



(RESEARCH ARTICLE)



The effects of a unique medium chain triglyceride complex on migraine symptoms: A beta pilot study

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Abstract

Purpose: Migraine headaches are among the most common worldwide medical issues, and various drug therapies only offer limited relief. Medium chain triglyceride (MCT) oil has demonstrated clinical benefits in multiple domains, from enhanced overall energy to increased brain function. This pilot study investigated the potential relief provided from a unique proprietary formulation, including a high concentration MCT-containing blend on migraine frequency, duration, and severity over 30 days.

Methods: Fourteen (n=14) chronic migraine sufferers (migraineurs) were prospectively selected to participate in the open-label trial of this patented complex. Participants were instructed to maintain a consistent lifestyle, health factors, and medications while consuming the study compound. Because of the current Corona virus pandemic, the original paper version of the migraine survey was converted to an electronic response form to allow subjects increased safety in rating episodes and symptoms.

Results: Overall, the subjects reduced the number of migraine episodes by 39% from the baseline period compared to after 30 days of using the supplement. The average episode duration decreased from 388 minutes to 152 minutes, a 61% reduction. Days/events missed due to migraine severity or complications were reduced from five per month to two per month, a decrease of 60%. A combined measure of specific symptoms also decreased according to subject rating, by an average of 32%.

Conclusion: In this beta pilot study, consumption of a high concentration MCT complex produced significant improvements in migraine symptoms in the three significant episode realms of frequency, duration, and lost days due to dysfunction. In addition, migraine symptom surveys can be converted to electronic record keeping, a benefit for both the patient and the clinician. These outcomes have provided further impetus to pursue a rigorous study of specific MCT products to reduce migraine symptoms. A formal confirmatory placebo-controlled trial has been initiated.

Keywords: Migraine; medium chain triglyceride; MCT; headache; Onabotulinum toxin A; serotonin; metabolism; pain; ketones; ketogenic; migraine prevention; 3-hydroxybutyrate.

1. Introduction

Migraine headache is the 3rd most prevalent global illness, with an estimated 12% of the overall population suffering from this condition, including about 40 million people in the U.S. Also, migraine has a high percentage of episodes resulting in both temporary and long-term disability due to lost employment, education, housework, recreation, and other activities [1-4].

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As this condition has been classified as a neurological disease, with a multiplicity of potential causes and factors, the diagnosis and treatment can be elusive [5-10]. Some migraineurs, depending upon the level of severity endured, do not seek help until the symptoms become so pervasive that it is apparent that the related morbidity and life disruption are overwhelming [11-14]. An additional consideration is that many sufferers are forced to miss work, education, or social events due to a migraine episode's length and severity. This factor has been attributed to why migraineurs may not admit symptoms, as there is a perceived negative social stigma to the condition.

While drug treatment for migraines has improved, it is not yet anywhere near 100% effective. There have been several types of drugs (as well as onabotulinum toxin A and neuromodulation for pain signaling) used historically to attempt to control symptoms [15, 16]. Relatively recently, pharmaceuticals have been approved directly for migraine prevention and treatment. There are two oral medications – ditans (5-HT receptor agonists of dopamine pathway) and gepants (calcitonin gene-related peptide receptor antagonists) used for treatment, as well as monoclonal antibodies administered by subcutaneous or intravenous injections targeted for prevention [17-19]. However, they have potential adverse side effects such as dizziness, nausea, fatigue, somnolence, and sedation. They are also expensive (up to several hundred dollars per month), yet some people may pay significantly less with commercial insurance [19, 20]. These drugs have been generally approved based on a reduction in episode frequency [21, 22]. The data shows that the best results (50% or more significant reduction in episodes) occur after taking the medications for extended periods. There appears to be increasing improvement, the longer the drug is taken.

