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Research Paper Review

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Targeted Alteration of Dietary Fatty Acids for the Treatment of Chronic Headache

Research Review By Dr. Colin O'Brien©

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Study Title:

Targeted alteration of dietary n-3 & n-6 fatty acids for the treatment of chronic headaches: a randomized trial

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Background Information:

Chronic daily headaches (CDH) are experienced by 3-4% of the adult and elderly population worldwide and are estimated to lead to loss of work and medical expenses adding up to billions of dollars per year (1). Conventional treatments for CDH rely mostly on medications that can be costly and may come with significant side effect profiles, while

rarely providing complete and lasting symptom resolution. While many alternative or complementary therapies exist, it has been suggested and anecdotally documented that dietary interventions can play a role in altering the course of CDH.

Omega-3 polyunsaturated fatty acids (n-3) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are well-known for their anti-inflammatory action, partly through their ability to generate anti-nociceptive mediators within the body (2). (Simopoulos) As such, n-3 fatty acids are widely supplemented and promoted as a part of a healthy diet. Omega-6 fatty acids (n-6) such as arachidonic acid (AA) and linoleic acid (LA), on the other hand, almost exclusively generate mediators with pro-nociceptive or pro-inflammatory properties. An overarching theory is that the standard American diet (or, SAD – appropriate, no?) consumes an excess amount of n-6 fatty acids relative to n-3's, thereby tipping the scales in favor of a pro-nociceptive dominant pathway. Many sources suggest that our ancestors consumed a ratio of n-6:n-3 around 1:1, whereas the current Western diet is closer to 15:1 (2). Moreover, various studies have found that when this ratio of fatty acid intake is closer to 1 (generally below 5), positive health effects and lower prevalence of chronic disease are present (2).

The aim of this review is to explore the possible association between omega fatty acid consumption in the diet and frequency and severity of chronic headaches in the adult population. Plausible mechanisms for this association will also be discussed.

Pertinent Results:

Sixty-seven subjects were randomized to either the H3-L6 intervention or the L6 intervention, although only 56 completed the 12-week study with 28 subjects per intervention group. Demographic characteristics were comparable between groups. Both groups were able to achieve the necessary dietary intakes of either n-3 and n-6 fatty acids, or simply a reduction in n-6 fatty acids for the L-6 intervention.

In erythrocyte measurements of Arachidonic Acid (AA), only the H3-L6 group was able to significantly reduce this value, whereas both the H3-L6 and L-6 groups showed significant reduction in Linoleic Acid (LA) levels. Only the H3-L6 group demonstrated a significant increase in EPA and DHA levels, with no changes found in the L6 group, as one would expect.

Anti-nociceptive and pro-nociceptive derivatives were measured in both groups. Compared to baseline, both intervention groups significantly increased n-3 EPA and DHA derived mediators and significantly reduced n-6 AA and LA derived mediators. However, the H3-L6 group produced statistically significantly more pronounced increases in n-3 EPA and DHA derived mediators compared to the L6 intervention.

In regards to clinical headache-related outcomes, both groups showed statistically significant improvements compared to baseline in all 4 categories (HIT-6 score, headache days, headache hours and severe headache days). In addition, the H3-L6 intervention group produced significantly greater improvements over the L-6 group in each category. Specifically, the H3-L6 group had -8.8 headache days per month vs -4.0 in the L6 group. Headache hours per day were reduced by 4.6 and 1.2, respectively, and the probability of

experiencing a severe headache day was reduced by 28% and 8%, respectively.

The proportion of subjects in the H3-L6 group at 12 weeks that used pain-related acute or adjunctive medication was also reduced by 37% and 43%, respectively. A sub-analysis of those individuals that used vasoactive abortive medications for migraines found a 33% reduction in use for those in the H3-L6 group, but no change in the L6 group.

Clinical Application & Conclusions:

In this relatively small yet interesting study, reductions in n-6 fatty acid consumption with simultaneous increases in n-3 fatty acid intake were associated with many positive impacts on CDH and health markers. These included statistically significant reductions in headache days, headache hours, severe headache days, HIT-6 score, pain-related medication use and favorable improvements in n-3 anti-nociceptive mediators and n-6 pro-nociceptive mediators. Although improvements were found for both the H3-L6 and the L6 groups, the most significant benefits were shown with the H3-L6 combination intervention on various parameters, above those of the L6 group. This study suggests that a H3-L6 dietary intervention is clinically effective for those suffering with CDH.

