GlaucoMag Study: Does Magnesium Improve Patients with Primary Open Angle Glaucoma (POAG)?

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ABSTRACT

Introduction: Primary open angle glaucoma (POAG) is a multi-factorial progressive optic neuropathy that results in gradual vision loss. Alongside an elevated intra ocular pressure (IOP), other factors influence the progression of retinal ganglion cells loss in POAG. Blood flow dysregulation and oxidative stress are believed to be important risk factors in the evolution of glaucomatous degenerative lesions. Magnesium is an essential cation for many reactions and enzyme activities in the human body. One of its crucial roles is vascular regulation and blood flow improvement by modifying endothelial function through endothelin (ET-1) and nitric oxide (NO) pathways. It is also considered as a neuro-protective molecule as it reduces the harmful effect of oxidative stress on retinal ganglion cells.

Objective: The objective of this study is to assess the impact of daily intake of Magnesium on the stabilization of the glaucomatous damages on optic nerve. Methods: It is a non-randomized monocentric clinical study. Patients having only POAG with an IOP values ≤ 19 mmHg and a visual acuity > to 5/10 were included. All patients had a daily supplementation of Magnesium for a period of at least 6 months each. All patients were assessed before the start of the study (T0), after 3 months of treatments (T1) and after 6 months of treatments (T2). At each visit, patients were given a full eye examination including IOP measures, perimetry, RNFL and GCC using OCT.

Results: 46 patients with a mean age of 54 years old and a mean IOP of 16 mmHg were included. At T1 and T2 the values of mean deviation have regressed compared to T0. The mean IOP have significantly lessened and the RNFL and GCC values on OCT were stabilized.

Conclusion: daily supplementation of Magnesium in patients with POAG has shown to be of great help on reducing the rate of progression of glaucomatous functional damage, therefore improving visual function and patients’ quality of life.

Keywords: Angle, Intraocular pressure, Glaucoma, Magnesium, Treatment.

I. INTRODUCTION

Primary open angle glaucoma (POAG) is an ocular neuropathy defined by a variable optic nerve damage with an open irido-corneal angle. It is a multifunctional neuropathy that results in progressive loss of retinal ganglion cells.

Patients with POAG can, nowadays, benefit from a wide range of treatments: medical, surgical, or even laser therapy. However, the decrease of the IOP isn’t an equivalent to the disease control. Many studies on glaucoma therapy (OHTS and EMGT) [1, 2] have shown the progression of retinal ganglion cells loss despite IOP control. Moreover, the normal tension glaucoma entity, in which the optic nerve damage doesn’t come along with a high IOP is now well recognized [3].

Magnesium is a mineral substance with a key role for the well-functioning of the human body. It helps regulate the blood pressure, enhance the nervous and muscular system, and supports the immune one as well. However, does magnesium have a role in improving patients with POAG?

The primary objective of our study was to determine whether patients with POAG that are under magnesium supplementation have better chances to ameliorate the course of their disease. Another end point of the study is to determine the reduction of IOP, the optic nerve damage control and the tolerability of the treatment. Finally, the patient’s life quality before and after the supplementation was also assessed.

II. MATERIAL AND METHOD

Our study, called GlaucoMag, is a non-randomized monocentric clinical study conducted at both Military teaching hospital of Rabat and Provincial hospital of Tetouan between December 2019 and March 2022.

In order to be included, patients had to be between 20 and 65 years old, had clinical signs of POAG (Cup-Disc asymmetry or alteration, localized or diffused defect of retinal nerve fiber layers), and IOP ≤ to 19 mmHg under antiglaucoma treatments over at least one year. The patients...
had to present a reliable Humphry 24-2 SITA standard visual field with the MD ≥ 1 dB per year.

