Original Research Article

Oral Magnesium Supplements for Management of Pediatric Asthma Patients

Abstract

Background: Asthma is the most widespread chronic paediatric condition, and Mg is one of the body's most plentiful ions. Due to its bronchodilator activity, it is used to treat acute asthma attacks by reversing bronchospasm. Our aim was to study the oral Mg supplementation effect as an adjuvant in the management of asthmatic children in between the attacks of asthma.

Methods: This case control study included eighty children, aged from 4 to 17 years old and were grouped into three groups group A, B, and control group. Group A included 40 moderate and severe asthmatic children who received oral Mg supplementation for two months plus ordinary treatment of asthma. Group B involved twenty asthmatic children who were given ordinary asthma treatment only and twenty healthy children with apparently age and sex matched were served as control group.

Results: Family history of allergies, serum Mg, pulmonary function tests were statistically significant different between studied groups. There was a negative significant relation between asthma severity and both of serum Mg and pulmonary function tests. A positive significant correlation was found between serum Mg and pulmonary function tests.

Conclusion: Serum Mg level and pulmonary function tests were significantly lower in asthmatic children. Children with asthma who were given oral Mg supplementation showed improvement in their pulmonary function tests and serum Mg level and asthma severity.

Keywords: Oral Magnesium Supplements, Asthma, Pulmonary Functions.

Introduction:

Asthma is a chronic lung illness manifested by inflammation of the airways and hyperresponsiveness of the airway smooth muscles [1]. Asthma symptoms involve chest tightness, shortness of breath, wheezing, coughing, and other respiratory problems, In the vast majority of cases, these symptoms are mild and may be managed with inhalers and allergen avoidance; nonetheless, they can occasionally cause life-threatening exacerbations. (Global Initiative for Asthma (GINA) 2020). The main stay of management of acute asthma therapy is corticosteroid inhaler and a beta-agonist. Standard therapies may be insufficient, and adjuvant therapies such as intravenous Mg sulphate may be administered in the emergency department [2].

Mg is the 4th most widespread mineral in the body, and it is required for more than 300 biochemical reactions that maintain a healthy immune system, a stable heart rhythm, strong bones, and normal muscle and nerve function [3]. Although the actual function of Mg in asthma is not completely understood, it is known that Mg acts as an anti-inflammatory agent in addition to inhibiting calcium-induced smooth muscle contraction [4].

Low Mg dietary consumption is accompanied with wheezing, bronchial hyperreactivity and impaired lung function according to epidemiological evidence [5].

Previous studies demonstrated that intravenous or inhaled Mg administration is effective in controlling acute asthma exacerbations; however, published investigations on the advantages of oral Mg supplements have produced conflicting conclusions [6].

The conflicting results may be explained through the significant problems in these researches regarding intervention duration, placebo use, randomization, baseline level of serum Mg and outcome measurements [7]. The aim of this research was to study oral Mg effect as adjuvant therapy in asthma management.

Meterials and Methods:

This case control research was carried out in Tanta University Hospital at pulmonology unit and at outpatients' clinics over a period of one year from December 2020 to December 2021. A total of 60 pediatric patients with an age range of 4 years to 12 years suffering from moderate to severe bronchial asthma according to Global Initiative for Asthma 2008 were recruited.

Exclusion criteria were other causes of wheezy chest than asthma. Patients treated with the potential to influence absorption or excretion of Mg, such as digoxin, diuretics or calcium-containing medications. Children younger than 4 years and those older than 17 years old with asthma. Causes of Hypermagnesemia, as renal failure. Inclusion criteria of controls included age and sex-matched children without asthma and other respiratory diseases such as pulmonary tuberculosis and pneumonia. Cases not receiving any medications that can influence level of Mg e.g., calcium blockers, diuretic therapy. Children devoid of chronic conditions such as renal diseases.

