Dietary Therapy could be an Important Factor in the Prevention of Headache Symptoms in Migraine (without Aura): A Case Study

Anna Kokavec

University of New England, School of Health, Armidale, NSW, 2351, Australia

Abstract Background/Aims: Early work suggests that migraine may be triggered by a diet-induced reactive hypoglycemia. The aim here is to report on the efficacy of dietary therapy in the management and treatment of headache symptoms in a chronic migraine (without aura) patient. Methods: A 51-year-old man previously diagnosed with chronic migraine (without aura) presented for treatment. The patient, upon request by his treating medical practitioner, had maintained a comprehensive headache diary, which included details of headache frequency and severity, time of headache onset, and headache-related medication usage for a period of six months. Several interviews were conducted to determine medical and complimentary health treatment history prior to the introduction of dietary therapy. As part of the dietary regimen the patient was required to: (1) completely eliminate alcohol, monosodium glutamate, artificial sweeteners, sugar, and food containing sucrose natural or otherwise from the diet; (2) modify the consumption of fruit, dairy, and fat; (3) eat at least six small meals per day; (4) ensure the interval between meals did not exceed 3 hours; (5) consume complex carbohydrate and a small glass of water at every meal and upon waking in the middle of the night; and (6) avoid all medication deemed to be unsuitable for hypoglycemic patients. The patient was also required to maintain his headache diary at all times. The results showed that the implementation of the dietary regimen successfully reduced the need for headache-related pain medication by at least 70% when compared to pre-treatment levels. Alternatively, subsequent deviation from the prescribed dietary regimen immediately resulted in a 2.5 fold increase in headache related pain medication usage. Conclusions: Dietary therapy may be effective in reducing headache frequency and should be explored when deciding on the best treatment and management strategy for migraine patients.

Keywords Migraine, Hypoglycemia, Insulin, Sucrose, Dietary therapy, Sugar

1. Introduction

In the last decade the recommended treatment for migraine has become largely pharmacological. It is now common for migraine patients to be advised to undertake some prophylactic treatment involving the continuous use of drugs like fluoxetine, a selective-serotonin re-uptake inhibitor or propranolol, a known β -Blocker. Moreover, the discovery of selective 5-hydroxytryptophan agonists, or triptans, has provided many migraine sufferers relief from the severely debilitating headache symptoms, which often result in the individual being unable to carry out even the most basic of functions during an attack. [1]

However, while drugs are often prescribed for the prevention or management of migraine these drugs are not only very expensive but also unsuccessful in preventing a recurrence of symptoms in all migraine sufferers. Early suggestions that migraine may be triggered by food allergies [2] or a reactive hypoglycemia [3] possibly due to hyperinsulinism [4], which can be managed without medication by the patient, have received little attention in the headache literature. The aim of this paper is to promote awareness of the potential contribution of diet to the development of headache symptoms in a chronic migraine (without aura) sufferer.

2. Case Study

Background

Mr. H was 51 years 4 months when he first presented for treatment. Enquiries into his medical history revealed that apart from being diagnosed with migraine (without aura) at age 12, there was little evidence of any major illness during his lifetime. Blood cholesterol, fasting glucose and liver function tests were reportedly normal. However, blood pressure at his last medical assessment was slightly elevated.

^{*} Corresponding author:

akokavec@une.edu.au (Anna Kokavec)

Published online at http://journal.sapub.org/fph

Copyright © 2014 Scientific & Academic Publishing. All Rights Reserved

Strenuous physical exercise was engaged in on a daily basis and a typical morning exercise routine would consist of a 5Km run followed by a 1Km swim and then later that evening a 40Km bicycle ride. However, the patient's physical presentation seemed at odds with the level of exercise being reported. Mr. H had an obvious "pot belly" and the excess weight seemed to be concentrated in the central midriff area.

Enquires relating to the patient's psychological health determined that within the last five years Mr. H had been diagnosed with a clinical depression, suffered from anxiety, and had experienced a panic attack on at least two occasions. However, Mr. H had refused the offer of anti-depressant medication by his treating medical practitioner. The patient also reported a history of poor anger management. He claimed to experience feelings of restlessness on a daily basis, more noticeably in the early evening, which made it difficult for him to relax. Mr. H developed tinnitus at the age of 38, and other conditions such as vertigo and poor eyesight were also reported during the interview.

