Prophylactic treatment of migraine with gamma-linolenic and alpha-linolenic acids

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Cephalalgia


Polyunsaturated fatty acids (PUFA) were administered to 168 patients over a period of 6 months in an open-label uncontrolled study. In 129 patients available for study 86% experienced reduction in severity, frequency and duration of migraine attacks, 22% became free of migraine and more than 90% had reduced nausea and vomiting. Self-medication changed to simple analgesics in the majority except in 14% of patients without improvement. □ Fatty acids, migraine, prophylaxis

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Current prophylaxis of migraine using drugs is unsatisfactory owing to side effects and limited effectiveness. Although the cause of migraine remains to be determined, a sterile inflammatory process and the mediators serotonin (5HT) and prostaglandin E2 (PGE2) appear to have a role in the migraine attacks (1–3). Prostaglandins, given intravenously, can cause hemicranial headache with accompanying symptoms of nausea and vomiting similar to reserpine-induced headache (3). Mild to moderate migraine headaches can be abolished by non-steroidal anti-inflammatory drugs (NSAIDs) (5). We postulated that long-term improvement in migraine might be possible by dietary modulation of the precursors of prostaglandins E2 (PGE2). This can be achieved by reducing dietary arachidonic acid (AA) (6), by decreasing production of AA by giving alpha-linolenic acid (ALA) (6,7), or by increasing prostaglandins of group 1 by substitution of gamma-linolenic acid (GLA) to provide a balance between PGE2 and PGE1 (8) (see Fig. 1).

We report here an open prospective study in which these dietary manipulations, combined with other non-pharmacologic measures, were associated with benefit to migraine sufferers.

Methods

In a prospective and open clinical study, we consecutively evaluated 168 migraine patients with and without aura diagnosed by the IHS criteria (9) using a modified questionnaire of the German migraine study (5). Over a period of 6 months they participated in a prophylactic program of care as follows.

Regular intake of GLA and ALA including coenzymes: vitamin B6, niacin, and antioxidants: vitamin C, D-alpha-tocopherol, beta-carotin (6 capsules daily = 1800 mg GLA and ALA). They were instructed to avoid high doses of arachidonic acid and their diet was adjusted to a dietary based carbohydrate and protein ratio of 5 : 1 (10). Self-medication was permitted only with acetylsalicylic (AS) or metamizol 20 min after taking metoclopramide, in cases of nausea and vomiting. Patients were instructed concerning incorrect techniques of self-medication, i.e. avoiding ergotamine, analgesic-ergotamine combinations, analgesic combinations and sumatriptan as drug of first choice.

Stress reduction and progressive muscle relaxation techniques (PR) were also recommended. Patients kept a pain diary. The 100-point-1-scale was used for pain assessment. Data were recorded at 2-month intervals.
Results

Baseline data

A total of 168 patients took part in this investigation, 129 of whom could be evaluated, forming the total group. Thirty-nine patients were rejected from this analysis because of incomplete record keeping. The total group was further divided into three subgroups, according to the patients' experience of success and failure, i.e. group 1 (n=82, improved migraine situation), group 2 (n=18, failure), and group 3 (n=29, free of migraine attacks).

At the beginning of the observation period, no patients expressed satisfaction with previous treatment. After 6 months, 111 (86%) considered their migraine problem had improved. Eighteen patients (14%) failed management while 29 (22%) were free of migraine.

After 6 months, the severity of attack was reduced from an average pain-rate of 88 points (min: 50, max: 100, SD=13) to 25 after (min: 1, max: 100, SD=25) in the total group, from 88 points pretreatment to 24 post-treatment in group 1, from 88 points pretreatment to 1 point post-treatment in group 3, and from 84 points pretreatment (min: 50, max: 100, SD=15) to 74 post-treatment in group 2 (min: 40, max: 100, SD=18). The differences were statistically significant in the total group, in groups 1 and 3, but not in group 2 (see Fig. 2).

