



Review

A CONCISE REVIEW OF COENZYME Q10 SUPPLEMENTATION IN THE PREVENTATIVE TREATMENT OF MIGRAINE

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Abstract

Migraine is a complex and heterogeneous syndrome that lacks clearly defined treatment. An effective prophylactic therapy with minimal side effect profile is of interest to patients and clinicians alike. CoEnzyme Q10, a critical member of the electron transport chain, has been proposed to play a role in the pathogenesis of migraine in certain patients. In this article, we provide a concise review of the proposed physiology of coEnzyme Q10 supplementation and its role in prophylaxis against pediatric and adult migraine. Robust data on this subject is lacking, though early evidence supports its routine use in clinical practice.

Keywords: migraine, supplement, coEnzyme Q10, prevention, headache, prophylaxis.

1. Introduction:

Migraine headache is a common condition which affects 12% of the population [1]. The condition is heterogeneous, lacks a universally effective treatment, and is among the world's leading cause of disability [2-3]. The etiology of migraine is not well understood, however several mechanisms have been proposed to define the pathogenesis. Given its tremendous expense and high prevalence, a safe and effective preventative therapy has been of longtime concern to patients and clinicians alike.

There is increasing interest in the use of nutraceuticals and supplements for treatment of migraine. Patient preference for their use include side effect profile, low cost and the perceived benefit of natural treatment. There is growing evidence to support the use of nutraceuticals, thus

physicians should be informed of the risks and benefits of their use in clinic practice. CoEnzyme Q10 is an inexpensive, over-the-counter supplement studied in the prevention of migraine in both adults and children. In this article, we provide a brief summary of the evidence for oral coEnzyme Q10 supplementation in the prevention of migraine.

2. Migraine Pathogenesis: Mitochondrial Theory and coEnzyme Q10:

Migraine is a complex condition influenced by genetic and environmental factors. The pathophysiology is heterogeneous and not fully understood, though mitochondrial micronutrient deficiency has been proposed to play a central role in a subtype of migraine [4]. Cellular production of

the energy dense molecule adenosine triphosphate (ATP) is dependent on a series of mitochondrial reactions influenced by certain cofactors. CoEnzyme Q10 is a key carrier of electrons in the mitochondrial electron transport chain and deficiency has been associated with several neurological, muscular, and nephrogenic diseases [5-7]. Neurons and myocytes have a higher relative concentration of mitochondria compared to other tissues, speaking to their unique dependence on ATP as a rapidly mobile energy supply [8]. It has been proposed these cell types are particularly susceptible to defects in oxidative phosphorylation, permitting certain pathologic processes related to migraine [9]. Impaired oxidative phosphorylation lends to a relative depletion of superoxide dismutase, a key enzyme in recycling reactive oxygen species [3]. It has been proposed this defect may cause compromised intracellular calcium metabolism and ultimately impaired vascular tone, which is thought to be related to migraine propagation [3]. Studies using positron emission tomography (PET) and functional MRI (fMRI) in migraine patients have demonstrated a relative ATP deficit secondary to mitochondrial dysfunction and lower serum levels of coEnzyme Q10 have been reported compared to controls [10-13]. The culmination of these findings suggest that the benefit of coEnzyme Q10 supplementation in migraine patients may be related to improved mitochondrial function. Not all patients seem to benefit from coEnzyme Q10 supplementation. It is possible those with deficiency procure the greatest response. Though the risks of supplementation appear to be low and a subset of patients benefit, more detailed studies are necessary to better understand that pathophysiology of coEnzyme Q10 as it relates to migraine.

3. Methods:

We conducted a literature review of PubMed and Ovid online databases using the following key words: migraine, coEnzyme Q10, prevention. The following limits were placed: English language, randomized controlled study, meta-analysis, review, book chapter. Brooke Army Medical Center Department of Medical Library assisted our literature search and utilized an inter-library loan program to access all articles. A total of seventeen

articles fit the selection criteria and were reviewed by the authors.

