

Comparison of Oral Magnesium Supplements with Placebo for Pregnancy-Induced Leg Cramps

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ABSTRACT

Background: Magnesium deficiency results in different types of complications in the pregnant females in pre and post delivery phase. This study is planned to check the impact of magnesium supplementation in terms of reduced leg cramps.

Objective: To compare the effectiveness of oral magnesium supplements versus placebo for pregnancy-induced leg cramps.

Study Design: Randomized control trial

Place and Duration of Study: Department of Obstetrics & Gynecology Department Unit 1, Lady Willingdon Hospital Lahore from 25th March 2017 to 30th September 2017.

Methodology: Two hundred pregnant women were enrolled. All patients were divided in two groups and each group comprised 100 patients. Group A received magnesium bisglycinate chelate (300 mg per day) and group B received placebo. All patients of both groups were followed for effectiveness. At the end of the 4th week, a detailed history was taken from patients about entirely free from leg cramps i.e. effectiveness.

Results: The mean age was 28.29±5.76 years. Gestational age was 27.74±5.25 weeks. The body mass index was >30 in 141 (70%). Majority of the females 57 (28.5%) have parity 3 while 55 (27.5%) were having parity 2. Overall efficacy was 71 (35.5%) and it was not noted in 129 (64.5%). It was found that efficacy of magnesium was in 45 (45%) and in placebo group 26 (26%) and this difference was statistically significant ($p < 0.05$).

Conclusion: Magnesium therapy appears to be effective in the treatment of pregnant induced leg cramps in the general population, but may have a small effect in pregnant women.

Key Word: Leg cramps, Pregnancy, Magnesium therapy

INTRODUCTION

Leg cramps were describe by Salvatore in 1961 as " sudden tonic or clonic involuntary contractions of the gastrocnemius muscle associated with severe pain". This definition discriminates leg cramps from restless legs in that the latter is not associated with pain.¹

Leg cramps are common in pregnancy; 30-45% of pregnant women suffer from leg cramps. Pregnancy-induced leg cramp tends to be more frequent during the second half of pregnancy, and mostly at night, resulting in sleep disruption which potentially introduces other complications.²

Leg cramps are involuntary, localized and usually painful skeletal muscle contractions, which commonly affect calf muscles.³ Muscle cramps arise from spontaneous discharges of the motor nerves rather than from within the muscle itself.⁴

Currently, there is no standard treatment for pregnancy-induced leg cramps; however, several studies have been conducted so far. Magnesium is the second most abundant intracellular cation and a cofactor for more than 300 metabolic reactions in the body.⁴ As pregnancy is a physiologic state of low serum magnesium compared with non-pregnant, shortage of magnesium may be one of the causes for cramping, which explains why there is a higher rate of leg cramps in pregnancy.⁵

Magnesium deficiency increases neuronal excitability and enhances neuromuscular transmission with muscle cramps as it has a curariform action on the neuromuscular junction and is associated with the release of acetylcholine from motor nerve terminals. Hence, magnesium supplementation may suppress excitable tissue and suppress muscle cramps.⁶

A study done by Dahle et al⁵ demonstrated the therapeutic effect of magnesium lactate/magnesium citrate against leg cramps in pregnancy at least twice a week when compared with placebo and found significant difference in terms of entirely free of leg cramps in both groups i.e. (10/34= 29.4% in magnesium group {dosage 5mmol (100mg); 3 times a day} versus 3/35=8.57% in placebo group) and treatment duration in this study was 3 weeks. Similarly another study done by Supakatisant and Phupong⁴ reported that patients with pregnancy-induced leg cramps at least twice a week and reported that efficacy (in terms of number of subjects without leg cramps after 4-weeks of treatment was

significantly higher in the magnesium group {dosage 100 mg 3 times a day} than the placebo group.

On the contrary, Nygaard et al¹ enrolled 38 pregnant women with leg cramps in their study. Treatment of oral magnesium supplementation {dosage of 5mmol 3 times a day} and placebo was prescribed. They found no significant effect of oral magnesium on frequency and intensity of leg cramps in pregnant women.

The rationale of this study is to compare the effectiveness of oral magnesium supplements with placebo as a treatment for pregnancy-induced leg cramps as no local study is available on this debate. Pregnancy induced leg cramps tend to be more frequent during the second half of pregnancy, and mostly at night, resulting in sleep disruption, which potentially introduce other complication like Lee & Gay⁷ reported that less sleep during pregnancy (less than 6 h per night) is associated with longer labour and increased rate of operative delivery. Since magnesium acts as a necessary activator of some 300 different enzymes and plays a central role in metabolism and muscle function. Pregnancy and lactation are among those processes that may be associated with a secondary magnesium deficiency. Some above mentioned studies reported that magnesium supplements helped in improvement of leg cramps but some showing that it made no difference. If we found the magnesium treatment effective in our population then we can recommend it as a treatment option for this patient group.

PATIENTS AND METHODS

In this randomized control trial conducted on 200 pregnant women with age group range 18 to 40 years, presenting with a history of painful leg cramps at least twice a week, with gestational age of 16 to 36 weeks assessed on LMP and having a singleton pregnancy (assessed on USG) with up to parity 4 were included whereas those with pre-eclampsia assessed, already taking magnesium or other treatment for leg cramps, Hypersensitivity to magnesium and Hb <10 mg/dl were excluded. Their demographic features i.e. name, age, parity, body mass index and address was recorded. The patients were divided in two groups and each group comprised 100 patients. Group A received magnesium bisglycinate chelate (300 mg per day) and group B received placebo. All patients of both groups were followed for effectiveness. At the end

of the 4th week, a detailed history was taken from patients about entirely free from leg cramps i.e. effectiveness. All the patients were followed-up and data was collected. Data was entered and analyzed through SPSS-20. Effectiveness was compared in both groups by using Chi-square test and P value ≤ 0.05 was considered as statistically significant.

