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ORIGINAL ARTICLE

Role of Magnesium in Migraine Prophylaxis among Females of Reproductive Age: A Safer Alternative to Teratogenic Agents

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ABSTRACT

Background: Migraine is a prevalent neurological disorder, particularly affecting females of reproductive age, and is often associated with significant disability and reduced quality of life.

Objective: To evaluate the effectiveness of magnesium supplementation in reducing the frequency, severity, and duration of migraines, as well as its impact on quality of life and medication usage, in females of reproductive age.

Methodology: This was a prospective observational study conducted at the Department of Neurology, Sialkot Medical College Sialkot from 1st February 2023 to 31st October 2023. A total of 175 females aged 18–45 years, diagnosed with episodic or chronic migraines, were enrolled. Participants self-selected their treatment regimen: 98 participants chose magnesium supplementation (Magnesium Group), while 77 participants either did not take magnesium or opted for other treatments (Non-Magnesium Group).

Results: At 6 months, the magnesium group showed significant reductions in migraine (6.4±2.3 to 3.2±1.8 days/month, p<0.01), severity (7.4±1.2 to 4.1±1.5, p<0.01), and duration (4.3±1.5 to 2.5±1.2 hours, p<0.01). The non-magnesium group showed smaller reductions in these outcomes. Additionally, the magnesium group reduced rescue medication usage (3.8±2.1 to 1.5±1.2 doses/month, p<0.01) and experienced significant improvement in quality of life (MIDAS score 28.3±12.1 to 15.4±9.3, p<0.01). Adverse effects were mild and limited to gastrointestinal discomfort in 12% of participants in the Magnesium Group, with no severe adverse events.

Conclusion: Magnesium supplementation significantly reduced migraine frequency, severity, and duration, and improved quality of life in females of reproductive age. The findings support magnesium as an effective, well-tolerated strategy for migraine prophylaxis.

Keywords: Role, Magnesium, Migraine Prophylaxis, Females, Reproductive age

INTRODUCTION

Magnesium is a crucial mineral involved in more than 300 enzymatic reactions within the human body, contributing to diverse physiological functions, including muscle function, protein synthesis, blood glucose regulation, and nerve function.[1] When considering magnesium's potential for migraine prophylaxis, its capacity to regulate neuronal excitability and influence vascular tone stands out among its many functions. Given the multifactorial nature of migraines, with underlying vascular, neural, and metabolic dysfunctions, magnesium has emerged as a promising therapeutic agent to mitigate the frequency and severity of these debilitating attacks, particularly in women of reproductive age.[2] Magnesium has been shown to have significant effects on brain metabolism, ion channels, and neurotransmitter regulation in migraine pathophysiology research. One of the key mechanisms through which magnesium may exert its effect in migraine prevention is through the regulation of calcium influx into nerve cells. Neurotransmitters such as glutamate and substance P, which are involved in pain pathways, are primarily released through calcium channels.[3]

Magnesium acts as a natural calcium antagonist, preventing excessive calcium influx into cells, which may lead to neurovascular hyperexcitability, the hallmark of a migraine attack. Magnesium can prevent or lessen the severity of migraine attacks by balancing calcium levels.[4] Researchers have also investigated how magnesium affects serotonin receptors in the brain. Serotonin, a neurotransmitter involved in mood regulation and vascular tone, is known to play a central role in migraine pathophysiology.[5] Magnesium has been shown to affects erotonergic transmission, which may lessen the vasodilation and vasoconstriction in the blood vessels that are linked to migraines. Moreover, magnesium has been shown to enhance nitric oxide (NO) production, which is known to relax blood vessels and improve blood flow, potentially mitigating the vascular constriction and dilation that contribute to migraine attacks. The frequency and severity of migraines can be affected by changes in sex hormones like estrogen and progesterone in women of reproductive age.[6]

Estrogen, in particular, has been implicated in the pathophysiology of menstrual migraines. Lower magnesium levels may be a factor in the onset of migraines, according to studies, particularly during the luteal phase of the menstrual cycle, when estrogen levels are at their highest. It is hypothesized that the hormonal changes associated with menstruation may exacerbate magnesium deficiency, thereby increasing migraine susceptibility.[7] This makes magnesium supplementation particularly relevant for this population, as it may help alleviate symptoms or prevent the onset of attacks and benefits of magnesium supplementation in migraine prophylaxis.[8]