Migraine history

Mr. H claimed he had his first migraine (without aura) attack at the age of 12 and other single migraine attacks occurred at the ages of 17 and 20, respectively. From the age of 20 the number of migraine attacks seemed to steadily increase and Mr. H claimed he noted a three-fold increase in headache frequency and some increase in migraine severity in the 12 months prior to our interview, at age 50. Mr. H could not offer any reason(s) as to why his headaches had suddenly became more frequent and severe. He reports having no alcohol at all after the age of 25. Similarly, the patient stopped smoking cigarettes at about the same time and has remained alcohol and smoke free for the last 26 years. A summary of migraine frequency is provided in Table 1.

 Table 1. Migraine frequency since migraine onset at age 12

Age	Migraine frequency	
20-25	Once every 3 months	
25 - 30	Once every 2 months	
30 - 35	Once every month	
35 - 45	1-2 times per month	
45 - 48	Once a week	
48 - 50	1-2 times per week	
50 - 51	2-3 times per week	

Table 1. Kokavec

The pain during a migraine attack seemed to almost always be localized to the right side of his head. However, on at least one occasion the pain was focused on the left side and on this occasion the pain of headache was so severe Mr. H lapsed into a coma and required emergency hospitalization for 3.5 days. Assessment of disability using the Migraine Disability Assessment (MIDAS) test [5] produced a score of 24, which suggested Mr. H had a "severe disability". The patient said that in the last 3 months he had experienced head pain on at least 30 days, he often woke up with a headache that would eventually pass, and on average the pain of headache on a scale of 0-10 (0 = no pain, 10 = unbearable pain) was about a 3-4. However, Mr. H admitted that the pain had been more severe prior to being hospitalized and he was very fearful that it could happen again so he made sure he took his migraine medication before the pain had an opportunity to become too intense.

Prior to Mr. H presenting for treatment he had kept a headache diary that included data with respect to the type of medication used for pain associated with headache. A sample of the diary for the 6-months prior to Mr. H presenting for treatment is presented in Table 2.

Over the last 20 years Mr. H reports trying a range of migraine treatments but states that in his opinion none of these have been effective in preventing the development of headache. He claims he tried ear candles on two separate occasions. On the first occasion he used the ear candle for thirty minutes each side and the headache disappeared completely. However, repeated use of this method resulted in no further headache relief. Mr. H commenced oxygen treatment two years prior but said this method was unreliable when the migraine pain is severe. Similarly, acupuncture and physiotherapy seemed to provide little benefit in the prevention of headache symptoms. Indeed, Mr. H reports that physiotherapy served to increase the frequency of headache immediately following treatment. A naturopath had earlier suggested taking glucosamine, but a significant worsening of headache frequency was noted so this treatment was immediately discontinued. Mr. H regularly took magnesium and calcium supplements with no beneficial or adverse affects being noted.

Medications used in the past include ibuprofen, paracetamol, and aspirin. However, Mr. H claims that none of these drugs seemed to provide relief during a severe migraine attack. Approximately 12 months prior to interview Mr. H was prescribed sumatriptan succinate (ImigranTM) in tablet form (100mg) and nasal spray (20mg) and he felt that this medication seemed to be highly effective in relieving the pain of migraine on most (but not all) occasions. When Mr. H was asked to elaborate on this comment he stated that the nasal spray was only effective when the headache was mild and when the pain was severe (which it had been several times in the six months prior), both type of medications only seem to dull the pain with the headache often still being present several days later.

When asked about food allergies Mr. H claimed there was no food he particularly disliked apart from chicken, but he had noticed that consuming peanuts and bananas would often promote the development of headache symptoms. His doctor had also advised that eating foods containing monosodium glutamate could cause a migraine to develop [6] and Mr. H agreed that this was true in his particular case.

