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Original Research Article

Effect of magnesium and zinc supplementation in the patients of essential hypertension

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ABSTRACT

Background: Primary hypertension is the most common (almost 95%) and it can easily be controlled through lifestyle modification by regular exercise and controlled diet plan. Magnesium and zinc supplementation can alleviate essential hypertension.
Methods: 73 hypertensive patients were recruited. Thrice in a row with interval of 5 minutes, twice a day for 7 days high BP monitoring was done and ensured daily intake of Mg (300 mg) and Zn (10 mg) for 4 weeks. Thereafter again 4th week home Blood pressure monitoring was done. Study was done from 25 April 2023 to 24 April 2024. Secondary hypertension was excluded after proper radiological and pathological investigations.
Results: Decrease in SBP by 6.9 mmHg, pre SBP 141±11.3 SD and post SBP 134±9.6 SD and DBP by 4.8 mmHg, pre DBP 91±7.8SD and Post DBP 86±73, observed after 4 weeks supplementation. In 30 medicated patients, antihypertensive showed decrease in SBP by 4.6 mmHg, pre SBP 137±11.5 SD and post SBP 132±9.6 SD with and DBP by 4.7 mmHg, Pre DBP 89.6±9.2SD and post DBP 84.9±8.7.
Whereas, in a group of 43, without any medicine exhibited decline in SBP by 8 mmHg (Pre SBP 144±10 SD and Post SBP 136±9.5 and DBP by 5 mmHg, pre DBP 92±6.8 SD and post DBP 87±0.6.3 SD. Value of $p<0.001$ in the study group.
Conclusions: Supplementation reduced blood pressure in all pre and post groups. The effect of supplementation had slighter edge on who were not taking antihypertensive medicine than were taking single medication or combined therapy.

Keywords: Systolic blood pressure, Diastolic blood pressure, Cardiac output, Essential hypertension, Primary hypertension

INTRODUCTION

Primary hypertension

There is many pathophysiology which explains the origin of primary hypertension such as change in the vessel wall stiffness and diameter either temporarily or permanently.

Arterial stiffness

Arterial stiffness refers to a reduction in elasticity and distensibility of arteries, and pulse wave velocity (PWV) is often used to represent the degree of stiffness in large arteries. An increment in PWV shows extreme blood vessel firmness and disabled in blood vessel dilatation capacity.

Arterial stiffness has been closely associated with an increased risk of essential hypertension, especially the isolated systolic hypertension.[1-3] Vice versa, systolic BP is also associated with a clinically significant progression of arterial stiffness.[4]

Sodium retention theory

Water-sodium retention is a key cause of abnormal increases in intravascular fluid volume. Diuretics (especially thiazide diuretics) are important in the control of hypertension caused by water-sodium retention.[5] Except secondary hypertension resulted from renal dysfunction, there is also a group of hypertensive patients related to water-sodium retention in essential hypertension, namely salt-sensitive hypertension. High-salt intake stimulator for primary hypertension caused by water-sodium reabsorption. Not all people will develop increased BP after consuming excessive salt. According to the blood pressure reactivity to salt-intake, patients are called salt-sensitive and salt-resistant, respectively.[6]

RAAS

Renin-angiotensin-aldosterone system is a consecutive peptidergic system that functions in the control of the renal, adrenal, and cardiovascular systems. RAAS directs BP primarily by influencing blood vessel narrowing and water-sodium maintenance in the body. Both circulating RAAS and tissue RAAS (cardiac RAAS, vascular RAAS, intra-renal RAAS, brain RAAS and adipose tissue RAAS) have been involved in the pathogenesis of essential hypertension and related target organ damage.[7]

Sympathetic dysregulation

Sympathetic dysregulation is also an important cause of essential hypertension.8 The sympathetic overdrive leads to increased cardiac output, increased systemic vascular tone, and elevated plasma catecholamine levels. Patients with hypertension can manifest as greater muscle sympathetic nerve activity (MSNA) and lower baroreflex response.[9]

