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Serum Magnesium in a Sample of Iraqi Adults with Essential Hypertension

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Abstract

Background Hypertension is a major cardiovascular problem across the globe. Electrolytes like magnesium are linked with the pathophysiology of essential hypertension by various studies.

Objective To evaluate the serum magnesium in patients with essential hypertension compared to healthy control.

Methods A case-control study recruited 45 patients with essential hypertension and 45 matched healthy control. The study was conducted in the Medical Outpatient Clinic in the Medical City Teaching Complex, Baghdad, from July 2016 to November 2016. Serum magnesium measured by Atomic Absorption Spectrophotometers (AAS).

Results Serum magnesium was significantly lower in patients with essential hypertension when compared to healthy control. Female had lowest serum Mg in the patients' group. Mg was low in obese hypertensive patients. Serum Mg tends to be lower with longer duration of hypertensin (r value-0.227) but it didn't reach statistical significance (p value 0.133).

Conclusion Serum magnesium levels were found to be low in hypertensive patients when compared with normotensive persons.

Keywords Hypertension, magnesium

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List of abbreviations: AAS = Atomic absorption spectrophotometry, ACEI = Angiotensin converting enzyme inhibitor, ARB = Angiotensin receptor blocker, BB = Beta blockers, DASH study = Dietary approach to stop hypertension, Mg = Magnesium, NO = Nitric oxide, RDAs = Recommended dietary allowances

Introduction

Magnesium (Mg) is the second most abundant intracellular cation, and fourth most abundant cation in the body [(1)]. In healthy people, blood plasma Mg concentrations range between 0.65-1.05 mmol/L [(2)].

Dietary survey data suggest that average Mg intake in western countries has been declining during the last century and is often below the recommended dietary allowances (RDAs) [(3)]. Although Mg is a cause of water hardness, drinking water accounts for 10% of daily Mg intake; Mg in drinking water is 30% better absorbed than dietary Mg, possibly because of Mg cations are in ionic form and so it is more available for quick absorption [(4,5)].

Many studies described an inverse correlation between the concentration of Mg in drinking water and the level of arterial blood pressure [(5)].

Changes in intracellular ions like sodium, calcium, and Mg have been related to the pathogenesis of hypertension. Mg was the target of many hypertension studies

considering that there is a significant inverse correlation between serum Mg level and incidence of cardiovascular disease [6].

Mechanisms for Mg depletion in experimental and human hypertension have been postulated to include impaired gastrointestinal absorption, increased urinary losses of Mg, and compromised cellular Mg handling. Chronic deficiency of Mg by way of reduced intake or malfunction in the Mg metabolism promotes the development of hypertension [7]. The DASH study (dietary approach to stop hypertension) demonstrates that diet rich in Mg produces a potent antihypertensive effect [8].

The main mechanisms by which low Mg contribute to hypertension is increased arterial stiffness, endothelial dysfunction, and vascular remodeling, and increase the sympathetic activity [7,8]. The peripheral vascular resistance may be modified by Mg through the regulation of responses to vasoactive agents, particularly (angiotensin, endothelin, prostacyclin, and nitric oxide). Mg deficiency results in decreased production of nitric oxide (NO), which is a potent vasodilator from endothelial cells along with decreased vasodilator response to acetylcholine and adenosine, low Mg promotes the synthesis and release of endothelin-1 which is a potent vasoconstrictor synthesized and released by endothelial cells, also low Mg associated with decrease smooth muscle cell-derived prostaglandin PGI2. All these lead to more vasoconstriction and increased vascular resistance and hypertension. In addition, hypertensive patients with high renin activity have low Mg than normotensive subjects, Mg ions compete with calcium ions for membrane-binding sites, lower levels of intracellular calcium and cause vasodilatation, Mg often referred to as calcium channel blocker [7].

In this study, we aimed to evaluate the serum magnesium in a group of Iraqi patients with essential hypertension compared to healthy control.

Methods

Setting and study design

A case-control study was conducted the Medical Outpatient Clinic in the Medical City Teaching Complex, Baghdad, from July 2016 to December 2016.

Ethical Consideration

The proposal of this study was made according to the scientific board of Internal Medicine in the Arab Board of Health Specializations in Iraq. All participants signed a written consent form explaining the study objectives, and all data were kept confidential during all stages of the work.