4. Discussion:

4.1. Mechanism of Action and Administration

A host of studies have suggested dysfunctional mitochondrial energy production may play a role in migraine pathogenesis [1, 3-4, 7-8, 11-12, 14-17]. CoEnzyme Q10 is an electronic transporter between complexes in the electron transport chain, resulting in the production of usable cellular energy. It is thought that subdued oxidative phosphorylation may cause cerebral vascular tone dysfunction through inhibited calcium ion metabolism and insufficient recycling of reactive oxygen species [3-4, 15, 17]. The combination of these cascades, particularly in those with coEnzyme Q10 deficiency, may propagate the headache syndrome.

CoEnzyme Q10 is most common given orally, though can be administered intravenously, and serum concentrations peak at 5-10 hours after oral administration [6]. Serum coEnzyme Q10 levels usually range between 0.7 and 1 mcg/ml and supplement of 100-150 mg per day can double the serum concentration. We were able to find no studies demonstrating further pharmacokinetics of supplementation [18]. Natural options include meat and poultry, but otherwise, oral doses up to 600 mg daily are well tolerated, with less than 1% of people experiencing nausea, diarrhea or epigastric discomfort [6, 10]. Routine dietary intake is likely much lower: the average intake in a Danish diet was reported to be 3 mg to 5 mg of coEnzyme Q10 per day [19]. Because coEnzyme Q10 deficiency is relatively common in patients who experience migraines and treatment is well tolerated, supplementation may be a safe option for migraine prophylaxis in some patients [6, 10].

4.2. Summary of Evidence in Adult Patients

We identified four studies and one meta-analysis that addressed the use of coEnzyme Q10 supplementation in the prevention of migraine in adult patients. In three additional studies, coEnzyme Q10 was given in combination with other supplements (L-carnitine, feverfew, magnesium). Of the observational studies conducted in adults, attack frequency and severity was significantly reduced in patients treated with

coEnzyme Q10. Supplementation was well tolerated, had few side effects and added benefit without significant increase in risk. A 2002 non-controlled, open label study showed a reduction in attack frequency (-55.3%) and headache days per month (-4.39 days; $p < 0.0001$) in treated patients compared to their baseline demonstrated by headache diary [6]. These results were affirmed by a 2005 follow-up blinded, randomized and controlled study, showing a reduction in attack frequency (-1.1 attacks per month; $p = 0.05$), 47.6% of these patients ($n = 21$) experienced a 50% reduction in headaches per month after three months of treatment compared to 14.3% of patients treated with placebo ($p = 0.02$) [4]. No significance was demonstrated in number of headache days, severity, and days with emesis when studies were blinded. It should be noted, the 2002 non-blinded study and the 2005 blinded study used two different doses of coEnzyme Q10: 150 mg daily versus 300 mg daily, respectively.

Similar results were published in a 2017 controlled but open-label trial, where attack frequency (-1.6 vs. -0.5 attacks/month; $p < 0.001$) and mean headache severity calculated by the Visual Analogue Scale (-2.3 versus -0.6; $p < 0.001$) were reduced [3]. A subsequent blinded study in 2019 confirmed these findings, demonstrating a significant reduction in frequency ($p = 0.018$), severity calculated by the Visual Analogue Scale ($p = 0.001$), and duration ($p = 0.012$) of attacks. This study also included analysis of serum markers thought to be related to the pathogenesis of migraine. Patients treated with coEnzyme Q10 had a significant reduction in calcitonin gene related peptide (CGRP) ($p = 0.011$) and tumor necrosis factor- alpha (TNF-alpha) ($p = 0.044$), but no significant difference in Interleukin-6 (IL-6) or Interleukin-10 (IL-10) [20]. In current practice, these markers are not routinely drawn to assess treatment response. It is difficult to draw comparisons between these trials due to the different doses of coEnzyme Q10 used (100 mg

daily versus 400 mg daily) and the inclusion of only women in the latter study.