Date	Medication	Pain Rating	Patient Comments
6 th May	1 x Imigran TM tablet (100mg)		
7 th May	1 x Imigran TM tablet (100mg)		
17 th May	1 x Imigran [™] tablet (100mg)		
22 nd May	Imigran [™] nasal spray (20mg) 1 x Imigran [™] tablet (100mg)	9	Nasal spray – nil effect
23 rd May	2 x ibuprofen (400mg)		
·	2 x ibuprofen (400mg)		
24 th Mov	1 x Imigran [™] tablet (100mg)		Neuroe exective
24 May	metoclopramide (Maxalon TM) tablet		Nausea excessive
	(10mg)		
7 th Jun	Imigran TM nasal spray (20mg)	6	
8 th Jun	1 x Imigran TM tablet (100mg)		
9 th Jun	1 x Imigran ^{1M} tablet (100mg)		
14 th Jun	2 x ibuprofen (400mg)	5	
	1 x Imigran [™] tablet (100mg)	U	
17 th Jun	Imigran ^{1M} nasal spray (20mg)	5	
22 nd Jun	Imigran [™] nasal spray (20mg)	8	Nasal spray did not work
22 Juli	1 x Imigran TM tablet (100mg)	0	rusur sprug and not work.
25 th Jun	Imigran [™] nasal spray (20mg)	1-4	Lasted 3.5 days.
	1 x Imigran ^{IM} tablet (100mg)		Medication at times ineffective
3 rd Jul	1 x Imigran [™] tablet (100mg)	2-5	
9 th Jul	Imigran [™] nasal spray (20mg)	3-5	Medication at times ineffective.
	1 x Imigran TM tablet (100mg)		
18 th Jul	1 x Imigran TM tablet (100mg)	3-5	Migraine persisted all day.
	1 x Imigran TM tablet (100mg)		Re-medication required.
19 th Jul	1 x Imigran TM tablet (100mg)	9.5	Hospitalized for 2 days.
26 Jul	1 x Imigran TM tablet (100mg)	2	
30 Jul	1 x Imigran TM tablet (50mg)	2	
3 rd Aug	1 x Imigran ^{1M} tablet (50mg)	1	
5 th Aug	1 x Imigran TM tablet (100mg)	1	
6 th Aug	1 x Imigran TM tablet (50mg)	2	
10 th Aug	$1 \times \text{Imigran}^{\text{TM}} \text{tablet (50mg)}$	2-4	
coth i	1 x Imigran TM tablet (50mg)		
12 th Aug	1 x Imigran TM tablet (50mg)	2	
15 th Aug	1 x Imigran TM tablet (50mg)	2	
16 th Aug	1 x Imigran TM tablet (50mg)	2	
22 nd Aug	1 x Imigran ^{1M} tablet (50mg)	2	
23 rd Aug	1 x Imigran TM tablet (50mg)	2	Migraine persisted
o th	1 x Imigran TM tablet (50mg)		
24 th Aug	1 x Imigran TM tablet (50mg)	2	
31 st Aug	1 x Imigran TM tablet (50mg)	2	
1 st Sep	$1 \times \text{Imigran}^{\text{TM}} \text{tablet (50mg)}$	2	Migraine persisted
	1 x Imigran ^{1M} tablet (50mg)		
4 th Sep	1 x Imigran ¹⁴⁴ tablet (100mg)	4	
-	$2 \times 100 \text{ proten} (400 \text{ mg})$		
23 rd Sep	1 x Imigran TM tablet (50mg)	1-4	Persisted all day
octh c	1 x Imigran tablet (50mg)	2	
20 Sep	1 x Imigran tablet (100mg)	3	
su sep	1 x Imigran TM tablet (100mg)	3	
9 th Oct	1 x Imigran Tablet (50mg) 1 x Imigran TM tablet (50mg)	2-3	Persisted all day
10 th Oct	1 x Imigran TM tablet (50mg)	2.2	
10 Oct	I X IIIIgian tablet (30 ling) Imigran TM pasal spray (20 mg)	2-3 5_6	
11 001	migran nasai spray (2011g)	5-0	

 Table 2.
 Medication diary for the 6 months prior to dietary intervention

 $11^{\text{th}} \, \text{Oct}$ Kokavec – Table 2 Assessment of the patient's dietary behaviour revealed that meals in general were nutritionally balanced and serving portions were relatively small. However, there was quite a noticeable excessive consumption of caffeine in the form of tea containing honey and milk (between 10-12 cups per day) and regular daily snacks containing high levels of refined sugar (chocolate, ice-cream, biscuits, sweets, soft drink).

Rationale for Dietary intervention

A migraine attack can occur after an overnight fast and the majority of migraine attacks have been noted between 0600 h and 1200 h. [7] Further research is consistent with these claims with more than 48% of migraine attacks reportedly occurring between 0400 h and 0900 h. [8] Inspection of diary data for this particular patient also supports these claims with Mr. H reporting headache symptoms prior to 0600 h in over 60% of his diary entries.