Because of this situation, many migraineurs may express a high interest in "natural" non-pharmaceutical treatments. Ketones have gained increased awareness in a variety of positive roles, from energy to brain health. They are essentially made in the liver from MCTs and sent to the brain for fuel. Also, recent attention to the benefits of both ketogenic diets and compounds such as MCTs [23, 24, 25], has engendered momentum to use these strategies and products for migraine reduction as well as cognitive improvements [26, 27]. In brain function related to fuel availability, ketones are used independently of glucose and take on more importance as one gets older. Additional investigation has shown that ketogenic programs, and more potently MCT products, positively influence a wide range of cognitive functions from basic thinking to potential effects in dementia [28-31]. While there are some probable reasons for this positive response, providing consistent fuel for the brain in ketones usually has demonstrated clinical benefits and is often attributed as the dominant initial cause of positive effects.

It has been theorized that ketogenic approaches, and specifically MCT compounds, would provide a natural path for migraine improvement. While positive overall, investigations with ketogenic diets do not differentiate between the ketogenic component's benefits versus the reduction of simple carbohydrates. Thus, with a ketogenic nutritional approach, it may have been that much lower carbohydrate levels were contributing factors in migraine reduction and more evenly available energy sources. To a degree, exogenous MCT products, which are ketogenic by themselves, likely have a mediating effect of lowering glycemic index, thus acting biologically as part of the overall total nutritional intake [32-35]. This approach may allow migraineurs to receive the benefits of a ketogenic strategy while permitting less dietary restriction.

The purpose of this pilot investigation was two-fold. First, can a specifically formulated MCT complex, without restriction and reference to other factors such as dietary regimes, lifestyle, or medications, reduce migraine symptoms, severity, duration, and episode frequency? If the initial results were favorable, it would provide the impetus for further study to determine potential relief in a rigorous clinical trial model. Secondly, because migraine sufferers are often incapacitated due to the symptom severity and duration, it was essential to determine if a revised migraine scale, based on previously validated questionnaires, could be converted to an electronic format that would allow migraineurs to more efficiently, safely (especially in light of COVID-19), and rapidly provide their insights and responses thereby improving accuracy and decreasing recall bias.

2. Material and methods

Migraine sufferers were recruited based upon initial criteria that included an average of six to 15 migraine episodes per month and a consistent lifestyle and medication regimen. Applicants were also instructed to have a capable smartphone, tablet, or computer for forms and rating scales. Those meeting all requirements were then instructed to fill out complete medical history forms, a standard consent form, and a detailed migraine description evaluation, which would be completed again at the end of the project (Table 1). This novel hybrid instrument was developed to avoid common problems noted with other scales. These issues include being too lengthy, requiring responses too frequently, prolonged study periods leading to recall bias and lowered compliance, as well as proprietary forms that required payment for use [36-39]. Subject applicants were then reviewed and approved by the Colorado Center for Health and Sports Science Institutional Review Board (CCHSS IRB), with fourteen (N=14) subjects being accepted into and completing the study.

For the 30 days before initiating supplement consumption, participants rated migraine frequency, duration, missed life episodes (employment, education, housework, and social activities), as well as individual symptom factors for average episodes. The individual factors were rated on a scale from 0-100, with significant rating points of 0 being no issues, 50 having moderate issues, and 100 showing severe issues. It appeared reasonable that this approach would allow the subject more latitude in assigning values to symptom severity. The symptom details to be monitored are listed in Table 1. It was also determined from a literature review and subject interviews that a combination of migraine scales and individual factors was the appropriate strategy to determine the most meaningful effects of the study supplement [40-43]. This strategy appeared to provide a greater view concerning how a unique MCT compound might or might not benefit migraineurs.

Table 1 Survey Parameters

Primary Survey Measures	Secondary Survey Measures
Number of Migraine Incidents	Light Sensitivity
Average Minutes per Incident	Sound Sensitivity
Number of Days/Events Lost Due to Migraines	Nausea
	Pain on One Side
	Vision Changes/Blurred Vision
	Vomiting
	Mood Changes
	Feeling Drained
	Vertigo/Dizziness
	Throbbing/Pulsating Pain

As this was a contact-less study during the global pandemic, the supplement was individually shipped to each participant. The product consisted of the proprietary MCT complex, Fuel4Thought™ (F4T™), employing a mild fruit-flavor taste profile. Subjects were instructed to take the supplement (generally with some food) at the same time every day at their preference. They were further directed to maintain consistent lifestyle patterns, work, medical treatments, and anything else that was part of the daily routine.

