

The Effects of Ingesting Magnesium during a Migraine

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### Abstract

The study design was a systematic literature search. The databases searched included the Medline, CINAHL, and Cochrane Central Register of Controlled Trails and Business Source Complete through the interface EBSCO HOST. There were fourteen full text articles included in the review and two abstracts where, the full text was not available, that were not included. The findings of the literature review indicate that serum magnesium in migraine patients was shown to be notably lower in numerous case-control studies compared to the healthy control patients and the level was related to the frequency of migraine attacks shown in Table 1. While testing magnesium serum levels may be a helpful indicator, it has limited results due to the fact that the test is not considered very accurate because levels in the blood stream may only represent 2% of total body stores, while the rest of body's magnesium is stored in bone or intracellularly (Tepper, D. 2013). The use of Mg for treatment has shown positive results, relatively low cost, minimal side effects, and has a safe pregnancy rating.

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### The Effects of Ingesting Magnesium during a Migraine

Magnesium (Mg) is the second most abundant cation in the body, essential in many intracellular processes, and plays a significant role in migraine pathogenesis (Mauskop & Varughese, 2012). Mg deficiency has several features which are relevant in the understanding of migraine pathophysiology such as neurotransmitter release, platelet aggregation, and vasoconstriction (Choi & Pamar, 2014). It is thought that during a migraine, those affected excrete an excessive amount of Mg caused from stress through urination and resulting in hypomagnesemia, an abnormally low level of Mg in the blood (Choi & Pamar, 2014). Hypomagnesemia seems more common resulting from an inadequate intake of Mg due to refined and processed food being consumed (Teigen & Boes, 2015). There are a number of experimental studies that have implicated the importance of Mg in the pathophysiology of migraines (Pardutz, A. Vecsei, L. 2012). Of total body Mg, 67% is stored in the bone and 31% is found intracellularly and only 2% is located in the extracellular space. Blood tests are insufficient for obtaining a true assessment of Mg total body store (Choi & Pamar, 2014). The question remains, does ingestion of Mg during a migraine reduce the effects or duration?

## Methods

This systematic literature review was completed in September 2015 using the abstract database platform of EBSCOHost to search Medline, CINAHL, and Cochrane Central Register of Controlled Trials. All databases were searched using the keywords ‘magnesium’, ‘migraine’, and ‘humans’. Exclusion criteria were if papers did not meet the criteria of assessing or utilizing magnesium in people who experience migraine. Steps included title review, abstract review and full text article review. Two independent reviewers, C. Harrison and K. Carlisle, identified articles for eligibility and abstracted information on patients, study design, outcomes, key results and study limitations.

## Results

After the search on the electronically indexed databases using keywords ‘magnesium’, ‘migraine’ and ‘humans’ fourteen full text articles were found to meet the criteria in obtaining information about the correlation between low serum Mg levels and the frequency and/or duration of migraine attacks. There were two abstracts where the full texts were not available to be reviewed that were not included. Shown below in Figure 1 are the outlined steps.

Of the fourteen articles that met the criteria, five were randomized controlled trials, three were case-control studies, one was a single center study, one was a retrospective medical record review, one was an expert review, one was an evidence base review, one was a narrative review, and one was a pilot/prospective study. Shown in Table 1 are the reviewed article summaries.

In the experimental trials that these articles included are based on 1848 patients being studied on the effects of Mg given either orally or intravenously to male and female adults, and adolescents. Only one double-blind randomized clinical trial of intravenous Mg for acute

migraine in adults showed that the reduction of pain relief was 7% lower in the Mg group compared with the control group (Choi & Parmar, 2014). Serum Mg in migraine patients was shown to be notably lower in numerous case-control studies compared to healthy patients and was related to the frequency of migraine attacks. While this may be a helpful indicator it is limited due to the fact that the serum test is not considered very accurate due to the fact that levels in the blood stream may represent only 2% of total body stores, with the rest of Mg stored in the bones or within cells (Tepper, 2013). Red blood cells Mg levels are more reliable but the test can be very expensive.

