Allergy UK

TESTING TIMES?

The Largest Food Intolerance Study
Is the Problem on the Plate or In the Mind?

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YORKTEST

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Dietary advice based on food-specific IgG results

Abstract

Purpose: To provide evidence that elimination diet based on food-specific IgG test results is an effective, reliable and valid aid to the management of chronic medical conditions.

Methodology / Approach: A postal survey, commissioned by Allergy UK, was carried out with 5286 subjects reporting a wide range of chronic medical conditions, who had taken a food-specific IgG enzyme-linked immunosorbant assay (ELISA) blood test. Questionnaires, issued three months after the results, were analysed to investigate the effect of eliminating the foods identified by the test. To check for response bias, a separate group of patients who had not responded were interviewed by telephone. The analysis and reporting of the data was carried out at the University of York.

Findings: 75.8% of patients who rigorously followed the diet had a noticeable improvement in their condition. 68.2% of patients who benefited from following the recommendations felt the benefit within three weeks. Those who reported more than one condition were more likely to report noticeable improvement. 81.5% of those that dieted rigorously and reported three or more co-morbidities showed noticeable improvement in their condition. For those who dieted rigorously and reported high benefit, 92.3% noticed a return of symptoms on reintroduction of the offending foods.

Practical Implications / Value: These data provide evidence for the use of elimination diet based on food-specific IgG blood test results as an aid to management of the symptoms of a range of chronic medical conditions.

KEY WORDS: ***Intolerance Food IgG ELISA Elimination Diet***

RESEARCH PAPER

Introduction

A role for food-specific IgG antibodies in the underlying mechanism of food intolerance (non-IgE mediated food allergy) has been proposed, as has the measurement of food-specific antibodies as a strategy for identifying foods to which a patient may be sensitive (Marinkovich, 1996). It is proposed that the presence of food-specific IgG indicates a potential sensitivity to that particular food and that the patient may achieve benefit by eliminating the food(s) from their diet. One recent study showed a consistent increase in IgG_4 antibody titres across the three Irritable Bowel Syndrome (IBS) subgroups compared to controls for wheat, beef, pork, lamb, and soya bean (Zar ***et al***, 2005), and a clinically significant improvement in symptoms has been observed in IBS patients eliminating foods identified by such a method (Atkinson ***et al***, 2004). However, the exact role of IgG antibodies as markers of food intolerance in general is not clear. IgG antibodies to food antigens are often present in healthy individuals and are generally considered to be part of the normal immune response to food allergens (Barnes, 1995).

Food intolerance has been associated with a myriad of chronic symptoms including headaches (Rees ***et al***, 2005), intestinal and skin symptoms (Sampson and McCaskill, 1985), behavioural changes and respiratory disorders (Pelikan, 1988). Currently, the best accepted method for diagnosing and confirming food intolerance is empirical, by elimination diet and subsequent challenge (Radcliffe, 2002). Using this method patients generally eat a restricted diet (elimination diet) for several weeks. If there is no symptomatic improvement during this time, it is assumed that the food type that has been restricted is not affecting their symptoms, and the process is repeated with another food type. This method is very laborious, and it is difficult to test all the combinations of food types that may be causing the problems.

Methodology

Patients

5286 subjects who had taken the YORKTEST foodSCAN 113 test for relief of chronic symptoms; 26.8% male and 72.4% female (0.7% did not reply to this question).

In terms of age range, 12.1% were under 30 years old, 38.0% were between 30 and 49 years old, 38.2% were between 50 and 69 years old, and 7.6% were 70 or over (4.1% did not report their age). The age distributions for the two genders were similar.

Method

YORKTEST Laboratories Ltd (York, UK) carry out an enzyme-linked immunosorbant assay (ELISA) test for food-specific IgG antibodies. In practice, a blood collection kit is sent direct to the consumer. The consumer uses the sterile lancet in the kit to collect the whole blood (finger prick) sample onto an absorbent 'wand'. This sample is then posted back to the laboratory. The sample is extracted from the 'wand', and then tested in the laboratory. The results of the semi-quantitative tests are sent to patients, and their medical practitioners (if involved), with classification scores in arbitrary units. Based on these results the patient is advised to stop or reduce the intake of the foods identified, and patients are entitled and encouraged to take advice on obtaining a balanced diet from an independent Nutritionist as part of the service. The service is compliant with the requirements of the European In Vitro Diagnostic Directive [1].