RESULTS

The mean age, mean gestational age and mean body mass index was presented in Table 1. Overall efficacy was 71 (35.5%) and it was not noted in 129 (64.5%) [Table 2]. It was found that efficacy of magnesium in 45 (45%) and 26 (26%) in placebo group. This difference was statistically significant ($p < 0.05$) between the groups (Table 3).

Table 1: Descriptive statistics of the patients (n=200)

Variable	Magnesium Group	Placebo Group
Age (years)	27.74±5.94	28.84±5.56
Gestational age (weeks)	27.98±5.28	26.97±5.21
Body mass index (kg/m ²)	26.23±4.67	27.24±5.32

Table 2: Distribution of the overall efficacy in the study group (n=200)

Overall efficacy	No.	%
Yes	71	35.5
No	129	64.5

Table 3: Comparison of the efficacy of the treatment versus placebo group

Efficacy of Treatment	Magnesium Group	Placebo Group	P value
Yes	45 (45%)	26 (26%)	0.004
No	55 (55%)	74 (74%)	

DISCUSSION

Many older people have experience of leg cramps at night. Leg cramps are also common during pregnancy with 33-50% of pregnant women experiencing leg cramps that also tend to get worse as the pregnancy progresses.⁸ There are many potential causes of night cramp, among them include over exercising, standing or sitting too long, cold weather, dehydration, and decreased amount of electrolytes which regulates muscle contractions and relaxation.⁹

Magnesium is one of the important electrolytes in the body. Deficiency of magnesium has been associated with a wide spectrum of symptoms, with leg cramps being one of them. Successful treatment of muscle cramps in patients with low magnesium level through intravenous infusion and supplementation of magnesium had been reported in some early case reports. As such, magnesium supplement has been widely marketed as a potential relief for night cramp.¹⁰ Guerrero et al¹¹ have shown the effectiveness of magnesium in eclampsia and preeclampsia, arrhythmia, severe asthma, and migraine. Other areas that have shown promising results include lowering the risk of metabolic syndrome, improving glucose and insulin metabolism, relieving symptoms of dysmenorrhea, and alleviating leg cramps in women who are pregnant.

Leg cramps occur in about 50% of pregnant women and subside after delivery.^{12,13} The mechanism for cramping is not known yet and is likely to be idiopathic, but it could be due to physiological changes in neuromuscular performance, weight gain, joint laxity in the final stages of pregnancy, impaired blood supply to lower body organs, and increased pressure on leg muscles during pregnancy.¹⁴ Pressure on blood vessels and nerves resulting from the enlarged uterus, imbalances between the intake and output of electrolytes and vitamins, and insufficient minerals intake might be other reasons for cramping. Hence, could increase glomerular filtration and greater needs of the fetus for receiving minerals from the mother (which reduces her serum calcium and magnesium levels).^{15,16}

Dhale et al⁵ conducted the studies in two hospitals of Sweden, 73 women with pregnancy-related leg cramps were randomly assigned to receive oral magnesium (15 mmol) or placebo daily for three weeks. They indicated that oral magnesium supplementation may be a valuable treatment option in the management of pregnancy-induced leg cramps. Similarly this

showed that significant improvement in the female who are presented with pregnancy related leg cramps.

In the present study, the efficacy was evaluated in magnesium as 45(45%) and in placebo group 26(26%) and this difference was statistically significant (p -value <0.05). These findings correspond to Supakatisant et al⁴ reported that efficacy (in terms of number of subjects without leg cramps after 4-weeks of treatment was significantly higher in the magnesium group {dosage 100mg 3 times a day} than the placebo group (i.e. 21/43= 48.8% vs 12/43=27.9%; P -value= 0.04). Another study done by Dahle et al⁵ demonstrated the therapeutic effect of magnesium lactate/magnesium citrate against leg cramps in pregnancy at least twice a week when compared with placebo and found significant difference in terms of entirely free of leg cramps in both groups i.e. (10/34= 29.4% in magnesium group {dosage 5mmol (100mg); 3 times a day} versus 3/35=8.57% in placebo group). Treatment duration in this study was 3-weeks. Though frequency of efficacy was no similar but it shows that magnesium is more effective than placebo.

On the contrary, Nygaard et al¹ enrolled 38 pregnant women with leg cramps for the treatment of oral magnesium supplementation {dosage of 5mmol 3 times a day} and placebo. They found no significant effect of oral magnesium on frequency and intensity of leg cramps in pregnant women. These findings are no in agreement with our study.

We are of the view that every pregnant woman should be supplemented with 240-480 mg (10-20 mmol) magnesium daily. Magnesium supplementation should start as soon as possible, continue until birth, and be continued postnatally, since the magnesium requirement of the body also increases during breast-feeding. Magnesium supplementation should not be discontinued some weeks before birth, since an effect on the beginning of spontaneous labour pain has not been proved.

CONCLUSION

When magnesium deficiency is agnostically assumed, magnesium deficiency exists with corresponding symptoms (e.g. calf muscle cramps, inadequate uterus, magnesium supplementation is essential. Notably, women in risk groups (e.g. patients with sprue, diabetics, metabolic syndrome and multiple births) have a higher magnesium requirement.

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