

FOOD INTAKE PRIOR TO A MIGRAINE ATTACK -STUDY OF 2,313 SPONTANEOUS ATTACKS

Katharina Dalton, M.R.C.G.P.

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SYNOPSIS

Sandler, Youdim and Hannington noted an inability to oxidise tyramine and phenylethylamine in dietary and non dietary migraine sufferers-1,883 female volunteers in Britain completed questionnaires detailing food intake during the 24 hours prior to spontaneous migraine attacks. Analysis of 2,313 attacks are reported. This revealed consumption of chocolate in 33%, cheese 40%, citrus fruits 21% and alcohol 23%. Fasting (5 hours day or 13 hours overnight) occurred in 67%. No dietary factors were isolated in 5%. Only 14% thought food caused their attacks and 2% blamed fasting. Sensitising factors analysed included age, time in menstrual cycle, pilltaking and hysterectomy. The findings suggest that in double blind trials designed to elucidate dietary factors, one needs to consider the patient's intake during the 24 hours prior to the administration of the test capsule. A new approach to treatment is suggested with elimination of specific foods and avoidance of fasting.

IT HAS BEEN postulated that there is a biochemical defect in migraine sufferers.¹ A highly significant reduction in the ability of migraine subjects to oxidase both tyramine and phenylethylamine when compared with non-migrainous controls has been noted. However, measurements of monoamine oxidase activity in platelets of migraine sufferers showed no difference between those with dietary and non-dietary migraine. The assumption that an individual has dietary migraine is not based on a scientific test, but on the ability of the sufferer to identify a specific food. Failure to identify a specific food does not necessarily imply a non-dietary basis for the migraine. There may be ignorance that certain foods can precipitate an attack; possibly a failure to observe the relationship; a lack of appreciation of the 12-24 hour interval between ingestion of the food and the onset of an attack; or no recognition of the effect of fasting. On the other hand the presence of a specific food eaten during the 24 hours prior to a migraine attack does not necessarily imply that it is the final precipitating factor of the attack, nevertheless this possibility does exist.

Previous studies on food in relation to migraine have concentrated on inducing migraine by the ingestion of tyramine^{2,3}, of phenylethylamine^{1,4} or by fasting.^{5,6,7,8} This paper reports the food intake of 1,883 women during the 24 hours immediately prior to the onset of a spontaneous migraine attack, and covers 2,313 attacks. It would appear to be the first large scale study of food intake prior to a spontaneous migraine attack.

METHOD

Volunteers were obtained in response to an appeal by the British Migraine Association asking for participants to assist in a survey of the hormonal effects on migraine in women.

Initially the volunteers completed a questionnaire about their migraine, general health, menstruation and pregnancies. They were then asked if they would assist further by recording over the next three months the dates of migraine and menstruation and also complete attack forms as used in previous surveys^{9,10} giving all food and drink consumed during the 24 hours immediately prior to an attack (only three attack forms were required from each participant).

Migraine was defined in accordance with the definition of the World Federation of Neurology and in each case the volunteer's description of her attack came within the definition of migraine. In addition all volunteers were asked when completing the 3 month record to grade the severity of their attacks on the following basis:

slight	- no medication needed.
mild	- medication needed.

moderate - unable to continue work.
severe - sufficient to require bed rest.

Only moderate and severe attacks were used in the analysis.

In a study of 500 patients with dietary migraine Hanington¹¹ found that the four most frequently cited foods were chocolate 75%, cheese and dairy produce 48%, citrus fruits 30% and alcohol 25%. The vasodilating amines, tyramine and phenylethylamine, are present in chocolate, cheese, citrus fruits and alcohol, and these four foods were selected for special study and will be referred to as "specific foods". (Dairy products other than cheese and yoghurt are excluded). In the analysis of the attack forms the following classification were made-"Chocolate" including drinks, cakes and puddings.

"Cheese" including yoghurt and dishes in which cheese is an essential ingredient, but excluding dishes in which cheese might have been an optional extra.

"Citrus fruits" including oranges, lemons and grapefruit either fresh or juice, but excluding drinks e.g. squash or foods, which might or might not contain citrus fruits.

"Alcohol" including drinks, but excluding foods which might have been cooked in alcohol, unless it was specifically stated that alcohol was used.

"Fasting" was limited to absence of food for 5 hours during the day or 13 hours overnight. If an attack was stated to have started on waking, and no time given, absence of food after 6 p.m. was considered fasting.

"Dietary factor" is used to include the consumption of specific foods and/or fasting.

Women under 45 years were divided into "takers", "ex-takers" and "non-takers" in respect of the oestrogen-progestogen oral contraceptive pill taken during the observed month. None of the women were currently taking progestogen-only contraceptive preparations.

Questionnaires were excluded if the volunteer was in poor health; requiring regular medication for some reason other than migraine; provided an uncertain diagnosis or the questionnaires were incompletely filled in. There was a total of 1,883 questionnaires suitable for analysis, of which 1,147 were in women between 15 and 45 years, 2,313 attack forms were analysed.