Genetics

Hypertension is closely related with qualities, and our understanding of the relationship between hereditary qualities and BP has been well moved forward in later years. More than 500 loci involved in the regulation of BP have been revealed by genome-wide association studies, taking the total number of BP genetic loci to over 1,000.[10] And BP is even discussed as a probable omni genic trait.[11]

Effect of Magnesium and Zinc

Magnesium is an important cation for the activity of many enzymes related to energy metabolism, e.g., serine racemase.[12] ATP diphosphohydrolase or myosin ATPase.[13,14] In addition, elevated levels of serum magnesium may lead to smooth muscle relaxation and vasodilatation due to antagonistic action on calcium receptors and channels.[15] On the other hand, the reduction of extracellular magnesium causes vasospasm, particularly important pathogenic factor for sudden death in ischemic heart disease, and for glaucoma and diabetic retinopathy.[16,17] Elevated extracellular magnesium leads to decrease of blood pressure through stimulated production of prostacyclin in endothelial cells and vascular smooth muscle cells and the inhibition of norepinephrine release from nerve endings.[18,19]

While Zinc reduces systolic BP only with non-consistent mechansim.[20] Secondary hypertension is purely due to either sudden or progressive changes in the system involved in it. Progressive renal artery stenosis and renal parenchyma disease can be example for it. Similarly, if we take a case of diabetes, it takes years to progress into hypertension. Inborn error in epithelial sodium channel (ENac) at DCT and collecting duct may lead to hypertension.[21]

Sudden causes may include hyperthyroidism and pheochromocytoma. These are conditions which demand immediate pharmacological and surgical intervention to control emergency and also require further routine medications and follow-up so that disease progression or regression could be monitored. These can be hereditary too that progress from one generation to other.

METHODS

Study design

This study was designed to determine the effect of minerals such as Magnesium and Zinc supplementation in the patients of essential hypertension. And to evaluate pre and post supplementation change in systolic blood pressure and diastolic blood pressure in the newly diagnosed hypertensive patients who were on antihypertensive medication and also among those not taking medicine at all despite being diagnosed hypertensive.

Measurements were taken 1 week prior to and at 4th week of Magnesium and Zinc supplementation. Home Blood Pressure Measurement was done where blood pressure was monitored twice a day for 7 days and each time 3 reading should be taken with 5 minutes apart for final declaration of Hypertension. Validated HEM-7156T Model OMRON digital BP Instrument was used as a research tool.

Study place

The study was conducted in the Department of Physiology, King George's Medical University, Lucknow in collaboration with Department of Medicine, KGMU, Lucknow, India.

Study duration

Study duration was one year from 25 April 2023 to 24 April 2024.

Subjects were taken from Medicine OPD, KGMU, Lucknow after taking ethical clearance from the Internal Ethical Committee of KGMU, Lucknow and informed consent taken either from the patients or from their guardian. A total number of 73 subjects allocated in the study. Hemodynamic parameter of SBP and DBP were taken and compared pre and post supplementation of magnesium and zinc. It was anticipated to show positive relation over essential hypertension so that diet modification could be implemented as early management rather been dependent on antihypertensive medicine.

Inclusive criteria

Inclusion criteria is characteristics that the prospective subjects must have if they are to be included in the study. In present study, inclusive criteria were newly diagnosed primary hypertensive patients, male and female (21-60 years). Blood pressure range>130/85 mmHg.

Exclusive criteria

Exclusive criteria are those characteristics that disqualify subjects from inclusion in the study. In present study exclusion criteria were, adult (Male and Female) below 21 years and above 60 years, who were co-morbid, who were secondary Hypertensive, taking Medicine for more than 6 months.

Participants

First of all, recruitment of patients was done on OPD of Medicine Department, KGMU and Hypertension Camp volunteers who were newly diagnosed either taking Anti-Hypertensive medicine as one group or those were not taking any medication. Patients were selected on random basis but keeping in mind their inclusion and exclusion criteria of age and comorbidity.

To rule out secondary hypertension, pathological and radiological investigations were ordered and then selected for supplementation. But patients were advised to not to change medicine and in salt intake during study duration. Exercise was also not advised if not done before study.

