# Can food hypersensitivity trigger a migraine attack?

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**Abstract**

Migraine is a common disorder. It occurs in 2 - 25% of the population. There have been many reports linking migraine with food hypersensitivity but the awareness of the relationship between migraine and food hypersensitivity by the medical community is far from universal. In a significant number of patients, food can trigger an attack of migraine. The exact mechanism by which food allergies provoke migraine is not known. High levels of specific IgE to food in migraineurs suggest an IgE-mediated hypersensitivity. This study was conducted to ascertain if there is an association of migraine with allergy in the local population. This is also the first local study where patients with migraine were skin tested in order to identify allergic basis for the attacks. The study found that almost 60% of the migraineurs had a history of allergy compared to 41.1% of non-migraineurs ($\chi^2 = 6.9$, $p = 0.0084$). Food allergy was found in 24.7% of migraineurs. 22% of migraineurs tested positive to foods that triggered their migraine. This strongly suggest that IgE-mediated hypersensitivity to food can precipitate migraine. The study found that it may be beneficial to skin test for food allergen in atopic individuals with migraine. This would help in identifying migraineurs who might benefit from an elimination diet.

Keywords: migraine; food hypersensitivity; allergy

## Introduction

Migraine is a common disorder. It occurs in 2 - 25% of the population (To & Wu, 1995; Lipton & Stewart, 1993; Rasmussen *et al.*, 1991). There have been many reports linking migraine with food and most investigators attribute this to pharmacological agents present in the food. It is generally accepted that food containing tyramine, phenylethylamine and monosodium glutamate can chemically trigger a migraine attack (Schuller *et al.*, 1996). The relationship between food allergy (IgE-mediated hypersensitivity) and migraine on the other hand has remained controversial.

Monro *et al.* (1980) demonstrated that two-thirds of severe migraineurs were allergic to certain foods. The radioallergosorbent test (RAST) for specific-IgE to food predicted migraine-provoking foods in patients who had benefited from elimination diet. Egger *et al.* (1983) found that 93% of 88 children with frequent migraine recovered on oligoantigenic diets. Mansfield *et al.* (1985) demonstrated that skin testing for food allergy was useful in determining which subjects would benefit from elimination diet. Despite these and other studies, the awareness of the relationship between migraine and food hypersensitivity by the medical community is far from universal (Mansfield, 1988).

Anderson (1995) discovered that mediators such as histamine and prostaglandins were found in few patients who were repeatedly challenged with specific foods. The hypothesis of neurogenic switching was proposed (Meggs, 1995) which provides a mechanism to explain how a stimulus at one site could lead to inflammation at a distant site. This provides a probable explanation of how allergen could exacerbate conditions such as migraine. Due to the renewed interest in food-induced migraine and a deficiency of local data, it was felt that a study was needed to ascertain if there is an association of migraine with allergy in the local population. This is also the first local study where patients with migraine were skin tested in order to identify allergic basis for the attacks. The skin prick test (SPT) was conducted as it has been demonstrated that SPT is useful for the diagnosis of food allergy (Aas, 1978; Chua, *et al.* 1976). Roger *et al.* (1994) found that the SPT had a sensitivity of 95% and a specificity of 92% when compared to the oral challenge test which is regarded as the "gold standard" in diagnosis of food allergy.

## Materials and Methods

Medical students from the Universiti Kebangsaan Malaysia were invited to participate in this study. A total of 533 students (299 females and 234 males) volunteered for the study. 420 of the participants were Malays, 87 Chinese, 14 Indians and 12 others. A detailed questionnaire based on the International Headache Society's (IHS) criteria for the classification of headache disorders was constructed (Headache Classification Committee of the IHS, 1988). The questionnaire included an extensive headache history, specific accompanying symptoms, trigger factors in particular food precipitants and personal and family history of allergy. The students were requested to fill the questionnaire

and this was conducted under supervision by the authors. Respondents were classified as having migraine if they fulfilled the IHS criteria. Migraineurs were then invited to undergo skin testing to a panel of food allergens. 126 student with no history of migraine or allergy served as a 'control' group and were also skin tested.

The Skin Prick Test (SPT) was carried out on the volar aspect of the forearm. The following food allergens were used: wheat, egg, milk, chocolate, cheese, rice, beef, banana, shrimp, mussels, crab and mixed nuts (Bencard UK). Histamine 1 mg/ml as a positive control and a negative control were also included (Bencard). A sterile lancet (Microlance, Becton Dickinson) was used to lift the skin through the drop of allergen. After 15 minutes the sizes of the wheals were measured. A wheal 3 mm or larger was considered positive. None of the subjects had taken any medication prior to the SPT that might interfere with the results.

Total IgE was measured using the kit Enzygnost-IgE micro (Behring) following the manufacturer's instructions. The statistical package SPSS was used for data entry and statistical analysis. A chi-square test was used to determine the significance of variables. Total IgE levels were analysed using the Wilcoxon Rank Sum test.

