Non-randomized ,comparative study of the occurrence and severity of constipation with Magnesium Sulphate and other laxatives in pediatric patients with cerebral palsy

Nermeen Elnahel[a], Elsayed Khalil[b], Ahlam Badawy[b]

[a]Department of Pediatric, [b]Department of Pediatric, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Nermeen Elnahel, MSc, Radwan Street, Tema, Sohag, Egypt. Postal Code: 82511;
Tel: 01004231328;
e-mail: nemozmemo27@gmail.com

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Introduction
In cerebral palsy (CP), one of the most common nonmotor problems is constipation. Several methods are used to manage constipation, such as increasing fluid intake, using a fiber diet, using oral laxatives, and rectal stimulants. One medication is magnesium sulfate ($MgSO_4$), which has a prominent role as an osmotic laxative.

Objectives
To assess the effect of oral $MgSO_4$ on constipation in patients with CP and to recommend it as a standard therapy to treat constipation in children with CP.

Patients and methods
This nonrandomized clinical study was done at the Neurology Unit of the Pediatric Department in Assiut University Hospital over 1 year (between October 2018 and October 2019).

Results
There was a significant increase of bowel movements in the magnesium group in the second, third, and fourth weeks of follow-ups (P = 0.05, 0.04, and 0.02, respectively). There was a significant difference in the mean number of doses used within a month in both groups (P = 0.03). Although failing to achieve statistical significance, a considerable improvement of straining in both groups was observed (P = 0.65, 0.2, and 0.2, respectively). We noticed a change in stool consistency from hard to soft in some cases, but others progressed to diarrhea with an insignificant difference between both groups (P = 0.72). Last, we recognized a noteworthy improvement in the abdominal pain and distention, even though it could not reach a statistical significance level (P = 0.31, 1, and 0.81).

Conclusion
Oral $MgSO_4$ is an effective drug for constipation in patients with CP.

Keywords:
cerebral palsy, constipation, magnesium sulfate

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Introduction

Cerebral palsy (CP) is a static disorder of the central nervous system presented with dysfunction in the musculoskeletal system. The incidence rate of CP is near 2–2.5 cases per 1000 live births [1,2]. Constipation is one of the most common nonmotor problems with a prevalence of up to 74% [3,4]. There are many risk factors for constipation, like, hypertonia, malnutrition, mental retardation, and lack of mobility. All these factors are leading to reducing the bowel movement and stool consistency, ultimately leading to reducing the quality of life of the child and parents as regards psychological and socioeconomical aspects. In CP patients, muscle cramps and unsuccessful defecation lead to stomach pain, which may aggravate the spasticity and advance chronic constipation and vice versa [5].

Nowadays, several approaches are available, both pharmacological and nonpharmacological, to control constipation in CP patients. These options combine intake of a large amount of fluid, eating fiber diet, biofeedback, receiving oral laxatives, and rectal medications [6]. One of the useful pharmacological tools is magnesium sulfate ($MgSO_4$). It acts as an osmotic laxative [7]. $MgSO_4$ acts through the intraluminal accumulation of hyperosmolar particles, this leads to retention of water in the intestinal cavity, as it is badly absorbed from the wall of the intestine. The process of water retention causes softening of stool and increasing intestinal peristalsis [8]. Another mechanism is through hasten – the transit to the small intestine – in fasting and fed state, and it increases the bowel movement and heaviness of stool, compared with other laxatives. The major side effect of $MgSO_4$ is decreasing the intestinal absorption of fat, protein, and carbohydrates after solid-food intake.

The two aims of this study were (a) to evaluate the efficacy of oral $MgSO_4$ in the treatment of constipation in patients with CP, and (b) to compare the effect of $MgSO_4$ to other known laxatives as regarding treating constipation.

Patients and methods

Study design

This is a nonrandomized clinical trial that was done at the Pediatric Neurology Unit and clinic at Assiut University Children Hospital, over 1 year between October 2018 and October 2019.

