Assessment of Serum Magnesium Levels in Stroke Patients and its Correlation with Severity of Neurological Disability

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ABSTRACT

Introduction: WHO clinically defines a stroke as 'the rapid development of clinical signs and symptoms of a focal neurological disturbance lasting more than 24 hours or leading to death with no apparent cause other than vascular origin'. Magnesium may play a preventive and therapeutic role in stroke, ischemic heart disease, and bronchial asthma. Aims and Objectives: To determine the levels of serum magnesium, evaluate the neurological status and to compare and explore the difference in serum magnesium levels in ischaemic and haemorrhagic stroke.

Material and methods: The present study was conducted in the Department of medicine, Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur (C.G.). Total 60 subjects including 30 stroke patients and 30 normal Individuals aged between 18-60 years of both sexes were included in the study. Age and Sex matched subjects were taken for the normal control group.

Results: Highest incidence of stroke was observed in 51-60 years of age group (mean age 51.10±14.74 years), 60% are male (n= 18), unconsciousness was present significantly (p=0.002*) higher frequency in Stroke group, and infract was the most common type of stroke (n= 23, 76.7%) observed. Sr. mg levels were significantly lower in stroke subjects and in subjects with mRS 3-6 compared to control subjects (p<0.0001*) and those with mRS 0-2 (p=0.004*). Systolic BP was significantly higher in stroke subjects (p=0.004*). mRS score was significantly lower in infarct subjects compared to hemorrhagic stroke subjects (p=0.003*).

Conclusion: Cerebrovascular disease predominates in the middle and later years of life. Men are more prone to thromboembolic stroke. Magnesium levels are significantly decreased in ischaemic stroke, though haemorrhagic stroke patients had a magnesium deficiency

Keywords: Ischaemic Stroke, Haemorrhagic Stroke, Magnesium Level, Neurological Disability

INTRODUCTION

WHO clinically defines a stroke as 'the rapid development of clinical signs and symptoms of a focal neurological disturbance lasting more than 24 hours or leading to death with no apparent cause other than vascular origin'.[1] Stroke is a clinical syndrome divided into two broad categories that define its pathophysiology:

Ischaemic Strokes: caused by sudden occlusion of arteries supplying the brain, either due to a thrombus at the site of occlusion or emboli from another part of the circulation. It accounts for 50% - 85% of all strokes worldwide.[2]

Haemorrhagic Strokes: caused by subarachnoid hemorrhage – arterial bleeding in the space between meninges and bleeding from one of the brain's arteries into the brain tissue or intra-cerebral haemorrhage. It accounts for 1% - 7% and 7% - 27% respectively of all strokes worldwide.[2]

Magnesium ions have a physiological role in multiple processes related to ischaemia. Magnesium (Mg) plays a significant role in multiple biological systems and acts as a cofactor in hundreds of enzymatic reactions in the human body. Low Mg level has been associated with increased risk of chronic diseases in prospective studies, including cardiovascular disease (CVD), type 2 diabetes, metabolic related diseases, and colorectal cancer. Mechanistic evidence supports a role for magnesium in cardiovascular diseases, including blood pressure, oxidative stress, endothelial function and thrombosis, and arrhythmia.[3] In the brain, magnesium is predominantly complexed with adenosine triphosphate. It is an important cofactor for cellular energy metabolism and protein synthesis. The daily magnesium requirement for a human being is 200-300 mg. Magnesium (Mg) deficiency correlates with a higher mortality and worse clinical outcome, particularly in critical care units. Magnesium has been directly implicated in hypocalcemia, tetany, hypokalemia, and arrhythmias. Magnesium may play a preventive and therapeutic role in stroke, ischemic heart disease, and bronchial asthma.[4] Patients with hypomagnesemia require frequent monitoring and magnesium replacement since this is correlated with adverse pathophysiological consequences, whereas hypermagnesemia is only a prognostic marker in patients with congestive heart failure.[5]

Although a lot of research work is being carried out on the serum magnesium levels in stroke patients and its correlation with neurological disability worldwide, there is a dearth of information in literature pertaining to the serum magnesium levels in stroke patients. Globally, the correlation of serum magnesium levels with neurological disability in stroke patients is also not extensively studied. Our study is a relevant

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step towards the future to overcome the lacuna in this field with the aim to determine levels of serum magnesium, evaluate the neurological status and to compare and explore the difference in serum magnesium levels in ischaemic and haemorrhagic stroke. The results of this study will help bridge the knowledge gap and provide population relevant data on the serum magnesium levels and related factors in stroke patients.