## Results

Of the 533 students that participated in the study, 73 (13.7%) were classified as having had migraine. The prevalence of migraine was 19.1% among females and 6.8% among males. The mean age of the participants was 22.9 years. Forty-two (57.5%) of the migraineurs had a history of allergy compared to 189 (41.1% ) of non-migraineurs ($\chi^2 = 6.9$, $p = 0.0084$). Forty (54.8%) of migraineurs had family history of allergy compared to 143 (31.1%) of nonmigraineurs ($\chi^2 = 13.4$, $p = 0.00025$). Food allergy was found in 24.7% of migraineurs. Table 1 gives the prevalence of the different types of allergies among migraneurs and nonmigraineurs. A large number of migraineurs had more than one type of allergy. 31% of migraineurs claimed that certain foods could trigger an attack of migraine. Food precipitants include chocolate, cheese, coffee, additives, milk, beans, seafood, beef and mutton. The commonest precipitants were cheese (16.4% of migraineurs), chocolate (13.7%) and coffee (5.5%).

Out of the 73 migraineurs, 32 were skin tested with a panel of 11 different food allergens. There was no positive correlation between a positive SPT and race, sex or age. Eleven of the 32 migraineurs (34.4%) and 1 of the 126 non-migraineurs (0.8%) were skin test positive to at least one or more food allergens. This was statistically significant ($p < 0.0001$). Of the migraineurs that were skin tested, 3 were skin test positive to only one food allergen, 4 were skin test positive to 2 - 3 food allergens and another 4 were positive to more than 3 different food allergens. The common skin test reactions were shrimp (21.9%), cheese (18.8%), crab (12.5%) and chocolate in (9.4%). Seven migraineurs had positive skin test to foods identified by them as trigger factors for their migraine. The foods involved being cheese in 6 subjects, chocolate in 3, milk in 1 and seafood also in 1. This demonstrates that 7 out of 32 (21.9%) migraineurs have immediate type hypersensitivity to the foods that precipitate their migraine. The migraineurs had a mean total IgE level of 234 IU/ml (the normal total IgE level is less than 100 IU/ml). In contrast, the control group (non-atopic, non-migraineurs) had a mean total IgE of 92 IU/ml. This difference was statistically significant ($p = 0.023$).

## Discussion

In this study, we found that allergy occurred in more than half of the students with migraine and in half of their first degree relatives. The link between migraine and allergy has also been demonstrated by others. In children, it has been shown that more migraineurs suffer from asthma than controls (Abu-Arefeh & Russel,1994). Chen & Leviton (1990) found that the prevalence of asthma was twice as high in children whose mothers had migraine than in children whose mothers had neither migraine nor allergies.

We found history of food allergy in 25% of migraineurs and this was statistically significant when compared to non-migraineurs. The role of food allergy and migraine has been debated for years. Monro *et al.* (1980;1984) found high levels of specific IgE to food in patienrs with migraine and subsequently was able to block food-induced migraine with sodium

Table 1. Prevalence of allergies in migraineurs and non-migraineurs

| Allergy | Migraineurs* | Non-migraineurs | p |
|---|---|---|---|
| Food allergy | 18 (24.7%) | 56 (13.3%) | <0.005 |
| Allergic rhinitis | 15 (20.5%) | 70 (15.2%) | NS |
| Asthma | 11(15.1%) | 42 (9.1%) | NS |
| Urticaria | 8 (11.0%) | 39 (8.4%) | NS |
| Atopic eczema | 7 (9.6%) | 43 (9.3%) | NS |
| Drug allergy | 7 (9.6%) | 33 (7.2%) | NS |

*42 Migraineurs had allergy with some having more than one type; NS = Not significant

chromoglycate. Vaughan (1996) in his review found that the data available clearly supports the role for food in the pathogenesis of migraine. On the other hand, there are studies that could not find proof of an IgE-mediated allergic mechanism in migraine (Padalier *et al.*, 1994; Pradalier & Launay, 1996).

Of the 32 subjects with migraine who were skin tested, 11 our of 32 (35%) were positive to one or more food allergens. A positive skin test indicates an IgE-mediated reaction to the particular allergen. It should be noted that only 0.8% of non-atopic subjects had a positive skin test. Of the 11 skin test positive migraineurs, 8 were allergic to multiple allergens. Seven of the 11 migraineurs were skin test positive to food identified by them as trigger factors for their migraine. This finding was interesting, as a review by Vaughan (1994) gave the opinion that the skin prick test did not demonstrate consistent efficacy in targeting clinically relevant food in food-induced migraine.

It is also interesting to note that the skin test demonstrated positivity in 6 subjects that specifically identified cheese as a trigger factor and 3 subjects that claimed chocolate as a trigger for migraine. It is generally thought that intolerance from pharmacologic agents in food cause migraine. Tyramine in cheese and phenylethylamine in chocolate are direct acting vasoactive amines. However, our results indicate that besides pharmacologic mechanisms, IgE-mediated hypersensitivity is involved in the pathogenesis of migraine as demonstrated by the positive skin test.

In agreement with other authors (Schuller *et al.*, 1996; Vaughan, 1994; Mansfield, 1988) we found that food allergy plays a role in a number of patients with migraine. We also feel that at least in our local population, it may be beneficial to skin test for food allergen in atopic individuals with migraine. This would help in identifying migraineurs who might benefit from an elimination diet.

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