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# Food Intolerance in Migraine

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## Abstract

Several factors can trigger migraine; among them, dietary factors play a very important role in the onset of migraine attacks. The aim of our study was to evaluate the incidence of food intolerances in a group of migraineurs, by using the Cytotoxic test.

30 consecutive patients suffering from migraine and coming to the Headache Center of S.Luca Hospital, Vallo della Lucania (SA) were examined. 23 were women, whose mean age was 28.2 years, range 13-47 years, 7 were men, whose mean age was 39.33 years, range 28-62 years. The Cytotoxic test is capable of identifying the presence of specific food intolerances by observing the appearance, the size, the shape or the integrity of leukocytes exposed to extracted food antigens or other materials derived from specific foods.

We found that: 12 women (52.17 %) and 3 men (42.85 %) were intolerant to tyramine. 3 women (13.05 %) and no man (0 %) were intolerant to milk 4 women (17.39 %) and 1 man (14.28 %) were intolerant to yeast. 4 women (17.39 %) and 1 man (14.28 %) were intolerant to Solanaceae. 5 women (21.74 %) and no man were (0 %) intolerant to coffee. 5 women (21.74 %) and no man (0 %) were intolerant to cocoa. 2 women (8.69 %) and no man (0 %) were intolerant to tea. 1 woman (4.35 %) and 1 man (14.28 %) were intolerant eggs. 1 woman (4.35%) and no man (0 %) were intolerant to pork. 1 woman (4.35 %) and no man were intolerant to sugar.

Our study showed a high incidence of food intolerance in migraineurs (in women more than in men). The dietary factors which gave more significant results were tyramine, yeast, solanaceae, coffee and cocoa. These results are in agree with those of other studies found in literature, proposing tyramine, coffee and cocoa as very important migraine-precipitating factors. Besides, there are few evidences about the comorbidity between migraine and intolerance to solanaceae. For this reason, further studies are requested to confirm this hypothesis.

Key words: migraine, food intolerance, cytotoxic test

## Introduction

Migraine is a neuro-vascular syndrome characterised by recurrent headache attacks associated with photophobia, phonophobia, nausea and vomiting. Migraine occurs in about 18 % of women and 6% of men, regardless of race or geographical location [1]. Currently, migraines are divided into two categories: migraine without aura (previously termed common migraine), and migraine with aura (previously also termed classical migraine) preceeded by a 15-20 minute episode of visual or sensory aura. Auras are most commonly visual alterations, such as hemianopsic field defects and scotomas that enlarge and spread peripherally [2] Visual auras are associated with spreading cortical depression; sensory auras are usually experienced as paraesthesias of the arm and face.

While the exact etiology of migraine headaches is unknown, several theories have been proposed. The vascular theory attributes migraines to an initial intra-cranial arterial vasoconstriction, resulting in reduced blood flow to the visual cortex, followed by a period of extra-cranial vasodilation [3]. Modern imaging techniques have shown that during a common migraine attack there are in fact only minor changes in cerebral blood flow, and the proposed initial vasoconstrictive phase may actually last much longer than the aura [4]. It has also been hypothesised that migraine sufferers have an inherent vasomotor instability and are more susceptible to the vasodilatory effects of certain physical and chemical agents. This point of view has been reinforced by the observation that organic nitrates, which are capable of delivering nitric oxide, trigger migraine attacks in migraineurs, at low doses, ineffective in normal subjects [5] .

Moskowitz's theory involves the trigeminovascular complex, which links the aura and the headache of migraine [6]. In this theory the trigeminovascular neurons release substance P and other neurotransmitters in response to various triggers .

The affected trigeminal nerve release of substances such as substance P, neurokinin A, calcitonin gene-related peptide, and nitric oxide which interact with the blood vessel wall to produce dilatation, protein extravasation, and sterile inflammation, stimulating the trigeminocervical complex as shown by induction of c-fos antigen by positron emission tomography (PET) scan.[7-9] This chain of events is further mediated by mast cells that release histamine and platelets that release serotonin. [8-15]

The release of these chemicals causes inflammation, and what is called peripheral sensitization. This is most likely, what results in the throbbing pain of migraine. Information then relayed to the thalamus and cortex for registering of pain and central sensitization explaining coetaneous allodynia. Involvement of other centers may explain the associated autonomic symptoms and affective aspects of this pain [12].

A relationship between food consumption and migraine has been widely suggested [16-21]. Some foods (such as cheese, chocolate or wine) are thought to be one of the well-known reasons triggering of migraine attacks according to consistent reports from the patients. It has been reported that diet with low-fat intake could reduce the headache frequency and intensity [22. On the other hand, some additives (such as triclorogalactosucrose or aspartame) may trigger attacks in some migraineurs [23-26]. However, it is neither easy nor very useful to organise routine diet according to robust protocols for many patients [27]. All this indicates that there is a need for an individualised approach of the diet to relieve migraine. One has to distinguish between inflammation-induced migraine and migraine caused by food via other mechanisms such as histamine-induced vasodilatation. IgG could be one of the markers to identify food which causes inflammation and could cause migraine attacks in predisposed individuals.

