

Effects of Magnetrex[®]

– Magnesium, Taurine, Citrus sinensis and Vitamin B6 – on Muscle Cramps and Anxiety in an Adult Population: A Retrospective Chart Review

ABSTRACT

INTRODUCTION

The development of effective interventions, including pharmacotherapy and dietary supplements, to alleviate symptoms of stress, anxiety, and related physiological discomfort such as cramps has gained considerable interest in recent years. In this context, several components like magnesium, taurine, Citrus sinensis, and vitamin B6 have individually shown promising effects on stress reduction, anxiety management and associated cramp reduction.

OBJECTIVES

To evaluate the potential effects of supplementation with Magnetrex[®] (Surveal Pharma), a combination of magnesium, taurine, Citrus sinensis, and vitamin B6, on signs and symptoms of stress and anxiety in adults as well as muscle cramps.

METHODS

A retrospective chart review design was employed among adults in Malta initiated on Magnetrex[®]. Data were extracted from medical records and Perceived Stress Scale (PSS) and Hamilton Anxiety Rating Scale (HAM-A) scales which were used to assess stress and anxiety symptoms,

respectively, at baseline and at four-month follow-up. Changes in stress symptoms, anxiety, and muscle cramps were analyzed, and linear mixed models adjusted for relevant covariates were performed to test changes in PSS and HAM-A scales from baseline to follow-up.

RESULTS

This study included 57 subjects who initiated Magnetrex[®] supplementation. Our results showed significant improvements in various stress symptoms and a significant decrease in the PSS and HAM-A scales, indicating lower levels of stress and less severity of anxiety symptoms after four months of Magnetrex[®] supplementation. Improvement in muscle cramps was also reported.

CONCLUSIONS

The results of this study suggest that supplementation with Magnetrex[®] may be effective in improving mental conditions such as stress and anxiety, and in reducing muscle cramps.

KEYWORDS

Magnesium, Vitamin B6, Taurine, Citrus sinensis, Stress Management, Muscle Cramps.

INTRODUCTION

In 2019, mental disorders affected around 970 million individuals, with a global prevalence representing approximately one out of every eight people, with anxiety and depression ranking as the most prevalent conditions.¹ Significant prevention and management efforts have been investigated to reduce the burden of these mental health problems². In keeping with this, the last decade has seen an expansion of novel therapeutic options, including several mineral agents and herbal compounds, for the treatment of stress and anxiety-related symptoms³.

Notable new evidence highlights the potential benefits of vitamin B6 in managing stress and anxiety, including a large cross-sectional study that found higher vitamin B6 intake in anxious and depressed people was associated with a lower risk of depression and anxiety⁴. Another compound that has received a lot of attention is magnesium. Although the evidence remains inconclusive, a systematic review suggested that magnesium may be beneficial in the management of mild anxiety symptoms⁵. In more severely stressed individuals, the beneficial synergistic effect of magnesium and vitamin B6 supplementation on anxiety⁵

and stress^{6,7} has been demonstrated. Concerning muscle cramps, the efficacy of magnesium is controversial. Studies have shown that supplementation with specific magnesium salts was not effective in reducing cramps⁸⁻¹⁰, while others have found a significant reduction in cramps in pregnant women^{11,12}.

Within the context of the limited clinical studies available, *Citrus sinensis* and taurine have emerged as compounds with potential roles in stress and anxiety management and in improving energy levels. Taurine, with its antioxidant and anti-inflammatory effects in the central nervous system, plays a role there. It acts as a cytoprotectant against stress-induced neuronal damage and is well known for its energizing anti-fatigue properties¹³. However, only animal studies have demonstrated the efficacy of *Citrus sinensis* in alleviating depression-like symptoms^{14,15}.

The aim of this study is to evaluate the response to Magnetrex[®], a combination of magnesium, taurine, *Citrus sinensis* and vitamin B6, in improving symptoms of daily fatigue, apathy and lack of energy, muscle cramps including nocturnal ones, and anxiety in adults. By evaluating the response to Magnetrex[®], we aim to add to the growing body of evidence supporting the potential benefits of its components in stress and anxiety management.

METHODS

DESIGN AND SETTINGS

We conducted a retrospective chart review of patients attending a sample of general practitioners in Malta, who were initiated on Magnetrex[®] tablets, a combination of magnesium bisglycinate (441 mg), taurine (100 mg), *Citrus sinensis* (250 mg), and vitamin B6 (1.96 mg) per tablet, for the relief of stress symptoms and anxiety, between August 2020 and December 2022. A 30-month period was needed due to the fact that patient visits to general practitioners during COVID-19 decreased considerably. Data were extracted from patients' medical records at a baseline time point corresponding to the initial visit and at a follow-up time point four months after baseline.