Figure 1:

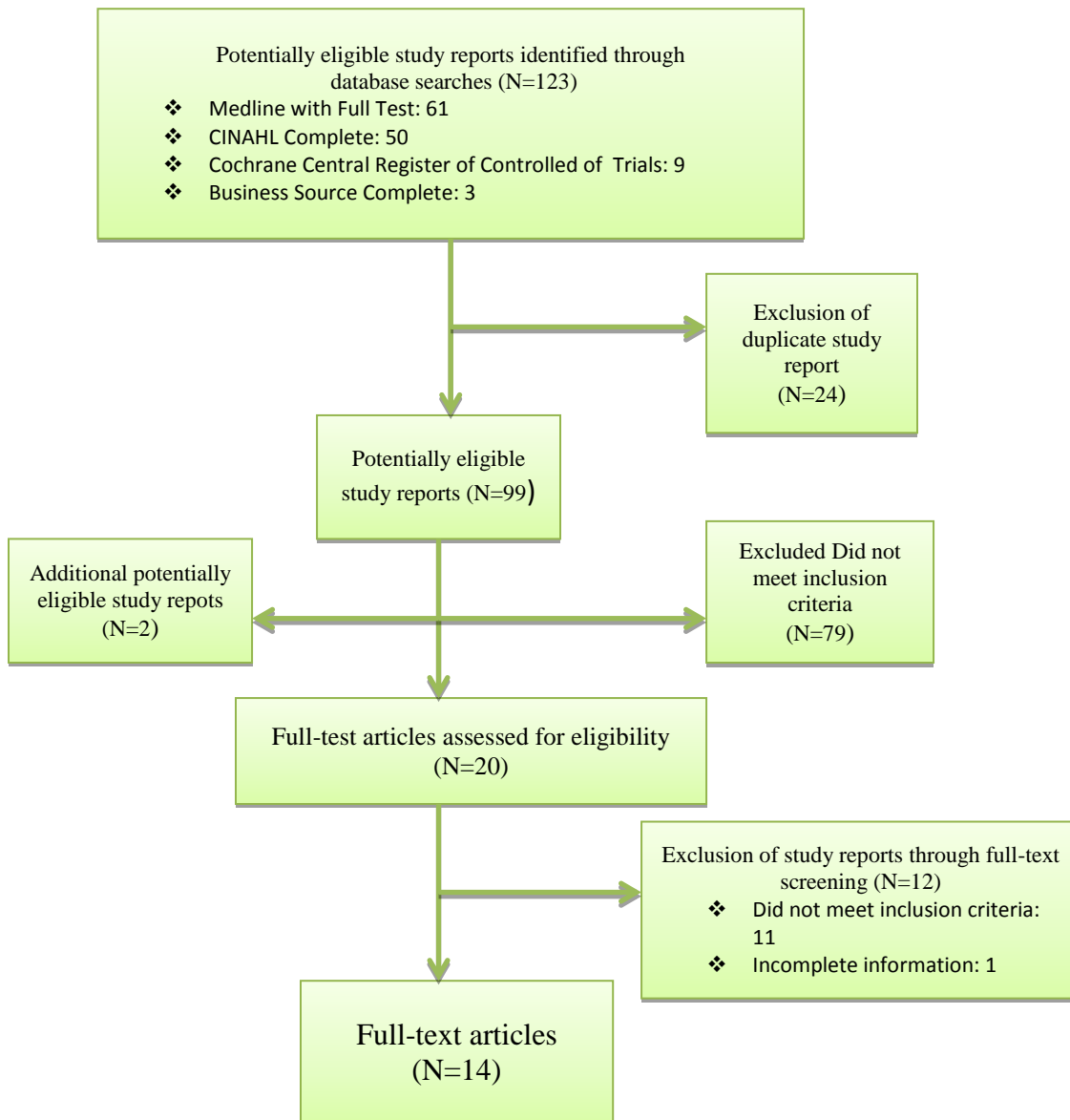


Table 1: Summary of Articles on Mg and Migraines Reviewed

<b>Authors</b>	<b>Type of Study</b>	<b>Numbers of Subjects</b>	<b>Outcomes / Measures</b>	<b>Findings</b>	<b>Limitations</b>
Bigal, M., Rapoport, A., Sheftell, F., & Tepper, S.	Placebo control study	81 patients	Attack frequency was reduce by 41.6%	reduction of at least 50% in intensity or duration of migraine attacks in hours at the end of the 12 weeks of treatment compared to baseline	69 patients were dropped from the study due to severe diarrhea and may not have absorb the Mg to obtain proper result
Choi, H. & Parmar, N.	Meta-analysis Double-blind RCT of IV Mg for acute migraine in adults	5 articles 295 patients were eligible for the meta-analysis	Experienced relief 30min following treatment was 7% lower in Mg group and 37% greater side-effects than in control group	Failed to show the significant beneficial effects with use of IV Mg and reduction of pain in migraineurs	Sample sizes, randomization method, clear inclusion criteria, placebo and follow-up Most studies were underpowered to detect primary and secondary outcomes, the study populations were the convenience sampling and some did not report inclusion and exclusion criteria in sufficient detail.
Gallelli, L., Avenoso, T., Falcone, D., Palleria, C., Peltrone, F., Esposito, M., Guidetti, V.	Single blind, balanced-recruitment, parallel-group, single-center study of outpatient children	160 children ages 5-16	Acetaminophen with Mg reduced significantly pain-relief timing but not for ibuprophen	Pain relief timing when from 48.5 minutes reduce to 35.5 minutes	Short time of pharmacological treatment, the absence of chronic migraine, the typology of study and the absence of randomization
