IMPACT OF MAGNESIUM SUPPLEMENTATION ON BONE MASS ACCRUAL IN ADOLESCENTS WITH SUBOPTIMAL MAGNESIUM INTAKE: A PILOT STUDY

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Abstract:

Pilot in the study was an attempt to test the influence of magnesium (Mg) supplement on the accrual of bone mass in poor dieting adolescents on magnesium. The researchers selected premenarchal girls of ages 8-14 years old and assigned them to magnesium oxide (300mg/day) or placebo in a span of one year. Dual energy x-ray absorptiometry (DXA) was used to measure the bone mineral density (BMD) and bone mineral content (BMC) at baseline, after 6 months, and after 12 months. The increase in total hip BMC was also significantly greater in the Mg-treated group than a placebo group especially in the neck of the femur, total hip and Ward area. Whereas, the effect on the spinal BMC and BMD was comparatively small, the effect was positive in support of Mg group. Mg supplement was also safe and well tolerated and linked with a reasonable compliance. This paper has confirmed the possibilities of Mg supplement on bone health in early teens, and more studies are required on bigger populations.

Keywords: Magnesium, Bone mass, Adolescents, Bone mineral content, Supplementation

INTRODUCTION

Diet has also been demonstrated to contribute largely to the occurrence of osteoporosis in old age, physical exercises and genetic factors (1-6). Nevertheless, the correlation between the bone mass at adulthood and the one at the bottom of the adolescence has not been studied carefully. Nevertheless, proper nutrition in the age of growth is regarded as an unquestioned insurance of lowering the osteoporosis rates in the age. Unlike, the role of calcium in keeping the bones of children healthy has been extensively studied (7–11), little has been conducted to comprehend the role of nutrition of magnesium (Mg) in that regard. Mg is a part of the mineral part of the bone and one of the essential components of the bone (1214), approximately, half of the entire magnesium in the body is concentrated in the bones, attached to the surface of hydroxyapatite (1516). Mg is a significant player in mineral homeostasis which is accompanied by the effect of balancing the release and action of parathyroid hormone (PTH) (17, 18) and the activation of vitamin D (19). Mg also activates the parathyroid and renal tubular cells extracellular calcium-sensing receptor, which is also an instant method by which Mg can have an impact on the body organs which contribute the core role in mineral homeostasis (20).

The nutritional surveys have discovered that the young American women lack magnesium in many occasions. Its daily dose of magnesium (RDI) in girls at the age of 9-13 and 14-18 years is 240mg/d and 360mg/d respectively (21). The magnesium intake of Third National Health and Nutrition Examination Survey (NHANES III) (1215 years old, 2016) was 206 (±7.6) mg/d (22). Although the body of research on the human intervention is small enough, it hints at the fact that magnesium supplementation could reduce bone turnover (23) and promote bone mass of some types of adults (24, 25). More importantly, bone degradation in case of magnesium deficiency in rats at high bone growth stages is directly related to osteoporotic status (26) and more recently, retarded bone growth, which is characterized by reduced osteoblast activity, high osteoclastic activity and loss of trabecular bone has been seen in magnesium deficient mice (27).On the basis of these observations, the hypothesis that magnesium undernutrition can stifle optimum bone growth during adolescence stage, was put forward.

To examine this we have conducted a pilot study and we discovered that magnesium supplement was well accepted and high rate of compliance and a positive increase of hip bone mineral content (BMC) in premenarchal girls.

METHODS

Study Design Overview

The study was designed to establish the safety and acceptability of the oral magnesium (Mg) supplementation to adolescents. The outcome goals considered to be the most important were to identify the effect size and evaluate the adherence to Mg supplementation. To further reduce the research; we selected the group of the girls aged between 8-14 years because of the active bone development and the possible absence of Mg at this age. Pediatric practices were used to recruit the subjects in the area. An estimated dietary Mg intake was utilized to select the volunteers who had dietary intake of less than 220 mg/day, another dietary intake was estimated using a 3-day dietary record and the estimated dietary intake was eradicated. The parents were made aware of the intended aim of the study, and the Mg of the subjects of the study, after the screening. It was an interventional, placebo, randomized and one year placebo trial which compared magnesium oxide to a control, a placebo. The initial assessment of the study subjects was done after 1, 6 and 12 months after the supplementation. Compliance and safety follow-up in the form of contact were conducted after 1-2 months to ensure the compliance. The study participants were to report to the study coordinator whenever he or she wanted to report any undesired events.

