy given for seasonal allergic rhinitis (hay fever).[2] Whilst evidence for the tolerogenic effect with other allergens is less robust, the principle remains generally accepted.

Interactions between upper and lower airway allergic disease have been highlighted in recent years, with consensus reached that treating the upper airway is important in individuals with both allergic rhinitis (AR) and asthma.[3] AR predisposes to the development of asthma;[4] AIT may reduce this progression.[5]

The study by Fritzsching et al.[6] uses a large health insurance database in Germany to investigate the association between prescriptions of AIT for AR, with or without asthma, and change in prescriptions for typical AR pharmacotherapy over a decade. Additionally, the data set was investigated for associations with changes in prescription of asthma medication, new asthma diagnoses, and exacerbations of asthma, including hospitalisations. Treatment with AIT was associated with a sustained reduction in prescriptions for AR pharmacotherapy, consistent with a long-term effect from the treatment. Perhaps more impressively, it was also associated with a reduction in asthma medication prescriptions, particularly short-acting beta-agonists (SABAs), as well as a reduction in asthma exacerbations. Conversely, no effect on protection from new onset asthma was found (in fact, a slight effect in the opposite direction was seen).

Obtaining clinical trial evidence of a beneficial effect of AR medications is difficult, with studies generally relying on participants completing daily or weekly symptom and medication use scores[7] and often the need to overcome a large placebo effect.[8] Keeping participants in a controlled trial of AIT for a decade has never been done and probably never will. Here, then, we have data covering a longer period than any available controlled trials. The data is, by its nature, less robust, though the authors have gone to considerable lengths to ensure matching of AIT-treated individuals and controls. A few caveats should be noted when interpreting the results. First, the data is not generalisable to an unselected asthmatic population. Cases were identified for their allergic rhinitis diagnosis, not their asthma diagnosis; moreover, asthma severity was generally mild to moderate (this is entirely consistent with international guidelines for the use of AIT, where uncontrolled or severe asthma is viewed as a contraindication to treatment, given the risk of severe reactions, including anaphylaxis.[9]) AIT should, therefore, not necessarily be expected to have the same impact in a more severe asthma cohort or in asthmatics without AR. Second, the data is not specific for the type of allergen (pollens, mites, animal danders etc.), allergen product (major allergen protein content may differ significantly between manufacturers; some products contain adjuvants), route of administration or schedule of treatment. The results, therefore, cannot be assumed to apply to all variations of the above.

There are barriers to AIT use and considerable variation in access to this treatment across Europe.[10] This dataset, where almost 2% of the population studied received at least one AIT prescription, is consistent with much greater use of AIT in Germany than in the UK. Whilst these results should encourage AIT use, further detailed data on cost implications are likely to be required to persuade national bodies, such as the UK's National Institute for Health and Care Excellence (NICE), to recommend its use more widely. This includes whether the long-term benefits to health and reduction in use of pharmacotherapy are sufficient to offset the short-term costs of the treatment and its administration.

For the clinician, it remains essential to select the patients who are most likely to derive benefit from AIT. These are individuals with severe disease, despite good levels of concordance in taking optimal pharmacotherapy, where there is evidence of allergic sensitisation

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(positive skin prick test and/or serum IgE) to relevant, causative allergen(s). There are many such patients out there.

Declaration of Interests

GS has received honoraria for presentations/lectures from ALK-Abello, UK and EUFOREA (European Forum for Research and Education in Allergy and Airway Diseases); he has received support for registration for an international meeting from Glaxo SmithKline, UK.

Contributors

As a sole author GS contributed to all aspects of this Commentary.

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