IgE-specific food allergy has been shown to be related with migraine supported by the success of individualised diet in controlling migraine attacks [28]. Non-IgE antibody mediated mechanisms have also been proposed in food allergy [29]. Aljada et al. [30] provided evidence for the pro-inflammatory

effect of food intake. IgG antibodies against food antigens have been found to be correlated with inflammation and intima media thickness in obese juveniles [31]. Several studies reported significant improvement in irritable bowel syndrome (IBS) by food elimination based on IgG antibodies against to food antigens [32-35]. Rees et al. [36] showed a beneficial effect of a diet guided by IgG antibodies to food in migraine patients. Recently, Arroyave Hernandez et al. [37] reported preliminary evidence that IgG-based elimination diets successfully controlled the migraine without need of medication.

Given the above evidences, the aim of our study was to evaluate the incidence of food intolerances in a group of migraineurs, by using the Cytotoxic test.

## Patients and Methods

The study was performed and approved by Neurophysiopatology Service, Headache Centre, S. Luca Hospital, Vallo della Lucania (SA),Italy.

30 consecutive patients suffering from migraine and coming to the Headache Center of S.Luca Hospital, Vallo della Lucania (SA) were examined. 23 were women, whose mean age was 28.2 years, range 13-47 years, 7 were men, whose mean age was 39.33 years, range 28-62 years. All patients suffering from migraine without aura (criteria ICDH-II) at least 3 years and were subjected to a laboratory evaluation through the cytotoxic test. The Cytotoxic test is capable of identifying the presence of specific food intolerances by observing the appearance, the size, the shape or the integrity of leukocytes exposed to extracted food antigens or other materials derived from specific foods.

Statistical analyses included parametric tests to compare means (paired and unpaired two sample *t*-test), non-parametric tests to compare medians (Wilcoxon test and Mann–Whitney test) and 2×2 chi-square test.

## Results

We found that: 12 women (52.17 %) and 3 men (42.85 %) were intolerant to tyramine. 3 women (13.05 %) and no man (0 %) were intolerant to milk 4 women (17.39 %) and 1 man (14.28 %) were intolerant to yeast. 4 women (17.39 %) and 1 man (14.28 %) were intolerant to Solanaceae. 5 women (21.74 %) and no man were (0 %) intolerant to coffee. 5 women (21.74 %) and no man (0 %) were intolerant to cocoa. 2 women (8.69 %) and no man (0 %) were intolerant to tea. 1 woman (4.35 %) and 1 man (14.28 %) were intolerant eggs. 1 woman (4.35%) and no man (0 %) were intolerant to pork. 1 woman (4.35 %) and no man were intolerant to sugar (See Table I). In women, there was a higher incidence of food intolerance (See Fig. 1).

## Discussion

Our study showed a high incidence of food intolerance in migraineurs (in women more than in men). The dietary factors which gave more significant results were tyramine, yeast, solanaceae, coffee and cocoa. These results are in agree with those of other studies found in literature, proposing tyramine, coffee and cocoa as very important migraine-precipitating factors [38-40].

Foods containing tyramine and other biogenic amines have long been suspected of triggering migraine [41-43]. Foods commonly identified as migraine triggers include (in order of importance): dairy products (eg, cheese), chocolate, eggs, citrus fruits, meat, wheat, nuts and peanuts, tomatoes, onions, corn, apples, and bananas [44]. Tyramine– and phenylalanine–containing foods, such as aged cheese, beer, and red wine, have also been implicated in migraine [43-44]. Although evidence is limited, dietary treatment of pediatric migraine with an allergen–free diet was effective in over 90% of subjects [45]. Elimination of certain food additives, including MSG, aspartame, and sodium nitrate, may also be helpful [46-47].

Experts are still trying to understand how tyramine can trigger migraines. One explanation is that tyramine can cause nerve cells in your brain to

release the chemical norepinephrine. Having higher levels of tyramine in our system -- along with an unusual level of brain chemicals -- can cause changes in the brain that lead to headaches.

Tyramines are derivatives of amino acids called tyrosine. After long periods of time, some of the tyrosine amino acids in foods such as aged cheeses or meats will naturally be converted by bacteria into tyramines. This same process can also occur in your intestinal tract if digestion is slow allowing bacteria the time to convert tyrosine into tyramine. For this reason, tyramine-sensitive individuals should take steps to support their digestive system as well as reduce foods containing pre-formed tyramine in their meal plan [48-49].

Although the reason tyramine causes toxic food responses such as migraines is not clearly understood, research suggests that people suffering from migraines may not adequately neutralize tyramine. While normally neutralized through a detoxification process in the intestine and liver before it is absorbed into the body, tyramine sensitive individuals are believed to have increased amounts of unneutralized tyramine that gets absorbed and circulated to the brain where it may interfere with normal brain functions causing the pain that is experienced as a migraine [48-49].

