Nutrition 38 (2017) 74–79

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

The effects of folic acid and pyridoxine supplementation on characteristics of migraine attacks in migraine patients with aura: A double-blind, randomized placebo-controlled, clinical trial

Gholamreza Askari Ph.D. [a], Morteza Nasiri M.Sc. [b], Hassan Mozaffari-Khosravi Ph.D. [c], Masod Rezaie M.Sc. [d], Mahdieh Bagheri-Bidakhavidi B.Sc. [e], Omid Sadeghi M.Sc. [f,*]

[a] Food Security Research Center and Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
[b] Department of Operating Room Technology, Paramedical School, Qom University of Medical Sciences, Qom, Iran
[c] Department of Nutrition, School of Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[d] Department of Nursing, School of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran
[e] Department of Nutrition, School of Health, Kerman University of Medical Sciences, Kerman, Iran
[f] Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:
Received 1 September 2016
Accepted 18 January 2017

Keywords:
Pyridoxine
Folic acid
Migraine
Headache

ABSTRACT

Objective: The aim of this study was to assess the effects of folic acid alone and in combination with pyridoxine on characteristics of migraine attacks in adult migraine patients with aura.
Methods: This double-blind, randomized placebo-controlled, clinical trial was conducted on 95 migraine patients with aura (age range 18–65 y) in Isfahan, Islamic Republic of Iran, in 2014. Patients were randomly allocated to receive folic acid (5 mg/d) plus pyridoxine (80 mg/d) or folic acid alone (5 mg/d) or placebo (lactose) for 3 mo. Characteristics of migraine attacks including headache severity, attacks frequency, duration, and headache diary results (HDRs) were obtained for each patient at baseline and at the end of the study.
Results: Folic acid plus pyridoxine intake resulted in a significant decrease compared with placebo in headache severity (-2.71 ± 0.08 versus -2.19 ± 0.05; $P < 0.001$), attack frequency (-3.35 ± 0.09 versus -2.73 ± 0.05; $P < 0.001$), duration (-7.25 ± 0.17 versus -6.5 ± 0.07; $P < 0.001$), and HDR (-74.15 ± 0.2 versus -72.73 ± 0.1; $P < 0.001$). Additionally, the reduction in these characteristics of migraine attacks in the folic acid plus pyridoxine group was significant compared with the group given folic acid alone ($P < 0.001$). However, these beneficial effects of the combined supplement became nonsignificant for attack duration compared with the folic acid–only and placebo groups after controlling for confounders. Folic acid intake without pyridoxine did not lead to a significant decrease in characteristics of migraine attacks compared with placebo group.
Conclusions: Supplementation of folic acid with pyridoxine could decrease the characteristics of migraine attacks including headache severity, attack frequency, and HDR; however, further studies are needed to shed light on the findings of the present study.

Introduction

Migraine is an intermittent neurovascular headache disorder that usually is characterized by recurrent headache, nausea, vomiting, sensitivity to light and sound, neck pain, muscle tension, photophobia, and phonophobia [1]. Migraine headaches are typically one-sided and throbbing. They last between 4 and 72 h [2]. This disorder is most prevalent in middle-aged individuals

This work was supported by the Food Security Research Center and Department of Community Nutrition, School of Nutrition & Food Science, Isfahan University of Medical Sciences, Isfahan, Iran (grant no. 392363).

OS, HMK, and MN contributed to the concept, design, data collection, and drafting of the manuscript. MN, MR, and MBB contributed to the statistical analysis and drafting of the manuscript. GA supervised the study. All authors read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

* Corresponding author. Tel.: +98 311 792 2658; fax: +98 311 668 2509.
E-mail address: omidsadeghi69@yahoo.com (O. Sadeghi).

http://dx.doi.org/10.1016/j.nut.2017.01.007
0899-9007/

and women [3]. The prevalence of migraine in Iranian adults is reported from 7.14% to 18.11% [4]. Based on International Headache Society (IHS) criteria, there are two major classes of migraine: migraine with aura (MA) and migraine without aura. These two subtypes have, to some extent, the same symptoms; however, 25% of patients with migraine perceive an aura, which is a transient disturbance in visual, sensory, language, or motor function and defined as a signal of headache occurrence [5].

Migraine headaches result in a substantial reduction in quality of life and have heavy costs for migraine sufferers [6]. Various drugs used to reduce migraine symptoms and frequency of migraine attacks often are expensive and have many side effects [7]. It has been shown that some nonpharmacologic therapies such as relaxation training, butterbur, vitamin D, riboflavin, magnesium, and coenzyme Q10 supplementation are effective for improving migraine symptoms [8–11]. Recently, it was reported that folic acid and pyridoxine supplementation can lessen migraine symptoms by affecting homocysteine levels [12,13]. In one study, folic acid and pyridoxine intake in combination with cobalamin decreased the severity and frequency of migraine attacks [12]; however, another study found that intake of these vitamins reduced the migraine severity but had no effects on frequency of attacks [13]. Earlier studies have mostly focused on combination effects of folic acid and pyridoxine but single effects of these vitamins have not been studied as frequently. Moreover, prior studies mostly have been confined to Western nations and data in this regard are scarce in Asian countries. Therefore, this study aimed to assess the effects of folic acid alone and in combination with pyridoxine on characteristics of migraine attacks in Iranian migraine patients.

