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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Effects Of Magnesium Oxide Treatment On Serum Electrolyte Levels In Constipated Children

Konstipasyonlu Çocuklarda Magnezyum Oksit Tedavisinin Serum Elektrolit Düzeyleri Üzerine Etkileri

Sevgi Ulusoy Tangül[1], Hülya İpek[2], Atilla Şenaylı[3]

[1]Department of Pediatric Surgery, Faculty of Medicine, Yozgat Bozok Univercity, Yozgat, Turkey
[2]Department of Pediatric Surgery, Faculty of Medicine, Hitit University Çorum Erol Olcok Training and Research Hospital, Çorum, Turkey
[3]Department of Pediatric Surgery, Faculty of Medicine, Yozgat Bozok Univercity, Yozgat, Turkey

ABSTRACT

Aim: Magnesium oxide (MgO) is a standard treatment for functional constipation. However, this medication has not been evaluated extensively for possible alterations of plasma magnesium (Mg) levels and other electrolytes. This retrospective study aimed to appraise the effects of serum magnesium with some other electrolyte levels after oral MgO treatment in children with functional constipation.

Material and Method: After the approval of the local ethical committee, archives of the patients who had been admitted to two different Pediatric Surgery outpatient clinics in different cities between 2014-2018 were evaluated. The demographic findings of the patients were recorded. For the diagnosis of chronic constipation, Rome-III classification criteria were used. After complete physical examinations, if there were no possible organic reasons other than chronic dietary problems, serum electrolyte levels were obtained and evaluated. Findings were evaluated statistically and discussed with the literature.

Result: The magnesium value was significantly higher in the constipation group ($p<0.05$) compared to the control group. In generalized linear models (GLM) results, the effects of calcium, potassium, and sodium levels on serum magnesium levels were significant ($p<0.05$). The effect of calcium and potassium levels on serum magnesium was statistically significant in the constipation group ($p<0.05$). In the control group, only the effect of chlorine level on serum magnesium was statistically significant ($p<0.05$).

Conclusion: MgO is a valuable treatment for constipation. However, especially by taking into account the dose adjustment, close follow-up of the patients for side effects is necessary to prevent patients from electrolyte imbalance.

Keywords: Constipation, magnesium, magnesium oxide, electrolyte

ÖZ

Amaç: Magnezyum oksit (MgO) fonksiyonel kabızlık için standart bir tedavidir. Ancak bu ilaç, plazma magnezyum (Mg) düzeyleri ve diğer elektrolitlerdeki olası değişiklikler açısından kapsamlı bir şekilde değerlendirilmemiştir. Bu retrospektif çalışma, fonksiyonel kabızlığı olan çocuklarda oral MgO tedavisi sonrası serum magnezyumunun diğer bazı elektrolit düzeyleriyle birlikte etkilerini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Yerel etik kurul onayı alındıktan sonra 2014-2018 yılları arasında farklı şehirlerdeki iki farklı Çocuk Cerrahisi polikliniğine başvuran hastaların arşivleri değerlendirildi. Hastaların demografik bulguları kaydedildi. Kronik kabızlığın tanısı için Roma-III sınıflandırma kriterleri kullanıldı. Tam fizik muayene sonrasında kronik beslenme sorunları dışında olası organik nedenler yoksa serum elektrolit düzeyleri elde edilerek değerlendirildi. Bulgular istatistiksel olarak değerlendirildi ve literatürle tartışıldı.

Bulgular: Konstipasyon grubunda magnezyum değeri kontrol grubuna göre anlamlı derecede yüksekti ($p<0,05$). Genelleştirilmiş doğrusal model (GLM) sonuçlarında kalsiyum, potasyum ve sodyum düzeylerinin serum magnezyum düzeylerine etkisi anlamlıydı ($p<0,05$). Kabızlık grubunda kalsiyum ve potasyum düzeylerinin serum magnezyumu üzerindeki etkisi istatistiksel olarak anlamlıydı ($p<0,05$). Kontrol grubunda ise sadece klor düzeyinin serum magnezyumu üzerindeki etkisi istatistiksel olarak anlamlıydı ($p<0,05$).

Sonuç: MgO kabızlık için değerli bir tedavi yöntemidir. Ancak özellikle doz ayarlaması dikkate alınarak hastaların elektrolit dengesizliğinin önlenmesi için yan etkiler açısından yakın takip edilmesi gerekmektedir.