All children involved in this research underwent: Careful history taking with stress on history of asthma regarding onset, course, duration of its symptoms, severity of symptoms, family history of allergies and smoking. Full clinical examination (general and systemic with stress on chest examination). Inspection: shape of chest, anteroposterior diameter, deformity, chest expansion, distress, retraction, and any visible pulsations. Palpation: position of trachea, apex, assessment of respiratory expansion and Tactile vocal fremitus. Percussion: degree and equality of resonance. Auscultation: breath sounds as regards intensity quality, prolongation of expiration, vocal resonance, and presence of additional sounds as wheezes and crepitations.

Anthropometric measurements were taken Weight in kilograms. Height in centimeters. BMI (Kg/m^2), Chest x-ray (postero anterior). **Investigations:** CBC, CRP, Kidney function test and Serum Mg level, Pulmonary function tests.

Maximum patient safety: Spirostik Complete utilises the spiraflow single use flow sensors and noseclip avoiding cross-contamination and enhancing the safety of the patient. The spiraflow flow sensor' lightweight and small design e aids in enhancing the patient compliance during tests, whilst ensuring reliable measurements and consistent results.

The tiny dead space volume of the flow sensors nearly eliminates rebreathing of CO2, allowing for comfortable lung function tests. This is a significant advantage for patients with increasing lung illness and for young children. The flow sensor and nose clip are easily interchangeable between patients, and the ergonomic "snap-in" handle allows the flow sensor to be switched without touching it. The flow sensor's design eliminates the need for additional components such as mouthpieces, and its one-time use eliminates the requirement for filters.

Spirometry procedure: Patient preparation before the test; avoid large meal, vigorous exercise. Wear loose, comfortable clothing. The patient was relaxed and had time to visit the toilet. Correct position of head and body; Sitting, upright. The head is upright or slightly leaned back. No leaning forward during the test. Manoeuvre of flow volume loop: The procedure was explained to the patients. Any contraindications were checked for as withholding bronchodilators. Height was accurately measured, standing (without shoes). The patient data were entered to the software. **The following data were obtained:** Forced expiratory volum in the first second (FEV1), Forced vital capacity (FVC). Forced expiratory volum in the first second to the forced vital capacity percent (FEV1/FVC%). Every patient did 3 successive trials: the one with the best performance was chosen

Statistical analysis

IBM SPSS software version 20.0 (Armonk, New York: IBM Corp.) was used to analyse the data given into the computer. Qualitative data were presented in the form of percentages and numbers. Distributional normality was tested using the Kolmogorov-

Smirnov test. The range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) were used to characterise quantitative data. The acquired findings were deemed significant at the 5% level. For categorical variables, a Chi-square test was employed to compare groups. To compare two groups using a student t-test with normally distributed quantitative variables. The paired t-test compares two groups using the same set of quantitative characteristics across the same time frames. Comparing two groups using Mann Whitney test for abnormally distributed quantitative data.

Results:

There was no statistically significant difference between the two groups regarding age, sex, residence, family smoking, weight, height and BMI, While There was statistically significant increase in asthma prevalence among children of positive family history of allergies.

Table 1: Comparison between the Studied groups as regards to demographic data, family history and anthropometric measurement

	Cases (N = 60)		Control (N = 20)		Test of Sig.	p
	No.	%	No.	%		
Age (years)						
Min. – Max.	4.0 – 12.0		4.0 – 12.0		t=	0.712
Mean ± SD.	7.83 ± 2.76		8.10 ± 2.85		0.371	
Median	8		8.5			
Sex						
Male	38	63.3	9	45	χ^2=	0.508
Female	22	36.7	11	55	0.439	
Residence						
Urban	33	55	8	40	χ^2=	0.696
Rural	27	45	12	60	0.152	
Family Smoking						
Yes	40	66.7	9	45	χ^2=	0.085
No	20	33.3	11	55	2.967	
Family History of Allergies						
Positive	42	70	8	40	**χ^2=**	**0.016***
Negative	18	30	12	60	**5.760***	
Weight (kg)					t	
Min. – Max.	16.0 – 33.50		18.0 – 34.0		0.205	0.838
Mean ± SD.	26.26 ± 5.79		25.95 ± 5.75		0.371	

Height (cm)				
Min. – Max.	95.30 – 150.0	98.20 – 148.30	0.344	0.732
Mean ± SD.	125.69 ± 18.07	127.29 ± 18.19	0.371	
BMI (kg/m^2)				
Min. – Max.	14.74 – 19.06	14.97 – 18.03	0.787	0.237
Mean ± SD.	16.58 ± 1.12	16.24 ± 1.11	0.371	

Regarding Hematologic Parameters, there was highly statistically significant higher eosinophilic count in asthmatic children compared to control group with no statistically significant difference as regard haemoglobin level and CRP among both groups. Serum Mg and pulmonary function tests were highly statistically lower in asthmatic children compared to control healthy children.

