

The Effect of Coenzyme Q10 as a Prophylactic Treatment in Episodic Migraine

Epizodik Migrende Koenzim Q10'un Profilaktik Tedavi Olarak Etkisi

Mufeed Akram TAHA¹

 0000-0001-5726-0733

Mohammed Jameel ABDULWAHHAB²

 0000-0002-9095-008X

Ahmed Mohammed MOSTAFA³

 0000-0002-1050-067X

¹Assistant Professor of Neurology,
Department of Medicine, University
of Kirkuk, College of Medicine,
Kirkuk, Iraq

²Department of Pharmaceutical
Industry, Kirkuk Technical Institute,
Kirkuk, Iraq

³Department of Neurology, Azadi
Teaching Hospital, Kirkuk, Iraq

ABSTRACT

Aim: Migraine is a neurological disorder characterized by recurring and often severe headaches. The aim of this study was to evaluate the effectiveness of coenzyme Q10 (CoQ10) in episodic migraine prophylaxis.

Material and Methods: In a prospective follow-up study, 80 patients with episodic migraine were enrolled according to the International Classification of Headache Disorders 3rd edition and divided into two groups. One group consisted of 40 patients who received CoQ10 oral 200 mg twice daily as monotherapy for three months, while the other group consisted of 40 patients who received CoQ10 as an adjunct therapy in combination with other prophylactic antimigraine drugs. The Migraine Disability Assessment (MIDAS) questionnaire was administered to both groups before and after three months of therapy. Throughout the three-month therapy period, patients recorded daily symptoms, allowing for observation of changes in symptom severity, number, and duration of attacks from baseline.

Results: Both groups that received CoQ10 supplementation exhibited positive responses. The group receiving adjunct therapy showed a statistically more significant reduction in the MIDAS ($p<0.001$), duration ($p<0.001$), and frequency ($p<0.001$) of attacks compared to the monotherapy group. Vomiting ($p<0.001$) in the adjunct therapy group completely disappeared and sound sensitivity ($p=0.002$) showed a dramatic response to treatment.

Conclusion: CoQ10 appears to have more beneficial effects as an adjunct than monotherapy in reducing the duration, frequency, and presenting symptoms such as nausea, vomiting, and light sensitivity, in addition to sound sensitivity that responded only to adjunct therapy than monotherapy among Iraqi patients with episodic migraine.

Keywords: Migraine disorders; coenzyme Q10; prophylaxis.

ÖZ

Amaç: Migren, tekrarlayan ve sıklıkla şiddetli baş ağrılarıyla karakterize bir nörolojik hastalıktır. Bu çalışmanın amacı, epizodik migren profilaksisinde koenzim Q10'un (CoQ10) etkinliğini değerlendirmektir.

Gereç ve Yöntemler: Prospektif bir takip çalışmasında, epizodik migreni olan 80 hasta Başağrısı Bozukluklarının Uluslararası Sınıflaması 3. basımına göre çalışmaya dahil edildi ve iki gruba ayrıldı. Bir grup, üç ay boyunca monoterapi olarak günde iki kez oral 200 mg CoQ10 alan 40 hastadan oluşurken, diğer grup ise diğer profilaktik antimigren ilaçlarla birlikte yardımcı tedavi olarak CoQ10 alan 40 hastadan oluşuyordu. Her iki gruba da tedaviden önce ve üç aylık tedaviden sonra Migren Dizabilite Değerlendirme (Migraine Disability Assessment, MIDAS) anketi uygulandı. Üç aylık tedavi periyodu boyunca, hastaların günlük semptomları kaydetmesiyle, başlangıçtan itibaren semptom şiddeti, atak sayısı ve süresindeki değişikliklerin gözlemlenmesine olanak sağlandı.

Bulgular: CoQ10 takviyesi alan her iki grup da olumlu yanıtlar gösterdi. Ek tedavi alan grup, monoterapi grubuna göre MIDAS'ta ($p<0,001$), atak süresi ($p<0,001$) ve sıklığında ($p<0,001$) istatistiksel olarak daha belirgin bir azalma gösterdi. Ek tedavi grubunda kusma ($p<0,001$) tamamen kayboldu ve ses duyarlılığı ($p=0,002$) tedaviye dramatik bir yanıt gösterdi.