Anahtar Kelimeler: Kabızlık, magnezyum, magnezyum oksit, elektrolit

Corresponding Author: Sevgi ULUSOY TANGÜL
Address: Department of Pediatric Surgery, Faculty of Medicine, Yozgat Bozok Univercity, Yozgat, Turkey
E-mail: sevguu@gmail.com

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INTRODUCTION

Constipation is a condition that can occur at any age, generally thought to be due to habitual dietary reasons. Ninety-five percent of constipations seen in childhood are functional (1-7). Functional constipation, occasionally, does not have distinctive signs and/or symptoms (8,9). Nevertheless, as defined in the literature, constipation was assumed to be an essential reason for magnesium deficiency in the body. As a result, magnesium-replaced treatments were installed in constipation treatments (10-12).

Magnesium Oxide (MgO) is one of the most used medications to treat constipation (8,13-17). The recommended dose for this purpose is 0.03 g MgO per kilogram daily (15).

In the stomach's acidic environment, MgO is converted to magnesium chloride (MgCl2). After several subsequent reactions, it undergoes pancreatic secretion in the duodenum as magnesium carbonate (MgCO3) (13). MgCO3 increases the osmotic pressure of the intestinal lumen fluid, which provides water diffusion to the intestinal lumen, increasing both the water content and volume of the stool. Increased volume stimulates the intestinal wall activating intestinal motility (18). When duodenal secretion in the duodenum interacts with MgO, side effects may be seen, especially in patients with intestinal disorders. In addition, since the use of MgO has consequences, such as effects on smooth muscle cells, it will be necessary to remember the effects of hypermagnesemia reflected in the clinic. Therefore, monitoring changes in serum Mg levels may be clinically necessary.

MgO studies encountered in the literature are mainly in the direction of the clinical effects of magnesium, especially its effects on kidney functions (14, 19). Although there are studies examining the severe side effects of magnesium, the effect of MgO treatment on serum magnesium correlation among magnesium and other electrolytes for constipation has been investigated insufficiently. This study aimed to evaluate the in vivo effects of magnesium oxide (MgO) treatment on serum magnesium and electrolyte levels in children with functional constipation.

MATERIAL AND METHOD

Ethics committee approval (2017-KAEK-189_2018.07.11_09) was obtained from Yozgat Bozok University Clinical Research Ethics Committee in accordance with the Declaration of Helsinki. The files of constipation patients who applied to Yozgat Bozok University Research and Practice Hospital Pediatric Surgery Clinic and Hitit University Pediatric Surgery Clinic between 2014-2018 were retrospectively analyzed. Patients with chronic constipation who received 1-2 g of MgO per dose 3 times daily for one week or longer according to the Rome III classification were included in the study. Phosphorus (P), sodium (Na), potassium (K), chlorine (Cl) and magnesium (Mg), and calcium (Ca) were evaluated in all (n=128) patients.

The control group (n=74), aged between 0 and 18 years, was randomly selected among the patients who applied to the Pediatric Surgery outpatient clinics between July 2016 and January 2018 for inguinal hernia and hydrocele and had no history of constipation. The patients' files were reviewed retrospectively, and the data were transferred to SPSS 17.0. Those with chronic kidney diseases, congenital heart diseases, endocrine disease-related electrolyte balance, bowel resection, short bowel syndrome, and Hirschsprung's disease were excluded from the study.

Nominal and ordinal parameters of the research were described with frequency analysis, whereas scale parameters were described with means and standard deviations. Kolmogorov Smirnov Test was used for the normality of scale parameters. Mann Whitney U test was used for non-normally distributed parameters, whereas the Independent Samples T-Test was used for normally distributed parameters. Fischer's Exact Test was used for differences between categorical parameters. Spearman's rho correlation was used for relational analysis at the univariate level, and Generalized Linear Model (GLM) was used for the multivariate level. All analyses were performed at SPSS 17.0 for windows at a 95% Confidence Interval with a 0,05 alpha significance level.

RESULTS

Age, gender, phosphorus, calcium, chlorine, potassium, and sodium levels between constipation and control groups were not statistically significant ($p>0.05$). The magnesium value was significantly higher in the constipation group ($p<0.05$). These distributions are shown in **Table 1**.