Recruitment and Enrolment

The paediatricians talked at length about the project on the phone upon the identification of the eligible participants as office posting or letter. Parental and child consent was covered in written form in case this would be in line with the inclusion/ exclusion criteria. During the study, any healthy and premenarchal Caucasian girl aged between 8-14 years was eligible as a study population. A parent and a child were interviewed with by a registered dietitian to provide the information related to the diet. Following the analysis of the nutritional histories, the research was limited to the individuals whose daily intakes of Mg were low (56.4) relative to the rest of the subjects whose intakes were above 220mg/day. A research nurse trained in paediatric endocrinology conducted physical examination on the participants and recorded the Tanner stage of breast development.

Randomization and Intervention

The magnesium oxide and placebo were introduced to the participants in 4 block ratios which were 1:1 using a random number table. Both the personnel and the research subjects were not aware of the treatment assignment. The magnesium supplementation was in two doses (twice daily) in capsule, which included magnesium oxide (300 mg of elemental Mg/day). The placebo was also made using the same powder of methylcellulose. They were prepared in cards of calendar capped capsules of two closed blister capsules. The highest limit of supply distribution was 1-3 months. Compliance was prompted and safety was observed by calling the coordinator of the study every month.

Outcome Measures

Baseline and 6 and 12 months supplementation Bone densitometry was assessed of lumbar spine and hip. The skeletal variable of major primary outcome was the bone mineral content (BMC) that is a direct variable, and is not altered by alterations in the bone area during growth. At this point, height and weight were measured and a full-fledged biochemical profile was obtained at this point and a month following supplementation that is presented in Table 1 and Table 5 respectively.

Bone Densitometry

The bone densitometry test was performed on four parts of the hip including; Femoral neck, trochanter, intertrochanteric regions of the femur diaphysis (forming total hip BMC) and Ward area by use of dual-energy x-ray absorptiometry (Hologic QDR 4500W bone densitometer; Hologic, Bedford, MA).

In the analysis of the scans of lumbar spine of the anteroposterior setups, pediatric software (Legacy Low Density Spine-revision C; Hologic) was analyzed. Two trained technicians carrying out all the scans were trained on the bone densitometry of children. The scans were confirmed until consistency ensued with respect to regions of scans that were done at a time in a particular subject.

Nutritional Analysis

The same was estimated by use of food preferences questionnaire to determine the daily Mg intake. The participants with an assumed daily intake of Mg of less than 220mg/day were requested to develop a 3-day nutritional journal that would be further discussed. The physical meeting contained food models and description of portions size in print and the instructions of food record were given. Name of the brand, size of portion based on household preparation measures and food preparation methods were recorded. These were to publish their intake in 2 weekdays and one day off weekend. The dietician would cross-examine the finished records and make any phone calls to get the missing information. Findings were forwarded to the respondents and only those that had an average of less than 220mg/day of Mg consumption were invited. There was a second 3-day food record that was taken in the middle of the study to determine consistency. A registered dietitian was used to conduct the nutrient analysis of Food Processor Program (ESHA Research, Inc., Salem, OR).

Statistical Analysis

Statistical analysis of BMC and bone mineral density (BMD) was carried out with SAS version 8.2 (SAS institute Inc., Cary, NC). The significance level used in all the tests was the one-sided P value of 0.1. The primary analysis at the end of the 12 months treatment was the comparison of the levels of changes and variability of changes of incremental BMC in the treatment group and the placebo group. Secondary surveys on the trends of BMC and BMD as per the maturity groups and skeletal locations based on treatment. Maturity groups The maturity groups were the prepubertal-early pubertal (Tanner 1 or 2 at enrolment), and mid-late pubertal (Tanner 3 or 4). The test of primary hypotheses was based on repeated measures analysis of covariance (ANCOVA) models of three areas of the hips (the neck of the femur, the total hip (that includes the neck of the femur, trochanteric region and intertrochanteric region), and the Ward area). The covariate of the model was baseline BMC. Some of the other interaction tests that were conducted were treatment by maturity group, treatment by location and treatment by baseline BMC (or BMD). ANCOVA of SAS was performed on the biochemical data, in terms of the treatment, time, and interaction effects. The parameters of biochemical parameters were statistically compared at the level of significance of 0.05- one sided at all samples of the same type.