A postal survey was carried out of subjects who had undertaken the YORKTEST foodSCAN 113 testing service; a test for the presence of IgG antibodies to one-hundred and thirteen different foods. Questionnaires were issued to subjects three months after the test results had been issued to them.

Information was analysed from two questionnaires. The information was analysed independently by the University of York. The outcome measures used for this study were categorical and based on self reported perceived improvements by the patients. For the purpose of analysis SPSS has been used, on the two data sets separately and on a combined data set of patients where the questions have been comparable. The analysis used non-parametric statistical tests where appropriate. The analysed data responses from both versions of the questionnaire have shown that statistically the results of the entire study combined are valid. The first database contained 2260 records and the second 3026; total 5286.

In order to check for response bias, a group of 107 patients who had taken the foodSCAN 113 test, and who had been tested between one year and eighteen months previously but who had not replied to the postal questionnaire, were interviewed by telephone. The results from this group were analysed separately and the results compared with the groups of patients who had replied to the postal questionnaire.

Results

Results from the 5286 responders have been analysed as follows:-

How rigorously was the dietary advice followed

Out of the 5211 subjects that responded to this question, 3626 (69.6%) reported that they had rigorously changed their diet as a result of the test, 1476 (28.3%) reported they had made a reasonable attempt to change their diet, and 109 (2.1%) reported they were unable to change their diet.

How much improvement di d patients experience

5103 (96.5%) subjects answered the question about benefit. 1114 (21.8%) reported high benefit (Score 5), 1526 (29.9%) reported considerable benefit (Score 4) and 1035 (20.3%) reported moderate benefit (Score 3). 914 (17.9%) reported zero or low benefit (Score 0 or 1), and 514 (10.1%) slight benefit (Score 2). 183 (3.6%) did not reply to this question.

In the absence of a quantitative outcome measure we define reporting high, considerable or moderate benefit as reporting noticeable improvement in their condition(s), thus 3675 (72.0%) of the patients that replied to this question reported noticeable benefit.

Relationship between adherence to dietary advice and improvement of symptoms

5057 subjects answered the questions about benefit and adherence to dietary advice. Table I shows the distribution of benefit by how successfully the patients were able to comply with the elimination diet.

Of those who rigorously followed their elimination diet, 2697 (75.8%) reported noticeable improvement. Of the 1436 subjects that made a reasonable attempt at the diet, 948 (66.0%) reported noticeable improvement.

take in Table I

Speed of improvement

4069 (77.0%) subjects replied to a question which asked, 'How long after altering your diet did you start to feel the benefits?' 630 (15.5%) reported feeling benefit within 4 days, 956 (23.5%) between 5 and 8 days, 1264 (31.1%) between 9 and 20 days, 1002 (24.6%) between 21 and 60 days, and 132 (3.2%) reported feeling benefit over 60 days after altering their diet. 85 (2.1%) reported feeling no benefit.

The length of time taken to benefit for those who rigorously dieted is shown in Figure 1. Out of the 2899 who showed a noticeable improvement from rigorously dieting, 2026 (68.2%) reported feeling benefit within 3 weeks of starting the diet.

take in Figure 1

There is a clear relationship between the overall amount of benefit and the speed with which it is felt, as shown in Figure 2. Those that improve the most are more likely to improve quickly, however it is clear that this may differ according to the particular condition suffered.

take in Figure 2

Females are more likely to report high benefit than males. 23.6% of females reported high benefit from the diet compared with only 17.3% of males (χ^2=57.3; p<0.001). There was no relationship between gender and how rigorously the diet was maintained. 70.3% of females and 68.2% of males dieted rigorously (χ^2=2.2; p=0.331). Gender did not have any influence on how quickly benefit was felt (χ^2=9.2; p=0.101). 50.3% males were 50 years old or older, whereas 46.9% females were 50 years old or older (χ^2=13.4; p=0.004). Age had a consistent effect on the amount of benefit reported. 25.4% of those under 30 reported high benefit, whereas only 16.1% of those 70 years old or older reported high benefit (χ^2=55.9; p<0.001). Age did not have any influence on how well patients dieted (χ^2=3.5; p=0.748).