Table 1. Age, gender and electrolyte levels of patient groups

	Control (n=74)	Constipation (n=128)	p
Age	8.80±4.53	9.11±4.59	0.653a
Gender, n (%)			
Male	36 (48.6)	61 (47.7)	0.504b
Female	38 (51.4)	67 (52.3)	
Phosphorus	4.41±0.60	4.52±0.76	0.267c
Glucose	96.64±10.80	94.28±14.30	0.149a
Calcium	9.35±0.47	9.37±0.54	0.798c
Chlorine	105.93±2.87	105.98±3.11	0.906c
Creatinin	0.57±0.11	0.57±0.11	0.775c
Magnesium	1.92±0.17	2.00±0.22	0.010a
Potassium	4.19±0.37	4.20±0.42	0.972c
Sodium	137.86±1.34	137.52±2.02	0.291a

a. Mann Whitney U test, b. Fischer's Exact Test, c. Independent Samples T-Test.

The mean value and the range of change of serum magnesium were higher in the constipation group (p<0.05). The serum magnesium level distribution in the constipation group was more scattered (**Figure 1**).

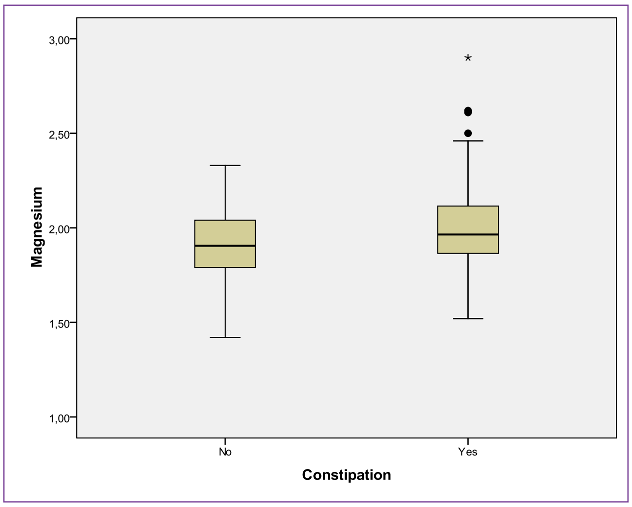

Figure 1. Serum magnesium level differences and ranges for patient groups

There was a statistical significance and positive correlation between serum magnesium and calcium (r=0.351; p<0.01) and potassium (r=0.224; p<0.05) in the constipation group. In the whole sample, serum magnesium (r=0.162; p<0.05), calcium (r=0.296; p<0.01), potassium (r=0.151; p<0.05), sodium (r=0.161; p<0.05), and There was a statistically significant and positive correlation between constipation (r=0.182; p<0.05) (**Table 2**).

Table 2. Spearman's rho correlation between serum magnesium levels and research parameters

	Control (n=74) (r)	Constipation (n=128) (r)	Total (n=202) (r)
Age	0.156	-0.098	-0.005
Gender	-0.091	-0.028	-0.049
Phosphorus	0.039	0.163	0.130
Glucose	-0.101	0.009	-0.049
Calcium	0.191	0.351**	0.296**
Chlorine	-0.282*	0.146	-0.001
Creatinin	-0.018	-0.009	-0.030
Potassium	0.052	0.224*	0.151*
Sodium	0.243*	0.162	0.161*
Constipation	-	-	0.182**

*p<0.05 **p<0.01

According to the GLM results, the positive effects of constipation, calcium, potassium, and sodium levels on serum magnesium levels were statistically significant (p<0.05). This means that increased constipation, calcium, potassium, and sodium levels cause an increase in serum magnesium levels. In the constipation group, the contribution of calcium and potassium levels to serum magnesium was statistically significant (p<0.05). Only the contribution of chlorine level on serum magnesium was statistically significant in the control group (p<0.05) (**Table 3**).

Table 3. Generalized Linear Model for effects of significant factors on magnesium level

Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test	p
			Lower	Upper	Wald Chi-Square	
All samples (n=202)						
(Intercept)	-1.487	1.0676	-3.579	0.606	1.940	0.164
[Constipation=No]	-0.087	0.0281	-0.142	-0.032	9.719	0.002
[Constipation=Yes]	0[a]	.	.	.	.	.
Calcium	0.085	0.0269	0.032	0.138	9.960	0.002
Potassium	0.073	0.0345	0.005	0.140	4.476	0.034
Sodium	0.017	0.0078	0.001	0.032	4.571	0.033
(Scale)	0.037[b]	0.0036	0.030	0.044		
Likelihood Ratio Chi-Square: 36.258; p<0.001						
Constipation (n=128)						
(Intercept)	0.603	0.3417	-0.067	1.272	3.112	0.078
Calcium	0.094	0.0348	0.026	0.162	7.331	0.007
Potassium	0.123	0.0446	0.036	0.211	7.668	0.006
(Scale)	0.043[a]	0.0054	0.034	0.055		
Likelihood Ratio Chi-Square: 17.559; p<0.001						
Control (n=74)						
(Intercept)	0.572	2.2526	-3.843	4.987	.065	0.799
Sodium	0.020	0.0145	-0.008	0.049	1.980	0.159
Chlorine	-0.014	0.0068	-0.027	0.000	4.191	0.041
(Scale)	0.026[a]	0.0043	0.019	0.036		
Likelihood Ratio Chi-Square: 7.279; p<0.05						

a. Reference category, b. Maximum likelihood ratio.

