Introduction

Type I food allergies, which result in immediate onset anaphylaxis and atopy, have been frequently described and involve mast cell-bound, allergen-specific IgE. Degranulation of the activated mast cell induces the release of vasoactive and inflammatory mediators, including histamine (Tortora & Grabowski, 2000, p769). Such IgE-mediated responses affect about 2% of the British population (Allergy UK, 2008) and are relatively easy to identify on account of their close temporal relationship with ingestion of a particular food.

Delayed onset food allergies, which appear to contribute to numerous chronic symptoms including fatigue, eczema, urticaria, rhinitis, migraine, rheumatoid arthritis, irritable bowel syndrome, inflammatory bowel disease, asthma and obesity (Gaby, 1998), affect as many as 45% of the population (Allergy UK, 2008) but are much more difficult to associate with ingestion of a particular food and are often overlooked.

The exact mechanisms of such abnormal responses to food are unclear but impaired gut barrier function may be involved. Intestinal permeability, evaluated by lactulose/mannitol ingestion, has been found to be altered in patients with non-IgE-mediated as well as IgE-mediated adverse reactions to food (Ventura et al, 2006).

The enzyme-linked immunosorbent assay (ELISA) has shown utility in screening for food-specific serum IgG (Husby, 1985) although the relationship between food-specific IgG antibodies and chronic symptoms is not well understood and the validity and reliability of the test has been questioned (Miller, 1998; Suen, 2003; Ko, 2004; Teuber & Beyer, 2007).

Exclusion diets based on detection of food-specific IgG antibodies have shown effectiveness in reducing chronic symptoms (Dixon, 2000; Atkinson et al, 2004; Zar et al, 2005; Hardman & Hart, 2007). The British Allergy Foundation commissioned an independent audit (University of York, 2002) of a survey conducted by York Nutritional Laboratory into the effectiveness of an IgG test and exclusion diet in reducing chronic symptoms in over 4000 individuals. The audit demonstrated that over 70% of the clients reported sustained improvements in symptoms.

In 2007, Allergy UK commissioned a postal survey of over 5000 subjects who had reported a large array of symptoms and chronic medical conditions and who had been tested with a food-specific IgG ELISA (Hardman & Hart, 2007). Over 75% of respondents who closely followed their exclusion diets noticed an improvement in their condition, and most did so within three weeks. On re-
introduction of the foods in question, over 90% experienced recurrence of their previous condition.

The relationship between weight gain and allergy is unclear. Increased body mass index has been linked to asthma and atopy in females (Hancox et al, 2005) and obesity has been correlated with serum IgE levels in children (Matsuda et al, 2006). The latter study showed a strong inverse correlation between the appetite-modulating hormone, ghrelin, and serum IgE, supporting a link between obesity and IgE.

A recent study (Wilders-Trushchnig et al, 2008) showed that obese children have higher food-specific IgG antibody titres than normal weight children and that such antibodies are closely linked to low-grade systemic inflammation. Increased vascular permeability, resulting from low-grade inflammation, has been proposed as a cause of weight gain in non-IgE-mediated food allergy, causing bloating and fluid retention (Merson, 2005).

An alternative theory is that chronic food allergy causes addiction to the foods to which the person is allergic. In gut dysbiosis, gluten and casein, two common food allergens, are not completely digested and are absorbed in the form of the opiate-like peptides, gluten exorphins and casomorphins, respectively (Elitsur & Luk, 1991, Pennington et al, 2007). These compounds affect the brain via the vagus nerve, and casomorphin has been shown to stimulate food intake in experimental animals (Bray, 2000).

Another possible connection between allergy and weight gain may involve the sympathetic nervous system. Patients with allergic rhinitis have been shown to have sympathetic hypofunction (Ishman et al, 2007) and disorder of sympathomimetic amines has been linked to increased vascular permeability and oedema in women who could not lose weight despite appropriate dieting (Check et al, 2008).

In another recently published study, Fetissov et al (2008) revealed that autoantibodies of IgG and IgA, specific to a number of appetite-regulating peptides, including ghrelin, are present in healthy, normal-weight women. The authors consider that either infections or a change in the composition of the intestinal microflora could trigger production of pathologic autoantibodies, altering peptidergic transmission with resulting metabolic consequences.