Patients with a visual acuity ≤ 0.5, a spherical equivalent out of the range of [-6, +3], presenting another form of glaucoma other than POAG, with a systemic or a neurological disease that could be responsible for the VF defect or optic nerve head changes, those who underwent an ocular surgery in the past 6 months, presumed or confirmed pregnant women and patients with poor collaboration were excluded.

A. Treatment with magnesium supplement

The treatment consisted of one tablet a day of 300 mg of Magnesium taken at night for 90 days. The patients continued to have their topical antiglaucoma treatment.

B. Examination

All patients were assessed before taking the treatment, time 0 (T0); after 3 months (T1) and 6 months of magnesium supplementation. At T0 medical history of patients was taken, and at each visit we’d conduct a complete ophthalmological examination including IOP measure using Goldmann tonometry. Then, each patient undergoes an automated perimetry using Humphry SITA standard 24-2 visual field, which would be taken into consideration only if the number of false positives and negatives < 30% and fixation lesions <15%.

All patients underwent a complete OCT glaucoma protocol scans using ZEISS OCT Cirrus 4000: First, both eyes of each patient were examined by the same operator and the, OHN and GCC scans were taken. Scans with a signal intensity index SSI less than 7/10 were excluded.

C. Statistical Analysis

In our study we used the following numerosity estimation to compare between two means. Null hypothesis means m1=m2 (m1: mean progression rate prior to the study, m2: mean progression rate after the treatment). The other hypothesis is m1=m2+d, d being the difference of the two means.

The sample size is 46 patients. The data was collected using Microsoft Office Excel and statistical program for Windows SPSS. The results were presented as means ± standard deviation.

The mean results of different parameters were compared between T0 (Before treatment) T1 (After 3 months) and T2 (After 6 months).

Primary outcome of the study is the rate if progression. It was compared based on 6 months before and after the Magnesium supplementation. Pearson correlation and linear progression were used to investigate possible interference on the rate progression such as: IOP, age and type of treatment. A level of p<0.05 was adopted for each analysis.

The Bonferroni correction was applied where there were several comparisons.

III. RESULTS

56 patients met the inclusion criteria of whom 5 patients were not included due to lack of collaboration during the study, 2 patients were declared pregnant after the start of treatment and 3 patients left the study voluntarily.

Therefore, a sum of 46 patients with POAG were included in our study with the mean characteristics that are listed in the table 1.

At the beginning of our study, the mean IOP was of 16.56±2.06 mmHg. At 3 and 6 months of treatment the IOP mean value dropped significantly (IOP = 15.73±2.13 and IOP= 13.93±2.73) mmHg respectively.

The MD values of visual field and the rate of progression were significantly improved throughout our study. At T1 (3 months) MD = -5.29±3.05 p<0.05 and at T2 MD= -5.29±2.95 p= 0.018.

As for the rate of progression, initially at -2.00±1.87 dB/year, it was estimated on the basis of 6 months at 1.01±2.75 dB/year. Therefore, no progression of the damage was noticed, as shown in Table II.

RNFL and GCC measured by OCT showed no significant variation throughout our study.

IV. DISCUSSION

The mean objective of our study was to demonstrate the effect of magnesium intake on the progression of functional and structural glaucomatous damage.

Elevated IOP has long been considered as key factor for POAG progression. However, other factors are now identified and are subject to study and drug development.

Oxidative stress and disturbed blood flow, for instance, are shown to be important risk factors in the progression of glaucomatous optic nerve damage [1], [2]. Therefore, many treatments with potential efficiency on blood flow regulation have been studied and suggested [3] such as carbonic anhydrase inhibitor and calcium channel blockers [4], [5].