MATERIAL AND METHODS

This was a hospital-based cross-sectional observational study, conducted in the Department of Medicine, Pt. JNM medical college, Dr. B.R.A.M. Hospital Raipur, among the patients presenting in OPD and admitted in medicine ward or intensive care unit from the period between June 2016-2017.

Study subjects

Subjects with clinically confirmed stroke (n=30) and equal number of age and sex matched subjects (n=30) for control group, aged between 18-60 years of both sexes, who gave informed consent were included in the study (Total n=60 subjects).

Subjects with Transient Ischaemic Attack (TIA), systolic blood pressure less than 90 mm of Hg, Presence of Bundle Branch Block or Atrioventricular Block, Serum Creatinine >3mg/dl, Clinical conditions, where there is a therapeutic indication of Magnesium Sulfate and Pregnancy were excluded from our study.

Data collection

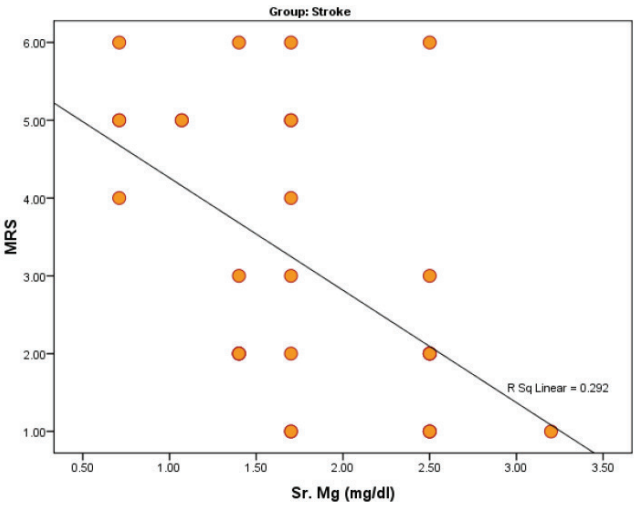
The institutional ethics committee of Pt. JNM Medical college Raipur, Chhattisgarh, approved this study protocol. Informed written consent was obtained from all study participants. Subject's brief history of the condition was sought and detailed clinical examination was performed. The severity of neurological impairment was evaluated in patients with clinically confirmed stroke using the modified Rankin Score (mRS) within 24 hours of admission. All the subject underwent for the estimation of serum magnesium levels.

STATISTICAL ANALYSIS

Data were expressed as a percentage and mean ± SD. Student's t-test was used to check the significance of the difference between two parameters in parametric data. Pearson correlation analysis was performed to check the correlation between two categorical variables. Fischer's exact test or Chi-square test was used to analyze the significance of the difference between frequency distribution of the data. A *P*-value <0.05 was considered as statistically significant.

RESULTS

The present study was conducted in the Department of



Correlation of MRS with Sr. Mg in study subjects (r= -.540, p= 0.002**)

Figure-1: Correlation of MRS with Sr. Mg in study subjects

Variables		Stroke Group	Control	Total	X^2	df	*P* value
Age (Years)	</=40	7 (23.3%)	7 (23.3%)	14	.000	3	1.000
	41-50	6 (20.0%)	6 (20.0%)	12			
	51-60	10 (33.3%)	10 (33.3%)	20			
	>60	7 (23.3%)	7 (23.3%)	14			
Sex	F	12 (40.0%)	12 (40.0%)	24	.000	1	1.000
	M	18 (60.0%)	18 (60.0%)	36			