The clinical registration number: NCT03471312.

Patients' characteristics and drug dosage: this study was conducted on 50 patients with CP and constipation, they were selected from two groups. The first one (group A) included 25 CP patients with chronic constipation and not responding to the usual laxative, they were given oral $MgSO_4$ in a dose of 5 up to 20 mg/day for 1 month with a weekly follow-up. The second group (group B) included 25 CP patients with chronic constipation who were on usual laxatives: seven patients were receiving glycerin suppository, eight patients were on lactulose syrup, and five patients on sodium picosulfate drops, and five patients were using a rectal enema.

We included patients who had all the following criteria: from 6 months to 18 years of age, patients diagnosed with spastic CP, their parents accept to participate in the study and sign the written consent, and had constipation according to Rome III criteria.

We excluded patients with any of the following criteria: severe growth retardation (children with CP and below the 10th percentile in weight and length charts), who fed with gastrostomy tube, suspected inborn error of metabolism, congenital malformations, or suspected and inherited the neurologic disease, and patients with cardiac, renal, gastrointestinal tract problems, or chronic diarrhea.

Study assays

All patients were subjected to five crucial steps: first, definition of constipation according to Rome III criteria before therapy. Rome III criteria include the frequency of defecation per week, straining, and stool form. Then, specifying any other gastrointestinal symptoms like abdominal pain, abdominal distention, and vomiting. Third, deciding the dose of the drug taken for 1 month. The next step was to follow up the same criteria of constipation and other gastrointestinal symptoms every week for 4 weeks after therapy. Last, recognizing any side effects that occurred during the study period.

Ethical consideration

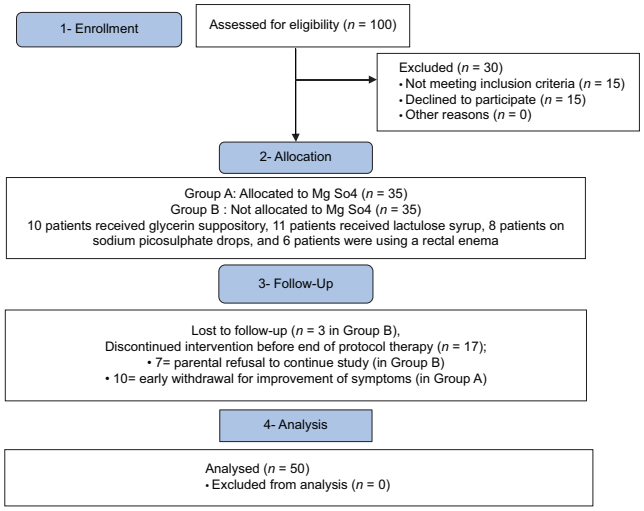
Acceptance of the study by an Ethical Committee of Faculty of Medicine, Assiut University. Security of all information was assured. Informed and written consent was obtained from all caregivers before accomplishment within the study, and after explaining the nature, purpose, and possible consequences of the study.

The IRB number: 17100473.

Statistical analysis

Data were collected and analyzed using SPSS (Statistical Package for the Social Science, version 20; IBM, Armonk, New York, USA). Continuous data were expressed in type of a mean ± SD or a median (range), whereas we declared nominal information as a frequency (percentage). χ^2 test was used to compare the nominal information of different groups, while the Student *t* test was employed to compare the means of continuous data among the studied groups. The level of confidence was kept at 95%, hence, *the P* value was significant if less than 0.05.

Consort flow diagram:



Results

The mean age of patients in group A was 3.413 ± 3.654 years, 13 (52%) cases were males, and 17 (68%) patients were from rural areas; while the mean age of group B was 2.73 ± 1.626 years, 10 (40%) cases were males, and 18 (72%) cases were from rural areas (Table 1). Both groups had insignificant differences regarding age, sex, and residence (P = 0.39, 0.88, and 0.09, respectively) (Table 2).