Data collection methods

In this study design, high BP monitoring was done on standard format through validated HEM-7156T BP machine for first week and thereafter single tablet which contained RDA approved 300 mg Magnesium and 10 mg Zinc for four weeks. Meanwhile on fourth week again a week-long BP measurement was done similarly.

Statistical analysis

Paired t-Test applied in IBM SPSS-25 to find out the association within Pre and Post mineral supplementation SBP and DBP in the whole sample as well as in those who were on anti-hypertensive medication and those were not taking anti-hypertensive medicine

Ethical approval

Written permission was taken from the Institutional Ethics Committee of King George's Medical University, Lucknow.

Written permission was obtained from the authorities of Department of Medicine and OPD in charge KGMU Lucknow, where the study was scheduled to be conducted. The purpose of the study explained to the concerned authorities. Informed consent was obtained from the participants who were enrolled for the study or their attendant or guardian. The purpose of the study well explained to the concerned participants and guardians.

RESULTS

Total number of participants taken in this Interventional cross-sectional study was 73. Subjects were taken within age limit. Mean age of participants was 40.49 years with standard deviation of 10.18 years (Table 1). On the gender basis, distribution of sample was not balanced. 56 male participants were 77 percent which was three time to female participants that were 17 which accounted 23 percent (Table 2). Decrease in systolic blood pressure by 6.9 mmHg. pre SBP 141±11.3 SD and post SBP134±9.6 SD and diastolic blood pressure by 4.8 mmHg, pre DBP 91 ±7.8SD and post DBP 86±73 observed after 4 weeks supplementation (Figure 1).

In 30 medicated patients, antihypertensive showed decrease in SBP by 4.6 mmHg. Pre SBP 137±11.5 SD and post SBP 132±9.6 SD with and DBP by 4.7 mmHg. Pre DBP 89.6±9.2SD and Post DBP 84.9±8.7 (Figure 2). Whereas, in a group of 43, without any medicine exhibited decline in SBP by 8 mmHg pre SBP 144±10SD and post SBP 136±9.5 and DBP by 5 mm Hg. Pre DBP 92±6.8 SD and post DBP 87±0.6.3SD (Figure 3). Data compared among pre and post Magnesium and Zinc supplementation groups to evaluate the effect of supplementation. For overall sample mean systolic blood pressure before supplementation was 141 mm Hg while post supplementation decrease recorded was 134 mmHg. Paired t-test with mean difference in systolic pressure of 6.9 mmHg, SD±6.9 and SE of mean 0.82.

Similarly, mean diastolic blood pressure before supplementation was recorded as 91 mmHg and it also decreased to 86 mm Hg with mean decrease in pressure of 4.8 mmHg with SD±6.9 and SE mean 0.81 in paired t-test. With 90% confidence interval and degree of freedom of 72, value of statistical t is 8.068 in pre and post SBP. And p value is less than 0.0001. So, the Null Hypothesis is failed and rejected. With 90% confidence interval and degree of freedom of 72, value of statistical t is 6.011 in pre and post DBP. And value of p is less than 0.0001. So, the null hypothesis is failed and rejected. In the group of

30 based on medication status analysed that patient on antihypertensive showed decrease in mean SBP by 4.6 mmHg with SD±5.9 and mean DBP by 4.7 mmHg with SD of 8.0 in paired t test.

Table 1: Statistical mean age of participants.

	Age (years)
Total (N)	73
Mean	40.49
SD	10.18
Minimum	22
Maximum	59
Median	38

Table 2: Percentage of gender distribution.

	Frequency (N)	(%)
Male	56	77
Female	17	23
Total	73	100

In non-medicated group of 43, with 90% confidence interval and degree of freedom of 42, value of statistical t is 7.104 in pre and post SBP. And value of p is less than 0.0001. So, the null hypothesis is failed and rejected. With 90% confidence interval and degree of freedom of 42, value of statistical t is 5.365 in pre and post DBP. And p value is less than 0.0001. So, the Null Hypothesis is failed and rejected.