Magnesium supplementation significantly reduced the frequency and severity of migraine attacks in adult men and women, according to a review of randomized control trials. One of the most commonly used forms of magnesium for migraine prevention is magnesium oxide, due to its high bioavailability and ease of administration. The frequency of migraines can be significantly reduced with minimal side effects at 360 mg per day.[9] Numerous studies have demonstrated that taking magnesium supplements significantly reduces the frequency of attacks in women who experience menstrual migraines. This is in addition to the well-documented effectiveness of magnesium in the prevention of migraines related to menstruation.[10] Magnesium may be beneficial to women with chronic or episodic migraines in addition to its role in menstrual migraines. A study examining magnesium levels in patients with chronic migraine revealed that many had suboptimal levels of magnesium, suggesting that supplementation may help correct this deficiency and alleviate migraine symptoms.[11] Magnesium supplementation was well-tolerated and had no significant adverse effects, making it an attractive option for long-term management. In addition, magnesium supplementation has been compared to conventional migraine treatments like antidepressants, beta-blockers, and anticonvulsants.[12] Although these medications are effective, they frequently come with a

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variety of side effects, such as weight gain, dizziness, and cognitive problems, which can have a significant impact on a woman's quality of life. In contrast, magnesium has a favorable safety profile, with side effects generally limited to gastrointestinal discomfort at high doses. As a result, many women prefer magnesium supplementation as a first-line or adjunctive treatment, particularly when seeking natural or complementary therapies.[13]

MATERIALS AND METHODS

This was a prospective observational study conducted at the Department of Neurology, Sialkot Medical College Sialkot from 1st February 2023 to 31st October 2023. A total of 175 females of reproductive age (18-45 years) diagnosed with episodic or chronic migraines, according to the International Classification of Headache Disorders (ICHD-3) were enrolled. All Female participants aged 18 to 45 years, diagnosis of episodic or chronic migraines as defined by the ICHD-3, regular menstrual cycles (between 21-35 days) or postmenopausal status, no history of major chronic diseases (e.g., diabetes, cardiovascular disease), no history of magnesium supplementation within the past 6 months and give the written informed consent were included. Those females with any major systemic illness such as severe liver or renal dysfunction, pregnant or breastfeeding women, history of allergic reactions to magnesium or any of its compounds, individuals on medications that interfere with magnesium absorption or metabolism (e.g., diuretics) and history of secondary headaches or any neurological disorder other than migraines were excluded. Participants were observed for 6 months, and their migraine frequency, severity, and other relevant data were tracked. Participants were not randomly assigned to any treatment group; instead, they were grouped based on their choice of treatment.

A total of 175 females diagnosed with episodic or chronic migraines, were enrolled. They were divided in two groups. Magnesium group comprised 98 participants who opted to self-administer magnesium supplementation (360 mg/day) and non-magnesium group comprised 77 participants who either did not take magnesium supplementation or chose other forms of migraine management. Participants were required to maintain daily headache diaries, noting the frequency, severity, and duration of each migraine episode. They were also instructed to record any medications taken for migraine relief. The MIDAS score was used to measure quality of life as well as changes in migraine frequency, severity, and duration at regular intervals, which were every three months. The researchers were able to monitor and record the progression of migraines in the context of magnesium supplementation or other self-chosen treatments thanks to this longitudinal approach. The change in the frequency of migraine attacks over the course of six months was the primary outcome measure of the study. The Visual Analog Scale (VAS) was used to measure the severity of the migraines, with scores ranging from 0 (no pain) to 10 (severe pain) as secondary outcomes. In their headache diaries, participants recorded the duration of each migraine episode and the number of rescue medications taken each month. The impact of migraines on participants' daily lives was assessed using the Migraine Disability Assessment (MIDAS) questionnaire at baseline and during follow-up visits. The data was analyzed using SPSS-26.0. Statistical significance was set at a p-value of less than 0.05.

RESULTS

The average age in both groups was 31.2±6.5 years in magnesium group and 30.8±6.2 years in non-magnesium group. The mean migraine was also similar between the groups at baseline, in the magnesium group was 6.4±2.3 days per month and the non-magnesium group was 6.8±2.5 days per month (Table 1).