There was an insignificant difference between both groups regarding the number of bowel movements before and after therapy (P = 0.57). After therapy, there was a negligible difference in the first week of follow-up (P = 0.95), but in the second week, third week, and fourth week of follow-ups, there were significant differences as P values of 0.05, 0.04, and 0.02, respectively (Table 3).

A significant difference in the mean number of doses taken within 1 month was detected (P = 0.03). In group A, the mean number of doses was 12.8 ± 11.66 that ranged from two doses up to 42 within 1 month. It was considered low compared with the mean number of doses of other laxatives in group B (21.48 ± 12.47), with a range from eight up to 56 doses within 1 month (Table 4).

The percentage of patients who had straining before and after treatment. Before therapy, we noted that 24 (96%) cases in group A and 25 (100%) in group B (P = 0.77) had straining. After therapy, it was observed that straining decreased during the first week, second week, and third week with an insignificant difference in both groups (P = 0.65, 0.2, and 0.2, respectively). During the fourth week of follow-up, we noticed a marked improvement in both sets, with only two (8%) cases in group A and six (24%) patients in group B who still suffered from straining (P = 0.03) (Table 5).

Before management, the stool consistency was classified as being hard–lumpy, or lumpy. Cases that presented with the hard–lumpy stool were nine (36%) cases in group A and 10 (40%) in group B, with an insignificant difference between them (P = 0.34).

Following the remedy, the categorization became broader and more divided between (hard–lumpy, lumpy, soft, and watery). In the first week of follow-up, there was an insignificant difference (P = 0.86) with six (34%) cases that became lumpy, 18 (72%) became soft, and one (4%) had a watery stool in group A. On the other hand, four (16%) cases developed a lumpy stool, and 21 (84%) patients had soft feces in group B.

In the subsequent weeks of follow-up, the second and the third weeks, there was a significant difference between both groups (P = 0.03), while in the fourth week of follow-up, the difference converted to be insignificant again (P = 0.99) (Table 6).

There was an insignificant difference between both groups regarding the occurrence of abdominal distention, pain, and vomiting before therapy. In follow-up, we noticed that the abdominal distention and pain reduced in both groups although they failed to achieve a significant statistical difference (P = 0.31, 1, respectively). There was no relation between therapy and vomiting in both groups, as there were cases that developed vomiting later during follow-up, while patients, who had vomiting before the start of the study, some improve, and others did not.

Diarrhea was the only side effect recorded in both groups in our study during the 4 weeks of follow-up. Table 7 shows a minimal difference between both groups regarding the development of diarrhea (P = 0.72).

Table 1 Demographic data of the studied groups

	Group A (N=25)	Group B (N=25)	P
Age (years)	3.413±3.654	2.733±1.626	0.39
Sex [n (%)]			
Male	13 (52)	10 (40)	0.88
Female	12 (48)	15 (60)	
Residence [n (%)]			
Rural	17 (68)	18 (72)	0.09
Urban	8 (32)	7 (28)	

Table 2 Quantity of bowel movements before and after therapy

Number of bowel movements per week	Group A (N=25)	Group B (N=25)	P
Baseline	1.42±0.58	1.52±0.56	0.57
1st week	4.72±2.54	4.68±2.11	0.95
2nd week	5.24±2.02	4.16±2.28	0.05
3rd week	5.36±1.65	4.16±2.39	0.04
4th week	5.64±1.62	4.24±2.29	0.02

Table 3 The mean sum of doses used within 1 month

Mean number of doses	Group A (N=25)	Group B (N=25)	P
	12.8±11.66	21.48±12.47	*0.03*

Table 4 Effect of therapy on straining in the studied groups

Straining	Group A (N=25) [n (%)]	Group B (N=25) [n (%)]	P
Baseline	24 (96)	25 (100)	0.77
1st week	7 (28)	5 (20)	0.65
2nd week	4 (16)	6 (24)	0.2
3rd week	4 (16)	6 (24)	0.2
4th week	2 (8)	6 (24)	0.03

Discussion

This nonrandomized clinical trial study was performed to evaluate the efficacy of oral $MgSO_4$ in the management of constipation in CP patients. $MgSO_4$ was given as 5 mg per dose up to four doses per day. Doses were on-demand and dependent on the patient's condition. We assessed the improvement in constipation through the increase in the number of complete spontaneous bowel movements, the rise in the overall sum of bowel movements per week, and the improvement of stool consistency, in comparison with other laxatives.