3. Results

The self-reported scale and questionnaire data compared migraine parameters and symptoms for the 30-day baseline period before supplementation to that after consuming the supplement for 30 days. Values are reported as simple, descriptive numbers since this pilot study utilized an open-label design with no control group (Table 2).

Total 30-day reported migraine frequency decreased from an average of 9.91 episodes to 6.03, a reduction of 39%. In addition, the maximum and minimum reported values also dropped in a parallel manner (Figure 1).

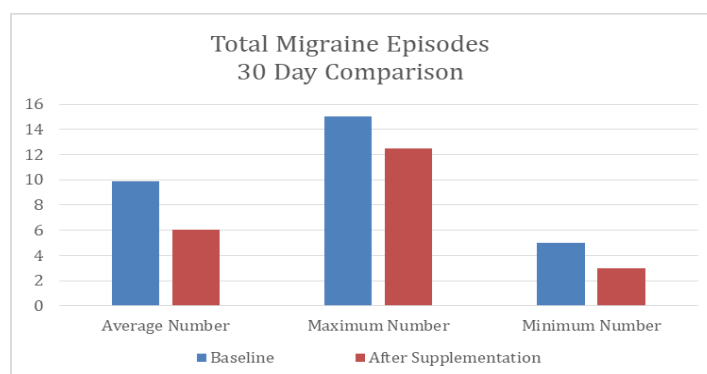
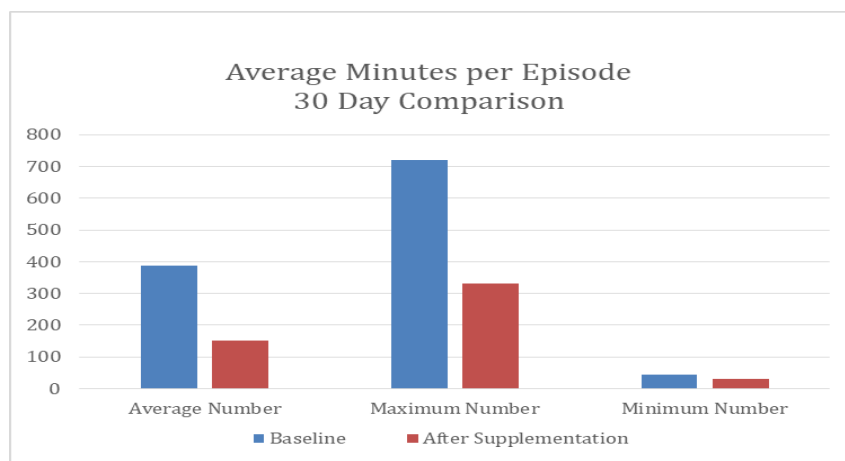


Figure 1 Total Migraine Episodes

Table 2 Overall Results Summary

Parameter/Variable	Baseline	After Supplementation	Change	% Change
<i>Primary Measures</i>				
Episodes/30 Day Average	9.91	6.03	-3.88	39%
Minutes per Episode	388	152	-236	61
Days Lost Work/School/Social	5	2	-3	60
<i>Secondary Measures</i>				
Throbbing, Pulsating Pain	77	51	-26	34
Light Sensitivity	62	34	-28	45
Sound Sensitivity	57	36	-21	37
Nausea	40	37	-3	7
Pain on One Side	72	54	-18	25
Vision Changes	32	25	-7	22
Vomiting	10	8	-2	20
Mood Changes	6	4	-2	33
Feeling Drained	61	38	-23	38
Vertigo/Dizziness	30	19	-11	37
Average	44.7	30.6	-14.1	32

The average duration per migraine episode also decreased from 388 minutes to 152 minutes. The maximum and minimum values were also reduced from the baseline to post-supplement period further indicating the group trend (Figure 2).

**Figure 2** Average Minutes per Migraine Episode

The number of days lost to migraine episodes in such areas as employment, education, housework, or social situations fell from an average of five per month to two per month (Figure 3). The maximum and minimum number levels also improved. For the maximum level, three subjects reported ten days lost during the baseline period, while only one participant lost ten days after supplementation. Four subjects reported no lost days during the baseline period for the minimum levels, which increased to seven participants who lost no days after supplementation.