In terms of migraine at 6 months, the magnesium group showed a statistically significant reduction from 6.4±2.3 days per month at baseline to 3.2±1.8 days per month at 6 months ($p<0.01$), reflecting a more than 50% decrease in migraine. This reduction is highly significant and suggests that magnesium supplementation plays an effective role in reducing the occurrence of migraines. On the other hand, the non-magnesium group showed a smaller reduction, from 6.8±2.5 days per month at baseline to 5.7±2.4 days per month at 6 months ($p<0.05$). The Magnesium Group also experienced a substantial reduction in migraine severity, with VAS scores decreasing from 7.4±1.2 at baseline to 4.1±1.5 at 6 months ($p<0.01$). This significant reduction in severity highlights the potential of magnesium to alleviate the intensity of migraines. Similarly, the non-magnesium group experienced a reduction in VAS score from 7.6±1.3 at baseline to 5.2±1.6 at 6 months ($p<0.05$) [Table 2].

The magnesium group demonstrated a significant reduction in the duration of migraine episodes, from 4.3±1.5 hours at baseline to 2.5±1.2 hours at 6 months ($p<0.01$). This reduction of nearly 40% in the duration of migraine attacks further emphasizes the potential benefits of magnesium supplementation in controlling not only the frequency and severity of migraines but also their duration. Conversely, the non-magnesium group showed a smaller reduction in migraine duration, from 4.5±1.6 hours at baseline to 3.8±1.4 hours at 6 months ($p<0.05$), reflecting a modest improvement in episode length. The magnesium group exhibited a marked decrease in the use of rescue medications, from 3.8±2.1 doses per month at baseline to 1.5±1.2 doses per month at 6 months ($p<0.01$) [Table 3].

According to quality of life, as measured by the MIDAS score, the magnesium group saw a significant improvement, with the score decreasing from 28.3±12.1 at baseline to 15.4±9.3 at 6 months ($p<0.01$). This reflects a considerable reduction in migraine-related disability and an improvement in daily functioning. Similarly, the non-magnesium group experienced an improvement in MIDAS score, from 29.1±13.4 at baseline to 21.2±11.2 at 6 months ($p<0.05$), although the change was less pronounced compared to the magnesium group (Table 4, Fig. 1).

Table 1: Baseline characteristics of study participants

Variable	Magnesium group (n = 98)	Non-magnesium group (n = 77)
Age (years)	31.2±6.5	30.8±6.2
Migraine (days/month)	6.4±2.3	6.8±2.5
Migraine severity (VAS)	7.4±1.2	7.6±1.3
Migraine duration (hours)	4.3±1.5	4.5±1.6
Rescue medication (doses/month)	3.8±2.1	4.1±2.4
MIDAS score	28.3±12.1	29.1±13.4

Table 2: Comparison of migraine at baseline and 6 months

Group	Baseline (MIDAS Score)	6 Months (MIDAS Score)	p-value
Magnesium group	6.4±2.3	3.2±1.8	<0.01
Non-magnesium group	6.8±2.5	5.7±2.4	<0.05
Migraine severity (VAS)			
Magnesium group	7.4±1.2	4.1±1.5	<0.01
Non-magnesium group	7.6±1.3	5.2±1.6	<0.05

Table 3: Comparison duration of migraine at baseline and 6 months

Group	Baseline (MIDAS Score)	6 Months (MIDAS Score)	p-value
Magnesium group	4.3±1.5	2.5±1.2	<0.01
Non-magnesium group	4.5±1.6	3.8±1.4	<0.05
Rescue medication usage			
Magnesium group	3.8±2.1	1.5±1.2	<0.01
Non-magnesium group	4.1±2.4	2.9±2.3	<0.05

Table 4: Comparison of quality of life (MIDAS) at baseline and 6 months

Group	Baseline (MIDAS Score)	6 Months (MIDAS Score)	p-value
Magnesium group	28.3±12.1	15.4±9.3	<0.01
Non-magnesium group	29.1±13.4	21.2±11.2	<0.05