Three trials studied the effect of various combinations of supplements including magnesium, riboflavin, and L-carnitine on attack frequency and severity. A double-blinded and controlled trial studying coEnzyme Q10 in combination with magnesium and riboflavin showed a decrease in attack severity ($p = 0.03$), reduction in burden of disease score (HIT-6) ($p = 0.01$), and subjective improvement in treatment efficacy ($p = 0.01$) [21]. An observational study with coEnzyme Q10, feverfew and magnesium supplementations found improvement in symptoms early in treatment, suggesting that repletion in patients with coEnzyme Q10 deficiency may be of benefit [22]. A trial of low-dose coEnzyme Q10 (30 mg daily) with L-Carnitine showed similar results, demonstrating decreased severity (-3.03, $p < 0.001$), duration (-7.67, $p < 0.001$), and attacks per month (-5.42, $p < 0.001$) [23]. Patients treated with coEnzyme Q10 and L-carnitine also had a significant reduction in their serum lactate concentration (-2.28 mg/dL $p = 0.002$), suggesting that lactate could be a marker of improved mitochondrial function in treated patients [23]. In summary, it seems patients may benefit from coEnzyme Q10 supplementation in combination with other nutraceuticals. Further study is necessary to determine if combination is better than coEnzyme Q10 alone, and to determine optimal supplement dose.

Given current research, the authors conclude coEnzyme Q10 supplementation is well-tolerated and is associated with reduction in certain disease burden parameters. CoEnzyme Q10 supplementation may also be of benefit when combined with other supplements that influence mitochondrial function (magnesium, L-carnitine, et cetera) to further reduce disease burden, though the best combination and dose remain unclear. A summary of these findings are in Table 1.

Table 1. Summary of CoEnzyme Q10 Supplementation in Adult Migraine Patients

Name	Study Design	Enrollment (n)	Dose of coEnzyme Q10	Study End Points	Conclusions
Guilbot A, et al. (2017)	Non-intervention observational prospective, non-controlled trial	62 males and females	CoEnzyme Q10 100 mg, feverfew 100 mg, and 112.5 mg magnesium daily	Number of headache days per month during third month of treatment; Quality of life score (QVM ¹), anxiety/depression (HADS ² , adverse outcomes	Significant decrease in headache days per month (-3.5 days, p<0.0001), 75% of patient had a 50% reduction of headache days per month by month three of supplementation, decrease in anxiety and depression scales (HADS), and increased quality of life (QVM). No change in intensity of headaches.
Gual C, et al. (2015)	Randomized, double-blind placebo controlled trial	130 males and females	CoEnzyme Q10 150 mg, riboflavin 400 mg, magnesium 600 mg daily	Attack frequency severity, burden of disease (HIT-6 ³), subjective evaluation of efficacy at four months (one month pre-intervention period)	Decrease in severity by 0.24 points on a 3-point scale (p=0.03), reduction of HIT-6 score of disease burden by 4.8 points (p=0.01), and better subjective evaluation of treatment efficacy versus placebo (p=0.01); non-significant difference in days per month (p=0.23)
Dahri M, et al. (2019)	Randomized, double-blind placebo controlled trial	45 females	CoEnzyme Q10 400 mg daily	Severity, frequency and duration of attacks; serum CGRP, IL-6, IL-10 and TNF-alpha levels at four months (one month trail period first)	Significant reduction in frequency (p=0.018), severity (p=0.001), and duration (0.012) of attacks; significant reduction in CGRP (p=0.011) and TNF-alpha (p=0.044), no significant difference in IL-6 and IL-10 levels.
Hajihashemi P, et al. (2019)	Double blinded, randomized, placebo controlled	56 males and females	CoEnzyme Q10 30 mg daily plus L-Carnitine 500 mg daily	Severity of attacks, duration, frequency, lactate	Decrease in serum lactate levels by 2.28 mg/dL (p=0.002), decreased severity of attacks by 3.03 on a 10-point scale (p<0.001), decreased duration of attacks by 7.67 hours (p<0.001), and fewer attacks per month by 5.42 days (<0.001) in treatment arm.
Rozen T, et al. (2002)	Open label trial, non-controlled	32 males and females	CoEnzyme Q10 150 mg daily	Attack frequency and one and three months, days per month with headache	Decrease in migraine frequency was 13.1% after one month of treatment and 55.3% after three months of treatment; reduction by 4.39 headache days per month at 3 months (p<0.0001); no adverse events.
Sandor P, et al. (2005)	Blinded RCT, placebo controlled,	42 males and females	CoEnzyme Q10 100 mg three times daily	Reduction in attacks from baseline at 4 months (3 months intervention)	Decrease 1.19 versus 0.09 attacks/month among coEnzyme Q10 and control groups respectively (p=0.05);