Table 2: comparison between two studied groups as regards hematologic parameter's pulmonary function tests.

	Cases (N = 60)		**Control (N = 20)**		**Test of Sig.**	**p**
	No.	**%**	**No.**	**%**		
Eosinophilic Count (Cells/Microliter)						
Min. – Max.	350.0 – 700.0		50.0 – 174.0		τ=	<0.001*
Mean ± SD.	553.33 ± 74.10		123.0 ± 35.55		34.598*	
Hemoglobin						
Min. – Max.	9.0 – 13.0		9.5 – 13.5		t=0.691	0.491
Mean ± SD.	10.80 ± 2.26		11.21 ± 2.49			
CRP						
Min. – Max.	1.0 – 13.0		1.0 – 7.0		U=	0.075
Mean ± SD.	7.50 ± 3.21		5.50 ± 3.54		594.5	
Serum Mg (mg/dl)						
Min. – Max.	1.50 – 2.30		1.80 – 2.30		**6.858***	**<0.001***
Mean ± SD.	1.79 ± 0.19		2.13 ± 0.18		594.5	
FVC						
Min. – Max.	51.60 – 79.0		82.40 – 92.20		**20.530***	**<0.001***
Mean ± SD.	65.65 ± 7.65		89.51 ± 2.74		594.5	
FEV1						
Min. – Max.	56.0 – 82.0		84.40 – 91.60		**19.898***	**<0.001***
Mean ± SD.	65.45 ± 8.32		89.02 ± 2.24		594.5	
FEV1/ FVC						
Min. – Max.	52.0 – 74.0		89.60 – 90.60		**28.069***	**<0.001***
Mean ± SD.	62.91 ± 7.54		90.28 ± 0.28		594.5	

Regarding Comparison of Asthma Severity Groups and Serum Mg level, there was no statistically significant difference between A1 and B1, A2 and B2 before receiving Mg supplementation in group A while There was statistically significant difference of serum Mg

after receiving Mg supplementation and between A1 and A2. But There's no statistically significant difference in B1 and B2.

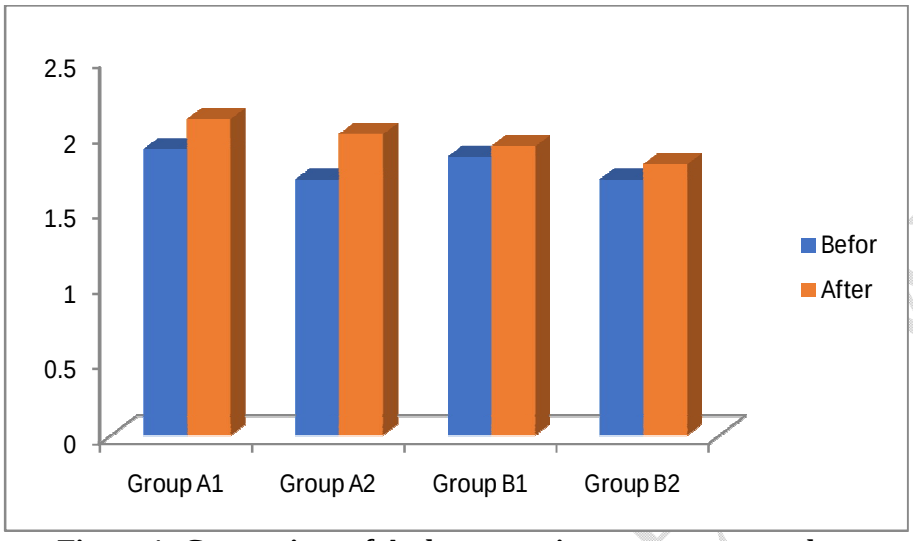

Figure 1: Comparison of Asthma severity groups as regards to serum Magnesium level

Regarding relation between asthma severity and serum Mg level in both Groups, serum Mg is statistically lower in severe asthma (A2, B2) than moderate (A1, B1) in before and after receiving oral Mg supplement.