Roberts [4] found that a large percentage of migraineurs also showed evidence of being hypoglycemic and an overnight fast could act as a trigger in vulnerable individuals. [9] Indeed, it has been known for some time that fasting can promote the development of migraine symptoms [10], with later studies confirming that fasting and/or the missing of one or more meals is sufficient to precipitate a migraine attack. [11-13]

Similar to that reported by Mr. H, individuals susceptible to migraine often report cravings for foods high in refined sugar [14] and ingestion of simple sugars in the past has been thought to trigger a migraine attack [3]. Dexter et al. [3] identified reactive hypoglycemia (i.e. serum glucose of less than 65 mg% or a drop of 75 mg% within 1 hour), in 76% of migraineurs assessed and subsequent dietary therapy aimed at eliminating refined sugar from the diet resulted in greater than 75% reduction in migraine frequency. Sucrose or common table sugar is the end product of the sugar refining process, a fairly involved process that effectively removes most of the natural nutrients normally found in sugar syrup leaving only pure carbohydrate in crystallized form. Therefore, eliminating sucrose from the diet in most cases should pose few nutritional problems as refined sugar largely consists of 'empty' calories.

Research has shown that animals fed a sucrose diet show significantly higher fasting serum insulin, glucose, triglyceride levels and demonstrated signs of insulin insensitivity. [15, 16] Furthermore, insulin levels during an OGTT are significantly greater in rats fed sucrose and relatively low sucrose levels in a high fat diet can produce significantly higher insulin levels after a glucose load. [17] Therefore, if migraine is caused by a reactive hypoglycemia due to diet-induced hyperinsulinism as suggested [3], and a combination of sucrose and fat can elevate insulin [17], then avoiding foods containing sucrose and fat, which provide little for the nutritional needs of the body, may be beneficial in the prevention of migraine symptoms. The dietary regimen recommended as a migraine preventative for Mr. H has to a large extent been reported by others [18] but the diet

also takes into account the additional research findings provided above.

3. Dietary Regimen

Requirement number 1: The migraine patient is asked to swap a diet high in refined sugar for one high in protein, natural sugars and carbohydrates (e.g. fruit, potatoes, rice, and wheat flour). The term 'refined sugar' applies to all food products containing added sucrose, glucose, fructose, and corn syrup. Additionally, foods high in sugar (e.g. dried or stewed fruit, grapes) or those containing natural sucrose (e.g. ripe bananas and peanuts) were also to be avoided. The use of honey as a sweetener was not encouraged due to this product also containing 'royal jelly', which contains sucrose.

Requirement number 2: At least six small meals were to be eaten throughout the day with the interval between feeding never exceeding three hours. It was also suggested that before retiring a snack high in complex carbohydrate (e.g. whole meal crackers) should be placed by the bed in the event that the patient woke up suddenly in the middle of the night. Furthermore, given the recent evidence that migraine may be due to dehydration [19] a glass of water was to be consumed prior to each meal. The elimination of refined sugar in the diet was counterbalanced by an increase in natural carbohydrate. Foods such as pasta, potatoes, rice and wholegrain breads and cereals were recommended for consumption at every meal. High protein foods such as meat combined with a range of vegetables, in particular potato, was recommended for the main meal. The consumption of fruit due to the high sugar content was restricted to only one small serving per day and only after a meal. Eating fruit such as green apples and most berries (including strawberries), was encouraged. Alternatively, grapes and bananas were not permitted.

Requirement number 3: Decreased dietary fat is associated with a decrease in headache frequency, intensity, duration, and medication intake [20], and "added" fat similar to that used in sandwiches, as topping on crackers, or melted on cooked vegetables was not permitted. However, the use of oils such as virgin olive oil when cooking food and flaxseed oil when preparing salads was allowed.

Requirement number 4: Alcohol may influence energy metabolism [21] and possibly promote the development of a pseudo-diabetic condition [22, 23]. Therefore, the consumption of all alcoholic beverages, regardless of the alcohol content, was not permitted.

Requirement number 5: Given the suggestion that a link may exist between migraine and hypoglycemia [4] the patient was advised to consult his doctor or pharmacist before taking any prescription or over the counter medication to determine whether the drug was suitable for hypoglycemic patients. In particular, the use of anti-inflammatory medication, aspirin, antibiotics, and anti-depressants (e.g. selective serotonin reuptake inhibitors), was to be replaced with something more suitable if at all possible.