Definition of the case, inclusion, and exclusion criteria

The study included 90 participants. The patient group consisted of 45 Iraqi adults with essential hypertension without any coexisting other diseases and being compliant with treatment for 6 months. The diagnosis of hypertension made by a certified physician with experience in managing hypertension. The physician should report about the patient's compliance prior to enrollment. This had been made through monthly visits to the Medical Outpatient Clinic in The Medical City of Baghdad.

The control group included 45 healthy non-hypertensive adults attending the Medical Outpatient Clinic.

Exclusion criteria: Subjects with diagnosed diabetes mellitus, lipid disturbance, heart failure, ischemic heart disease, chronic kidney disease, thyroid disease, Cushing syndrome, drugs (steroid, oral contraceptive pills, anabolic steroids, diuretics, aminoglycoside, laxatives), history of recent illness, recent use of multivitamins and tonics, alcoholism and pregnancy.

Measurement

Serum Mg measured by using Atomic Absorption Spectrophotometry (AAS), model Buck 210 VG- USA, using standardized procedure by air acetylene. Laboratory

measurements were performed at the Toxicology Unit, the Medical City-Baghdad. Body mass index (BMI) is a measure of body fat based on height and weight that applies to adult men and women. The formula is BMI = kg/m^2 where kg is a person's weight in kilograms and m^2 is their height in meters squared. A BMI of 25.0 or more is overweight, while the healthy range is 18.5 to 24.9.

Blood pressure measured by using the auscultatory method. It was measured twice on both arms.

Low serum magnesium (1.7 to 2.2 mg/dl) is the primary outcome of the study

Statistical analysis

Data of the study groups (patients and controls) were entered in computerized database software (Microsoft excel software 2010), all variables were coded and transferred into statistical analysis computerized package; IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Chi-square was used to assess the significance of differences between patients and controls in categorical variables. Student's independent (t) test was used to assess the significance of differences between study groups in continuous variables. Level of significance (p-value) ≤ 0.05 considered significant.

Results

The study recruited 45 patients with essential hypertension with age range from 18-75 years. The patients group included 16 males and 29 females, while the control group included 17 males and 28 females. (Table 1).

Table 1. Gender Distribution of the study group

Gender	Control group No. (%)	Patient group No. (%)	*p-value*
Male	17 (38)	16 (36.0)	1.000
Female	28 (62)	29 (64.0)	

The odds ratio of having lower serum Mg in a hypertensive patient was 7.72 (Table 2).

Serum magnesium was significantly lower in patients with essential hypertension when compared to healthy control. Female had lowest serum Mg in the patients' group (Table 3).

Table 2. Serum magnesium level in the study groups

Magnesium (mg/dl)	Hypertension No. (%)	No Hypertension No. (%)
Low	16 (35.5)	3 (6.6)
Normal	29 (64.5)	42 (93.3)
Total	45	45

The odds ratio is 7.72 (95% CI:5.31-9.52, P=0.042)

Table 3. Comparison of serum magnesium means of the study groups (t-test)

Group	No.	Mean	SD	SE	95% CI	*p-value*
Control	45	1.68	0.21	0.03	(1.6219-1.7470)	<0.0001
Patient	45	1.15	0.18	0.02	(1.1147-1.1853)	

There was no correlation between age, and serum Mg. Serum Mg was lower in patients with higher BMI (p value 0.019). It tends to be lower with longer duration of hypertension (r value-0.227) but this didn't reach statistical significance in this study (Table 4).

Table 4. Correlation between Mg levels, Age, duration of hypertension and BMI

Parameter	Serum Mg		Relationship
	r	p	
Age	0.026	0.864	No
Duration of hypertension	-0.227	0.133	No
BMI > 25	-0.35	0.019	Yes

Degree of significance (α=0.05), negative r values indicate inverse relationship, and positive sign indicate direct relationship

There was no significant effect of different types of water supply on serum Mg values (Table 5).

There was no relationship between serum Mg and the type of antihypertensive medications (Table 6).

Table 5. Unadjusted mean Mg levels in relation to water consumption types.