DATA COLLECTION

Data collection was sourced from medical records of patients 18 years of age or older who had reported symptoms of daily stress such as fatigue, apathy, lack of energy, and generalized anxiety disorder, and pregnant women in the 2nd or 3rd trimester with sleeping difficulties, stress, anxiety, and muscle cramps. The data which was collected excluded patients who were taking other similar supplements, those receiving lithium for neurological treatment, and those in the first trimester of pregnancy.

DATA COLLECTION AND OUTCOME MEASURES

A convenience sample of 17 general practitioners practicing in Malta, whose practice utilized a system of patient medical records, was selected for this study. The physicians were informed of the purpose and the conduct of the study. Data from both the baseline and follow-up visits were extracted from patients' medical records and the data was used to compile electronic case report forms (e-CRF). e-CRFs were either compiled by the physicians in an anonymous manner or by a medical representative since some physicians opted to fill the CRF as a hard copy and give this to a medical representative in order for the data to be transferred to a soft copy. The hard copies filled by the physicians and handed to the medical representative were totally anonymous.

The baseline characteristics which were extracted from patients' medical records included age, sex, weight, height, occupation, tobacco smoking, alcohol consumption, current medication, and food supplement use including nutraceuticals, although not all medical records contained the required information. Patient medical history was also collected, such as pregnancy status, presence of cardiovascular disease, hypertension, diabetes, chronic kidney disease, cancer, if known, psychiatric disorder (general anxiety disorder or depression), and family history of psychiatric illness. The presence of stress signs and symptoms, including headache, tense muscle cramps, presence of muscle cramps including nocturnal ones, fatigue, anxiety/worry/phobias, difficulty falling asleep, irritability, outbursts of anger/hostility, boredom/depression, eating a lot or not enough, gastrointestinal symptoms (flatulence, cramps, diarrhoea, constipation), and any restlessness/tics/itching were collected at baseline and follow-up visits. Not every medical record contained the required information. Data from the use of two scales were collected at baseline and after four months of Magnetrex[®] supplementation: Perceived Stress Scale (PSS) and Hamilton Anxiety Rating Scale (HAM-A).

The PSS consists of 10 items and is used to measure participants' perceptions of stress. Each question has 5 response options depending on how often patients feel a certain way, ranging from "never" to "very often". The total score was calculated according to the official scoring system by summing across all items, which range from 0 to 40. Higher scores indicate higher levels of stress. The HAM-A scale was used to assess the severity of anxiety symptoms. It consists of 14 items scored on a scale from 0 "not present" to 4 "severe". The scores were summed to produce a total score ranging from 0 to 56, with higher scores representing more severe anxiety symptoms.

ETHICAL CONSIDERATIONS

The study was an observational analysis of pre-existing medical records and did not involve direct contact with participants. The participating physicians provided the anonymized patients' records from which data was extracted for the study. As a result, data collection did not require the study researchers to meet the patients in person.

STATISTICAL ANALYSIS

Baseline characteristics of patients were summarized using descriptive statistics, i.e., means and standard deviations (SD) for quantitative continuous variables and frequencies and percentages for categorical variables. Changes in the presence of stress signs and symptoms and the presence of muscle cramps at 4 months from baseline were assessed using the McNemar chi-square test. Two-tailed paired sample t-tests were used to compare changes from baseline for the PSS and HAM-A scales. Baseline to follow-up changes in PSS and HAM-A scores were assessed using linear mixed models adjusted for sex, concomitant medication, smoking, alcohol use, presence of other psychiatric illness (depression, anxiety), diabetes, and hypertension. A p-value less than 0.05 was considered statistically significant. All statistical analyses were performed with Stata v17.0 software.

RESULTS

PATIENT CHARACTERISTICS

A total of 57 subjects were reviewed, of which 32 (56.1%) were female. Table 1 shows the characteristics of the patients at baseline. The mean age was 50.4 (standard deviation [SD]=14.3) years, and the mean weight was 70.1 (SD=14.4) kg. Medication and dietary supplement use were reported by 38.6% and 24.6% of participants, respectively.

Five of the participants (8.8%) had cardiovascular disease, 16 (28.1%) had hypertension, and 4 (7%) had diabetes. While a large proportion of subjects (24.6%) had a psychiatric disorder including anxiety or depression, none had cancer or kidney disease (Table 2).