Table 5 Effect of therapy on the consistency of stool in the studied groups

	Group A (*N*=25) [*n* (%)]	Group B (*N*=25) [*n* (%)]	*P*
Baseline			
Hard–lumpy	9 (36)	10 (40)	0.34
Lumpy	16 (64)	15 (60)	
Soft	0	0	
Watery	0	0	
1st week			
Hard–lumpy	0	0	0.8
Lumpy	6 (24)	4 (16)	
Soft	18 (72)	21 (84)	
Watery	1 (4)	0	
2nd week			
Hard–lumpy	0	0	0.03
Lumpy	3 (12)	7 (28)	
Soft	21 (84)	18 (72)	
Watery	1 (4)	0	
3rd week			
Hard–lumpy	0	1 (4)	0.03
Lumpy	1 (4)	7 (28)	
Soft	23 (92)	17 (68)	
Watery	1 (4)	0	
4th week			
Hard–lumpy	0	1 (4)	0.99
Lumpy	0	5 (20)	
Soft	25 (100)	19 (76)	
Watery	0	0	

Table 6 Frequency of other gastrointestinal-tract symptoms in the studied groups

Abdominal pain	Group A (*N*=25) [*n* (%)]	Group B (*N*=25) [*n* (%)]	*P*
Baseline	18 (72)	17 (68)	0.75
Follow-up	0	1 (4)	0.31
Abdominal distention			
Baseline	12 (48)	15 (60)	0.19
Follow-up	2 (8)	2 (8)	1
Vomiting			
Baseline	4 (16)	3 (12)	0.68
Follow-up	5 (20)	1 (4)	0.81

Table 7 Side effects in the studied groups (diarrhea)

	Group A (*N*=25) [*n* (%)]	Group B (*N*=25) [*n* (%)]	*P*
Side effects (diarrhea)	5 (20)	2 (8)	0.22

John Callen patented $MgSO_4$ in 1818, its other name is the Epsom salt, and it was used over years in the treatment of constipation. Being an osmotic laxative [9], it acts by hurrying small-intestinal transit and reducing the intestinal absorption of fat, protein, and carbohydrates following hard-meal intake; it enhances the frequency and heaviness of stool [7]. Our study included two groups: group A, which received oral $MgSO_4$ as a drug under trial, and group B, which received other laxatives. Regarding baseline data before the start of the study, there were insignificant differences in bowel movement, stool consistency, and diarrhea between both groups. Most cases in both groups had two times or fewer bowel movements per week before ragmen, we considered this low number of bowel movements as constipation according to Rome III criteria. After the first week, the difference in the sum of bowel movements between both groups was still negligible. Although from the second week to the fourth week, the difference became significant. There was an increase in the frequency of stool per week in the $MgSO_4$ group compared with the other group. Our results were like a previous study [10], which told about taking 1 l of $MgSO_4$-rich water per day for 1–2 weeks, resulted in a significant improvement of the gastrointestinal tract transit time in patients with chronic idiopathic constipation. This laxative effect remained till the fourth week of treatment and was associated with a satisfactory safety profile [11]. Another study [12], which studied the efficacy and safety of oral $MgSO_4$ in CP patients with constipation, showed that $MgSO_4$ had an adequate response, with using 10 mg/kg/day of oral $MgSO_4$ regularly as a single dose in the morning for 1 month, they found that there was a statistically significant increment in bowel movements per week after therapy compared with before it.