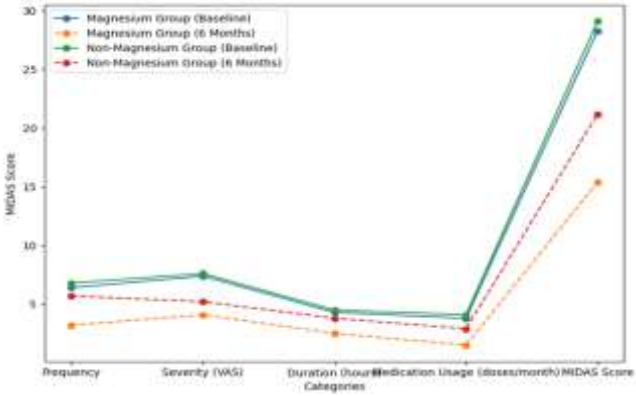

Fig. 1 Comparison of MIDAS core

DISCUSSION

The results of this study highlight the significant role of magnesium supplementation in the prophylaxis of migraines in females of reproductive age and found that magnesium supplementation led to a considerable reduction in migraine frequency, severity, and duration, as well as a reduction in the use of rescue medications. As indicated by the MIDAS score, there were also improvements in quality of life. Previous research has suggested that magnesium may help manage migraines, particularly in those with magnesium deficiency, which is common in chronic migraine sufferers. These findings are consistent with these findings. The significant reduction in migraine frequency among magnesium group participants is one of this study's most notable findings. The magnesium group saw a greater reduction in the number of migraine days per month (from 6.8 to 5.7 days per month) by more than 50%, while the non-magnesium group saw a smaller decrease. This decrease in the frequency of migraines is consistent with other studies that have shown that taking magnesium supplements can reduce the number of migraine attacks.[14] In a randomized controlled trial conducted by Ziaei et al[15] found that taking magnesium supplements significantly decreased the frequency of migraines in migraine sufferers who were experiencing migraines related to menstruation. Similarly, the decrease in migraine severity, measured by the Visual Analog Scale (VAS), was more pronounced in the magnesium group. Although the non-magnesium group also showed improvement, it was not as significant. These results suggest that magnesium supplementation may not only reduce the frequency of migraines but also mitigate the intensity of migraine attacks, providing both preventive and symptomatic relief. The exact mechanisms underlying this effect are thought to involve magnesium's role in regulating neurotransmitter release, including serotonin, and its ability to stabilize blood vessels by reducing vasospasm and vasodilation, both of which are implicated in migraine pathophysiology. Participants in the magnesium group showed a significant decrease in the average duration of their migraines, from 4.3 hours at the beginning to 2.5 hours after six months. Because prolonged migraine attacks are frequently linked to increased disability and a greater reliance on acute pain medications, this reduction in duration is especially significant.[16] In contrast, the non-magnesium group only observed a modest reduction in the duration of migraines, indicating that magnesium may play a unique role in both reducing the duration of pain after an episode and preventing migraines altogether. A further benefit of magnesium supplementation was the reduction in the use of rescue medications. While the non-magnesium group only saw a 30% decrease (from 4.1 to 2.9 doses) in rescue medication use per month, the magnesium group saw a reduction of more than 60% (from 3.8 to 1.5 doses).[17] This reduction in medication usage is of particular clinical significance as it may lessen the potential for medication-overuse headaches, a common problem among migraine sufferers who frequently use pain-relief medications.[18] The significant difference in rescue medication usage between the two groups supports the hypothesis that magnesium supplementation can provide a degree of migraine relief that reduces the need for acute medication.

Quality of life was assessed using the MIDAS score, and the results showed a marked improvement in the Magnesium Group, with the MIDAS score decreasing from 28.3 to 15.4, reflecting a reduction in migraine-related disability. Other studies have shown that taking magnesium supplements can reduce the frequency and severity of migraine attacks, which in turn can improve daily functioning and improve quality of life.[19] The MIDAS score for the Non-Magnesium Group also decreased, but the change was less significant, indicating that magnesium supplementation may be more effective in improving the quality of life for those suffering from chronic or episodic migraines. The findings of this study are in line with the growing body of evidence supporting the role of magnesium in migraine prophylaxis.[20]

There are several limitations that should be acknowledged. First, the lack of randomization and blinding introduces the possibility of selection bias, as participants self-selected their treatment regimen. This means that the results may not be fully attributable to magnesium supplementation alone, as other factors (e.g., lifestyle changes, concurrent treatments) could have influenced the outcomes. Additionally, the absence of a placebo group limits our ability to draw definitive conclusions about the effectiveness of magnesium in comparison to a non-active treatment.

CONCLUSION

Magnesium supplementation (360 mg/day) significantly reduces the frequency, severity, and duration of migraines in females of reproductive age. The study demonstrated that magnesium supplementation led to substantial improvements in migraine-related outcomes, including a decrease in the use of rescue medications and better quality of life, as reflected by the MIDAS score.

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