Table 3: Relation between asthma severity and serum Magnesium level in both Groups

s. Mg	Asthma severity				t		p	
	A1 (n =18)	A2 (n =22)	B1 (n =9)	B2 (n =11)	A	B	A	B
	Mean ± SD.	Mean ± SD.	Mean ± SD.	Mean ± SD.				
Before	1.90 ± 0.17	1.70 ± 0.14	1.90 ± 0.17	1.70 ± 0.20	**4.001***	**2.360***	**0.002***	**0.030***
After	2.10 ± 0.16	2.0 ± 0.14	2.0 ± 0.17	1.80 ± 0.19	**4.183***	**2.395***	**0.012***	**0.028***

Regarding Comparison of Asthma Severity Groups and pulmonary functions, there was no statistically significant difference of pulmonary function tests between A1 and B1 and between A2 and B2 before and after receiving Mg supplementation and between A1, and A2, But there's no statistically significant difference in B1 and B2.

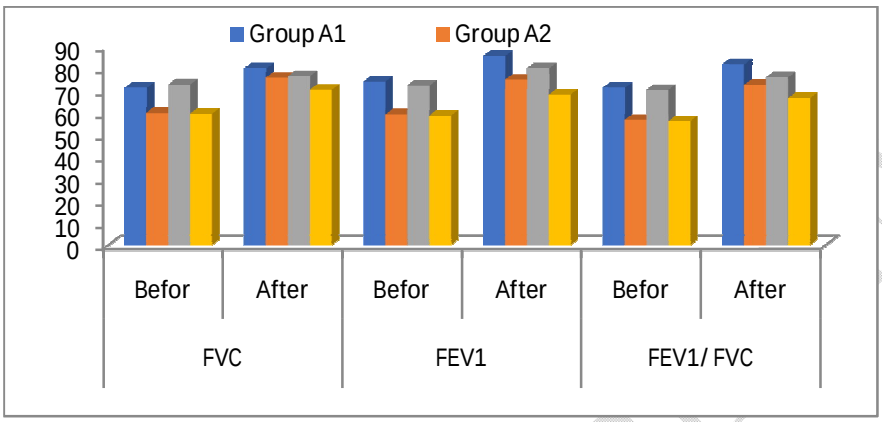

Figure 2: Comparison of Asthma severity groups as regards to pulmonary functions

Regarding Relation between Asthma Severity and pulmonary function tests, they were statistically significant lower in A2, B2 compared with A1, B1 of asthmatic children.