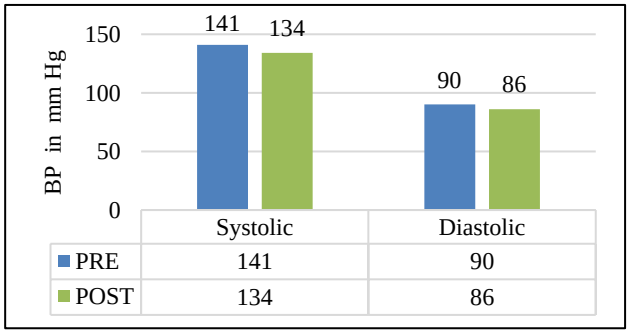

Figure 1: Statistical mean and standard deviation of whole sample.

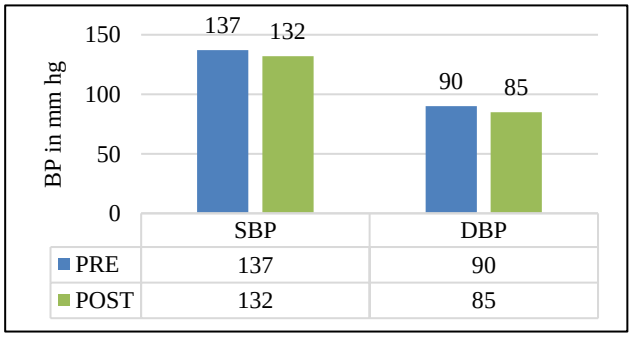

Figure 2: Statistical mean and standard deviation of participants (on medication).

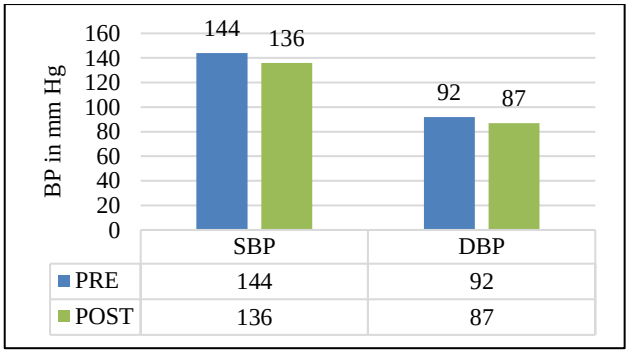

Figure 3: Statistical mean and standard deviation of participants (non-medication).

Whereas, in a group without any medicine exhibited decline in in mean SBP by 8 mmHg with SD±7.4 and mean DBP by 5 mmHg with SD±6.1 in paired t- test.

DISCUSSION

Similar studies have been done in the past to determine the effects of minerals such as magnesium and zinc on hypertension separately. Duration of studies varied and ranging from 4 weeks to 20 weeks, sample size was taken less than fifty in almost all the cases and amount of magnesium given in a dosage of as small as 300 mg to 1000 mg per day to evaluate its effect on both systolic and diastolic blood pressure. Salts used in different studies were different such as magnesium oxide, magnesium pidolate even magnesium sulphate.

According to Motoyama T et al Sano H et al Fukuzaki H, et al oral magnesium supplementation in patients with essential hypertension. Hypertension (Dallas, Tex.: 1979), 13 (3), 227–232. A 4-week study of oral magnesium supplementation (Magnesium oxide-1000mg per day) was conducted in small sample of 21 outpatients with uncomplicated essential hypertension. During the study, blood pressure and intra erythrocyte sodium concentration decreased significantly and oral magnesium supplementation lowered the blood pressure through the activation of a cell membrane sodium pump and may reduce serum lipid concentration. Oral magnesium appeared an effective treatment in lowering blood pressure. Thus, oral magnesium supplementation emerged as nonpharmacological treatment for essential hypertension.[22]