	intention to treat				50% attack rate responder was 47.6% compared to 14.3% among coEnzyme Q10 and control groups respectively (p=0.02); no significant difference in headache days, severity, and days with vomiting
Shoeibi A, et al. (2017)	Open label, add-on, controlled trial	73 males and females	CoEnzyme Q10 100 mg daily	50% reduction attacks/month at 4 months (3 total months intervention)	Decrease in attacks per month by 1.6 vs. 0.5 among coEnzyme Q10 and control groups respectively, (p<0.001); decrease in mean headache severity by 2.3 vs. 0.6 among coEnzyme Q10 and control groups, respectively (p<0.001). No side effects observed.

1Hospital Anxiety and Depression Scale

2Qualité de Vie et Migraine questionnaire

3Headache Impact Score

4.3. Summary of Evidence in Pediatric Patients

A 2007 open-label, randomized and placebo controlled trial of pediatric patients (average age 13.3 +/- 3.5 years) with low serum coEnzyme Q10 (below 0.7 mcg/m) compared weight based treatment to placebo [10]. Supplementation resulted in reduced attack frequency (19.2 +/- 9.8 to 12.5 +/- 10.8 days per month, p<0.001), with 46.5% of participants having a 50% reduction in headache frequency. PedMIDAS, a pediatric headache severity index, calculated prior to and following treatment, showed a decrease in headache severity from 47.4 +/-50.6 to 22.8+/-30.6 (p<0.001) [10]. This was among the largest trials conducted on the subject, with 1550 patients enrolled and 252 analyzed at follow-up. Interestingly, 74.6% of the enrolled pediatric patients with qualifying headache syndrome (ICHD-II headache criteria) were deficient in serum coEnzyme Q10.

A 2011 cross over study of 120 pediatric patients (13.6 +/- 2.6 years) enrolled in a multi-specialty headache clinic were given 100 mg of coEnzyme Q10 or placebo for sixteen weeks, followed by the opposite treatment for the same duration. At the end of thirty two weeks, there was no significant difference in end points (headache frequency, migraine frequency, headache severity, headache duration) [14]. Prior to treatment group flip, there

was no significant difference between groups (p>0.5), though both had some degree of clinical improvement that was first reached by the supplementation group. The slightly more rapid decline in symptom burden in the treatment group suggests coEnzyme Q10 replenishment may have an early and limited benefit [14]. Similar improvement in both groups suggests an intrinsic therapeutic benefit to a multidisciplinary clinic and makes it difficult to draw conclusions about the specific role of coEnzyme Q10 [14].

One study with interesting findings but limited generalizability evaluated the response of 18 children with Neurofibromatosis I-related headaches to supplementation with ginkgolide B, coEnzyme Q10, riboflavin, and magnesium in a non-controlled trial. At six months, these children experienced fewer attacks per month (-42.96%; p < 0.001), lower VAS headache intensity (-32.98%; p < 0.001), and fewer headache hours per month (-16.26%; p < 0.001).

The heterogeneity of these studies in their end points, design, inclusion criteria, and dosages make comparisons among them challenging. Regardless, the authors conclude early evidence supports the use of coEnzyme Q10 supplementation in pediatric migraine patients due to the low side effect profile and likely

therapeutic benefit in deficient patients. A summary of these findings is in Table 2.