Gertsch, E., Loharuka, S., Wolter-Warmerdam, K., Tong, S., Kempe, A., & Kedia, S.	Retrospective medical record review	20 patients rages 13-18 years old	7 patients (35%) showed favorable response with no major effects	Children with acute headaches experienced minimal side effects when infuse with 20mg/kg IV Mg	Inability to examine recurrence rate of headache symptoms within 24 hours, non-standardized pain assessments, and potential reported bias
Mauskop, A. & Varughese, J.	Review Double-blind, placebo-controlled randomized trial	43 References 24 women with menstrual migraines	Keywords: migraine, aura, deficiency, intravenous and Mg 400mg Mg Reduction of the frequency of attacks in the Mg group (41.6%) was much better than the placebo group	A daily dose of 400mg of Mg could benefit up to 50% of migraine sufferers pain, if 1 <sup>st</sup> dose doesn't work you can double it Up to 50% of patients with migraines could potentially benefit from Mg treatment	Mg decreases the effect of metoclopramide Increased Mg levels can cause a side-effect of diarrhea and abdominal pain Serum levels are entirely inaccurate while RBC Mg is more reliable, both are mostly useful if they show a deficiency
Pardutz, A. & Vecsei, L.	Double-blind, placebo-control clinical trials with Mg <sup>2+</sup> and	Migraine prophylaxis 337 patients and migraine attack	For prophylaxis patients the overall results was a decrease of volume of attack, duration and	Effective in migraine therapy but since far more powerful drugs available definitely not needed to	Relatively sparse number of relevant clinical studies has not yielded sufficient