Medical conditions

The information obtained from asking which was the primary condition that concerned patients was grouped into diagnostic categories. As previously mentioned this question was not asked of all patients as it was only part of the first questionnaire. Of the 2221 replies 38.0% were gastro-intestinal, 13.7% were dermatological, 10.7% were neurological, 10.1% were respiratory, 9.4% were psychological, and 6.2% were musculo-skeletal. 11.9% were categorised as 'other'.

The distribution of benefit reported varied according to the medical condition of most concern is shown in Table II. For example, 40.6% of patients reporting psychological problems as their main concern report high benefit from dieting rigorously, whereas only 21.0% of those reporting respiratory or musculo-skeletal problems as the main concern reported high benefit.

take in Table II

The length of time the patient has had their primary condition does not appear to be associated with benefit felt from dieting rigorously (χ^2=10.1; p=0.604), nor the pattern of dieting behaviour (χ^2=3.3; p=0.769).

In the second questionnaire patients were asked to state all the conditions that concerned them, so data on co-morbidities became available. There were 3026 subjects who responded to the questions, and 4818 conditions stated. Of all of these reported conditions 1805 (37.5%) were gastro-intestinal, 635 (13.2%) were dermatological, 591 (12.3%) were neurological, 445 (9.2%) were respiratory, 708 (14.7%) were psychological, and 411 (8.5%) were musculo-skeletal. 223 (4.6%) were categorised as 'other'. 61.1% of patients had gastro-intestinal problems either as a main or subsidiary condition. 24.0% of patients had psychological problems either as a main or subsidiary condition.

55.1% of patients reported only one condition, 27.3% reported two conditions and 15.2% reported three or more conditions. Patients with co-morbidities were more likely to report noticeable improvement. Of the 2029 who dieted rigorously, 70.1% of the 1086 with one condition reported noticeable improvement, 78.0% of the 587 with two conditions reported noticeable improvement, and 81.5% of the 356 with three or more conditions reported noticeable improvement (χ^2=31.6; p<0.001).

Reintroduction of foods

In the second questionnaire, patients were asked if they had reintroduced any of the offending foods after starting the diet. Subjects were asked specifically to say whether the result of reintroducing foods was a strong return of symptoms, a slight return of symptoms, or no change. Of the 3026 subjects that responded to the second

questionnaire, 2275 (75.2%) said they had reintroduced offending foods either on purpose or by accident.

2219 of these patients also answered the question regarding the return of symptoms. 824 (37.1%) reported a strong return of symptoms, 902 (40.6%) reported a slight return of symptoms, and 493 (22.2%) reported no change. That is 77.7% reported the return of symptoms after the reintroduction of offending foods.

Information concerning the conditions under which patients deliberately reintroduced offending foods was not collected but the advice the patients received on dieting did suggest that under certain circumstances foods could be introduced after a period of time. Those reporting more benefit were more likely to feel a return of symptoms after reintroducing offending foods. For those who dieted rigorously and reported high benefit, 92.3% felt a return of symptoms after reintroducing offending foods.

Follow-up with the non- responders

A follow-up, by telephone, was carried out of subjects who had not responded to the postal questionnaire. This showed that of the 107 patients interviewed, 103 (96.3%) altered their diet, compared with 97.9% for the postal survey respondents. Of the 107 subjects, 73 (68.2%) rigorously dieted compared with the 69.6% who rigorously dieted based on the postal survey. There appears to be no significant difference between responders and non-responders to the postal survey in terms of the way they changed their diet based on the results.