Date	Medication	Pain rating	Comments
15 th Oct	1 x Imigran TM tablet (50mg)	2-3	
9 th Nov	1 x Imigran TM tablet (100mg)	2-3	Consumed MSG
13 th Nov	1 x Imigran TM tablet (100mg)	4-5	Excessive exercise, forgot to eat
17 th Dec	1 x Imigran TM tablet (100mg)	4-5	Consumed sucrose
17 th Jan	1 x Imigran TM tablet (100mg)	2-3	Consumed sucrose
31 Jan	1 x Imigran TM tablet (100mg)	4-5	Medication ineffective
51 Jali	1 x Imigran TM tablet (100mg)		Suffering influenza
20 th Feb	1 x Imigran TM tablet (100mg)	1-3	Consumed sucrose
6 th Mar	1 x Imigran TM tablet (100mg)	1-2	Consumed sucrose
4 th Apr	1 x Imigran TM tablet (100mg)	1-2	Forgot to eat and Sleep disrupted

Table 3. Medication diary for a 6-month period after introduction of dietary regimen aimed at optimizing glucose control

Kokavec – Table 3

Requirement number 6: Monosodium glutamate, which is also called 'Additive 621', is found in large quantities in hydrolyzed vegetable protein. Foods containing monosodium glutamate and aspartame are known migraine triggers [6], possibly due to the adverse effect of monosodium glutamate on the release of hormones such as serotonin [24, 25], a decrease in which has long been associated with the development of migraine symptoms. The patient was advised to check the labeling of prepared food and in particular frozen foods, canned and dry soups, potato chips and other prepared snack foods, diet foods and weight loss powders, cured meats, sauces, salad dressings, and Asian food.

Effect of Dietary Therapy on Migraine Frequency

Mr. H reportedly adhered to the dietary regimen to the best of his ability for a period of six months. After 3 months the MIDAS was re-administered and Mr. H achieved a score of 4, which was much lower and consistent with a "little or no disability" rating. The next 3 months resulted in Mr. H achieving a score of 7 on the MIDAS, which was slightly higher and consistent with a "mild disability". However, he acknowledged that he had mistakenly consumed sucrose on at least three occasions and deviated slightly on at least one other occasion. Diary data showing medication history while attempting the dietary regimen, including pain rating is provided in Table 3.

Mr. H developed a headache nine times while attempting the dietary regimen over a six month period. Each time a headache developed Mr. H claimed he could link it back to either some food that he ate and later found contained sucrose, monosodium glutamate, artificial sweetener; not eating within the three hour time period and engaging in strenuous exercise; not eating within the three hour time period and enduring emotional stress; or taking anti-inflammatory medication for a sport injury.

During the six-month period that Mr. H eliminated refined sugar from his diet he was surprised to find that despite eating more food across the 24 h day he had steadily lost a total of 35 pounds in weight. All signs of his "pot belly" and weight around his central area disappeared and his blood pressure was assessed by his medical doctor to be normal.

However, the dietary regimen, while initially being manageable, proved to be extremely difficult for the patient to adhere to over time. Mr. H claimed he constantly had sugar cravings and was finding it increasingly difficult to maintain the willpower required to completely eliminate refined sugar from his diet with the result being a negative effect on mood. Following the dietary regimen was also hard when eating out or socializing with others.

Within a period of six-months, despite being advised that a deviation from the dietary regimen would likely increase headache frequency, Mr. H chose to re-introduce small amounts of refined sugar into his diet. However, foods such as bananas, peanuts, butter and margarine, and those containing monosodium glutamate or artificial sweetener were still avoided. Furthermore, Mr. H continued to maintain his six-meal schedule during the day. Unfortunately, re-introducing refined sugar into the diet resulted in Mr. H developing a headache severe enough to require medication on 24 occasions during the 6 months period.

Statistical analysis utilizing a Chi-squared goodness of fit test showed a significant difference in medication usage when refined sugar was included, omitted, and re-introduced into the diet (χ^2 (DF = 2) = 18.29, P < .05). Inspection of the raw data revealed that the number of times Mr. H needed to use medication for pain associated with headache was much lower when refined sugar was voluntarily omitted from his diet. Additionally, self-report data confirmed that even a reduced amount of refined sugar is sufficient to promote a 2.5 fold increase in pain medication usage for headache in this patient.

4. Discussion

The present case study is successful in drawing attention to the difficulties and frustrations experienced by migraine sufferers when attempting to find an appropriate treatment for their condition. Mr. H, while trying a number of headache treatments, claims that only triptan medication (e.g. ImigranTM) by alleviating headache symptoms (most of the

time), has been the most effective in improving his quality of life. However, even this medication is not completely effective in treating the pain of migraine or preventing a migraine attack from developing.

In the past it was suggested that the elimination of refined sugar could promote a reduction in migraine frequency. [3] Similarly, eliminating refined sugar from the diet and altering dietary behaviour promoted a significant reduction in the need for headache-related pain medication. Furthermore, it was possible to retrospectively link any headache episodes to specific aspects of non-adherence to the dietary regimen.