Cambridge Nutritional Sciences Ltd, which developed the first food-specific IgG food allergy self-test, noted that many of their clients experienced unexpected weight loss after an exclusion diet based on the results of the IgG ELISA Food Detective™ test. A pilot study, the Fresh Start trial, therefore, aimed to determine whether weight loss would occur in overweight subjects subsequent to the elimination of any foods that showed a positive result in the Food Detective™ test, while maintaining the same calorific intake.
Methods

A total of 42 participants (37 women, 5 men), selected from an initial questionnaire (N1), were allocated to 13 nutritionists from throughout the UK. Each nutritionist was asked to monitor 5 overweight candidates who had been unsuccessful in keeping weight off with previous diets.

Selection Criteria

Strict guidelines were used to select participants for the Fresh Start Trial. The chosen subjects were: a) 13-20 kg overweight, b) aged 18-50 years old, c) had tried other diets unsuccessfully in the past, d) were not on medications that could affect body weight or Food Detective™ test results, e) had not experienced any recent change in lifestyle or exercise, f) had not been diagnosed with any of the conditions in Table 1, and g) had at least three symptoms commonly associated with food allergy.

Study Procedure

The participants were weighed prior to the study and then acted as their own control during a 1-week lead-in period, during which time they were asked to keep a food diary and eat their usual diet. The participants were also asked to keep all till receipts for all food purchases in the following 3 months.

One week later, each participant was weighed again and a Food Detective™ IgG test (Cambridge Nutritional Sciences Ltd) was conducted. The test is an enzyme immunoassay which detects raised levels of IgG antibodies to 59 commonly eaten foods. Each participant was advised to eliminate from their diet all the foods showing a positive test result, and to substitute alternative foods which would maintain the calorific value of their meals. Each volunteer was asked to complete a food diary for the subsequent 12 weeks and not to change their diet, supplements or exercise routine in any other way.

Participants were weighed every 2 weeks during the 12-week study period and checked both for compliance in eliminating positive foods, and for symptoms. At the end of 12 weeks, the participants were weighed and completed a feedback questionnaire.

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<th>Table 1. Exclusion criteria - diagnosed conditions.</th>
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Results

Weight Loss

Of the 42 participants who were selected for the trial, ten (23.8%) dropped out after the second consultation on receiving their Food Detective™ results.

Of the 32 subjects who took part in the study, 4 were later found either to be taking drugs or had conditions that may have affected weight loss and were thus excluded from the analysis. The final weight loss results and statistical analysis are presented for 28 participants (26 women, 2 men). A t-test for paired comparisons was applied to the data. Eight-week and 10-week data were not available for one participant who completed 12 weeks of the trial.

Of these 28 subjects, 24 (85.7%) lost between 0.1 kg and 8.2 kg of weight (average weight loss 2.86 kg; p=<0.05), 3 (10.7%) gained between 0.5 kg and 5.3 kg of weight and 1 person (3.5%) remained at the same weight.

Twenty (71.4%) participants completed the whole 12 weeks, with 21 (75.0%) completing 10 weeks, 23 (82.1%) completing 8 weeks and another 4 (14.2%) participants (2 women, 1 man) completing 4 weeks.

Of the 20 participants who completed 12 weeks of the trial, 18 (90.0%) lost between 0.3 kg and 6.8 kg (average -2.88 kg; p=<0.05), 1 (5.0%) gained 0.5 kg and 1 (5.0%) remained at the same weight, with a total average weight loss of 2.57 kg (p = <0.05).

Of the 21 participants who completed 10 weeks of the trial, 18 (85.7%) lost between 0.9 kg and 8.2 kg (average -3.38 kg; p = <0.05), and 3 (14.3%) gained between 0.3 and 0.9 kg (average +0.57 kg), with a total average weight loss of 2.82 kg (p = <0.05).

Of the 23 participants who completed 8 weeks of the trial, 19 (82.6%) lost between 0.2 kg and 7.2 kg (average -2.87 kg; p = <0.05), and 4 (17.4%) gained between 0.5 kg and 2.6 kg (average +1.25 kg), with a total average weight loss of 2.15 kg (p = <0.05).

Other Symptoms

Before the start of the trial, the most common symptoms reported by the 42 selected subjects were abdominal bloating (n = 30), fatigue (n = 29), excessive wind (n = 25), bloat (n = 25), headache (n = 24), water retention (n = 21), itchy skin (n = 21), depression (n = 20), skin problems (n = 19), constipation (n = 18), stomach cramps (n = 18), diarrhoea (n = 16), anxiety (n = 16) and insomnia (n = 15). Less commonly reported symptoms were migraine, asthma, eczema, rhinitis, fibromyalgia, sinusitis and facial puffiness (n = 2 to12).