Of those 103 who altered their diet, 101 reported how much they had benefited. Of these, 65 (64.4%) reported noticeable improvement. The comparative percentage for the postal questionnaire was 73.0%. Response bias was present in that a larger percentage of those who responded to the postal questionnaire showed noticeable

benefit from following an elimination diet than a sample of non-responders contacted by phone.

Discussion

The current study was not a randomised controlled trial. All the measures considered were categorical and based on self reported perceptions so quantification of comparisons was not possible. However, there was consistent evidence that noticeable benefit was gained from removing offending foods from the diet. 75.8% of those that rigorously followed the recommended diet had a noticeable improvement in their condition. 68.2% of those that benefited from following the recommendations felt benefit within 3 weeks of following the diet. The survey covered subjects with a wide range of medical conditions, and it was clear that those who reported more than one condition were more likely to report noticeable improvement. 81.5% of those that dieted rigorously and reported three or more co-morbidities showed noticeable improvement in their overall condition.

Data from a randomised controlled trial, looking at the effect of following an elimination diet on Irritable Bowel Syndrome (Atkinson ***et al***, 2004), showed similar percentages of benefiting subjects. The trial indicated that food exclusion for 12 weeks based on the results of the presence of a food-specific IgG ELISA test resulted in significantly improved symptoms compared to a "placebo diet" comparison group. Furthermore, this improvement was reversed upon 4 week reintroduction of the offending foods, and a significantly greater treatment effect was observed in patients adhering to the diet.

The observation of a clear relationship between adherence to the diet and outcome is critical in showing that the diet is an 'active treatment'. Similarly the fact that over

three-quarters of subjects who reintroduced offending foods back into their diet, whether on purpose or by accident, showed reoccurrence of their symptoms. These two criteria are the basis for the diagnosis of 'food intolerance' by the laborious elimination diet process which, it appears, can be largely 'bypassed' by following a diet based on the results of food-specific IgG testing. The percentage of patients reporting noticeable improvement suggests that such specified elimination diets are a valid intervention in the relief of certain symptoms. The degree of success varies with the type of problem being experienced. Having chronic symptoms does not seem to diminish the effect of dieting on the chances of improvement.

Many patients with chronic conditions would rather have a dietary solution to their problem than have to take medication, and this has obvious economic benefits. The results of these analyses go some way towards establishing the validity and reliability of ELISA testing for IgG-mediated food intolerance, and subsequently following an elimination diet based on the results, as an effective aid to the management of certain medical conditions. To complete this process further research is required to establish normal ranges for raised IgG levels from different groups, including those who do not perceive any symptoms as well as research to find the relationship between severity of symptoms, level of antibodies and the degree of benefit from dieting.

Footnote

[1] Examination Certificate (Annex III, section 6 of the Directive 98/79/EC on In Vitro Diagnostic Medical Devices), UL International (UK) Ltd, Report Number 05CA45655, Certificate Number 440.

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Table I. Level of benefit in relation to adherence to dietary recommendations

Level of Benefit	Dieted			
	Rigorously	Reasonably	Not at all	Total
Zero / Low	576 (16.2%)	270 (18.8%)	49 (79.1%)	895 (17.7%)
Slight	286 (8.0%)	218 (15.2%)	3 (4.8%)	507 (10.0%)
Moderate	595 (16.7%)	431 (30.0%)	3 (4.8%)	1029 (20.3%)
Considerable	1107 (31.1%)	410 (28.6%)	4 (6.5%)	1521 (30.1%)
High	995 (28.0%)	107 (7.5%)	3 (4.8%)	1105 (21.9%)
Total	3559 (100.0%)	1436 (100.0%)	62 (100.0%)	5057 (100.0%)

Pearson's Chi-Square $?^2$=523.28 (p=<0.001)

Figure 1. Time between start of diet and feeling benefit for those who dieted rigorously