CHANGE IN STUDY OUTCOMES BETWEEN BASELINE AND FOLLOW-UP

Table 2 shows the changes in stress signs and symptoms, muscle cramps including nocturnal ones from the PSS and HAM-A scale results between the baseline visit and follow-up visit four months after initiation of Magnetrex® supplementation. There was a statistically significant improvement in all stress signs and symptoms compared to baseline, along with a statistically significant decrease in PSS from 17.7 ± 7.5 to 14.0 ± 6.3 and HAM-A from 12.0 ± 8.4 to 6.1 ± 16.0 scales, indicating lower levels

Table 1. Sociodemographic and lifestyle characteristics of patients (n=57).

	Mean	Standard deviation
Age (years)	50.4	14.3
Weight (kg)	70.1	14.4
Height (cm)	163.7	7.9
	Frequency	Percentage
Sex		
Women	32	56.1
Men	25	43.9
Pregnancy	1	1.8
Chronic medication use	22	38.6
Supplements use	14	24.6
Tobacco use	7	12.3
Alcohol consumption	7	12.3
Medical conditions		
History of coronary artery disease	5	8.8
Hypertension	16	28.1
Diabetes	4	7
Kidney Disease	0	0
Cancer	0	0
Psychiatric Disorders	14	24.6
Family history of psychiatric illness	0	0
Summary statistics are expressed as mean and standard deviation for continuous variables and as frequency and percentage for categorical variables.		

of stress and less severe anxiety symptoms, respectively, between baseline and follow-up.

After adjustment for sex, concomitant medication, smoking, alcohol use, presence of other psychiatric illness, diabetes, and hypertension, the linear mixed models showed a statistically significant decrease in mean PSS scale (coefficient = -3.7, $p < 0.001$, 95% CI: -5.2 to -2.2) and mean HAM-A scale (coefficient = -5.9, $p < 0.001$, 95% CI: -7.6 to -4.2) between baseline and follow-up (Table 3).

DISCUSSION

In this study, stress- and anxiety-related symptoms assessed by the PSS scale, and severity of anxiety symptoms assessed by HAM-A scale significantly improved after four months of Magnetrex® administration.

This is consistent with the results of several studies on the individual components of Magnetrex®. The observed reduction in stress and anxiety symptoms is consistent

Table 2. Signs and symptoms appearing at least once a day for patients initiated on Magnetrex[®] at baseline and 4-month follow-up.

	Baseline	Follow-up	P-value
	n (%)	n (%)	
Headache	11 (19)	4 (7)	<0.001
Fatigue	28 (49)	9 (16)	0.001
Anxiety and phobia	25 (44)	10 (18)	<0.001
Sleeping difficulties	13 (23)	4 (7)	<0.001
Irritability	13 (23)	7 (12)	<0.001
Anger and hostility	4 (7)	0 (0)	<0.001
Depression or boredom	3 (5)	2 (4)	<0.001
Irregular eating habits	6 (11)	5 (9)	<0.001
Gastrointestinal symptoms	4 (7)	2 (4)	<0.001
Restlessness, tics or itching	11 (19)	1 (2)	<0.001
Tense Muscles or cramps	26 (46)	3 (5)	<0.001
Presence of muscle cramps	22 (39)	11 (19)	<0.001
Night cramps (n=22)	11 (50.0)	1 (4.5)	<0.001
Intensity of cramps evaluated using NRS or FRS	3	0	
	Mean ± SD	Mean ± SD	
PSS Score ± SD	17.7 ± 7.5	14.0 ± 6.3	<0.001
HAM-A Score ± SD	12.0 ± 8.4	6.1 ± 16.0	<0.001

PSS: Perceived Stress Level; HAM-A: Hamilton Anxiety Rating Scale; NRS: Numerical Rating Scale; FRS: Faces Rating Scale; SD: Standard deviation.

with previous research suggesting the potential benefits of magnesium in the treatment of anxiety⁵, depression¹⁶, and stress⁶. Another study also showed that a reduction in HAM-A score in depressed patients was associated with higher levels of magnesium¹⁷, highlighting, along with our results, the impact of magnesium on stress and anxiety management.

A number of studies have found positive effects on measures of stress and anxiety following vitamin B6 supplementation, which actively relieves symptoms

Table 3. Linear mixed models for the change in PSS and HAM-A scores between baseline and after four months of Magnetrex[®] use.

	Coefficient	95% CI	P-value
PSS Score	-3.7	-5.2 to -2.2	<0.001*
HAM-A Score	-5.9	-7.6 to -4.2	0.010*

*models adjusted for sex, concomitant medications, smoking, alcohol, presence of other psychiatric illnesses, diabetes, and hypertension

associated with depression and anxiety^{4,18}. Our findings are consistent with these results and suggest that vitamin B6 was one of the main drivers of our results and provides a partial explanation for the effects that we found.