The attack frequency per year was significantly reduced in 111 of 129 patients (86%) (see Fig. 3). Group 1 was similar to the total group. Group 3 showed a reduction from 36 attacks/year before treatment to no attacks. The duration of attacks is shown in Fig. 4. There was a significant reduction in the total group and in groups 1 and 3. Baseline data did not differ between groups.

There was a significant reduction in nausea and vomiting in every group, except in group 2 nausea (*p<0.01, **p<0.1) (Figure 5). Nausea and vomiting were more effectively treated by self-medication after prophylaxis (Fig. 5), not only in the successful groups, but also in group 2 (n=18), in which nausea was reduced in 11 from 16 patients and vomiting in 6 from 11 patients.

Self-medication

Six months after treatment, patients were also able to change their use of ergotamine, ergotamine combination drugs and sumatriptan to NSAIDs, which had previously not been possible (Fig. 6). Medication practice was unchanged in group 2. Only 1 patient (5.5%) took NSAID alone, and 1 (5.5%) metoclopramide alone, 6 (33%) sumatriptan alone (11%), 2 ergotamine alone, and 8 (44%) ergotamine combination drugs alone. Two of those patients (11%) additionally took combination analgesics, including spasmyloytic agents, and 8 (44%) added NSAID.
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Discussion

The prospective and open design of our study is a problem, but it was considered unethical to administer placebo for 6 months. A shorter length of time would have missed a successful outcome in a proportion of our patients. Also, a high number of patients could be studied over the extended period of 6 months.

Although our results may be explained by a placebo effect or a "regression to the mean", onset of improvement was 3.2 months on average, with a maximum of 6 and a minimum of 1 month. Such a late placebo effect is unlikely. The regular attendance at our clinic because of frequent treatment failure speaks also against "regression to the mean".

Another reason for the success of prophylaxis by change in nutrition habits might be proper instruction of their use as well as the addition of procedures such as relaxation and biofeedback. In group 3 for example, 96% of the patients used drugs which we expressively encouraged them not to take. None of this group was satisfied before or after treatment. The reverse was true in group 2. There was a complete change in self-medication and patients learned to take antiemetics 20 min before analgesics to permit better resorption. Group 4, which was free of migraine, had only mild headache and seldom used analgesics. This group, however, may have been less severely affected at onset because they used only NSAIDs to treat migraine and thus may have been more sensitive to prophylaxis. Theoretically, then, changing self-medication alone might explain the improved outcome. At this time, however there are no rigorous studies which suggest that removing migraine-inducing substances such as ergotamines promotes successful prophylaxis. Therefore, we believe our results may be best explained by our dietary regime and supplements.

The question why change from allopathic medicine to a nutrition combination, consisting of n-6 and n-3 fatty acids with their coenzymes and antioxidants, works can only be answered hypothetically. Iversen et al. showed that LTB4 is reduced by evening primrose-oil, which contains 15–20% pure GLA (8). Furthermore, the quantity of PGE2 in relation to PGE1 can be raised in favor of PGE1, which promotes an anti-inflammatory effect. The disadvantage of a short elimination half-time is compensated by regularly administering 20 mg of pure GLA to ensure a high take-up of PGE1. At the same time, this can be achieved by reducing dietary arachidonic acid, which in turn reduces PGE2. Sterile neurogenic inflammation may explain the head pain of migraine (2) and may be mediated in part by prostaglandins, PGE2 and leukotriene B4. Prostaglandin E2 can be reduced by cyclooxygenase inhibitors, but it is difficult to influence leukotriene synthesis, once begun. Thus, a prophylactic approach to prevent leukotriene synthesis seems appropriate.

There may also be an influence of this therapy on thromboxane A2 synthesis. Stabilizing platelet membranes reduces aggregation, which releases serotonin. Although platelet aggregation possibly plays only a minor role in neurogenic inflammation, serotonin release can cause a migraine-like headache (3).

References

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