

Diet and Migraine (2007)

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Migraine is a highly prevalent population problem and typically chronic over time. Therefore any headache risk related to diet has important implications. The number of foods and substances contained within foods reputed to trigger migraine is large (See Partial Listing). Some of the most commonly cited food triggers of migraine are major sources of important nutrients. Current dietary instructions in medical offices may include the removal of those selected foods "reported (believed) by the patient" to trigger attacks, and/or avoidance of all foods "listed to trigger attacks." Avoidance of these foods and substances requires detailed attention to eating plans and is typically time-consuming and difficult. Over years or decades, dietary restrictions for migraine that emphasize food scrutiny and avoidance likely are not innocuous. I therefore report the evidence for current dietary migraine recommendations.

[Alcohols and Wines](#)

Nicoli and Sicuteri recruited 307 volunteers with migraine without aura to complete a questionnaire every time they consumed alcohol. No correlation was found between alcohol consumption and migraine attacks, but when the two events coincided, spirits and sparkling wines were most likely imbibed. Stressful events and onset of migraine were positively related. Kanny studied 8 healthy and 16 wine-intolerant subjects with histamine-rich and histamine-free wine in double-blind oral provocation studies. No headaches occurred with either type of wine, and no change in plasma histamine levels was found in either group. In a study by Jarman on 5-HT release from platelets there was no difference in wine-sensitive, wine-insensitive and control patients. Littlewood challenged patients with migraine who believed red wine, but not other alcohol types, caused their headaches. Red wine or vodka was consumed cold out of dark bottles with equal alcohol content, with flavor and color "disguised." Red wine triggered attacks in 9/11 with a 3 hour time lag, while vodka triggered 0/8.

[Aspartame](#)

Schiffman published in NEJM a study involving 40 inpatient headache subjects studied with 30mg/kg aspartame. Diet was tightly controlled as were additional variables, with headache experienced in thirty-five per cent of patients taking aspartame and forty-five per cent with placebo. Commentaries have included that study design may have eliminated endogenous or exogenous factors which act synergistically with aspartame to trigger headaches. Koehler studied 25 episodic migraine subjects with 300mg QID aspartame in a 13-week crossover study. Only forty-four percent of the ITT group completed the study and reported increased frequency of headache triggered by aspartame. In another DBPC trial Van den Eeden used 30mg/kg/d aspartame in 32 subjects with only 18 completers in a crossover randomized trial. Only those subjects "very sure" of their aspartame sensitivity reported increased headaches with aspartame. Stegink, in a DBPC crossover trial, used 6 non-headache subjects reporting glutamate but not placebo sensitivity. They received aspartame 34 mg/kg or sucrose 1g/kg in orange juice. No subject reported symptoms after either sucrose or aspartame loading. Case reports on aspartame sensitivity are published by Newman, Blumenthal and Johns.

[Monosodium Glutamate \(MSG\)](#)

There are no RCTs specific to migraine subjects. Walker, in Regulatory Toxicology & Pharmacology reports that blood glutamate levels, known to be neurotoxic in mice, were not achieved in humans even after bolus doses of 150 mg/kg. Walker further states, "High usage of MSG in ethnic cuisines does not represent a situation in which intake might achieve unsafe levels, even among individuals claiming idiosyncratic intolerance of such foods." Tarasoff's RDBPC crossover study provided no proof of evidence for a small subset of subjects truly sensitive to MSG. Yang performed a double-blind, placebo-controlled, randomized oral challenge study in self-identified MSG-sensitive

subjects. In random double-blind sequence, they received either 5 gm MSG or placebo. Subjects who reacted underwent re-challenge with placebo and 1.25, 2.5 and 5 gm MSG. Positive re-challenge was defined as reproduction of more than 2 specific symptoms ascertained by a pre-challenge interview. In 61 subjects, 29.5% responded to neither challenge, 9.8% to both, 24.6% to placebo and 36.1% to MSG only. Total and average severity of MSG symptoms in sensitive subjects after ingestion of MSG was greater than values after placebo. Analysis revealed a threshold re-challenge dose of 2.5 grams of MSG. Headache occurred more frequently after MSG than after placebo. Methodological errors have been detailed by Martin regarding positive RCTs.

Nitrates/Nitrites

Henderson and Raskin studied a single patient with moderate headache following consumption of frankfurters, bacon, salami, and ham. In a single-blind multiple-drink study, 8/13 nitrites and 0/8 sodium bicarbonate drinks produced headache. They concluded that pharmaceutical nitrates produce headache, while dietary nitrates/nitrites may in susceptible individuals.

Tyramine

Tyramine is perhaps the most studied migraine trigger substance. There are multiple positive studies, mostly from Hannington, published in the 1960s to early 1970s using 125mg of tyramine (possibly the same patients and studies multiply reported). Hannington also published at least one negative study as well. There are multiple additional negative studies. In these trials, when double blind, the placebo rates were unusually high. The Ziegler trial has been criticized for not selecting "tyramine"-sensitive headache subjects. Salfield and Forsythe performed two independent negative pediatric trials, while Medina and Diamond found no difference in headache indices when using high, low or regular tyramine diets, although improvement occurred in all 3 groups, leading to a conclusion that a special diet helps. Sandler studied tyramine metabolism and found no differences in tyramine sulfoconjugation following an oral tyramine load in 30 migraine patients compared with 14 non-headache controls, or in diet sensitive and non-diet sensitive migraine patients and controls when depressed patients were removed from the analysis.

Others

There are no RCTs, or only negative trials, for cheese, chocolate, dairy products, soy isoflavones and vegetables.

Strength of Evidence

Standard evidence grading supports Grade B evidence for alcohol, aspartame, MSG and nitrates. Even the grade B evidence for MSG lacks data specific for migraine. All others discussed are Grade C with no positive results or at least 2 dissenting studies.

Conclusions

There is little to no evidence for "diet substances" as migraine triggers. All trigger factors are experienced occasionally; not consistently, and are endogenous in the majority of patients. Subjective sensitivity to foods should be examined critically before concurring with elimination, and practitioners should advise that foods play a limited role as migraine triggers, and dietary restrictions have generally not been proven. Therefore we should advise elimination

of proven precipitating factors and avoidance of general dietary restrictions. Perhaps we should even counter detail with explicit recommendations NOT to avoid dairy products, citrus fruits and vegetables. Finally, this is not to say that food cannot trigger headache or that food allergy does not exist, but evidence is currently inadequate for implementation across headache populations.

Partial List of Dietary Triggers

Cheese

Chocolate

Citrus fruits

Ham, Bacon, Hot dogs

Dairy products and Yogurt

Fatty and fried foods

Asian foods

Coffee, tea, colas

Food dyes, additives

Artificial sweetener

Wine, beer