Table 2. Summary of CoEnzyme Q10 Supplementation in Pediatric Migraine Patients

Name	Study Design	Enrollment (n)	Dose of CoEnzyme Q10	Study End Points	Conclusions
Slater S, et al. (2011)	Cross over, double-blinded, randomized, placebo-controlled, add on	72 male and female children and adolescents ages 6 to 17 years (at time of cross over)	CoEnzyme Q10 100 mg daily plus multidisciplinary headache clinic	Headache frequency, migraine frequency, headache severity, headache duration	Improvement in both treatment and placebo, without difference between groups in headache frequency ($p>0.05$), migraine frequency ($p>0.05$), or headache severity ($p>0.05$). Improvement in both groups suggests benefit of multidisciplinary clinic.
Hershey A, et al. (2007)	Open label, randomized, placebo controlled	1550 male and female children and adolescents, ages 3 to 22 years.	CoEnzyme Q10 1-3 mg/kg daily in patients below the reference	Attack frequency and PedMICAS ¹	Reduction in attack frequency from 19.2 +/- 9.8 to 12.5 +/- 10.8 days per month ($p<0.001$). 46.3% of treated patients experienced 50% reduction in headache frequency. Improved PedMIDAS score from 47.4 +/- 50.6 to 22.8 +/- 30.6 ($p<0.001$)
Carotenuto M, et al. (2013)	Non-controlled, add on trial	18 male and female children and adolescents, ages 6 months to 18 years, with Neurofibromatosis I (NFI).	CoEnzyme Q10, Riboflavin, Ginkgolide B, Magnesium supplement twice daily for six months	Attack frequency, severity (VAS scale), duration and PedMIDAS ¹ score	After six months of treatment, encountered 6.41 fewer attacks per month (-42.96% $p < 0.001$), a decrease by -2.79 of headache intensity on VAS score (-32.98% ; $p < 0.001$), 2.16 fewer headache hours per month (16.26% ; $p < 0.001$); and decrease in PedMIDAS score by -22.4 (-92.47 , $p < 0.001$).

¹ PedMICAS Headache Severity Score

5. Conclusions:

There is evidence to support the routine use of coEnzyme Q10 in the prophylactic treatment of migraine in both adults and pediatric patients. Supplementation is well tolerated, though there is insufficient evidence to determine the optimal dose and frequency of supplementation. Further studies should be conducted to determine the optimal patient subgroup and treatment dose.

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References:

- [1.] Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007; 68: 343-349.
- [2.] Bianchi A, Salomone S, Caraci F, et al. Role of magnesium, coenzyme Q10, Riboflavin, and vitamin B12 in migraine prophylaxis. In *Vit and Hormones*; Gerald Litwack, Eds.; Elsevier Science: United States, 2004; Colume 69, pp.297-308.
- [3.] Shoeibi A, Olfati N, Soltani Sabi M, Effectiveness of coenzyme Q10 in prophylactic treatment of migraine headache: an open-label, add-on, controlled trial. *Acta Neurol Belg*. 2017; 117, 103-109.
- [4.] Sandor P, Clemente L, Coppola G, et al. Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized controlled trial. *Neurology*. 2005; 64, 713-715.
- [5.] Littarru G, Tiano L. Clinical aspect of coenzyme Q10: an update. *Curr Opin Clin Nutr Metab Care*, 2005, 8,641-646.
- [6.] Rozen T, Oshinshky M, Cebeline C, et al. Open label trial of coenzyme Q10 as migraine preventive. *Cephalalgia*. 2002; 22;:137-141.
- [7.] Quinzii, C and Hirano M. Coenzyme Q and Mitochondrial Disease. *Dev Disabil Res Rev*. 2011; 16(2): 183-188. DOI: 10.1002/ddrr.108.
- [8.] Gasparini, C.F., Sutherland, H.G., et al. Studies on the Pathophysiology of Migraine. *Current Genomics*. 2013 Aug; 14(5): 300-315. doi: 10.2174/13892029113149990007.
- [9.] Yorns, W., Hardison, H. Mitochondrial Dysfunction in Migraine. *Seminars in Pediatric Neurology*. 2013 Sep. DOD - 10.1016/j.spen.2013.09.002
- [10.] Hershey A, Powers S, Vockell A, et al. Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine. *Headache*. 2007; 47, 73-80.
- [11.] Orr S, Venkateswaran S. Nutraceuticals in the prophylaxis of pediatric migraine: Evidence-based review and recommendations. *Cephalalgia*. 2014; 34(8), 568-583. DOI: 10.1177/0333102413519512
- [12.] Russo, A., Silvestro, M., Tedeschi, G. et al. Physiopathology of Migraine: What Have We Learned from Functional Imaging? *Curr Neurol Neurosci Rep*. 2017 Oct; 17, 95. Doi: 10.1007/s11910-017-0803-5
- [13.] Fila, Michal., Pawlowska, Elzbieta., et al. Mitochondria in Migraine Pathophysiology - Does Epigenetics Play a Role? *Archives of Medical Science*. 2019 Jul; 15(4): 944-956. doi: 10.5114/aoms.2019.86061
- [14.] Slater SK, Nelson T, Kabbouche M, et al. A randomized, double-blind, placebo-controlled, crossover, add-on study of Coenzyme Q10 in the prevention of pediatric and adolescent migraine. *Cephalalgia*. 2011; 31(8), 897-905. DOI: 10.1177/0333102411406755
- [15.] Volta G, Carli D, Zavarise P, et al. P026. Pilot study on the use of coenzyme Q10 in a group of patients with episodic migraine without aura. *The Journal of Headache and Pain*. 2015; 16(Suppl 1), A186.
- [16.] Zeng Z, Li Y, Lu S, et al. Efficacy of CoQ10 as supplementation for migraine: A meta-analysis. *Acta Neurol Scand*. 2019; 139, 284-293. DOI: 10.1111/ane.13051
- [17.] Sagermani R, Boncimino A. The use of nutraceuticals in children's and adolescent's headache. *Neurol Sci*: 2017; 38(suppl 1), S121-S124. DOI 10.1007/s10072-017-2896-7
- [18.] Redulieu E, Nilsson IM, et al. Determination and levels of coenzyme Q10 in human blood. *Analytical Biochemistry*. 1968; 23:132-40.
- [19.] Weber C, Bysted A, Holmer G. Coenzyme Q10 in the diet—daily intake and relative bioavailability. *Mol Aspects Med*. 1997;18(suppl):S251S254.
- [20.] Dahri M, Tarighat-Esfanjani A, Asghari-Jafarabadi, M, Hashemilar M. Oral coenzyme Q10 supplementation in patient with migraine: Effects on clinical features and inflammatory markers. *Nut -Neurosci*. 2019; 22(9), 607-615. DOI 10.1080/1028415X.2017.1421039

- [21.] Gual C, Diener H, Danesch U, et al. Improvement of migraine symptoms with a proprietary supplement containing riboflavin, magnesium and Q10: a randomized, placebo-controlled, double-blind, multicenter trial. *The J of Headache and Pain*. 2015; 16(32), 1-8. DOI 10.1186/s10194-015-0516-6
- [22.] Guilbot A, Bangratz M, Ait Abdellah A, Lucas C. A combination of coenzyme Q10, fever, feverfew and magnesium for migraine prophylaxis: a prospective observation study. *BMC Complement Altern Med*. 2017; 17(433), 1-7. DOI 10.1186/s12906-017-1933-7
- [23.] Hajihashemi P, Askari G, Khorvash F, et al. The effects of concurrent Coenzyme Q10, L-carnitine supplementation in migraine prophylaxis: A randomized, placebo-controlled, double-blind trial. *Cephalalgia*. 2019; 39(5), 648-654. DOI: 10.1177/0333102418821661.
- [24.] Carotenuto M, Esposito M. Nutraceuticals safety and efficacy in migraine without aura in a population of children affected by neurofibromatosis type I. *Neurol Sci*. 2013; 34, 1905-1909. DOI 10.1007/s10072-013-1403-z
- [25.] D'Onofrio F, Raimo S, Spitaleri D, Casucci G. Usefulness of nutraceuticals in migraine prophylaxis. *Neurol Sci*. 2017; 38(Suppl 1), S117-S120. DOI 10.1007/s10072-017-2901-1.