Table-1: Comparison of age and sex distribution between groups

Variables		Stroke Group	Control	Total	X^2	df	*P* value
Conscious-ness	Conscious	20 (66.7%)	30 (100.0%)	50 (83.3%)	12.000	2	.002*
	Altered	3 (10.0%)	0 (0%)	3 (5.0%)			
	Unconscious	7 (23.3%)	0 (0%)	7 (11.7%)			
Pallor	Absent	12 (40.0%)	20 (66.7%)	32 (53.3%)	4.286	1	.069
	Present	18 (60.0%)	10 (33.3%)	28 (46.7%)			
Clubbing	Absent	24 (80.0%)	29 (96.7%)	53 (88.3%)	4.043	1	.103
	Present	6 (20.0%)	1 (3.3%)	7 (11.7%)			
Cyanosis	Absent	28 (93.3%)	30 (100.0%)	58 (96.7%)	2.069	1	.150
	Present	2 (6.7%)	0 (0%)	2 (3.3%)			
Icterus	Absent	22 (73.3%)	26 (86.7%)	48 (80.0%)	1.667	1	.197
	Present	8 (26.7%)	4 (13.3%)	12 (20.0%)			

Table-2: Comparison of clinical findings between groups.

Variables		Frequency	Percent
General Condition	Fair	17	56.7
	Poor	5	16.7
	Very Poor	8	26.7
Type of stroke	Haemorrhage	7	23.3
	Infarct	23	76.7

Table-3: General condition in stroke subjects

Variables		N	Mean	SD	T	*P*-Value
Group	Stroke	30	1.75	.673	-6.211	<0.0001*
	Control	30	2.83	.665		
mRS	0-2	15	2.09	.58	3.130	.004*
	3-6	15	1.41	.59		

Table-4: Comparison of Sr. Mg levels between study groups and mRS score

Parameters	Group	N	Mean	SD	t	*P*-Value
Age (Years)	Stroke	30	51.10	14.88	0.00	1.00
	Control	30	51.10	14.88		
Pulse (/min)	Stroke	30	89.93	12.36	1.37	0.176
	Control	30	85.67	11.78		
BP Systolic (mmHg)	Stroke	30	139.00	19.18	3.01	0.004*
	Control	30	126.07	13.58		
BP Diastolic (mmHg)	Stroke	30	86.00	8.55	1.97	0.054
	Control	30	82.00	7.14		

Table-5: Comparison of various parameters between study groups

	Type of stroke	N	Mean	SD	min	max	F	*P*-Value	Post hoc
Sr. Mg (mg/dl)	Infarct	23	1.72	0.74	0.71	3.2	19.238	0.0001*	I≠H>N
	Hemorrhagic	7	1.89	0.43	1.4	2.5			
	None	30	2.83	0.67	1.7	4.1			
mRS	Infarct	23	2.65	1.58	1	6	10.732	.003*	
	Hemorrhagic	7	4.86	1.46	2	6			

Table-6: Comparison of serum Mg levels and mRS between subjects with a different type of stroke

medicine Dr. B.R.A.M. Hospital, Raipur and included total 60 subjects. Out of total 60 subjects in this study 30 belongs to stroke group presenting to OPD or inpatient wards and 30 age and sex-matched healthy normal controls from June 2016 to October 2017.

Table no 1 showing a comparison of age and sex distribution between groups and it reveals that the maximum incidence of stroke was observed in 51-60 years of age group (mean age 51.10±14.74 years). Among stroke group 60% are male (n= 18) and 40% were female (n=12).

No significant difference was observed in age and sex distribution in two groups indicating that both groups were age and sex matched (*P*=1.00).

Table no 2 shows a comparison of clinical findings between groups and it reveals that unconsciousness was present significantly (*P*=0.002*) higher frequency in Stroke group. No significant difference was found between study groups regarding pallor, clubbing, cyanosis, and icterus.

Table no 3 shows general condition and type of stroke in stroke subjects and we found that most of the subjects having a fair general condition (n= 17, 56.7%) and infract were the most common type of stroke (n= 23, 76.7%).

Fig. no 1 Shows correlation of MRS with Sr. Mg in study subjects and a moderate downhill correlation (r=-0.54, *P*=0.002) was found between two parameters.

Table no 4 show comparison of Sr. Mg levels between study groups and mRS score and it reveals that Sr. mg levels were significantly lower in stroke subjects and in subjects with mRS 3-6 compared to control subjects (*P*<0.0001*) and those with mRS 0-2 (*P*=0.004*).

Table no 5 shows a comparison of various parameters between study groups and it reveals that systolic BP was significantly higher in stroke subjects (*P*=0.004*). No significant difference was observed between study groups regarding Age, Pulse rate, and diastolic BP.

