

PB-PG-0609-19254 – NIHR Research for Patient Benefit Programme – Final report

Project title: Enabling people with the oral allergy syndrome to eat fresh fruit

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Plain language summary

Many people with early season hay fever have problems eating fruit. This is due to a cross-reaction between proteins in pollen and proteins in tree-fruits such as apples, pears, peaches, cherries, plums etc.

It is possible to desensitise people against pollen allergy, but it is not clear whether this will alter their ability to eat apples. Previous studies had given different answers.

In our allergy service, we use a short-course vaccine to treat tree pollen allergy, with seven injections of a chemically modified pollen extract (Allergovit, produced by Allergopharma, a division of Merck).

This study aimed to find out whether treatment with Allergovit vaccine for birch pollen allergy has any effect on people's ability to tolerate apples. A total of 40 patients were screened for the study; 6 were excluded as they failed to meet inclusion criteria. 32 received the medication they were randomised to. Although some individuals saw an improvement in their ability to eat tree-fruits, overall there was no detectable benefit for those randomised to active treatment compared to the placebo group.

We conclude that this vaccine is not a suitable treatment to enable patients with pollen-related fruit allergies to become more tolerant of apples

Keywords

food allergy; hay fever; specific immunotherapy; apple; birch pollen

Summary of research findings

The overall objective of the project was to establish whether a particular form of birch pollen specific immunotherapy could attenuate symptoms of the oral allergy syndrome. This was tested using a standard immunotherapy vaccine that we use routinely in our allergy service to treat hay fever due to tree pollen.

Our primary endpoint was a change in the threshold of fresh apples that can be eaten by the subject. This was assessed using a double blind placebo controlled food challenge, and backed up by open apple challenges, using a visual analogue scale.

A total of 32 patients were randomised and contributed data. 17 of these received active treatment and 15 received placebo. Mean age was 39.4 (SD 11.4); 7 were male and 25 female. 20 subjects completed the study while 9 withdrew. Seven of these withdrew consent, one was lost to follow-up and one started new medication which made them ineligible to continue. Data from 3 patients was missing.

In terms of the primary outcome, no difference was observed between the baseline and first year food challenges ($p=0.67$) or between the baseline and second year challenges ($p=0.86$).

The study was designed on the basis of 20 patients completing each arm. Unfortunately we did not manage to recruit sufficient numbers of patients to deliver that. However, as there was no discernible trend towards any effect in the subjects we did study, we are confident that we have not missed a true effect due to the small numbers.

On the open apple challenges, comparing year 1 to baseline, we observed a mean fall in VAS score of 20.3 points for the active group ($n=10$) and a drop of 15.4 points for the placebo group ($n=13$) ($p=0.41$). Similarly there was no significant difference in VAS after the open apple challenge at two years ($p=0.77$).

A limited number of secondary variables have been analysed. Skin test sensitivities for mid-seasonal tree pollens showed a clear reduction in the active group compared to the placebo treated group (mean reduction 5.7mm diameter relative to placebo; $p=0.0024$). A small reduction (not statistically significant) was seen in the early seasonal tree pollen skin tests.

No significant reductions were seen in skin sensitivity to grass pollen, apple sap or commercial apple extracts. These results are consistent with the pollens contained within the treatment vaccine and confirm that this was immunologically active, even if there was no benefit in terms of fruit tolerance.

Original protocol summary:

We will conduct a randomised, double-blind, placebo-controlled study of birch pollen immunotherapy (BP-SIT) in 50 patients with OAS. Patients with tree pollen allergy and a history of the oral allergy syndrome will be enrolled and their level of pollen sensitivity assessed by skin, blood and conjunctival tests. Sensitivity to apple will be assessed by food challenge with apple. After randomisation half will receive BP-SIT and half will receive matching placebo injections for 2 seasons. The injections will start 7 weeks prior to the start of birch pollen season and be given once weekly for 7 weeks.

Subjects will complete a diary of their hay fever symptoms during pollen season and they will then be re-evaluated by food challenge tests, blood tests and conjunctival tests following 1 and 2 seasons of therapy, at a point outside the birch pollen season.

1.1 Primary Outcome measure: A change in the response to apple in a disguised, double-blind, graduated food challenge

1.2 Secondary outcome measures:

- Symptom control during birch pollen hay fever season.
- A change in the threshold to birch pollen in the conjunctival provocation tests
- A change in the IgG and IgE levels in the serum as a result of immunotherapy

1.3 Population: 50 male and female adult patients (18+), with the oral allergy syndrome recruited from the South of England.

1.4 Sites and laboratories: Recruitment, screening and clinical tests will be carried out at CIRU, Royal Sussex County Hospital, Eastern Road, Brighton, BN2 5BE. Lab work will be done at either the Immunology department at the Royal Sussex County Hospital or the Brighton and Sussex Medical School.

1.5 Phase: Phase 4 therapeutic use trial

1.6 Study Duration: November 2011 to May 2014

1.7 Subject Participation duration: Approximately 2 years

1.8 Description of intervention: The active and placebo vaccines will be supplied by Allergopharma. The immunotherapy is an aldehyde-modified allergen extract. The details of the investigational product can be found in the summary of product characteristics booklet. 2 different concentrations of IMP will be used. Strength A contains 1000 units/ml and strength B contains 10 000 units/ml. The dose will be up-titrated in accordance with patient response over the 7 weeks.

A placebo solution will be supplied as a comparator. The placebo preparation used is the verum solution without any added allergen substance, also termed Allergovit diluent. The vials containing the placebo solution are identical in appearance to the trial preparation of the active product.

Patient and public involvement

We involved patients in defining the research question, making sure that the desirable outcome was relevant to them. We had a lot of interest from patients in taking part in the study; we also heard from a number of patients who would have liked to take part but were unable to give up their time to do so. We also had a lot of interest from staff members who suffer with the syndrome and responded to the open advertisement.

As the outcome is essentially negative and relates to one particular type of vaccine, the main dissemination will be professional.

Data sharing statement

See link

[\[https://www.nihr.ac.uk/documents/nihr-position-on-the-sharing-of-research-data/12253\]](https://www.nihr.ac.uk/documents/nihr-position-on-the-sharing-of-research-data/12253) for the NIHR position of the sharing of research data. The NIHR strongly supports the sharing of data in the most appropriate way, to help deliver research that maximises benefits to patients and the wider public, the health and care system and which contributes to economic growth in the UK. All requests for data should be directed to the award holder and managed by the award holder.

Disclaimer

This project is funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0609-19254). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

This final report has not been peer-reviewed. The report was examined by the Programme Director at the time of submission to assess completeness against the stated aims.

This project was carried out between March 2012 and March 2015.