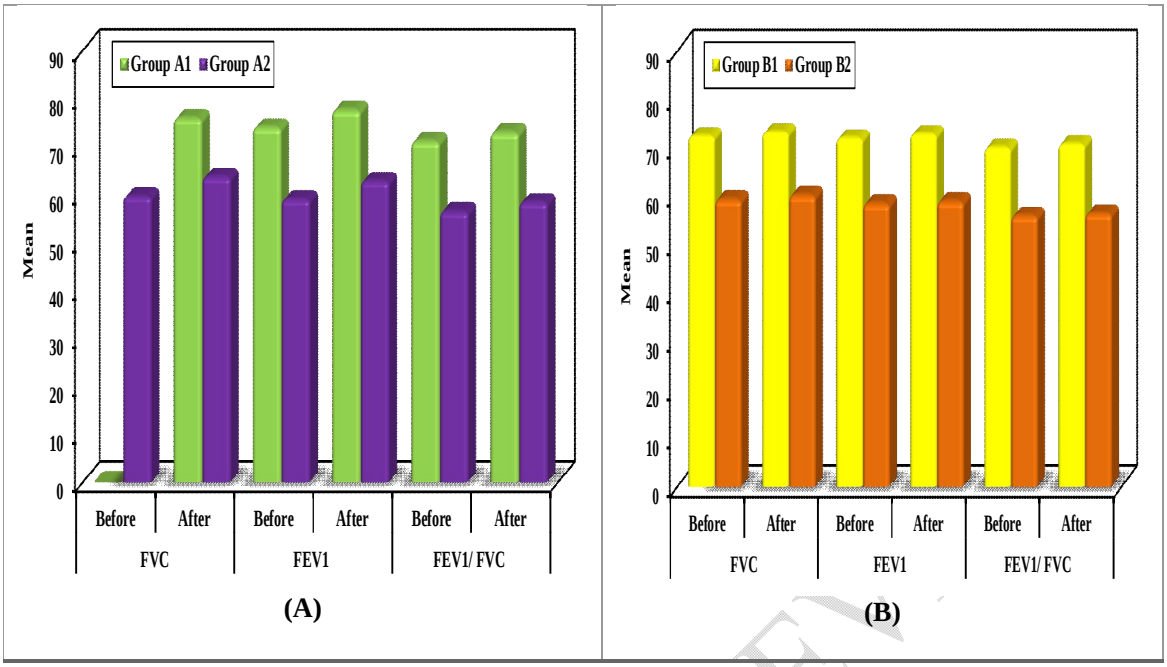

Figure 3: Relation between Asthma severity and pulmonary functions in both groups

Regarding Correlation between Serum Mg and Pulmonary Functions in both Groups, a positive significant correlation existed between serum Mg level and each of FVC, FEV1, and FEV1/FVC ratio in both groups.

Table 4: Correlation between serum Mg and pulmonary functions in both groups

		Serum Mg							
		Before		After		Before		After	
		A1 (N =16)	A2 (N =24)	A1 (N =28)	A2 (N =12)	B1 (N =9)	B2 (N =11)	B1 (N =12)	B2 (N =8)
FVC	r	0.740	0.800	0.914	0.631	0.941	0.936	0.910	0.924
	p	**0.01***	**0.01***	**0.001***	**0.002***	**0.001***	**0.002***	**0.001***	**0.003***
FEV1	r	0.711	0.795	0.672	0.713	0.965	0.985	0.905	0.873
	p	**0.001***	**0.001***	**0.002***	**0.001***	**0.001***	**0.001***	**0.001***	**0.002***
FEV1/ FVC	r	0.900	0.882	0.936	0.748	0.966	0.965	0.952	0.952
	p	**0.001***	**0.001***	**0.001***	**0.001***	0.001*	0.002*	0.003*	0.001*

Regarding Comparison between children with moderate, severe Asthma and controls as regards to serum Mg level, there was statistically significant lower of serum Mg level with increase of asthma severity.

Table 5: Comparison between Children with Moderate, Severe Asthma and Controls as Regards to Serum Mg level

Serum Mg level	Moderate	Severe	Control (N=20)	F	p	p_1	p_2	p_3
Before	(N = 25)	(N = 35)						
Min. – Max.	1.70 – 2.30	1.50 – 2.20	1.80 – 2.30	**39.899***	**0.006***	**0.002***	**0.001***	**<0.001***
Mean ± SD.	1.90 ± 0.17	1.70 ± 0.16	2.13 ± 0.18					
After	(N = 40)	(N = 20)						
Min. – Max.	1.75 – 2.50	1.60 – 2.30		**10.964***		**0.001***		
Mean ± SD.	2.10 ± 0.19	1.93 ± 0.18						

Regarding Comparison between Children with Moderate, Severe Asthma and Controls as Regards to Pulmonary Functions, there was statistically significant lower of pulmonary functions compared to control group.