RESULTS

During the 24 hours prior to a spontaneous attack of migraine, chocolate was consumed by 33%, cheese by 40%, citrus fruits by 21% and alcohol by 23%. Fasting was present in 67%. In only 5% was there no dietary factor present (Table 1). The final question on the attack form was "What do you think caused this attack?" Only 14% mentioned food, while 2% thought fasting could have been responsible for the attack. In contrast stress, worry, frustration and tension received frequent mention. The questionnaires completed in the initial stages of the survey asked "What brings on an attack?" to which 28% replied certain foods and 5% mentioned fasting (Table 2). Thus the appreciation of a dietary factor preceeding a migraine attack is poor, even when the evidence is provided by the volunteer herself.

An analysis of 2,313 attack forms in respect of age showed there was a progressive decrease in specific foods from 79% in those under 30 years to 69% in those over 50 years, and a progressive increase in

TABLE 1

**Dietary Factors in 2,313
Spontaneous Migraine Attacks**

	No. 2,313	%
Total Attacks		
Chocolate	766	33%
Cheese	914	40%
Citrus fruits	482	21%
Alcohol	536	23%
Specific food	1,703	74%
Fasting	1,551	67%
No dietary factor	111	5%

Some attacks involved more than one factor.

TABLE 2

Recognition of Dietary Factor		
Total attacks	2,313	
Thought food caused this attack	331	14%
Thought fasting caused this attack	57	2%
Total questionnaires	1,883	
Thought food caused attacks	553	28%
Thought fasting caused attacks	93	5%

the incidence of fasting from 69% in the under 30 years to 76% in those over 50 years. (Table 3). No differences were noted in respect of parity and dietary factors.

The dietary factors present in women under 45 years were analysed in respect of takers, ex-takers, non-takers of the pill and those in whom a hysterectomy (and/or oophorectomy) had been performed. A

TABLE 3
Dietary Factors and Age in 2,313 Attacks

Age	- 30 %	- 40 %	- 50 %	+ 50 years %
Chocolate	37	41	34	26
Cheese	44	44	33	36
Citrus Fruits	18	16	24	23
Alcohol	30	25	17	20
Specific Foods	79	77	73	69
Fasting	69	68	72	76

Some attacks involved more than one factor.

higher proportion of takers were influenced by consuming cheese 48% and alcohol 28% before an attack, while in those who had a hysterectomy a high percentage were influenced by consuming chocolate 47% or had been fasting 91% before an attack. (Table 4).

TABLE 4
Dietary Factors in Women Under 45 Years

	<i>Number of Attacks</i>	<i>Chocolate %</i>	<i>Cheese %</i>	<i>Citrus Fruits %</i>	<i>Alcohol %</i>	<i>Fasting %</i>
Takers	262	35	48	20	28	75
Ex-Takers	344	33	44	16	26	73
Non-Takers	488	41	34	18	23	61
Hysterectomy	55	47	29	25	18	91
Probability		<2.5%	<0.1%			<0.1%

TABLE 5
Dietary Factors Present in Menstrual Cycle

Day of Cycle	1-4 %	5-8 %	9-12 %	13-16 %	17-20 %	21-24 %	25-28 %	Total Attacks
Chocolate	28*	11	10	16	12	8	5	326
Cheese	29*	14	9	16	11	7	14	349
Citrus Fruits	30*	13	10	11	11	7	17	169
Alcohol	27*	14	9	14	11	7	18	249
Fasting	31*	14	10	12	10	9	14	596

* Probability exceeds 0.1%.

Of the 2,313 attacks there were 872 (38%) which occurred within 28 days of menstruation and these were distributed according to the seven 4-day phases of the menstrual cycle. This group excluded those with amenorrhoea due to pregnancy, lactation, hysterectomy, menopause and pill taking, those with unduly long cycles and those who failed to record menstruation accurately. During day 1-4, 29% of all attacks were experienced, compared with an expected incidence on an even distribution of 14%. There was a significant increase in all the different dietary factors in attacks which occurred during days 1-4, compared with days 5-28, thus chocolate was consumed by 28%; cheese 29%; citrus fruits 30%; alcohol 27% and fasting was present in 31% (Table 5). The probability of such a high incidence occurring by chance during one of the seven menstrual phases exceeds one in a thousand in each instance.

DISCUSSION

The information on which this study is based was provided by 1,883 volunteers, who completed self-administered postal questionnaires. The data, therefore, could not be validated. However Waters and O'Conner¹² showed there was no significant difference in the validity of information on migraine obtained from self-administered postal questionnaires and that obtained from questionnaires administered by a trained field worker.

It should be appreciated that the volunteers in this study assumed that the main purpose was to investigate the role of hormones rather than dietary factors. Nevertheless most of them were meticulous in completing the attack forms in great detail.