Table no 6 shows a comparison of serum Mg levels and mRS between subjects with a different type of stroke, a significant difference was detected between three groups (*P*<0.0001*). Further, in post hoc analysis, Sr. Mg. was found to be significantly lower in Infarct and haemorrhagic stroke subjects (*P*<0.0001*) compared to normal subjects. Though Mg was found to be lower in infarct subjects compared to haemorrhagic stroke subjects, the difference failed to reach statistical significance. mRS score was found to be significantly lower in infarct subjects compared to hemorrhagic stroke subjects (p=0.003*).

DISCUSSION

A stroke is caused by the interruption of the blood supply to the brain and cuts off the supply of oxygen and nutrients causing damage to the brain tissue.

Our study findings reveal that both study groups were matched adequately corresponding to age and sex. Anaemia was more prevalent in females irrespective of study group *i.e.* in both stroke group and in the otherwise healthy normal group, females lead in the frequency of anaemia, probably due to nutritional factors.[6]

This study shows a male predominance of cerebrovascular accidents, which is in consensus with the previous studies. And the incidence of cerebrovascular accidents is more in elderly probably because most of the risk factors for stroke such as hypertension, dyslipidemia, stress, and smoking *etc.* are present in males more frequently compared to females.[7,8]

Serum magnesium levels are inversely associated with cardiovascular risk factors such as hypertension. Though pulse rate and diastolic blood pressure between two groups in this study have no significant difference but systolic blood pressure is significantly higher in stroke patients, which may be attributable to the lower level of serum magnesium. Study by Kaur, Prabhu, and Thakur (2012) found that the serum magnesium levels were significantly lower in stroke patients and the serum magnesium levels were not significantly higher in haemorrhagic stroke when compared with ischaemic stroke.[9]

The level of serum magnesium is significantly lower in stroke patients when compared to healthy subjects. The patients of haemorrhagic stroke also observe the significantly lower level of serum magnesium compared to healthy normal subjects. Serum magnesium levels tend to be higher but not significantly higher in hemorrhagic stroke when compared to ischaemic stroke.

Serum magnesium is an indispensable element for man. It is an indispensable activator of over 300 enzymes in a human being. Hypomagnesemia leads to neuromuscular hyperirritability, tremors, increased vascular resistance, coronary vasospasm, and hypertension. Magnesium deficiency triggers vasoconstriction, enhances vascular endothelial injury and hence leads to atherosclerosis and stroke.

The present study observes a statistically significant correlation between mRS score (modified Rankin Scale) and serum magnesium level which indicates that severity of a stroke is inversely related to the level of serum magnesium. Saberi, Hatamian, Esmaeilzadeh and Heydarzadeh (2011) Concluded reciprocal statistical correlations between the serum magnesium level and Rankin $Score_0$ and Rankin $Score_{1w}$.[10]

Modified Rankin Score, a novel manual tool to stratify severity of neurological disability in sick individuals. Patients with higher scores (3-6) depict the significantly lower level of serum magnesium when compared to those scoring lower (0-2). This reconfirms the reciprocal correlation of mRS (discrete) to serum magnesium levels (continuous).[10]

Siegler, Boehme, Kumar, Gillette, Albright and Martin-Schild (2013) assumed higher serum levels of magnesium may contribute to improved outcome following ischaemic stroke, which possibly is related to vessel recanalization. Magnesium ions have a physiological role in multiple processes related to ischaemia and the relation of magnesium deficiency and cardiovascular disease is well established.[11]

The present study is not an interventional study, and this been the limitation of the present study and the expected gain, had the patients been given Magnesium as the part of their treatment, cannot be commented upon.

CONCLUSION

Cerebrovascular disease predominates in the middle and later years of life. This condition has become a worldwide concern as it is causing morbidity, mortality, and disability in developed and developing countries. Men are more prone to thromboembolic stroke. Magnesium levels are significantly decreased in ischaemic stroke, though haemorrhagic stroke patients had a magnesium deficiency. Magnesium deficiency predisposes atherosclerosis, the known modifiable risk factor for stroke. Despite our best effort, there are limitations of our study, which includes Small sample size, we have not taken general population, and lack of a control group. These limitations can be overcome in the future studies.

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