Sonuç: CoQ10 Iraklı epizodik migren hastalarında monoterapiye göre sadece yardımcı tedaviye yanıt veren ses duyarlılığına ek olarak süreyi, sıklığı ve bulantı, kusma ve ışığa duyarlılık gibi semptomların ortaya çıkışını azaltmada yardımcı olarak monoterapiden daha yararlı etkilere sahip gibi görünmektedir.

Anahtar kelimeler: Migren bozuklukları; koenzim Q10; profilaksi.

Corresponding Author

Sorumlu Yazar

Mufeed Akram TAHA
mufeedakram@uokirkuk.edu.iq

Received / Geliş Tarihi : 05.01.2023

Accepted / Kabul Tarihi : 17.07.2023

Available Online /

Çevrimiçi Yayın Tarihi : 07.08.2023

INTRODUCTION

Migraine is a chronic disorder characterized by recurrent and often severe headaches, commonly accompanied by symptoms such as nausea, vomiting, and sensitivity to light and sound (1). Migraine stands as a prevalent neurological condition on a global scale, impacting a staggering number of individuals surpassing 1 billion. Its prevalence is estimated at around 10%, with 6% affecting males and 14% impacting females. However, the occurrence of migraines varies across different regions, with higher rates observed in Europe at 15% and North America at 13%, while relatively lower rates are found in Asia at 9% and Africa at 5% (2). The primary goal of migraine treatment is to reduce the frequency and intensity of migraine attacks, and while there are several medications available, only a few of them act as preventive measures. There is substantial evidence that supports the positive impacts of Coenzyme Q10 (CoQ10) and L-carnitine supplements in reducing lactate levels in the bloodstream and alleviating symptoms associated with migraines (3).

Moreover, it has been hypothesized that inhibiting cortical spreading and the subsequent accumulation of MMP-9, a protein involved in the breakdown of the blood-brain barrier, could contribute to nerve inflammation and the worsening of migraines (4). The disruptions in the brain's energy demand and/or production observed in migraines are likely significant enough to induce oxidative stress (5). While limited clinical trials have been conducted, some have shown the potential of CoQ10 as a prophylactic treatment for migraines (6,7). Micronutrients like magnesium, vitamin B2, and CoQ10 have received significant attention for their potential in managing migraines (8). However, studies specifically investigating the effectiveness of CoQ10 as monotherapy versus adjunct therapy with other drugs are lacking.

Therefore, the aim of this study was to investigate the effectiveness of CoQ10 in migraine prophylaxis and its impact on reducing the frequency and severity of migraine attacks.

MATERIAL AND METHODS

A prospective follow-up study, from January 2021 to January 2022, was conducted in the outpatient neurology clinic of the Azadi Teaching Hospital in Kirkuk. Informed oral consent was obtained from all patients. The study focused on 80 patients diagnosed with episodic migraine, who were divided into two groups. One group comprised 40 patients who received CoQ10 oral 200 mg twice daily as monotherapy for three months. The other group consisted of 40 patients who received the same dose as adjunct therapy alongside other prophylactic antimigraine drugs.

The dose adjustment plan for CoQ10 supplementation was based on a review article (9) that synthesized findings from six relevant studies investigating the use of CoQ10 in various doses ranging from 30 mg to 800 mg daily. The review article provided a comprehensive analysis of the dose-response relationship and efficacy of CoQ10 supplementation in similar populations.

Considering the range of doses examined in the reviewed studies, we selected a daily dose of 400 mg of CoQ10 as the appropriate dosage for our study. This dose was

determined based on the reported efficacy and safety profile in previous literature, aiming to provide a sufficient therapeutic effect while minimizing the potential for adverse effects.

The diagnosis and classification of migraine patients in the study were based on the International Classification of Headache Disorders 3rd edition (ICHD-3). Prior to and following the three-month therapy period, the Migraine Disability Assessment (MIDAS) questionnaire was conducted in both groups. Over the course of the three months, daily monitoring and recording of changes in mean duration, number of migraine attacks per day, severity, and accompanying symptoms such as nausea, vomiting, vertigo, and light and sound sensitivity took place. The study excluded participants who met any of the following criteria: pregnancy, breastfeeding, other types of headaches apart from episodic migraine, smoking, history of brain injury in the last two years, history of allergies, stroke, inflammation, autoimmune diseases, other chronic diseases such as cardiovascular diseases, diabetes, rheumatoid arthritis, digestive disorders, or neurological diseases, history of antioxidant supplements in the last three months, history of contraceptives, non-steroidal inflammatory drugs, corticosteroids, history of alcohol consumption, change in the dose or type of regular drugs, or evidence of incompatibility with supplement intake.