RESULTS

TABLE 1. Densitometric measures of bone mass at enrollment

Measure	Mg-treated (mean ± sd)	Placebo (mean ± sd)
BMC (g)		
Spinal column	28.50 ± 6.00	29.12 ± 8.25
Ward's district	0.690 ± 0.15	0.740 ± 0.18
An all-around hippie	18.45 ± 4.60	18.00 ± 5.90
Bone area (cm²)		
Spinal column	40.10 ± 5.55	41.00 ± 7.10
Ward's district	1.15 ± 0.11	1.17 ± 0.10
Total hip	25.50 ± 4.20	24.90 ± 5.15
BMD, BMC/bone area (g/cm²)		
Spinal column	0.712 ± 0.080	0.710 ± 0.115
Ward’s area	0.600 ± 0.110	0.630 ± 0.125
Total hip	0.725 ± 0.090	0.730 ± 0.120

TABLE 2. Combined overall hip measures of bone mass (as change from baseline)

Measure	Least square mean (g)	Standard error (se)	P value
BMC			
Group as a whole		0.0534	
Medications	1.1205	0.06205	0.065
Using placebos	1.0143	0.06010	
A half-group of Tanners		0.2967	
Treatment	0.9756	0.06235	0.112
Using placebos	0.9274	0.06110	
3 & 4 Tanners		0.0991	
Treatment	1.1523	0.0741	0.070
Placebo	1.0300	0.0712	
BMD			
Group as a whole		0.8444	
Medications	0.1210	0.03625	0.087
Using placebos	0.1158	0.03589	
A half-group of Tanners		0.6357	
Treatment	0.1053	0.03602	0.136
Using placebos	0.1105	0.03562	
Tanner 3/4 group		0.5854	
Treatment	0.1402	0.03710	0.045
Placebo	0.1236	0.03685	

The aim of the research was to establish how magnesium (Mg) supplement affects bone mass in terms of the change in bone mineral content (BMC) and bone mineral density (BMD) in the different age groups. The densitometric measurements of the bone mass of the Mg-treated and placebo group can be viewed in the densitometric scale of the baseline values of the bone mass during the time of enrolment (Table 1). The lumbar spine value of Mg-treated group in the BMC scenario was 28.50 + 6.00 g, which is marginally lesser than the placebo providing 29.12 + 8.25 g. Similarly, the same was observed in the case of area and total hip BMC of Ward where a slightly lower value of Mg-treated group than the placebo was observed. In terms of bone area, the Mg-treated group had also slightly lower values of the lumbar area spine and total hip, but there was no significant difference in the value of the area enjoyed by the Ward in the two groups. The same tendency might be noted in the Mg-treated BMD population where the values of lumbar spine, Ward area and total hips were not different to that of the placebo population. Under general hip analysis of bone mass (Tables 2 and 3), the measurement of the BMC at baseline showed that there was a linear yet insignificant increase of Mg treated group versus the placebo. Concerning Mg-treated group, the means of the Mg-treated group of 1.1205 0.06205 g and 1.0143 0.06010 g of placebo group increased by 0.05. Its dissimilarity was more at the level of Tanner 3/4 and a higher proportion of the Mg-treated people increased in comparison with their placebo counter-parts but with a low significance value. Likewise on the same aspect in respect of BMD, there was a slight, but persistent advantage in Mg-treated group on the total cohort and Tanner 3/4 cohort, less so in Tanner 1/2 cohort. Such results indicate that magnesium supplemental effect can positively impact bone mass accrual in specific circumstances in older adolescents. Nevertheless, these trends are to be further supported by more research on a small sample with a longer follow-up period.