Regarding migraine by solanaceae, these may contain toxic alkaloids, *solanine* and *chaconine*. These alkaloids present in the greatest concentrations just underneath the skin and increase proportionately with age and exposure to sun light. Cooking at high temperatures (over 170 °C) partly destroys these toxic substances [50,51]. When consumed in sufficient amounts, these compounds may cause headache [50,51].

Regarding migraine by caffeine, excessive caffeine consumption or withdrawal from caffeine can cause headaches when the caffeine level abruptly drops. The blood vessels seem to become sensitized to caffeine, and when caffeine is not ingested, a headache may occur [52].

Sigmon et al. [52] investigated the biological mechanisms of caffeine withdrawal in a new study. Consumers of coffee and other caffeinated products have often reported that caffeine withdrawal brings with it many after effects such as headache, fatigue, feeling less alert, less energetic and experiencing difficulty concentrating. In the study, the researchers looked at brain electrical activity and blood flow during caffeine withdrawal to examine what was taking place physiologically during acute caffeine abstinence, including the likely mechanism underlying the common "caffeine withdrawal headache." They examined caffeine's effects in a double-blind study, which involved the administration of caffeine and placebo capsules. The researchers measured each participant's response to the caffeine or placebo using three different measures, brain electrical activity via electroencephalogram (EEG); blood flow velocity in the brain via ultrasound; and participants' self-reports of subjective effects via questionnaires. It was shown that stopping daily caffeine consumption produces changes in cerebral blood flow velocity and quantitative EEG that are likely related to the classic caffeine withdrawal symptoms of headache, drowsiness and decreased alertness. More specifically, acute caffeine abstinence increased brain blood flow, an effect that may account for commonly reported withdrawal headaches [52].

Regarding migraine by cocoa, this contains high proportions of condensed tannins and although researchers are not certain what the exact mechanism is behind cocoa migraine, most are currently in agreement that the neurotransmitter serotonin is involved. Some researchers suggest that, at least in some cases, low levels of utilizable serotonin may account for a propensity to migraine. According to agricultural studies, tannins are believed to bind with nutritional components in the digestive tract, and to bind to the wall of the digestive tract itself. Although proline absorption appears to be most effected by tannins' complexing with proteins, other amino acids, including tryptophan (a precursor to serotonin), are also effected. Starches, needed by the body in the production of serotonin, are easily bound by tannins. It seems possible that

as a result of this binding, diets high in tannins could result in reduced utilizable levels of serotonin. In individuals who are susceptible to migraine, such a reduction of serotonin may lead to an increase in the number and severity of their migraines.

Therefore, our study confirm a strong relationship between food intolerance and migraine considering that tyramine, coffee and cocoa are very important migraine-precipitating factors. Besides, there are few evidences about the comorbidity between migraine and intolerance to solanaceae. For this reason, further studies are requested to confirm this hypothesis.

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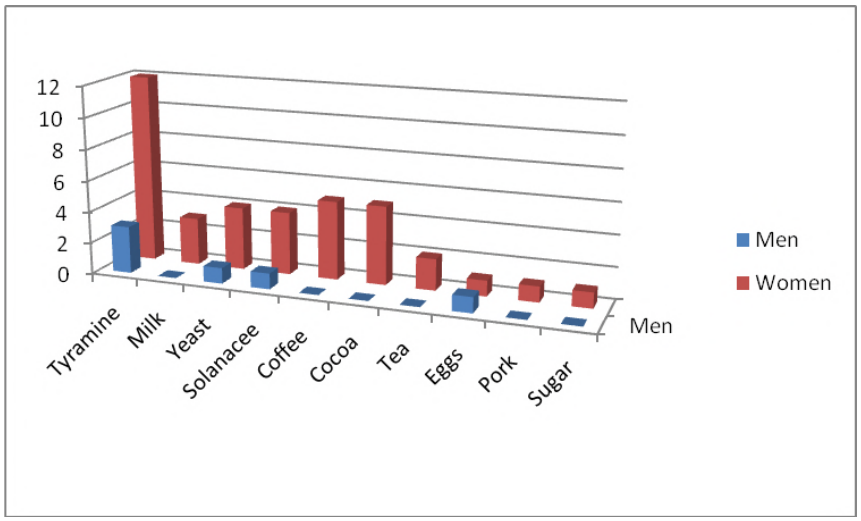


Fig. 1: Intolerance in migraineurs: women vs men

| Substance | Women | Men |
|---|---|---|
| Tyramine | 12 (52,17%) | 3 (42.85%) |
| Milk | 3 (13,05%) | 0 |
| Yeast | 4 (17,39%) | 1 (14,28%) |
| Solanacee | 4 (17,39%) | 1 (14,28%) |
| Coffee | 5 (21,74%) | 0 |
| Cocoa | 5 (21,74%) | 0 |
| Tea | 2 (8,69%) | 0 |
| Eggs | 1 (4,35%) | 1 (14,28%) |
| Pork | 1 (4,35%) | 0 |
| Sugar | 1 (4,35%) | 0 |

Table I: Food intolerance in migraineurs