DISCUSSION

Magnesium is the fourth most abundant mineral in the body, and it is a cofactor of over 300 enzymatic reactions (12). Clinically, approximately 0.3% of body magnesium level is found in plasma. Therefore, measuring the plasma magnesium level is insufficient to show the whole magnesium level in the body (20).

There are some clinical situations that magnesium-consisting treatments are performed, such as constipation. It is known that the therapeutic effect of MgO in constipation is to increase the osmotic pressure in the intestinal lumen and to ensure water transfer to the intestinal lumen. Consequently, the liquid content and the increased stool volume stimulate the intestinal wall and run the impulsive motor activity (13).

Although some studies have shown the side effects and negative aspects of magnesium treatment, MgO is still widely preferred in the treatment of constipation today. In addition, as Dupont and Hebert reported, compounds such as magnesium-rich mineral water are also used to treat constipation (21).

Mori et al. evaluated the use of traditionally-used magnesium oxide compounds for laxative purposes in Central Asia had severe side effects, especially in patients with kidney failure, in addition to its advantages in constipation (13). Therefore, there is a possibility of aggravation of renal or intestinal disorders with MgO as a side effect after constipation treatment.

Laxatives containing magnesium are widely used to treat constipation (16, 17). Although rare, iatrogenic hypermagnesemia with these laxatives has also been reported in the literature (22, 23). In addition, although MgO is generally used as a laxative, its effects on serum magnesium levels have yet to be adequately studied.

Tatsuki et al. reported the serum magnesium level as 2.4 mg/dL in MgO-treated constipation patients aged 1 to 14 years (19). In our study, the mean magnesium of the control group was 1.92 mg/dL, and the mean of the constipation group was 2.00 mg/dL. The difference between the groups was statistically significant. This result reveals the increase in magnesium levels after MgO usage for constipation. Secondly, our study shows that other electrolyte levels were not affected after MgO usage, even in various gender and age factors.

On the other hand, Generalized Linear Model (GLM) results showed that the effects of sodium, potassium, and calcium levels on serum magnesium levels significantly differ in all constipated patients. Calcium was the most influential factor in constipation among these electrolytes. These findings show that the relationship between serum magnesium level and calcium and potassium in the constipation group is significant compared to normal individuals.

Calcium (Ca), magnesium (Mg), phosphorus (P), and magnesium (Mg) are necessary nutrients for cellular energy metabolism and human bone growth. Ca, Mg, and P are essential for bone health and enhancing cardiac, pulmonary, and neurological function (24, 25). It has long been reported that in humans, hypomagnesemia frequently coexists with hypocalcemia and that calcium intake influences the retention of magnesium and vice versa. All living cells depend on complex interactions between magnesium and calcium, some of which are relatively primitive on the evolutionary scale (26).

In several experimental, clinical, and observational investigations, micronutrients like calcium, magnesium, and potassium have been studied for their individual effects on high blood pressure (27). There is minimal research on how dietary sodium in combination with calcium and magnesium consumption affects (28-30). However, there has yet to be research the relationship between calcium, magnesium, and potassium in constipation patients with a direct comparison nature research design. This increases the originality of our results.

This study retrospectively examined the relationship between the use of MgO and other electrolytes in treating functional constipation in children. Although using MgO as a laxative is common, it can disrupt the electrolyte balance in the body at both univariate and multivariate levels and cause unwanted complications. We thought that the research makes an essential contribution to the literature, and we firmly believe that expanded or repeated studies will support the findings in this study.

Study Limitations

One of the most critical limitations of the study is that it is not prospective. Results from the study can be generalized with multicenter and prospective studies on functional constipation.

CONCLUSION

Using MgO in treating constipation is beneficial, especially considering dose adjustment and other electrolyte balances. In addition, it would be appropriate to follow up with the patients closely regarding side effects.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Yozgat Bozok University Clinical Researches Ethics Committee (Decision No: 2017-KAEK-189_2018.07.11_09).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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