Magnesium is known to be involved in many cellular processes such as energetic metabolism, maintaining a normal cellular membrane function, and enhancing enzyme activities in protein, carbohydrate, and fat metabolism [6], [7]. Studies have also demonstrated that Mg improves the ocular blood flow in patients with glaucoma and protects ganglion cells from oxidative stress [1], [2], [8]. Thereby, exhibiting both neuro protective effects and enhancing blood flow, Mg may serve as a potential therapy in POAG.
A. Physiological Ocular Effects of Magnesium

Magnesium is the second highest intracellular cation in human body, and it has been linked to almost all basic metabolism processes, such as fat, protein and carbohydrate. It is also a co-factor for over than 300 enzymes [9]. It also plays a key role in DNA and RNA production as well as maintaining a normal nerve, muscle, and cardiac activity.

As for the eye, animal experimental studies have shown that Mg has a critical role in the development and well-functioning of the eye [10]. Multifocal necrosis of retinal pigment epithelium has been associated with Mg deficiency in rates for instance [10]. Additionally, hypomagnesemia has been linked to necrosis and myelination disorder in optic nerve [11]. A study also showed that patients with diabetic retinopathy were declared to have low blood levels of Mg [12]. All of these finding and more show that Mg has great role in ocular well development and function, making it a with potential high therapeutic value.

B. Role of Magnesium Deficiency in Glaucoma

As previously shown, ocular blood flow reduction is considered to be a contributing factor for POAG [11]. Moreover, the resultant ischemia may damage the trabecular meshwork and therefore increase IOP [13]. As magnesium optimizes ocular blood flow by reducing cytokines levels and free radicals’ production, as well as enhancing ocular vasodilatation which minimizes neuronal loss and ganglion cell damage, it may be of great value as an add-on therapy in glaucoma treatment [14].

On the other hand, oxidative stress is known to cause the over production of Nitric Oxide (NO) which is a strong neuro-destructive agent [15] resulting in ganglion cells loss and glaucoma [15], [16]. Moreover, oxidative stress is responsible for increasing Endothelin-1 levels (Et-1), which is a powerful vasoconstrictor, disturbing the optic nerve blood flow [17].

Et-1 production not only interferes with oxaplastic transport and reduces optic nerve blood flow, but it also activates astrocytes [18]. Once activated, astrocytes contribute to production of NO, free radicals and Et-1 creating thus a cycle of axonal destruction [19]. Magnesium is known to be a reliable anti-oxidative agent that not only reduces oxidative stress but also indirectly inhibits the activation of astrocytes, preventing thereby neuronal loss and ganglion cells destruction [20].

C. Clinical Reflections

Many studies suggested the benefit of magnesium supplementation therapy in improving ocular function. Gasper and al. [21] evaluated the effect of oral intake of Mg in 10 patients with glaucoma. A video nail-fold capillaroscopy was used to evaluate the optic nerve blood flow. By the end of one month of Mg supplementation both blood flow and visual field improved [20].

Another study of Aydin and al. [22] proved the efficiency of oral intake of Mg supplementation on improving visual field pachymetry in 15 patients with glaucoma. After 4 weeks of therapy, VF mean deviation and standard deviation were statistically improved compared to placebo group [22].

In agreement to literature data, we observed, on our study, an important improvement in perimetric damage and rate of progression after merely 3 months of daily magnesium intake, as well as a stabilization of structural damage of optic nerve. After 6 months follow-up the rate of improvement continued to progress. This highlights the highly probable therapeutic value of magnesium supplementation in glaucoma treatment.

Our study, however, has its limitation, as the data should be compared with a placebo group having the same clinical characteristics, and a randomized clinical trial would be of a better proof to the exact place of magnesium supplementation in glaucoma treatment. This only opens doors to more research grounds for a better understanding of the matter.

V. CONCLUSION

In conclusion, Magnesium had a key role in regulating and maintaining a well function of ocular tissues. The contribution of Mg levels in the process of glaucoma may be attributed to its many virtues in regulating ocular blood flow (ON and trabecular meshwork), reducing oxidative stress’s harmful impact on ganglion cells and optic nerve, and preventing the over production of some damaging molecules. Therefore, Mg may be of great value in glaucoma treatment, representing, thereby, a fresh ground for further clinical research.

REFERENCES