As regards stool consistency, the $MgSO_4$ cluster showed a 100% improvement, all patients developed soft stools at the end of the work. This result was gradual, at first, within the initial week of follow-up, there was associate-degree insignificant modification relating to the stool texture among each team. Then, within the second and third weeks, a considerable discrepancy was noted between each team. Within the fourth week, all patients in each team became within the soft stage. These results were per the results of an alternate study [11] that proved the laxative impact of $MgSO_4$-rich natural drinking water. No important impact of $MgSO_4$ was noted within the initial week, 1 week after, the constipation was reduced in 21% of controls and 30.9% of cases within the $MgSO_4$ cluster. The $MgSO_4$ cluster conjointly had a reduced range of laborious or lumpy stools and a considerable decrease within the want for different medication. Safety was remarkably guaranteed, with no dangerous facet effects among patients who drank magnesium water. In another study conducted by Bothe *et al.* [13] (2017), the modification within the range of complete spontaneous gut movements per week became additional in the active cluster when put next to placebo when half-dozen weeks. The mean range of spontaneous gut movements considerably enhanced over the course of the study, with important variations in stool consistency of spontaneous gut movements, and therefore, the associated symptoms regarding constipation improved considerably with the natural drinking water as compared with placebo.

In line with the improved objective parameters of gut performance, the study participant's veteran associate-degree improvement in straining. At the start of the medical care, nearly all the cases were complaining of straining (96%), this range was reduced into only 8% after 1 month, with a big distinction in each team.

Diarrhea was the sole facet impact recorded in each team in our study throughout the complete 4 weeks, with associate-degree small distinction between each team. Naumann *et al.* [14] reported that the utilization of sulfate-rich drinking water was related to wonderful results. No major adverse effects were reported, solely delicate to moderate adverse effects, probably not associated with the treatment (abdominal distention and diarrhea). A review paper showed associate-degree association between higher sulfate content in water and increased stool frequency, however, no correlation was found with looseness of the bowels, up to 2800 mg/l, or different adverse effects, even in infants.

Last, in our study, patients used oral $MgSO_4$ on-demand, like different laxatives, we tend to detect patients who took $MgSO_4$ less oftentimes compared with the management cluster. The mean range of doses of oral $MgSO_4$ in group A was 12.8 ± 11.66, which ranged from two doses up to 42 doses within 1 month, whereas the mean range of doses of different laxatives in type B was 21.48 ± 12.47, with a variety from 8 up to 56 doses inside an equivalent period.

Some limitations of the current work includes no methodology for analysis: the concentration of bodily fluid magnesium when oral administration of $MgSO_4$. A study that aims to work out the bodily fluid magnesium concentration in medicine cases receiving magnesium cathartics for chronic constipation can facilitate in establishing the optimum therapeutic dose. Furthermore, no safety measures were done to the participants such as hemoglobin, hematocrit, complete blood count, excretory organ and liver-performance tests, uric acid, potassium, and metal, that was thanks to the shortage of monetary support. In addition, the sample size may need to be too little to administer a firm conclusion. Additional clinical trials with a bigger sample size could be required to research the impact of the oral $MgSO_4$ on chronic constipation in spastic CP. However, our study confirms the helpful impact of oral $MgSO_4$ on gut performance in CP patients with purposeful constipation in a very-less-frequent dosing plan than the opposite laxatives.

Using $MgSO_4$ could facilitate to cut back epithelial duct discomfort and therefore the development of comorbidities oftentimes related to constipation in CP kids. Finally, this would possibly improve the health-related quality of life and, later on, scale back the economic burden on healthcare resources.

Conclusion

In conclusion, the results of our study have confirmed that oral magnesium sulfate is also compelling various-to-different notable laxatives to treat constipation, particularly in patients with CP, because it is extremely effective, has fewer facet effects, and a tiny low dose is needed to attain sensible compliance.

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Conflicts of interest

There are no conflicts of interest.

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