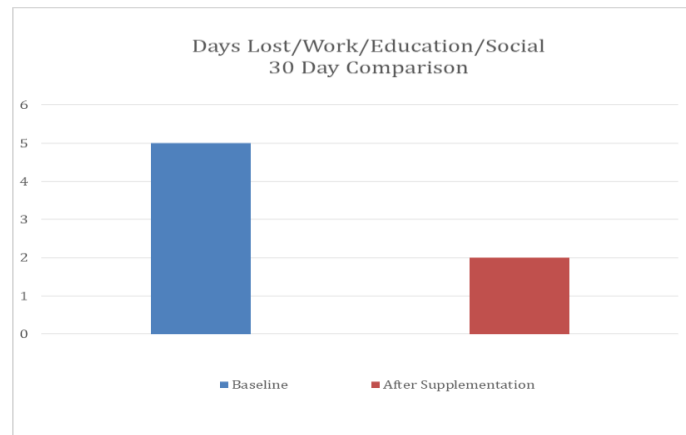


Figure 3 Days Lost to Migraine Episodes

The secondary migraine symptoms also showed decreases across the scale after consuming the supplement. (Figure 4). In this self-reported section, subjects were directed to rate the amount of disability or effect during each migraine incident. The scale allowed flexibility since subjects could use the sliding scale to add fine points of effect for each parameter. Percentage decreases were as follows: throbbing pain 34%, light sensitivity 45%, sound sensitivity 37%, nausea 7%, single-sided pain 25%, vision changes 22%, vomiting 20%, mood changes 33%, feeling drained 38%, and vertigo/dizziness 37%. The average decrease for the combination of all secondary measures was 32%.

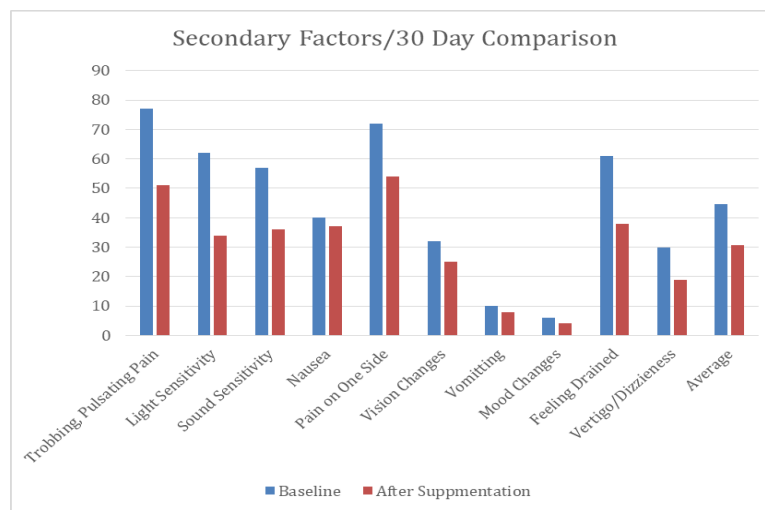


Figure 4 Changes in Secondary Symptom Areas

4. Discussion

As this was a beta trial with a limited number of subjects and no placebo control group, the results should be considered observational and exploratory. However, the degree of beneficial outcomes was substantial, considering that the study compound was a natural supplement and not a pharmaceutical drug. While not directly comparable, the results appear quite favorable in terms of positive effect compared to migraine medications that recently received regulatory approval and became commercially available [15, 18].

In addition, while not formally reported, a survey of subjects after the initial 15 days of consuming the supplement already showed dramatic improvement, which was further heightened during the last 15 days of supplementation. A substantial portion of the ultimate 30-day benefit was already reported in the interim (15 days) survey for migraine frequency, duration, and symptom severity. This result trend appears to conform to what is observed for approved preventive pharmaceuticals that routinely demonstrate increasing benefit the longer the drug is taken [17, 22, 44].