Material and methods

Study design

This was a parallel, double-blind, randomized placebo-controlled trial with all those involved—investigator, patients, and the researcher who delivered the drug—being blinded to the therapeutic option. The trial was registered in the Iranian Registry of Clinical Trials.

The trial was approved by the Institutional Review Board and Ethics Committee of Isfahan University of Medical Sciences (Isfahan, Iran). This study followed declarations of Helsinki, and written consent was obtained from all patients, and verbal explanation about the research and assurance of confidentiality and anonymity was provided before the enrollment.

Participants

This study was performed in Khorshid and Emam Mosa Sadr clinics of Isfahan University of Medical Sciences, Isfahan, Islamic Republic of Iran, from January 8 through April 16, 2014. The study included individuals who were referred to recruitment centers who were between the ages of 18 and 65 y; had history of migraine for ›5 y; had a 1-y history of severe, recurrent, and long-lasting migraine attacks (at least one attack per mo lasting 4 h); had a current diagnosis of MA approved by an experienced neurologist according to IHS (third revision) beta diagnostic criteria [5]; and were receiving routine treatment of migraine. We selected patients with MA based on previous studies [14,15] reporting that homocysteine levels are high in these patients. *Migraine attack* was defined as one-sided headache with aura in each situation in a day. Individuals were excluded if they were taking vitamin supplements or had clinical cardiovascular diseases, previous stroke, and chronic renal failure, which may increase homocysteine levels.

Sample size was determined by formula suggested for randomized clinical trials, with type I error of 5%, type II error of 20%, study power of 80%, and serum level of homocysteine as a key variable. The number of needed samples was calculated as 30 participants. To get a more confident result with a 20% dropout rate, we considered 34 patients in each group.

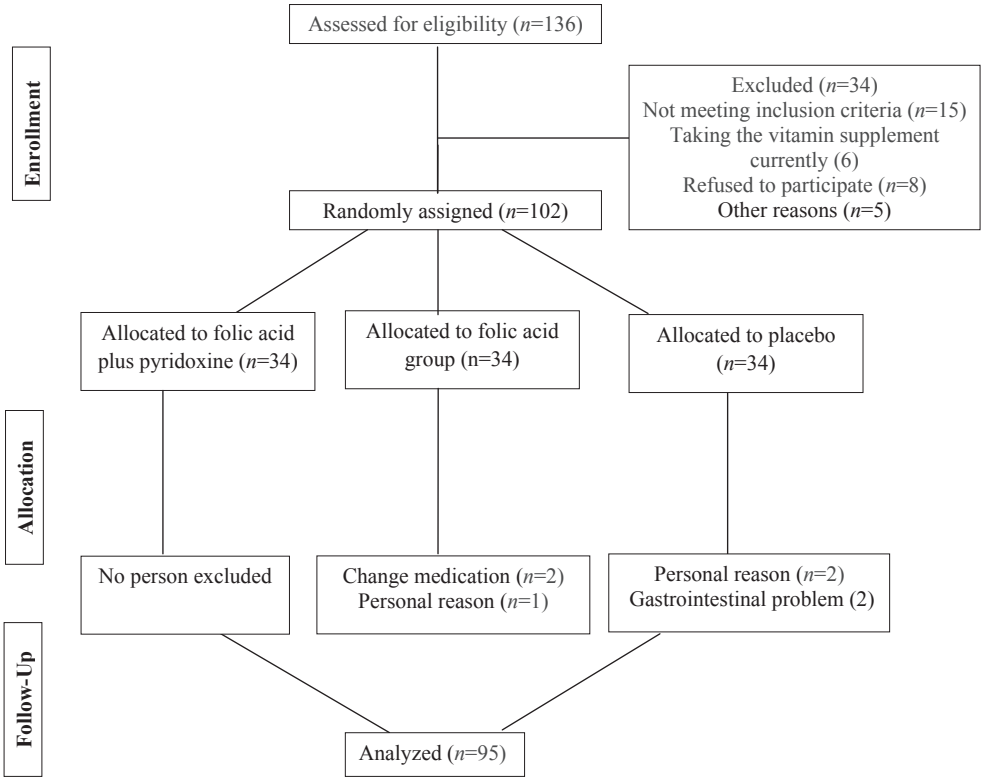

Fig. 1. Summary of patient follow-up.