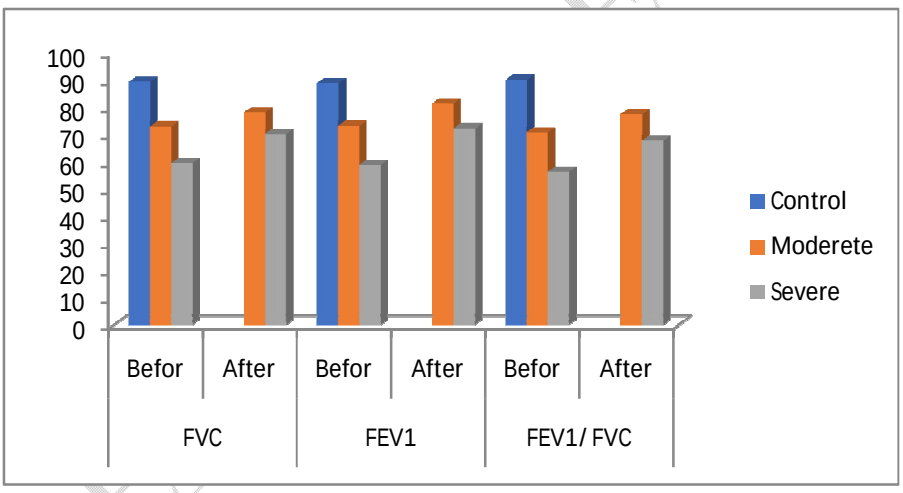

Figure 4: Comparison between Children with Moderate, Severe Asthma and Controls as Regards to Pulmonary Functions

Discussion:

Asthma is a chronic lung illness manifested by inflammation of the airways and hyperresponsiveness of the airway smooth muscles. [1]. Asthma symptoms involve chest tightness, wheezing, coughing, shortness of breath and other respiratory problems. In the majority of cases, these symptoms are mild and manageable with inhalers and allergen avoidance, but they can occasionally cause life-threatening exacerbations. (Global Initiative

for Asthma (GINA) 2020). Mg is the 4th most prevalent mineral in the body, and it is required for more than 300 biochemical reactions that maintain a healthy immune system, strong bones, normal muscle and nerve function and a stable heart rhythm, a robust immune system [3]. Although the exact function of Mg in asthma is not completely understood, it is known that Mg acts as an anti-inflammatory agent in addition to inhibiting the Ca+2-induced contraction of smooth muscle.[4].

In concordance with Shaaban et al. [9] who reported that asthma was more common in boys than girls before puberty and a higher prevalence in females than in males as adults.

Asthma gender differences cannot be explained by a single straightforward explanation due to the disease's complexity. Possible causes are hormonal fluctuations and genetic predisposition. Our result is not in line with Shaaban et al. [9] who showed that (37.8%) of asthmatic patients lived in urban areas and (62.2%)in rural areas. Also, Yawn [10] is not in accordance with our results.

In accordance with Hom, et al. [11] who investigated no association between increased BMI and increased asthma severity. However, Cassol et al. [12] didn't agree with our result. Their study showed a positive association between obesity and asthma severity, but this research was on adolescents.

In accordance with Abdul Rahman Al-frayh et al. [13] who observed that 18% and 20.6% of asthmatics didn't have a positive history of asthma in the immediate family and in relatives, 48.1% and 46.1% had immediate family and relatives with a positive history Therefore, the presence of high familial accumulation aggregation and atopy in the immediate family and relatives was identified as a major risk factor for the development of paediatric asthma.

Our result is in accordance with Julian Casciano et al. [14] who stated significantly more patients with moderate-severe asthma had a higher peripheral eosinophil count than

patients with mild asthma. Also, in accordance with Lee et al. [15] who found positive correlation between total eosinophilic count (TEC) and severity of asthma especially marked in (EIB) exercise-induced bronchoconstriction in children.

In accordance with Ogbuka [16] who reported that children with asthma had significantly lower serum Mg levels than children without asthma. Also, this result is in keeping with similar studies by Alamoudi et al., Oladipo et al., and Agin et al. [17-19] who reported that in asthmatic patients serum Mg level was significantly lower compared to their controls, also it was discovered that hypomagnesemia is a prevalent condition in chronic asthma.