It appears that exogenous MCT products and ketogenic diets can improve brain energy by increasing ketone and overall energy levels [26]. It also seems that MCTs have a function in repairing specific brain-cell damage. Another set of factors

to be considered is the relationship between the flora of the intestines and documented weight maintenance, and various applications from cognitive health to performance improvement [45, 46, 47]. In further physiological terms, MCT oils have been demonstrated to aid in energy regulation, both with regular activity and intense exertion [48-51].

Several mechanisms of action may be implicated in the effects related to ketogenesis in migraineurs. Mounting scientific data has recently shown that migraines are, in significant part, a response to cerebral energy deficiencies or oxidative stress levels exceeding those that can be managed by natural physiologic antioxidant activity. Ketones are an alternative fuel source for the brain and may address certain deficiencies in the human brain to adequately manage glucose metabolism that is imbalanced in migraines. Ketones act as signaling molecules for energy substrates and thus may manage other components of migraine physiology such as underlying mitochondrial function, inflammation, and oxidative stress.

Oxidative stress has injurious effects on cells, tissues, organs, body proteins, lipids, and DNA. If damage occurs to neurons, resulting neurological conditions may occur, including migraine headaches. In addition to excess free radicals, acute and chronic inflammatory reactions also contribute to the spectrum of injury. Neurogenic inflammation, cellular extravasation, vasodilatation, mast cell activation, and the release of pro-inflammatory mediators may stimulate trigeminal nerve afferents leading to symptom sensitization in the migraineur [52, 53]. Exogenous ketogenic MCT can impact these factors and improve migraine pathophysiology. Simultaneously, the ketone body 3-hydroxybutyrate, the principle ketone produced by MCTs metabolism and the active ketone agent for brain energy, can reduce inflammation and address aspects metabolic-related disorders. Ketones appear to have a strong anti-inflammatory response. Thus, various likely causative mechanisms in migraines may account for the positive MCT effect, including metabolites as signaling molecules, efficient mitochondrial energy generation, oxidative damage, inflammation, brain stimulation, and hyper-excitability, and even signaling feedback with the overall human microbiome [23, 26, 51].

Finally, it is theorized that the MCT combination used in this study also resulted in the subjects having more energy with subsequently improved attention to lifestyle, thereby mitigating migraine frequency and severity. Healthy intestinal flora and function are related to serotonin and dopamine, compounds that improve mood and may modulate migraine headaches [54]. Robust microbial health while reducing harmful bacterial levels can lower brain inflammation and other positive health benefits [24, 55, 56, 57, 58]. Quality of life factors, as noted previously, are serious components of the disease, and their improvement is a significant positive aspect of the management and improvement of the migraineurs' experience.

5. Conclusion

This study introduces a natural, safe, cost-effective supplement intended to address migraine symptoms and rapidly provides beneficial effects. The supplement also shows improvements in episode frequency, duration, symptom severity, and limitation of daily activities. The product does not require a prescription and has not been associated with adverse side effects. In conclusion, there is now an efficacious alternative to pharmaceutical drugs in the challenge to improve the quality of life in migraineurs. It appears that this supplement can also be used alone or in combination with other drug and non-pharmaceutical interventions to address this disabling chronic medical condition. While this study had limited participant numbers and no control group, the results were so encouraging that a formal confirmatory clinical trial is being undertaken.

Compliance with ethical standards

Acknowledgments

The manufacturer of the product, Healthy Extracts (HE), provided the product for the study. Otherwise, HE had no input to study design, data gathering, or final format. GMH and RAF provided content relative to MCT background and mechanistic interactions from their extensive knowledge and experience with MCT products. They were not involved in study design, data acquisition, or initial study authorship. NEW was responsible for study design, research mechanics and protocol, and subject monitoring. In addition, NEW was the initial author of the paper and orchestrated the final form.

Disclosure of conflict of interest

RAF and GMH are shareholders in HE but did not contribute to study design, data collection, or result analysis. All parties did review the final document for accuracy. NEW reports no conflicts of interest with the project.

Statement of informed consent

All subjects were provided with an informed consent as to the study's purposes and possible side effects and alternatives. These were affirmed verbally with each subject before signature and then given to the CCHSS IRB for review and approval. Subjects were informed that results would be pooled into overall results, but no self-identifying information would be released during or after the study.

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