Water	Control group			Patient group			p-value
	No.	Mean	Grouping	No.	Mean	Grouping	
Municipal	31	1.6842	A	35	1.1417	B	
Soft	3	1.6667	A	8	1.1700	B	0.146
Mixed	11	1.7413	A	2	1.1233	B	

Table 6. Relationship between mean Mg level and antihypertensive treatment

	BB patients	ACEI/ARBS Patients	Combination therapy Patients	
S. Mg (mg/dl)	1.144	1.115	1.251	
	BB vs. ACEI/ARBS		p-value	0.637
	BB v. Combination therapy		p-value	0.931
	ACEI/ARBs vs. Combination therapy		p-value	0.579

BB; Beta Blockers, ARB; Angiotensin receptor blocker, ACEI; Angiotensin converting enzyme inhibitor

Discussion

Epidemiological evidence suggested that Mg plays an important role in regulating blood pressure [3].

In this study, there was a statistically significant ($p<0.001$) difference of mean serum Mg between patient group (1.1500) and control group (1.68). It is consistent with the results of Sarmah [6].

This study showed that female hypertensive patients had the lowest serum Mg levels, however, there was no statistically significant correlation between gender and serum Mg levels. This was compatible with the results of Bohnen et al. that found no effect for gender on Mg level [9]. This low Mg level in women may be related to the effect of estrogen. Women at childbearing age and during

pregnancy have lower levels of Mg. Estrogens-induced lowering of serum Mg is not associated with increased urinary Mg output or decreased Mg absorption, which support the premise that estrogen shifts Mg to tissue [10].

Here, we found a progressive decrease in serum Mg with increasing age. The Mg concentration in red blood cells is lower in middle age people suffering from hypertension in compared to healthy subjects. However, other studies showed no effect for age on Mg level Low serum Mg with increasing age, could be explained by reduced intake in elderly, reduced intestinal absorption, reduced bone stores, excess urinary loss, and drugs effect. Both aging and Mg deficiency has been linked to excessive production of O_2-derived free radicals and inflammation, which could be at least one of the mechanisms of hypertension and age-associated CV diseases [8,9].

In this study, serum Mg was significantly low in obese hypertensives. This was supported by the results from Corica et al. [11]. The possible explanation is that increased visceral adiposity predisposes to reduced insulin sensitivity, which in turn may worsen Mg status. This may be part of metabolic syndrome. Magnesium supplementation in such patients with hypomagnesemia can be effective in the treatment of Metabolic syndrome [12].

We found an inverse correlation between the duration of hypertension and Mg level (r= -0.227, p=0.133) but this didn't reach statistical significance. It is imperative to say that the older the patient with longer hypertension history may have a lower serum magnesium value. We may need to test for magnesium after one year of the onset of hypertension. Increased urinary losses may be implicated [13].

There was no statistical difference between patients and controls in regard to the types of drinking water. Demineralized water produced through reverse osmosis process removes 93-97% of calcium and Mg. Although it's beneficial to remove water hardness, such water may lead to Mg deficiency if consumed for prolonged period. Demineralized water is commercially available as bottled water or through home installed systems. A retrospective study assessed Mg and calcium content in drinking water in subjects who died from hypertension compared with those who died from other causes demonstrated that Mg levels in drinking water were inversely related to the risk of death from hypertension [4,5].

There was no statistically significant correlation between hypomagnesemia and the type of antihypertensive medications. A targeted metanalysis showed that the addition of oral magnesium supplements decreases high blood pressure (SBP > 155 mmHg) in hypertensive subjects on anti-hypertensive medication [14]. In this study, we didn't assess the effect of diuretic as per the exclusion criteria.

In this study, it was difficult to assess the effect of nutritional habits and life styles of the study participants which could be affected by other factors like residence and socioeconomic status. This may be a potential area for future studies and possible interventions.

In conclusion, low serum magnesium is prevalent in patients with essential hypertension. It's important not to overlook low magnesium in evaluating patients with hypertension. A further and larger study may disclose the exact prevalence of low magnesium in Iraqi population and may pave the way for possible preventive strategies.

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Author contribution
Dr. Athab collected the data; Dr. Al-Taee reviewed the literature; and Dr. Ali designed the study and written the manuscript. All authors reviewed and approved the manuscript.

Conflict of interest
Authors declare no conflict of interest.

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