Our results in accordance with the researches done by Shaikh et al. and Yuvara jan et al. [20, 21] but with varying prevalence , although the origin of hypomagnesaemia in chronic asthmatic patients is unknown, it may be connected to increased urine Mg loss as a side effect of corticosteroid , B2-agonist, , or genetically determined therapies or inadequate intake of Mg in asthmatics

In accordance with Alamoudi [18] who discovered among chronic asthmatics that the hospitalizations frequency with low Mg (40%) was significantly higher than among those with normal Mg (11.8 %), and Das et al. [22] who discovered a statistically significant relationship between serum Mg level (normal or deficient) and past and future exacerbations. This can be interpreted by the fact that low serum Mg levels can promote airway hyperreactivity and hyper-responsiveness making chronic asthmatics with low Mg levels more susceptible to acute asthma exacerbations and bronchoconstriction. Hypomagnesemia can result in bronchoconstriction and, subsequently, an elevation in the hospitalisation rate among chronic asthmatics.

In Hala A. et al. [23] study, they found that hypomagnesaemia was much more prevalent in moderate and severe chronic asthmatic patients, also acute asthmatic attacks were associated with a statistically significant reduction in serum Mg levels.

The study done by Olga Bede et al. [24] agreed with our study, she reported that deficiency of Mg can occur in in moderately asthmatic children, and can be avoided with adequate long-lasting Mg supplementation, she also found the significant decrease in the use of bronchodilator in children with moderate asthma Vs. the placebo group suggested the Mg supplementation benefits.. Olga Bede et al. [24] found that Mg has positive benefits on the airways. A low intake may increase the likelihood of developing asthma or persistent airflow obstruction in individuals. A consumption of 200–600 mg of Mg per day was previously demonstrated to be associated with increased FEV1 and decreased bronchial hyperreactivity.

Fuhlbrigge et al. [25] found a significant correlation between FEV1 % and asthma symptoms and severe asthma exacerbations requiring oral corticosteroids, visits to the emergency department, and hospitalizations.

In accordance Narges Fathi et al study . [26] that used 340 mg of Mg citrate daily or placebo for 2 months and found that after 2 months of oral Mg supplementation, significant FVC (P= 0.002), FEV1 and the FEV1/FVC ratio changes were observed. This study provides evidence that in mild and moderate asthmatic patients, oral Mg supplementation can enhance lung function.

The study done by Hala A. et al. [23] found that with Mg sulphate infusion, there was a considerable increase in FEV1 and PEFR, which is consistent with Rolla et al. (1991) and Devi et al. (1997). However, Mohammed and Goodacre (2007) found weak evidence that I.V Mg sulphate improves respiratory performance in adults.

The study done by J Britton, et al. [27] found that a 100 mg/day increase in Mg intake was associated with a 27.7 ml increase in FEV1; he concluded that dietary Mg consumption

is independently associated with lung function and the incidence of self-reported wheezing and hyper-reactivity of the airway in the general population.

Our study disagrees with A Fogarty, et al. [28] who reported that regular dietary supplementation with vitamin C or Mg does not offer any therapeutic benefit to the conventional treatment for asthma in primary care patients. It is likely that supplementation is only helpful in cases with a reduced baseline intake of these nutrients (Mg and vit. C and Mg), and that the lack of benefit in this trial is due to the fact that these participants had relatively high baseline daily intakes.

Limitations of the study were, Serum Mg level may not accurately reflect Mg store in the body because Mg is an intracellular cation so a more accurate assessment of Mg status is given by erythrocytic Mg estimation , a 24-hr recall of dietary intake was insufficient to assess the dietary intake of subjects, hence it is difficult to determine the Mg quantity eaten at each meal. Further follow-up is needed.

Conclusions:

Asthmatic children with moderate and severe asthma who received asthma treatment in combination with oral Mg supplementation had an improvement in their pulmonary function tests and serum Mg level to provide better symptoms control in paediatrics. Serum Mg level and pulmonary function tests were significantly lower in asthmatic children. A significant correlation between hypomagnesaemia and reduced pulmonary function tests was proven. Pulmonary function tests and hypomagnesaemia were significantly related with severity of asthma.

Consent

An informed written consent was obtained from the patient' guardian.

Disclaimer

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