In addition to the primary outcome measure, weight loss, the participants also reported on these other symptoms, every 2 weeks during the 12-week study. The majority of the 32 participants who took part in the trial reported an improvement in other symptoms as well as a change in body weight, after eliminating foods that showed a positive response in the Food Detective™ test.
In particular, 11 (34.4%) reported an improvement in fatigue/energy levels, 9 (28.1%) noted an improvement in abdominal bloating, 6 (18.75%) noted improved skin condition, 3 (9.4%) reported that headaches were reduced or eliminated, and 8 (25.0%) reported an improvement in general health.

Other symptoms that showed a significant improvement included constipation, insomnia, eczema, mood problems, poor hair and nail condition, premenstrual syndrome and joint problems.

**Discussion**

The trial investigated the association between exclusion of foods identified as positive in the IgG Food Detective™ ELISA test and loss of body weight in overweight subjects. The results showed that when IgG-positive foods were eliminated for each subject, significant weight loss was obtained over a 12-week period, despite maintaining calorie intake. In addition, an improvement in feeling of wellbeing was reported by most of the participants.

Although the exact role of IgG in food intolerance is not clear, a number of other studies have shown clinical benefit when foods identified by a serum IgG antibody ELISA have been eliminated from the diet. Atkinson et al (2004) conducted a double-blind, randomised, controlled study in 150 patients sensitive to at least one food in the food-specific IgG ELISA. After a 12-week period, a true exclusion diet resulted in a 10% greater decrease in symptoms than did a sham exclusion diet, and in those participants who were fully compliant, this reduction in symptom score increased to 26%. A small prospective audit (Rees et al, 2005) showed that excluding specific foods, identified in an IgG ELISA, resulted in considerable benefit in 38% of migraine sufferers after 2 months. Drisko et al (2006) not only found a significant improvement in IBS symptoms in 20 patients following a food elimination and rotation diet, but after 1 year, there was still significant adherence to the diet with minimal IBS symptoms and perceived control over the condition. This long-term follow-up minimises the likelihood that placebo played a major role in the therapeutic effect. Hardman & Hart (2007) found nearly a 76% noticeable improvement in a variety of chronic symptoms in subjects who had been IgG tested and who had rigorously followed an exclusion diet.

In the Fresh Start trial, although 90% of subjects completing the trial lost an average of nearly 3 kg, there may be other factors which could have contributed to the weight loss observed in these subjects on withdrawal of IgG-positive foods. There would have been substantial expectation from the participants that improvement in their condition and weight loss may occur following an exclusion diet, and this would contribute to the perceived therapeutic effect. Medical conditions characterised by highly subjective symptoms without a proven physiological correlation, such as those reported in this study, are believed to be especially susceptible to very strong placebo responses (Kaptchuk, 2002). A control group given a sham exclusion diet, as used by Atkinson et al (2004), would help to minimise any placebo effect in a future extended trial.

In addition, a longer follow-up period, such as that used by Drisko et al (2006), may reduce the likelihood that the placebo effect has influenced the results. It
would be interesting to determine if weight loss would continue in participants who maintain their exclusion diet over a longer period, or whether weight loss would tail off but be sustained.

The most crucial factor in a study of weight loss, in relation to a food elimination diet, is ensuring that calorie intake is maintained during the study period. Close monitoring of the participants’ diets and calculation of calorific intakes is paramount, otherwise any weight loss results would be open to question.

The participants’ other symptoms, although a secondary outcome measure, were recorded as ‘improved’ or ‘worsened’. A method of grading the severity of the symptoms, such as the ‘measure your own medical outcome profile’ (MYMOP) (Paterson, 1996), before and after food exclusion, would more easily quantify any improvement or exacerbation in a future trial.

There are other interesting questions, not addressed by this study, such as whether weight loss was greater or more likely in relation to particular symptoms or groups of symptoms. For instance, if gastrointestinal symptoms were resolved by food exclusion, would this result in greater weight loss than resolution of, say, skin conditions. It would also be interesting to determine the pattern of weight loss in relation to elimination of particular IgG-positive foods, and whether there is a correlation with age.

This small, non-placebo-controlled study has produced some interesting results, demonstrating significant ($p = <0.05$) weight loss subsequent to the exclusion of foods found to be positive in the Food Detective™ test. A future placebo-controlled study should determine if weight loss can be sustained over a longer period following IgG-positive food exclusion in a larger group of overweight people.

References