This study was approved by the clinical research ethics committee of the University of Kirkuk - College of Medicine (date: 15.11.2022, number: 19).

Statistical Analysis

Data entry and analysis were performed using IBM SPSS Statistics v.26 (Statistical Package for Social Sciences, IBM Inc., Chicago, USA) software. Descriptive statistics included frequency and percentage for categorical data, while mean and standard deviation were calculated for continuous data. Normality assumptions were assessed using the Kolmogorov-Smirnov test, and skewness values. Categorical variables were compared using the Chi-square test, or Fisher's exact test for small frequency cells. For quantitative parameters, independent t-tests were employed to compare the means, and Mann-Whitney U tests were used to compare the number and duration of migraine attacks between both studied groups. Statistical significance was set at a p-value of less than 0.05.

RESULTS

The analysis involved 80 patients, with an average age of 30.49±8.06 (range, 15-45) years. The majority of the patients were female (n=57, 71.3%). There were no statistically significant differences in sex (p=0.083) and age (p=0.134) between the two groups.

There was a statistically significant difference (p<0.001) in the MIDAS questionnaire score prior to treatment between the adjunct therapy and monotherapy groups, with the adjunct therapy group showing a higher severity. However, the adjunct therapy group exhibited a greater decrease, from 3.63±0.49 to 1.05±0.22, in the MIDAS score compared to the monotherapy group which dropped from 3.00±0.78 to 2.75±0.84. Moreover, there was a statistically significant difference (p=0.003) in the number of migraine attacks before treatment between the adjunct therapy and monotherapy groups, with the adjunct therapy

group experiencing more frequent attacks. This difference became even more significant ($p<0.001$) after treatment initiation in the adjunct therapy group (median number of attacks dropped from 9 to 0) compared to the monotherapy group (dropped from 7 to 3). Additionally, there was a statistically significant difference ($p<0.001$) in the reduction of migraine attack duration per hour between the adjunct therapy and monotherapy groups when comparing before treatment initiation (Table 1).

There were no significant changes in presenting symptoms related to the aura, vertigo, nausea, and light sensitivity before and after therapy in both groups, except for vomiting ($p<0.001$), which was significantly more prevalent in the adjunct therapy group before starting therapy but completely disappeared after therapy. Moreover, sound sensitivity ($p=0.002$) showed a dramatic response to treatment in the adjunct therapy group compared to the monotherapy group (Table 2).

Table 1. Comparison of demographics, MIDAS, number of attacks, and duration of attacks between groups

	Adjunct Therapy (n=40)	Monotherapy (n=40)	p
Sex, n (%)			
Female	32 (80)	25 (62.5)	0.083
Male	8 (20)	15 (37.5)	
Age (years), mean±SD	29.12±8.18	31.85±7.81	0.134
MIDAS, mean±SD			
Before Treatment	3.63±0.49	3.00±0.78	<0.001
After Treatment	1.05±0.22	2.75±0.84	<0.001
Number of attacks, median (min-max)			
Before Treatment	9 (5-24)	7 (3-10)	0.003
After Treatment	0 (0-1)	3 (1-5)	<0.001
Attack duration (hour), median (min-max)			
Before Treatment	21 (10-72)	24 (8-72)	0.400
After Treatment	1 (0-6)	5 (1-24)	<0.001

MIDAS: migraine disability assessment, SD: standard deviation, min: minimum, max: maximum

Table 2. Comparison of migraine symptoms before and after CoQ10 treatment between groups