As per Ferrara LA et al and Iannuzzi R et al, long-term magnesium supplementation in essential hypertension. Cardiology In this study, Magnesium Pidolate a different salt, is given for 6 months and proper serum level was also evaluated. Thereafter decrease in SBP or DBP and decrease in peripheral resistant observed which in short term showed significant reduction in overall BP while remain insignificant for long term use of it on resting BP. It was double blind clinical trial in a very small group of 18 candidate. Conversely placebo group also exhibited the same observations. Effect of magnesium on

sympathetically stimulated BP was also evaluated. Overall effect of mineral supplementation on resting as well as sympathetically stimulated BP ineffective with very slight reduction in peripheral resistance in forearm.[23]

Our study aimed to establish effect of mineral supplementation on essential hypertension among local population of Lucknow. The result stated the decrease in both systolic and diastolic blood pressure after supplementation of Magnesium and zinc that supported the hypothesis taken in this study. Similar results were already found in earlier studies done at different zone of the world but their sample size was smaller than this study. Thus, it supported that magnesium antagonize the effect of calcium on smooth wall of blood vessels. Whereas zinc effectively played crucial role in major enzymatic activities to maintain elasticity of vessel wall as this concept was adopted to explain the cause and effect here.

In my study, in whole sample, there was decrease in systolic and diastolic blood pressure, though the sample selected were group of patients taking antihypertensive medicine and more than half of them were not on medicine. It was also observed that younger population up to 50 refrain medicine. Beyond 50 population were on antihypertensive medicine of same group. In a separate group of antihypertensive medicine but non-compliance, systolic and diastolic blood pressure decreased significantly. In non-medication group the result is same.

In nutshell, the study arrived at conclusion that minerals have impacted the vessel wall and reduced blood pressure of both systolic and diastolic. Although, the correlation was significant statistically yet not effective in the reduction of blood pressure in hypertension. This may be due to small sample size, geographical limitations and time constraint as well as financial limitation to cover up longer sample size.

Serum magnesium and zinc level could also be performed to establish a link, had financial support and enough study duration been granted for the comprehensive study. As per earlier studies, this link of minerals and its impact on hypertension is almost coherent but all those studies remain of very small size. Though I had larger sample than earlier studies, I also conclude with similar but less strong result.

After considering complete result of study, we can say that mineral supplementation has little and positive impact on the essential hypertension though not sufficient enough to treat hypertension. For stronger establishment of these results, we have to conduct pre and post supplementation serum magnesium and zinc level test, involved other hemodynamic component, future study with larger sample size and indifferent geographical regions. It would be better to compare results with normal individuals.

Limitations of the study was significant correlation of minerals on hemodynamic parameters of SBP and DBP was not found because of small sample size. Time and resources limitation were factors behind it. Serum Magnesium and Zinc estimation could have established further stronger correlation. Other hemodynamic parameters should be used to determine comprehensive link of minerals supplementation on essential hypertension.

Better conclusion could be derived if study was also compared with normal subjects. Study was done in one limited geographical area of Lucknow. It would fetch better outcome if samples from different geographical distribution were taken. Anthropometric parameters should also be included.

CONCLUSION

This study will out loud mineral supplementations as crucial factor as adjunctive therapy to antihypertensive medication to combat primary hypertension at early age and prevent damage on vital organs such as reduce retinal damage, cardiovascular, renal, cerebral mortality and morbidity as well as reduce the huge burden of non-communicable disease which account almost 95% in the society.

In conclusion, oral magnesium and zinc supplementation for 4 weeks reduced both systolic and diastolic blood pressure in the patients with essential hypertension. Similar results were also reported in the sub groups who were on antihypertensive medication and those were not taking any medication. The effect of supplementation had slighter edge on who were not taking antihypertensive medicine prior and during supplementation period. On the other hand, mineral supplementation on those were taking single medication or combined therapy during whole study period had almost negligible effect. Despite, change in the pressure are not sufficient to switch anti-hypertensive medication into supplementation alone. And those are not taking medicine, their blood pressure is still in the range of damaging vital organs in long term. Thus, supplementation can play crucial role as adjunctive therapy for hypertensive medication rather major role in reducing blood pressure.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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