In the past it has been suggested that migraine can be triggered by a reactive hypoglycemia [3], caused by hyperinsulinism. [4] There is usually evidence of hypercortisolism in hyperinsulinemic patients [26], and similarly cortisol is elevated in migraine sufferers. [27] Furthermore, Mr. H reported a history of tinnitus, poor eyesight, and vertigo all of which have been known to occur with hyperinsulinemia. [28] Moreover, a significant association between polymorphisms in the insulin receptor gene and migraine pathogenesis has been confirmed [29], which further suggests that a link may exist between migraine and pancreatic function.

The level of serum insulin can be greatly affected by the type of carbohydrate in the diet [30] and comparisons with starch show that the consumption of sucrose can result in a 20% increase in insulin level. [31] Furthermore, in carbohydrate-sensitive individuals a sucrose diet can promote an even higher level of insulin. [32, 33] Carbohydrate-sensitive individuals demonstrate increased insulin binding because of a failure of plasma insulin to down regulate the number of receptors [34], and a spontaneous reactive hypoglycemia can occur due to the enhanced insulin-mediated glucose uptake. [35]

However, simply eliminating refined sugar from the diet may on its own not be an effective long-term solution for the prevention of migraine. Despite the patient experiencing a significant reduction in migraine frequency while following the dietary regimen, this it appears was not sufficient to prevent non-adherence to the dietary regimen. Over time, sticking to the dietary regimen proved to be extremely difficult and there was a noticeable negative affect on mood when refined sugar was eliminated from the diet. The patient has a history of clinical depression, anxiety, and panic attack and co-morbidity with mood disturbance is a common finding in the migraine population. [36, 37]

Including a small amount of refined sugar in the diet post-treatment resulted in a 2.5 fold increase in headache-related medication usage. Given that Mr. H reported keeping other factors constant this could suggest that consuming sucrose and not other factors such as eating behaviour, presence of hypoglycemia unrelated to refined sugar, or monosodium glutamate was the trigger for the development of headache symptoms in this patient.

Individuals susceptible to migraine often report cravings for foods high in refined sugar [38], and whether this is because sugar has analgesic properties [39] is unknown. It is well accepted that a connection exists between not only the serotonergic system and mood disturbance but also between the serotonergic system and migraine itself. The level of transmitter that serotonergic neurons release may be altered with food intake and carbohydrates with a higher glycemic index may have a greater serotonergic effect than carbohydrates with a low glycemic index. [40] Supplementation with sucrose can produce a higher glucose and insulin peak [41] and increased hippocampal serotonin level. [42] In animals, serotonin produces hypoglycemia via activation of 5-HT₁ and 5-HT₂ receptors [40], which by increasing serum insulin levels significantly inhibits glucose-induced hyperglycemia and increases glucosestimulated insulin release. [43] Of interest is that while sucrose can significantly increase insulin level, the insulin level can also affect the uptake of tryptophan by the brain and influence the synthesis of cerebral serotonin. [44] Thus, when these findings are considered together it is tempting to conclude that the preference for refined sugar often shown by migraine sufferers could to some extent is linked to impairment in serotonin synthesis and/or release.

Increased incidence of severe hypoglycemia can result in hypoglycemic unawareness [45], and selective serotonin reuptake inhibitors have been shown to cause decreased awareness of hypoglycemia [46], possibly due to these drugs (e.g. fluoxetine), promoting hypophagia. [47] Food intake is inhibited by serotonin [48] and there is clear evidence for a selective and dose-dependent effect of hypothalamic serotonergic stimulation on carbohydrate intake. [49] Drugs such as fluoxetine prevent the reuptake of serotonin and the increased level of serotonin can subsequently affect the neuropeptide Y system and promote a satiety signal in hypothalamic regions in the brain. [50]

5. Conclusions

A significant reduction in migraine frequency was shown to occur in a chronic migraine (without aura) patient by introducing a dietary regimen devoid of refined sugar. The findings here are consistent with earlier reports claiming that removing refined sugar from the diet can result in a 75% reduction in migraine symptoms [3]. Thus, careful monitoring of a patient's dietary behaviour may be important when prescribing ongoing medical treatment for the prevention and management of migraine symptoms.