Although this interventional trial contains many limitations for application into practice, at this point it would be prudent to consider the following:

1. Previous trials examining only an increase in n-3 supplementation for the prevention of migraines found no statistically significant improvement (3). Perhaps no beneficial effect was seen because this intervention failed to reduce overall intake of n-6 fatty acids. A plausible explanation for the discrepancy found between these two trials would be that n-3 supplementation alone without reduction of n-6 intake is not sufficient to adequately alter pro- and anti-nociceptive mediators for clinical benefit. This is supported by the fact that even the L6 group showed an improvement in levels of anti-nociceptive n-3 EPA and DHA mediators, without directly supplementing or augmenting their n-3 intake.
2. Fish, flaxseed and walnuts are significant sources of n-3 fatty acids that can be increased in regular dietary intake. Highly processed foods using vegetable oils (such as sunflower, safflower and corn) are relatively high in n-6 fatty acids and void of n-3. Foods such as potato chips, corn chips, french fries and pasta are typically made with these oils and should be reduced if trying to lower overall intake of n-6. As many studies have demonstrated, the relative intake of n3:n6 is extremely important because of competition between the polyunsaturated fats in physiological pathways (2).
3. CDH is a multifactorial concern that cannot necessarily be explained by psychological, physiological or physical imbalances alone. Dietary factors must, at minimum, be considered as playing a role in aggravating or causing CDH in those patients without a clear causative pathogenesis.
4. In spite of the shortcomings mentioned in the forthcoming ‘Strengths and Weaknesses’ section, this trial does provide a unique insight into possible dietary management of those with CDH. *Altering n-3 and n-6 intake through dietary means is a very safe and cost effective method for possibly reducing frequency and severity of CDH in many patients with this debilitating condition.* This is especially useful in

those individuals with poor dietary habits at baseline and those patients that experience significant side effects or poor response to medications.

Study Methods:

Adults experiencing headaches greater than 4 hours per day for more than 15 days per month for at least 3 months were enrolled by a study neurologist. Participants were also under the care of a physician for headache management for at least 2 years. Viable participants also completed the MIDAS migraine disability assessment, ultimately classifying individuals with CHD into 1 of 3 classes: 1) chronic migraine; 2) CDH with migraine features; or 3) CDH without migraine features. Participants were additionally required to report demographics and those suffering from secondary headaches due to known causes such as trauma or vascular disorders were excluded from the trial.

For the 4 weeks before beginning any interventions, participants continued usual care and used an online daily headache diary to record headache characteristics and medication use. After this pre-intervention stage, participants were randomized into a high n-3 + low n-6 (H3-L6) group or simply a low n-6 (L-6) group for 12 weeks. Targeted reductions in n-6 Arachidonic Acid (AA) and Linoleic Acid (LA) amounts per day were given for both groups while a target level of n-3 EPA and DHA was only given to the H-3-L6 group.

A registered dietitian provided dietary counsel at randomization and at every 2-week interval throughout the study. Average intakes for n-3 in the H3-L6 group were 47mg/day pre-intervention and 1482mg/day during the intervention. The L6 group consumed on average only 76mg/day of n-3 during the intervention. Both the H3-L6 and L6 groups maintained AA intake below 195mg/day for both pre- and post-intervention, with LA reductions from 6.4-7.4% of total energy intake being reduced to 2.4-2.5% of total energy intake during intervention.

The primary clinical outcome of this study was the Headache Impact Test (HIT-6), a headache-related disability tool based on self-reported pain, social functioning, cognitive functioning, psychological distress and other markers. Daily headache diaries were also utilized to generate information regarding headache hours per day, severe headache days and medication use (including acute, preventive or adjunctive). Finally, erythrocyte fatty acid levels, n-3 derived anti-nociceptive mediators and n-6 pro-nociceptive mediators were also tested at randomization and weeks 4, 8 and 12.

Study Strengths / Weaknesses:

This study is the first trial to evaluate an H3-L6 dietary intervention for clinical pain reduction in CDH. It is also unique that the comparison group used had an active intervention of lowered n-6 intake, as opposed to not changing dietary omega fatty acid intake at all. This “active” style of intervention was still considered intensive and perceived by participants as credible and beneficial. Therefore, the placebo effect related to any dietary change or coaching given from a trained nutritionist was removed or blunted significantly by this tactic.

Another noteworthy strength of this study includes the use of laboratory-analyzed fatty acid

composition of foods to allow for greater control over nutrient intake, instead of relying on dietary recall alone. Along the same lines, erythrocyte fatty acid analysis at regular intervals throughout the trial allowed for higher suspicion of causality and correlation between clinical outcomes and dietary changes. For example, if no changes in pro-nociceptive or anti-nociceptive mediators were detected even in the presence of clinical CDH outcomes, perhaps other mechanisms for improvement would be considered more plausible.

Despite these strengths, a number of shortcomings are present with this study. Firstly, although an active intervention group as a comparison was used, there was no true placebo group in order to gage the amount of possible placebo effect with dietary change and CDH. The present trial was relatively small with only 56 subjects completing the study and a relatively high dropout rate (11 of 67 participants; 16.4%). Larger trials must be completed to confirm or deny the findings of this study.

As with any dietary intervention used in outpatient populations, there is the risk of unintended dietary factors contributing toward the findings. For example, although n-3 and n6 intakes were highly regulated, other micronutrients could not be completely monitored and, therefore, some other nutrients may have contributed to the favorable effects of the H3-L6 group. Finally, although alterations in erythrocyte and tissue levels of fatty acids can plausibly reduce CDH through inflammatory or vascular pathways, this study cannot prove causation or the definitive mechanism of action.

Additional References:

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