	Adjunct Therapy (n=40)	Monotherapy (n=40)	p
Aura, n (%)			
Before Treatment	4 (10.0)	5 (12.5)	>0.999
After Treatment	3 (7.5)	5 (12.5)	0.712
Nausea, n (%)			
Before Treatment	40 (100)	38 (95.0)	0.493
After Treatment	2 (5.0)	0 (0.0)	0.493
Vomiting, n (%)			
Before Treatment	40 (100)	14 (35.0)	<0.001
After Treatment	0 (0.0)	0 (0.0)	N/A
Light sensitivity, n (%)			
Before Treatment	33 (82.5)	30 (75)	0.412
After Treatment	0 (0.0)	1 (2.5)	>0.999
Sound sensitivity, n (%)			
Before Treatment	24 (60.0)	23 (57.5)	0.820
After Treatment	0 (0.0)	9 (22.5)	0.002
Vertigo, n (%)			
Before Treatment	24 (60.0)	22 (55.0)	0.651
After Treatment	0 (0.0)	3 (7.5)	0.240

CoQ10: coenzyme Q10, N/A: not applicable

DISCUSSION

This study aimed to assess the effectiveness of CoQ10 as a prophylactic treatment for episodic migraines among Iraqi patients and compare its use as monotherapy versus adjunct therapy with other prophylactic antimigraine drugs. Migraine imposes a significant burden on patients' lives, particularly during moderate to severe attacks (10). Numerous medications have been approved for both the acute and preventive treatment of migraines (11).

To provide a brief summary of the study and discuss the relevant literature, it is important to note that the mean age of the patients included in this study was 30 years. This finding aligns with a previous study conducted in Iraq which also reported a mean age of 35 years for migraine patients (12). However, a recent study from Italy showed a higher mean age of 49 years among migraine patients (13). It should be noted that the Italian study focused on patients with established chronic migraine, which may account for the higher mean age in their sample. Additionally, the higher prevalence of aggravating factors, such as stress, in Iraq could contribute to the younger age of migraine patients in our study.

Regarding gender distribution, the majority (71.3%) of patients in our study were female, consistent with other Iraqi studies reporting that 60-70% of migraine sufferers are female (14,15). This observation aligns with the general understanding that females tend to express migraine symptoms more frequently than males (16,17). Migraine without aura was the most common type of migraine in our study, with over 88% of participants not experiencing aura. This finding is in line with previous studies that have shown migraine without aura to be the most prevalent type (15,18).

In terms of the treatment approach, all patients in our study were prescribed CoQ10 as a prophylactic treatment for their migraines. We observed notable reductions in the MIDAS score, number of migraine attacks, and duration of headache attacks after treatment. The MIDAS score demonstrated a significant decrease after treatment, indicating an improvement in migraine-related disability. Similarly, the number of migraine attacks experienced by patients showed a significant reduction after treatment.

Additionally, the duration of migraine attacks was notably decreased. These findings align with previous studies, particularly clinical trials, which have reported significant reductions in MIDAS, number, and duration of migraine attacks following CoQ10 treatment (3,19,20).

Some studies have also shown a decrease in serum lactate levels among patients receiving CoQ10 as a prophylactic treatment for migraines (3,19). However, a meta-analysis study highlighted that while CoQ10 may reduce the frequency of migraine attacks, it does not appear to reduce their severity or duration (21). It is important to note that meta-analyses may have high heterogeneity, and their results should be interpreted with caution.

One of the diagnostic criteria for migraine listed by the ICHD-3 is the presence of phonophobia and photophobia during attacks. Phonophobia, or sensitivity to sound, is commonly seen during acute attacks (22,23). In our study, 59% of the patients were associated with phonophobia. However, it is important to note that we considered these symptoms during both attack and inter-attack periods, whereas previous studies focused only on symptoms during attacks. Interestingly, we found that sound sensitivity did not respond well to CoQ10 as monotherapy compared to adjunct therapy with other prophylactic antimigraine drugs.

Coenzyme Q10 supplementation has shown promising effects when used in combination with other supplements, as demonstrated in two separate studies (8,24). In their research, a fixed combination of *Andrographis paniculata*, feverfew, vitamin B2, magnesium, and CoQ10 supplementation was utilized for episodic migraine prophylaxis. The results indicated a significant improvement in migraine attacks, duration, and symptoms in both study groups. Notably, the adjunct treatment group exhibited a significantly lower MIDAS score, number of migraine attacks, and duration of migraine attacks compared to the monotherapy group. This suggests that adjunct therapy may yield better outcomes than monotherapy.