	migraine prophylaxis and migraine attack	90 patients	intensity and for migraine attack patients ~50% success rate with 1000mg IV Mg <sup>2+</sup>	be use by every migraineur	evidence
Samaie, A., Asghari, N., Ghorbani, R., & Arda, J.	Case control study	100 patients: 50 International Headache Society (IHS) and 50 control	Measured serum Mg levels 1.86 +- .41mg/dL vs. 2.10 +- .23mg/dL by xylidyl blue method Serum total Mg level was notably lower in the migraine group compared to control group	Averages of Mg levels significantly reduced in patients with migraine compared to healthy control group Serum Mg level might predict migraine attacks and its symptoms as well as might help physicians to determine optimal dose	In the group with migraines, there was not significant difference found in serum Mg levels within and between attacks Absence of randomization
Shahrami, A., Assarzagdegan, F., Hatamabadi, H., Asgarzadeh, M., Sarehbandi, B., & Asgarzadeh, S.	Clinical double-blind randomized	70 adults from International Classification of Headache Disorders (ICHD)	1g/100mL Mg/saline vs. 8mg/10mg/100mL dexamethasone/ metoclopramide/ saline Significant decrease in pain severity at 20-min interval from 8.0 to 5.2	10-scale standard numeric rating scale (NPS) Data at 20min 35% vs. 9.8% /1hr 71.25% vs. 26.8% /2hr 91.75% vs. 69.5% Mg was more effective in decreasing pain severity compared to treatment of dexamethasone/metoclopramide	Short follow-up time, no placebo group, dexamethasone might decrease metoclopramide effects
Sprouse-Blum, A., & Gogineni, A.	Narrative Review with Double-blind RCT	4 References 81 patients	Prophylaxis with 600mg oral Mg oxide a day slightly decreases frequency and severity of migraines	Slightly larger decrease in migraineur. 42% to 16% and 7.6 to 4.0 compared to 7 to 7 (n/c)	No correlation between prophylaxis levels and attack frequency.
Sun-Edelstein, C., & Mauskop, A.	Expert review	134 references	400mg of chelated Mg, Mg oxide or slow-release Mg	Recommend in patents with symptoms suggestive of hypomagnesemia (migraine headache, premenstrual syndrome, cold extremities and leg or foot muscle cramps)	Mauskop, A. is the inventor of Migralex
Sun-Edelstein, C., & Mauskop, A.	Pilot Study and Prospective Study	Pilot Study 40 patients and prospective 270 women patients	In the pilot study 86% of patients with low serum Mg had pain relief and for the prospective study 45% of the women had low serum Mg during menstrual attacks	Low ionized Mg in migraine patients improved symptoms after two weeks trial of drinking mineral water containing Mg	Future trials should focus on patients with deficiencies and ionized or red blood cell Mg
Talebi, M., Savadi-Oskouei, D., Farhoudi, M., Mohammadzade, S., Ghaemmaghami hezaveh, S., Hasani, A., & Hamdi, A.	Case control study	140 migraine patients and 140 control patients	Of the migraine group 40 patients had aura and 100 did not, average serum levels were 26.14+-10.31 significantly lower than the control at 31.09+-4.32	No significant difference between the mean level of serum Mg in patients with and without aura, however, there was a significant linear relationship between the amount of serum Mg and frequency of headache Highest relationship was between low Mg level and frequency of headache therefore Mg	Mg serum levels were only measured headache free, limited to middle age patients with female dominance



				prophylactic treatment is recommended	
Teigen, L., & Boes, C.	Evidence-based review	76 references Mg assessment in migraine studies(16), Mg intervention trials (4), & migraine prevention therapies	Outcomes results were mixed ranging from Mg serum levels were not significantly different to RBC levels were significantly lower in migraine group	With limited evidence, increasing the dietary intake of Mg offers an alternative solution than supplementation for migraine prophylaxis willing to make lifestyle changes.	Limited research and evidence on oral Mg intake
Tepper, D.	Narrative review	n/a	Mg oxide effective dosage 400 to 500mg/day or Mg sulfate intravenously 1 to 2 grams	Consider using Mg as a prevented strategy to reduce the frequency and or severity of migraines	No references given

## Discussion

This review identified a wide variety of results when it came to using Mg for prophylactic and/or treatment of migraines. Ingestion of Mg during a migraine to reduce the effects has a plausible hypothesis. Mg can affect both regulation of blood flow and neural function – both of which are physiological factors important in migraines. Studies taken have theorized that migraineurs have lower brain Mg during attacks and may be Mg deficient. Mg deficiency may also be relative to females suffering from menstrual migraines. While there was no true evidence to show that Mg can prevent migraine attacks, taking 400mg of Mg oxide can help decrease frequency of attacks and decrease the duration (Sun-Edelstein, C., & Mauskop, A. 2009). Intravenous Mg sulfate showed significant improvement in the treatment of acute migraine attacks in emergency room studies (Pardutz, A. & Vecsei, L. 2012). Mg therapy has shown positive results, has a relative low cost, minimal side effects, and a safe pregnancy rating this review supports the use of Mg for prevention and treatment of migraines. This review did not find clear evidence to determine if Mg therapy was effective in prevention of migraines when given prophylactically, but most studies showed about a 50% success rate at decreasing migraine attack frequency and/or decreasing pain-relief timing (Mauskop. & Varughese, 2012). Since there is still much to be learned about Mg therapy it cannot be relied upon as a first-line therapy to more well-documented pharmaceuticals used for migraine therapy, however can be useful as adjunct therapy and for patients looking to use more natural alternatives.

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