The recognition of dietary factors in precipitating migraine has usually depended on the patient's history, rather than precise observation of food intake during the preceding 24 hours. Pearce¹³ found that migraine attacks were caused by specific foods in 13%, alcohol in 11% and hunger in 7%, while Selby and Lance¹⁴ considered about 25% of attacks were provoked by eating certain foods, particularly fatty foods, chocolates and oranges. In this study of the food intake during 24 hours prior to an attack an incidence was found of 74% for specific foods and 67% for fasting (Table 1). This study also emphasises the poor recognition of these factors. Immediately after an attack only 14% thought the attack was provoked by specific foods and 2% by fasting. (Table 2). Sandler, Youdim and Hanington¹ noted that the defect in tyramine and phenylethylamine metabolism was present in both dietary and non-dietary migraine sufferers, but absent in non-migraine controls.

During the 24 hours prior to a moderate or severe migraine attack a dietary factor was isolated in 95% of the 2,313 attacks studied. Further study is now needed, and in particular a study of dietary factors in spontaneous attacks in men. If this high incidence of a dietary factor is confirmed then the arbitrary division of dietary and non-dietary migraine can be abandoned, and attention focussed on those factors which increase an individual's sensitivity to specific foods and fasting.

In only 26% of the attacks studied specific foods were not consumed and in only 5% of the attacks were dietary factors not isolated. This could mean that a few volunteers may have forgotten to mention all foods consumed; the occasional chocolate or alcoholic drink may have been missed or the onset of migraine may have occurred more than 24 hours after the ingestion of the specific foods.

There are other foods which contain tyramine and phenylethylamine which were excluded from this study, e.g. avocado contains 23 ug/g tyramine. There may also be other vaso-dilating amines to which certain individuals are sensitive e.g. onions or fatty foods. Alternatively some migraine attacks may have been due to some other etiology.

The present findings suggest that although the final precipitating factor in migraine attacks may be the ingestion of specific foods in those with a biochemical defect in amine metabolism, sensitizing factors may be present at an earlier stage (Table 6). Fasting may be a sensitizing factor, possibly by lengthening the time after the ingestion of the specific food from the

TABLE 6**Factors Influencing the Timing of a Migraine Attack**

1. *Biochemical factor.* Inborn error of amine metabolism with inability to oxidise tyramine and phenylethylamine. (Sandler, Youdim & Hanington¹).
2. *Sensitizing Factors*, including:
 - a. Changing levels of menstrual hormones e.g. menstruation, puerperium, hysterectomy, pilltaking.
 - b. Stress causing alteration in adrenal hormone levels.
 - c. Lack of sleep and alteration of the diurnal rhythm affecting the hypothalamus.
3. *Precipitating Factor.* Ingestion of specific foods and/or fasting.

more usual 3-12 hours¹ to 24-36 hours. The changing of levels of menstrual hormones¹⁵ would appear to be another sensitizing factor, but there may well be others, e.g. stress causing alteration in adrenal hormone levels, or lack of sleep or alterations of diurnal rhythm affecting the hypothalamus.

The different foods involved in migraine suffered by takers and non-takers of oral contraceptives could reflect changes of food habit or tastes, although there were no differences in respect of age or parity. The finding that the greatest differences occur during the first four days of menstruation suggests a hormonal influence increasing the sensitivity to specific foods.

The attack rates after cheese (48%) are significantly higher among takers among those with hysterectomy, fasting (91%) is even higher (Table 4). This suggests that exogenous (in takers) and endogenous (after hysterectomy) alterations in levels of menstrual hormones are also sensitizers.

Moffet et al⁵ consider the double blind controlled trial vital to elucidate dietary factors. It is worth emphasizing, however, that in controlled and double blind trials of the induction of attacks by tyramine^{2,3} phenylethylamine^{1,5} or fasting⁵⁻⁸ none had considered dietary factors in the 24 hours prior to an attack. Moreover, there was no mention of the phase of the menstrual cycle at which the attempt to induce an attack was made. These variables appear to be as important as the test substance used, be it active or placebo.

If it is accepted that all migraine attacks have a dietary factor then a new approach to the management of migraine is opened up. While the inborn biochemical defect cannot be remedied much can be done to prevent spontaneous attacks. Routinely, sufferers should be asked to complete attack forms for the 24 hours prior to an attack and an effort made to isolate the dietary factor in each individual. Sensible and individual dietary advice needs to be given to patients, but not of the kind provided to one volunteer who wrote, "I have been advised to avoid all milk products, eggs, fish, fruit, meat, cheese, sweet foods, tea and coffee, yet I still have severe attacks!" Actually her attacks were due to day-time fasting.

Critchley and Ferguson⁵ pointed out that "missing a meal in the course of a busy day or unwanted exertion on an empty stomach" could provoke migraine. In this study that observation was amply confirmed with attacks following day-time fasting of 5-8 hours incurred by shopping, swimming or boating expedition; when walking 12 miles; car breakdowns and flight delays; and no food taken from mid-day until 8 or 9 p.m. in anticipation of an evening dinner party. The management of migraine should include the recognition that attacks can be precipitated by fasting. It is reasonable to assume that in this study consideration of this one factor might have eliminated two thirds of the migraine attacks.

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Reprint requests to

Katharina Dalton, M.R.C.G.P.
 Clinical Assistant
 Department of Psychological Medicine
 University College Hospital
 86 Harley Street
 London W. 1., England