These findings align with the growing understanding of the metabolic mechanisms involved in migraine pathogenesis. It has been proposed that migraines may be triggered by a deficiency of cerebral energy or the accumulation of oxidative stress beyond the control of antioxidants (25). CoQ10, as an antioxidant, may help mitigate these mechanisms and provide therapeutic benefits in migraine management.

Furthermore, a recent study conducted in Iran focused on the efficacy of CoQ10 as a prophylactic treatment for migraine headaches in children (26). The study concluded that CoQ10 holds great value as a treatment option for children with migraines, particularly due to its relatively fewer side effects, especially during long-term use. This suggests that CoQ10 supplementation may be a viable and well-tolerated treatment approach for pediatric migraine patients.

Overall, these findings highlight the potential benefits of CoQ10 supplementation, as a prophylactic treatment in improving migraine outcomes and reducing the burden of migraines in both adults and children. Further research and clinical trials are warranted to better understand the precise mechanisms of action and optimize the use of CoQ10 in migraine management.

One limitation of our study is that the number of patients included was not sufficiently high, which can be attributed to the fact that it was self-funded. As a result, we had to carefully consider practical factors when determining the sample size. Although a larger sample size would have been preferable to improve statistical power and precision, limitations such as limited resources forced us to adopt a balanced approach that prioritized feasibility while still allowing us to draw meaningful conclusions.

CONCLUSION

Coenzyme Q10 has shown greater efficacy as an adjunct therapy compared to monotherapy in reducing the duration, frequency, and presenting symptoms of episodic migraines among Iraqi patients. The addition of CoQ10 to the treatment regimen resulted in significant improvements in symptoms such as nausea, vomiting, light sensitivity, and sound sensitivity, with the latter specifically responding only to adjunct therapy rather than monotherapy.

Ethics Committee Approval: The study was approved by the Ethics Committee of the University of Kirkuk - College of Medicine (15.11.2022, 19).

Conflict of Interest: None declared by the authors.

Financial Disclosure: None declared by the authors.

Acknowledgments: None declared by the authors.

Author Contributions: Idea/Concept: MAT; Design: MAT; Data Collection/Processing: MAT, MJA, AMM; Analysis/Interpretation: MAT, MJA, AMM; Literature Review: MAT, MJA, AMM; Drafting/Writing: MAT, MJA, AMM; Critical Review: MAT, MJA, AMM.

REFERENCES

1. Iba C, Ohtani S, Lee MJ, Huh S, Watanabe N, Nakahara J, et al. Migraine triggers in Asian countries: a narrative review. *Front Neurol.* 2023;14:1169795.
2. Ashina M, Katsarava Z, Do TP, Buse DC, Pozo-Rosich P, Özge A, et al. Migraine: epidemiology and systems of care. *Lancet.* 2021;397(10283):1485-95.
3. Hajhashemi P, Askari G, Khorvash F, Reza Maracy M, Nourian M. The effects of concurrent Coenzyme Q10, L-carnitine supplementation in migraine prophylaxis: A randomized, placebo-controlled, double-blind trial. *Cephalalgia.* 2019;39(5):648-54.
4. Ashina M, Tvedskov J, Lipka K, Bilello J, Penkowa M, Olesen J. Matrix metalloproteinases during and outside of migraine attacks without aura. *Cephalalgia.* 2010;30(3):303-10.
5. Borkum JM. Brain energy deficit as a source of oxidative stress in migraine: a molecular basis for migraine susceptibility. *Neurochem Res.* 2021;46(8):1913-32.
6. Yaghini O, Hoseini N, Ghazavi MR, Mansouri V, Nasiri J, Moosavian T, et al. A comparative study on the efficacy of coenzyme Q10 and amitriptyline in the