REFERENCES

- [1] Goadsby PJ. Post-triptan era for the treatment of acute migraine. Curr Pain Headache Rep 2004;8:393-398.
- [2] Monro J, Carini C, Brostoff J. Migraine is a food-allergic disease. Lancet 1984;2(8405):719-721.
- [3] Dexter JD, Roberts J, Byer JA. The five hour glucose

tolerance test and effect of low sucrose diet in migraine. Headache 1978;18:91-94.

- [4] Roberts HJ. Migraine and related vascular headaches due to diabetogenic hyperinsulinism. Observations on pathogenesis and rational treatment in 421 patients. Headache 1967;7: 41-62.
- [5] Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. Neurology 2001;56(6 Suppl 1):S20-28.
- [6] Scopp AL. MSG and hydrolyzed vegetable protein induced headache: Review and case studies. Headache 1991;31: 107-110.
- [7] Solomon GD. Circadian rhythms and migraine. Cleve Clin J Med 1992;9:326-329.
- [8] Fox AW, Davis RL. Migraine chronobiology. Headache 1998;38:436-441.
- [9] Peroutka SJ. Serum glucose regulation and headache. Headache 2002;42:303-308.
- [10] Critchley M. Migraine. Lancet 1933;1:123-126.
- [11] Blau JN, Cumings JN. Method of precipitating and preventing some migraine attacks. BMJ 1966;2:1242-1243.
- [12] Blau JN, Pyke DA. Effect of diabetes on migraine. Lancet 1970;2:241-243.
- [13] Marsters JB, Mortimer MJ, Hay KM. Glucose and diet in the fasting migraineur. Headache 1986;26:243-247.
- [14] Jacome DE. Hypoglycemia rebound migraine. Headache 2001;41:895-898.
- [15] Hallfrisch J, Lazar F, Jorgensen C, Reiser S. Insulin and glucose responses in rats fed sucrose or starch. Am J Clin Nutr 1979;32:787-793.
- [16] Reiser S, Hallfrisch J. Insulin sensitivity and adipose tissue weight of rats fed starch or sucrose diets ad libitum or in meals. J Nutr 1977;107:147-155.
- [17] Hallfrisch J, Cohen L, Reiser S. Effects of feeding rats sucrose in a high fat diet. J Nutr 1981;111:531-536.
- [18] Low R. Victory over migraine. New York, Henry Holt and Company, 1987.
- [19] Blau JN. Water deprivation: A new migraine precipitant. Headache 2005;45:757-759.
- [20] Bic Z, Blix GG, Hopp HP, Leslie FM, Schell MJ. The influence of a low-fat diet on incidence and severity of migraine headaches. J Womens Health Gend Based Med 1999;8:623-630.
- [21] Becquet D, Fauldon M, Hery F. In vivo evidence for an inhibitory glutamatergic control of serotonin release in the rat caudate nucleus: involvement of GABA neurons. Brain Res 1990;519:82-88.
- [22] Brewerton TD, Murphy DL, Mueller EA, Jimerson DC. Induction of migraine-like headaches by the serotonin agonist m-chlorophenylpiperazine. Clin Pharmacol Ther 1988;43: 605-609.
- [23] Kokavec A, Crowe SF. Alcohol consumption in the absence

of adequate nutrition may lead to activation of the glyoxylate cycle in man. Med Hyp 2002;58:411-415.