DISCUSSION

This research offers some data to confirm the hypothesis that the magnesium (Mg) supplement has a positive effect on the accrual of bone mass among the adolescents with poor Mg absorption. The percentage change in the total hip bone mineral content (BMC) of the people who were given Mg was also significant as compared to the percentage change of the total hip bone mineral content (BMC) of the students who were given the placebo. Subgroup analysis, which was pegged on the maturity (girls in Tanner stage 1 to Tanner stage 3 and 4 to each) revealed that, there was no statistically significant difference in the effects of Mg supplementation in each of these maturity groups, however, there was no statistically significant difference in the effects in each of these maturity groups. In addition, the hip location results were compared between the two hips and the results showed that BMC change was more favourable in Mg-supplemented group in total hip, the femur neck and Ward area. This effect on skeleton was achieved without significant increase in the levels of minerals or bone turnover indices. Moreover, the Mg-supplemented group had a better (but not significantly) increment in the spinal BMC as well as bone mineral density (BMD) compared to the placebo group. Mg (300 mg/day) 300 mg magnesium oxide as 2 doses of 300 mg each of the forms of capsules were safe, well-tolerated and reasonably adherent to the use. The weight gain of placebo and Mg-supplemented groups was not significantly different. Dietary Mg and BMD (3135) have been proven to be correlated. Coincidentally, Mg during the early adolescence was linked with the mass of the calcaneal bone at the young adulthood (35) Mg during premenopausal women was linked with varying levels of spinal bone density (34) to suggest that Mg does play some role in bone mineralization in the early to adolescence phase. The other result of the NHANES data analysis was a correlation between dietary Mg and hip BMD in some of the groups including younger men who were not Hispanics (36). Limited amount of interventional research has been done on the impact of Mg on the bone. The bone turnover indicators in healthy young men on day 5 reduced in those who were fed on Mg supplementation (360mg/day) (23). The randomized controlled trial of the postmenopausal female population with osteoporosis that was not controlled showed that Mg supplements were related to improving the BMD of 60 percent of the women (24). In a controlled trial of the use of placebo control with individuals with gluten-sensitive enteropathy, there was a significant increase of BMD in the group using Mg supplements compared with the group using placebo control after 6 months (25). These studies suggest that Mg supplementation has application in the development of the bone-mass, but the studies have not been significantly undertaken on healthy young people, but the elderly with some complication in their health. Due to the reality that the suboptimal levels of Mg intake were identified in the U.S. dieting surveys (21, 22, 37), Mg supplementation can be considered one of the significant variables to be considered in the periadolescent population. Our hypothesis was that early adolescence stage was critical stage in terms of improvement of Mg intake and thus we planned to conduct this pilot study to determine the outcome of Mg supplementation on this group. In order to reduce the variance in bone mass between the genders and ethnicities, we have narrowed down to the Caucasian females. We picked the half of the screened subjects that had the lowest percentage to obtain Mg intake because this would represent the most likely beneficers of the intervention. The selection of researchers population and the general compliance rate was self-motivation (73 percent). There was 12 per cent dropout rate randomly selected on the treatment and maturity group. Some of the weaknesses of this study include small size of the study. The absence of pre-data could not predetermine the quantity of the sample and statistical power to place oneself in a situation to identify the changes on the anatomical sites (37,38). This implies that the possibilities of such outcomes cannot be overemphasized since the differences are low in their level of significance. Nevertheless, we affirm that in a bigger study we would have been able to make more conclusive findings, since the predispositions that informed Mg supplementation were fundamentally similar at the various pubertal phase and at the various locations. The results would not be applicable to those who have more Mg intake, boys and other ethnicities because we sampled the girls with mean Mg below 220 mg/day. Finally, this pilot study was positioned to illustrate that Mg supplementation positively impacted on bone mass accrual after 12 months in peripubertal Caucasian girls with sub optimum daily intake of Mg. The supplement was acceptable and non-toxic. Majority of the future researches rely on the study to justify the skeletal effects of Mg in children.

CONCLUSION:

The pilot study presents some evidence that magnesium (Mg) supplementation is a potentially useful intervention on bone mass accrual in adolescents with the sub-optimal Mg intake, specifically, pre-menarchal girls. The findings also showed that Mg-supplemented group had much better bone mineral content (BMC) at the hip than the placebo group and the responses between the various locations of hip such as the femur neck, total hips and Ward area were also good. The difference in the mass and densities of the spinal bones were not that high, though, they were in favor of the Mg group. The toleration to supplementation was good, no side effects were experienced and there was reasonable compliance and this was also an indicator that this may be among the interventions that can be employed to enhance the bone health of young adolescents. Nevertheless, a study with larger cohort size and extended follow-ups is needed to demonstrate the effectiveness of the Mg supplementation and develop a more rigid conception of the impact it has on the skeletal development as some of the results were insignificant and the sample size was small. The research paper can be used to form the basis of future studies based on the role of Mg to the bone health of adolescents.

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