In this regard, several studies have previously demonstrated the synergistic effect of magnesium and vitamin B6 in reducing stress in a highly stressed population^{6,7}. While our results are consistent with this trend, measuring the exact magnitude of this synergistic effect remains challenging. In addition, this finding is consistent with the results of a study of subjects with chronic psychological stress and fatigue, which showed that supplementation with a combination of minerals and vitamins, including magnesium, taurine, vitamin B6, and other ingredients, resulted in significant improvements in subjectively perceived stress¹⁹.

While there is evidence that taurine and Citrus sinensis are effective in treating depression and anxiety-like symptoms in animals^{14,15,20-23}, to our knowledge, no studies have examined their effects on stress and anxiety in humans. Therefore, it is important to acknowledge that the effects observed in our study may be due to the interaction of the components of Magnetrex[®] rather than their individual efficacy. While the inclusion of taurine and Citrus sinensis in the formulation of Magnetrex[®] added unique insights to our study and to the evolving strategies and interventions for stress and anxiety management, the exact contribution of these compounds in the context of stress and anxiety relief warrants future investigation.

As discussed above, data on the role of magnesium in reducing cramps have shown inconsistencies. Our results support previous findings demonstrating the potential of magnesium in the treatment of muscle cramps. This discrepancy may be due to the different forms of magnesium used, the differential effect of magnesium in different populations, baseline magnesium levels, and potential interactions with other agents. The form of magnesium used in Magnetrex[®],

magnesium bisglycinate, offers several advantages in the administration of magnesium over other salts. Studies have demonstrated the high bioavailability and safety of magnesium bisglycinate and efficacy at lower doses, outperforming inorganic magnesium salts such as magnesium carbonate, oxide and sulphate, and some organic salts such as magnesium citrate or lactate in certain preparations. Magnesium absorption from magnesium bisglycinate was 2.3 times greater than from magnesium carbonate, 3.6 times greater than from magnesium sulfate, and 8.8 times greater than from magnesium oxide^{24,25}. This appears promising for the reduction of muscle cramps and increases the possibility of synergistic effects of magnesium, taurine, hesperidin, and vitamin B6 contributing to the observed improvements and physiological benefits of Magnetrex®.

LIMITATIONS

The main limitation of our study was the convenience sampling nature of physician recruitment which may have resulted in a non-representative sample of patients, limiting the generalizability of the results to the broader Maltese population. In addition, the lack of a control group and the lack of adjustment for other variables that were not collected in the study and that may be important to adjust for in the analysis, prevented us from distinguishing between the true effects of Magnetrex® and other potential factors that could affect stress, anxiety and muscle-related outcomes, such as diet and lifestyle changes, life events, and the presence of nutrient deficiencies or concomitant interventions given to patients at the same time as Magnetrex®. Another limitation of the study is the relatively short follow-up period of 4 months, which did not allow for seasonality to be taken into account when assessing changes in outcomes. Furthermore, considering that the study was retrospective, some data may not have been collected in its entirety, including baseline characteristics of patients, patient medical history and presenting ailments. Given these limitations, our findings are considered exploratory and require confirmation in appropriately designed randomized controlled trials.

CONCLUSION

In conclusion, the novelty of this study is the demonstration that a combination of chelated magnesium bisglycinate, taurine, Citrus sinensis, and vitamin B6 can have a positive synergistic effect in improving stress and anxiety-related symptoms and reducing cramps in adults. Therefore, this study suggests that Magnetrex® may be a suitable nutraceutical for improving mental wellbeing in selected patients suffering from anxiety and cramps.