- [24] Kokavec A, Crowe SF. Effect on plasma insulin and plasma glucose of consuming white wine alone after a meal. Alcohol Clin Exp Res 2003;27:1718-1723.
- [25] Kokavec A, Crowe SF. Effect of moderate white wine consumption on serum IgA and plasma insulin under fasting conditions. Ann Nutr Metab 2006;50:407-412.
- [26] Fruehwald-Schultes B, Kern W, Born J, Fehm HL, Peters A. Hyperinsulinemia causes activation of the hypothalamus-pituitary-adrenal axis in humans. Int J Obesity 2001;25:S38-S40.
- [27] Ziegler DK, Hassanein RS, Kodanaz A, Meek JC. Circadian rhythms of plasma cortisol in migraine. J Neurol Neurosurg Psychiatry 1979;42:741-748.
- [28] Kazmierczak H, Doroszewska G. Metabolic disorders in vertigo, tinnitus, and hearing loss. Int Tinnitus J 2001;7:54-58.
- [29] McCarthy LC, Hosford DA, Riley JH, Bird MI, White NJ, Hewett DR et al. Single-nucleotide polymorphism alleles in the insulin receptor gene are associated with typical migraine. Genomics 2001;78:135-149.
- [30] Moser PB, Behall KM, Kelsay JL, Prather ES. Carbohydrate tolerance and serum lipid responses to type of dietary carbohydrate and oral contraceptive use in young women. J Am Coll Nutr 1986;5:45-53.
- [31] Crapo PA, Reaven G, Olefsky J. Plasma glucose and insulin responses to orally administered simple and complex carbohydrates. Diabetes 1976;25:741-747.
- [32] Reiser S, Bohn E, Hallfrisch J, Michaelis OE 4th, Keeney M, Prather ES. Serum insulin and glucose in hyperinsulinemic subjects fed three different levels of sucrose. Am J Clin Nutr 1981;34:2348-2358.
- [33] Reiser S, Hallfrisch J, Michaelis OE 4th, Lazar FL, Martin RE, Prather ES. Isocaloric exchange of dietary starch and sucrose in humans. Effects on levels of fasting blood lipids. Am J Clin Nutr 1979;32:1659-1669.
- [34] Bhathena SJ, Reiser S, Smith JC, Revett K, Kennedy BW, Powell A, Voyles NR, Recant L. Increased insulin receptors in carbohydrate-sensitive subjects: mechanism for hyperlipaemia in these subjects? Eur J Clin Nutr 1988;42:465-472.
- [35] Kergoat M, Bailbe D, Portha B. Effect of high sucrose diet on insulin secretion and insulin action: a study in the normal rat. Diabetologia 1987;30:252-258.
- [36] Radat F, Irachabal S, Swendsen J, Henry P. Analgesic abuse and psychiatric comorbidity in headache patients. Encephale 2002;28:466-471.
- [37] Neuhauser H, Lempert T. Vertigo and dizziness related to migraine: a diagnostic challenge. Cephalalgia 2004;24:83-91.
- [38] Jacome DE. Hypoglycemia rebound migraine. Headache. 2001;41:895-898.
- [39] Blass EM, Hoffmeyer LB. Sucrose as an analgesic for new-born infants. Pediatrics 1991;87:215-218.
- [40] Lyons PM, Truswell AS. Serotonin precursor influenced by

type of carbohydrate meal in healthy adults. Am J Clin Nutr 1988;47:433-439.

- [41] Yamada J, Sugimoto Y, Kimura I, Takeuchi N, Horisaka K. Serotonin-induced hypoglycemia and increased serum insulin levels in mice. Life Sci 1989;45:1931-1936.
- [42] Smolders I, Loo JV, Sarre S, Ebinger G, Michotte Y. Effects of dietary sucrose on hippocampal serotonin release: microdialysis study in the freely-moving rat. Br J Nutr 2001;86:151-155.
- [43] Sugimoto Y, Kimura I, Yamada J, Watanabe Y, Takeuchi N, Horisaka K. Effects of serotonin on blood glucose and insulin levels of glucose and streptozotocin-treated mice. Jpn J Pharmacol 1990;54:93-96.
- [44] Baumann P, Gaillard J. Insulin coma therapy: decrease of plasma tryptophan in man. J Neural Transm 1976;39: 309-313.
- [45] Hepburn DA, Patrick AW, Eadington DW, Ewing DJ, Frier BM. Unawareness of hypoglycaemia in insulin-treated diabetic patients: prevalence and relationship to autonomic neuropathy. Diabet Med 1990;7:711-717.

- [46] Sawka AM, Burgart V, Zimmerman D. Loss of awareness of hypoglycemia temporally associated with selective serotonin reuptake inhibitors. Diabetes Care 2001;24:1845-1846.
- [47] Dryden S, Frankish HM, Wang Q, Pickavance L, Williams G. The serotonergic agent fluoxetine reduces neuropeptide Y level and neuropeptide Y secretion in the hypothalamus of lean and obese rats. Neuroscience 1996;72:557-566.
- [48] Routh VH, Stern JS, Horwitz BA. Adrenalectomy increases serotonin turnover in brains of obese Zucker rats. Physiol Behav 1995;58:491-499.
- [49] Leibowitz SF, Alexander JT, Cheung WK, Weiss GF. Effects of serotonin and the serotonin blocker metergoline on patterns and macronutrient selection. Pharmacol Biochem Behav 1993;45:185-194.
- [50] Dryden S, Wang Q, Frankish HM, Williams G. Differential effects of the 5-HT 1B/2C receptor agonist mCPP the 5-HT1A agonist flesinoxan on hypothalamic neuropeptide Y in the rat: evidence that NPY may mediate serotonin's effects on food intake. Peptides 1996;17:943-949.