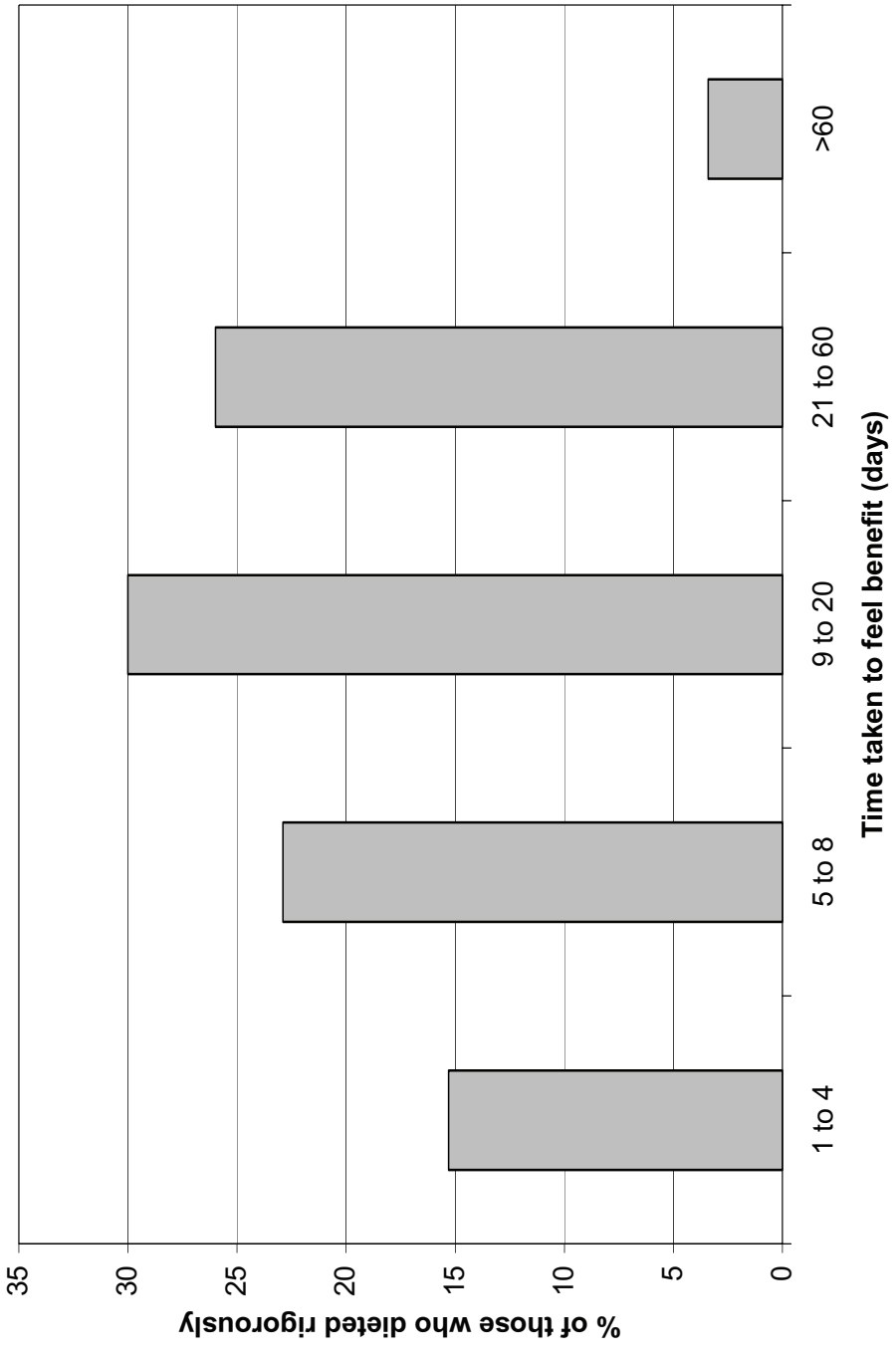
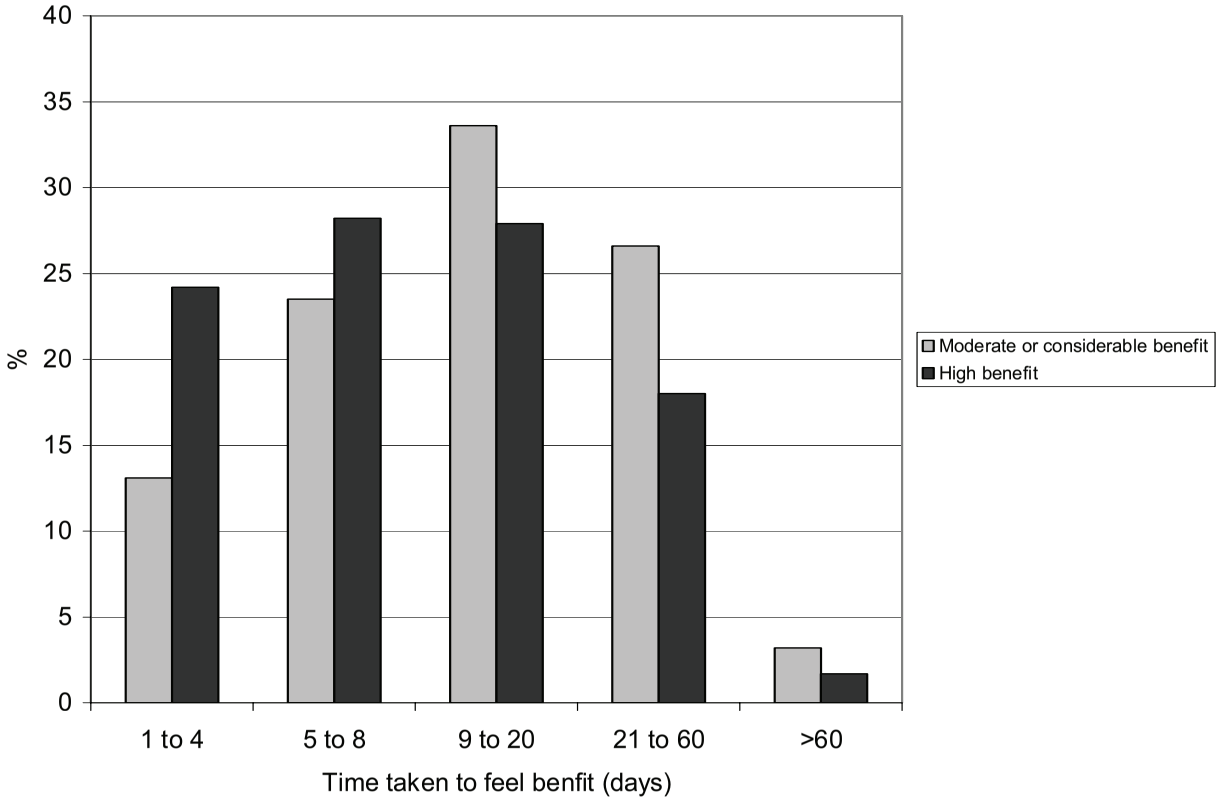


Figure 2. Relationship between overall benefit and how quickly subjects begin to feel benefit



Pearson's Chi-Square $?^2$=163.3 (p=<0.001)

Table II. Benefit by main medical condition for those who dieted rigorously

	Level of benefit reported		
	Low or none	Moderate or considerable	High
Gastro-intestinal	108 (19.7%)	287 (52.5%)	152 (27.8%)
Respiratory	39 (28.3%)	70 (50.7%)	29 (21.0%)
Neurological	34 (22.1%)	72 (46.8%)	48 (31.2%)
Dermatological	48 (23.6%)	106 (52.2%)	49 (24.1%)
Musculo-skeletal	36 (36.0%)	43 (43.0%)	21 (21.0%)
Psychological	27 (18.9%)	58 (40.6%)	58 (40.6%)
Other	38 (20.7%)	97 (52.7%)	49 (26.6%)

Pearson's Chi-Square $?^2$=32.3; p=0.001

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