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REFERENCES

1. Global Burden of Disease Study 2019. Institute for Health Metrics and Evaluation. Available from: <https://vizhub.healthdata.org/gbd-results>
2. Wainberg ML, Scorza P, Shultz JM, et al. Challenges and Opportunities in Global Mental Health: a Research-to-Practice Perspective. *Curr Psychiatry Rep* 2017;19(5):28.
3. Garakani A, Murrrough JW, Freire RC, et al. Pharmacotherapy of Anxiety Disorders: Current and Emerging Treatment Options. *Front Psychiatry* 2020;11:595584.
4. Kafeshani M, Feizi A, Esmailzadeh A, et al. Higher vitamin B6 intake is associated with lower depression and anxiety risk in women but not in men: A large cross-sectional study. *Int J Vitam Nutr Res Int Z Vitam-Ernahrungsforschung J Int Vitaminol Nutr* 2020;90(5-6):484-92.
5. Boyle NB, Lawton C, Dye L. The Effects of Magnesium Supplementation on Subjective Anxiety and Stress - A Systematic Review. *Nutrients* 2017;9(5):429.
6. Pouteau E, Kabir-Ahmadi M, Noah L, et al. Superiority of magnesium and vitamin B6 over magnesium alone on severe stress in healthy adults with low magnesemia: A randomized, single-blind clinical trial. *PLoS One* 2018;13(12):e0208454.
7. Noah L, Dye L, Bois De Fer B, et al. Effect of magnesium and vitamin B6 supplementation on mental health and quality of life in stressed healthy adults: Post-hoc analysis of a randomised controlled trial. *Stress Health* 2021;37(5):1000-9.
8. Garrison SR, Korownyk CS, Kolber MR, et al. Magnesium for skeletal muscle cramps. *Cochrane Database Syst Rev*. 2020;9(9):CD009402.
9. Moretti A. What is the role of magnesium for skeletal muscle cramps? A Cochrane Review summary with commentary. *J Musculoskelet Neuronal Interact* 2021;21(1):1-3.
10. Liu J, Song G, Zhao G, et al. Effect of oral magnesium supplementation for relieving leg cramps during pregnancy: A meta-analysis of randomized controlled trials. *Taiwan J Obstet Gynecol* 2021;60(4):609-14.
11. Barna O, Lohoida P, Holovchenko Y, et al. A randomized, double-blind, placebo-controlled, multicenter study assessing the efficacy of magnesium oxide monohydrate in the treatment of nocturnal leg cramps. *Nutr J* 2021;20(1):90.
12. Supakatisant C, Phupong V. Oral magnesium for relief in pregnancy-induced leg cramps: a randomised controlled trial. *Matern Child Nutr* 2012;11(2):139-45.
13. De Luca A, Pierno S, Camerino DC. Taurine: the appeal of a safe amino acid for skeletal muscle disorders. *J Transl Med* 2015;13:243.
14. Offor SJ, Orish CN, Frazzoli C, et al. Augmenting Clinical Interventions in Psychiatric Disorders: Systematic Review and Update on Nutrition. *Front Psychiatry* 2021;12:565583.
15. Zhang LL, Yang ZY, Fan G, et al. Antidepressant-like Effect of Citrus sinensis (L.) Osbeck Essential Oil and Its Main Component Limonene on Mice. *J Agric Food Chem* 2019;67(50):13817-28.
16. Botturi A, Ciappolino V, Delvecchio G, et al. The Role and the Effect of Magnesium in Mental Disorders: A Systematic Review. *Nutrients* 2020;12(6):1661.
17. Garalejić E, Bojović-Jović D, Damjanović A, et al. Hamilton anxiety scale (HAMA) in infertile women with endometriosis and its correlation with magnesium levels in peritoneal fluid. *Psychiatr Danub* 2010;22(1):64-7.
18. Field DT, Cracknell RO, Eastwood JR, S et al. High-dose Vitamin B6 supplementation reduces anxiety and strengthens visual surround suppression. *Hum Psychopharmacol* 2022;37(6):e2852.
19. Armbrorst D, Metzner C, Altheheld B, et al. Impact of a Specific Amino Acid Composition with Micronutrients on Well-Being in Subjects with Chronic Psychological Stress and Exhaustion Conditions: A Pilot Study. *Nutrients* 2018;10(5):551.
20. El Idrissi A, Boukarrou L, Heany W, et al. Effects of taurine on anxiety-like and locomotor behavior of mice. *Adv Exp Med Biol* 2009;643:207-15.
21. Wu GF, Ren S, Tang RY, et al. Antidepressant effect of taurine in chronic unpredictable mild stress-induced depressive rats. *Sci Rep* 2017;7:4989.
22. Zhu Y, Wang R, Fan Z, et al. Taurine Alleviates Chronic Social Defeat Stress-Induced Depression by Protecting Cortical Neurons from Dendritic Spine Loss. *Cell Mol Neurobiol* 2023;43(2):827-40.
23. Watanabe M, Ito T, Fukuda A. Effects of Taurine Depletion on Body Weight and Mouse Behavior during Development. *Metabolites* 2022;12(7):631.
24. Vynckier AK, Vanheule G, Vervaeke C, et al. Types of Magnesium Salt and Formulation Solubility that Determines Bioavailability of Magnesium Food Supplements. *J Nutr Food Sci* 2020;10:781.
25. Siebrecht S. Magnesium Bisglycinate as safe form for mineral supplementation in human nutrition. Online. 2013. Available from: <https://www.semanticscholar.org/paper/Magnesium-Bisglycinate-as-safe-form-for-mineral-in-Siebrecht/d3ec33570bc26330097284c53a4a5c3815be905>