- prophylactic treatment of migraine headaches in children: A randomized controlled trial. *Adv Biomed Res.* 2022;11:43.
7. Hoffman W, Luster JD, Izurieta R. A concise review of coenzyme q10 supplementation in the preventative treatment of migraine. *J Med Case Rep Rev.* 2020;3(8):717-24.
 8. Vikelis M, Dermitzakis EV, Vlachos GS, Soldatos P, Spingos KC, Litsardopoulos P, et al. Open label prospective experience of supplementation with a fixed combination of magnesium, vitamin B2, feverfew, *Andrographis paniculata* and coenzyme Q10 for episodic migraine prophylaxis. *J Clin Med.* 2020;10(1):67.
 9. Sazali S, Badrin S, Norhayati MN, Idris NS. Coenzyme Q10 supplementation for prophylaxis in adult patients with migraine-a meta-analysis. *BMJ Open.* 2021;11(1):e039358.
 10. Zhu B, Coppola G, Shoaran M. Migraine classification using somatosensory evoked potentials. *Cephalalgia.* 2019;39(9):1143-55.
 11. Ducros A, de Gaalon S, Roos C, Donnet A, Giraud P, Guégan-Massardier E, et al. Revised guidelines of the French headache society for the diagnosis and management of migraine in adults. Part 2: Pharmacological treatment. *Rev Neurol (Paris).* 2021;177(7):734-52.
 12. Esmael ZF, Hamdan FB. Blink reflex study in patients with migraine. *Iraqi J Med Sci.* 2022;20(2):175-82.
 13. Iannone LF, Fattori D, Benemei S, Chiarugi A, Geppetti P, De Cesaris F. Long-term effectiveness of three anti-CGRP monoclonal antibodies in resistant chronic migraine patients based on the MIDAS score. *CNS drugs.* 2022;36(2):191-202.
 14. Mustafa WW, Mohammed SS, Naser ZA. Migraine headache and gender differences of Bagdad city population/Iraq. *Indian J Forensic Med Toxicol.* 2021;15(1):1787-92.
 15. Almohammadawi KOM, Alhilfi HSQ, Alkhalidy RAA. Clinical characteristics of migraine: A prospective cross-sectional study over nine years. *F1000Research.* 2018;7:1973.
 16. Ofowwe GE, Ofili AN. Prevalence and impact of headache and migraine among secondary school students in Nigeria. *Headache.* 2010;50(10):1570-5.
 17. Güneş M, Özeren E. Effectiveness of bilateral greater and lesser occipital nerve blocks in the prophylaxis of episodic migraine. *Duzce Med J.* 2021;23(1):93-6.
 18. Androulakis XM, Sen S, Kodumuri N, Zhang T, Grego J, Rosamond W, et al. Migraine age of onset and association with ischemic stroke in late life: 20 years follow-up in ARIC. *Headache.* 2019;59(4):556-66.
 19. Nattagh-Eshstivani E, Dahri M, Hashemilar M, Tarighat-Esfanjani A. The effect of coenzyme Q10 supplementation on serum levels of lactate, pyruvate, matrix metalloproteinase 9 and nitric oxide in women with migraine. A double blind, placebo, controlled randomized clinical trial. *Eur J Integr Med.* 2018;21:70-6.
 20. Hendrix C. Migraine-prophylactic and acute migraine treatments. *Evidence-Based Use of Supplements.* 2021;4.
 21. Parohan M, Sarraf P, Javanbakht MH, Ranji-Burachaloo S, Djalali M. Effect of coenzyme Q10 supplementation on clinical features of migraine: A systematic review and dose-response meta-analysis of randomized controlled trials. *Nutr Neurosci.* 2020;23(11):868-75.
 22. Yang W, Chu B, Yang J, Yu Y, Wu J, Yu S. Elevated audiovisual temporal interaction in patients with migraine without aura. *J Headache Pain.* 2014;15(1):44.
 23. Kalita J, Misra UK, Bansal R. Phonophobia and brainstem excitability in migraine. *Eur J Neurosci.* 2021;53(6):1988-97.
 24. Guilbot A, Bangratz M, Ait Abdellah S, Lucas C. A combination of coenzyme Q10, feverfew and magnesium for migraine prophylaxis: a prospective observational study. *BMC Complement Altern Med.* 2017;17(1):433.
 25. Gross EC, Lisicki M, Fischer D, Sándor PS, Schoenen J. The metabolic face of migraine-from pathophysiology to treatment. *Nat Rev Neurol.* 2019;15(11):627-43.
 26. Yaghini O, Hoseini N, Ghazavi MR, Mansouri V, Nasiri J, Moosavian T, et al. A comparative study on the efficacy of coenzyme Q10 and amitriptyline in the prophylactic treatment of migraine headaches in children: A randomized controlled trial. *Adv Biomed Res.* 2022;11:43.