

Correlation between Serum Calcium and In-Patient Mortality among Patients with Hemorrhagic and Non-Hemorrhagic Cerebrovascular Disease

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ABSTRACT

Introduction: Cerebrovascular disease is the second most frequent cause of death worldwide. This study was designed to assess the correlation between ionized calcium and clinical outcomes of Cerebrovascular events.

Methods: The study included 225 cases diagnosed with cerebrovascular disease and undergone a CT scan. Calcium (ionized calcium) was measured within 1-2 hrs. Of sample collection. The time frame of the study was from December 2016 till December 2017.

Result: Out of 225 participants the mean age of patients who have had infarction was higher compared to those who had haemorrhage (59.77±13.29 vs. 54.85±11.74, p value=0.097). Significant correlation was noted between hypertension and cerebrovascular disease. Also Significant difference between sex and type of cerebrovascular accidents was not established (p value =0.128)

Conclusion: Serum calcium was found to be associated with clinical outcome among stroke patients found to have infarction. High incidence of favourable clinical outcome among those who have normal level of serum calcium compared to those who have low serum calcium level was found.

Keywords : Cerebral Infarction; Hemorrhagic Stroke; Serum Calcium.

INTRODUCTION

Stroke, along with its devastating and long term complications is one of the leading causes of morbidity/mortality in the world. Stroke incidence and mortality are increasing in less developed countries in which the lifestyles and population restructuring are rapidly changing.¹

The calcium ion (Ca²⁺) is a ubiquitous intracellular messenger during and immediately after an ischemic period and it influences the cascade of events that lead to subsequent neuronal injury. Under ischemic conditions, release of glutamate from the neurons and glia activates the N-methyl-D-aspartate (NMDA) receptor and triggers the rapid translocation of Ca²⁺ from extracellular to intracellular spaces in cerebral tissues. Experimental results indicate that Ca²⁺ can have a harmful effect on neurons under acute ischemic conditions.² Calcium has also been studied with regards to its association with clinical outcomes after stroke. Total and ionized calcium levels are found to directly correlate with ischemic stroke

and high dietary calcium has been associated with reduced risk of stroke.³ Higher albumin-corrected calcium levels are also showed to be prognostic markers of early neurologic outcome and long-term mortality of acute ischemic stroke in a study carried out previously.⁴ Serum calcium also correlates with the size of cerebral infarct and clinical outcomes as shown by different studies.^{5,6,7} These results indicate that calcium level may serve as a potential therapeutic target for improving stroke outcome as it was proven that serum calcium level serves as a clinical prognosticator. In contrast, the systematic review of 8 randomized clinical trials have showed that calcium supplements in monotherapy were associated with a significant increased risk of acute myocardial infarction and an increased risk of stroke.⁸ It has also been found that calcium supplements were associated with an increased risk of atherosclerosis as measured by coronary artery calcification, whereas they found the opposite effect with dietary calcium which could be explained by the abrupt

increase of serum calcium that seems to occur after the intake of calcium supplements and not with dietary calcium.⁹ Intermittent increases in serum calcium sustained over long periods could ultimately promote vascular calcification and the development of atherosclerosis. This could occur particularly when there is a positive calcium balance (eg, after calcium intake >1400 mg/day). Consequently, intermittent increases in serum calcium sustained over long periods could ultimately promote vascular calcification and the development of atherosclerosis. This could occur particularly when there is a positive calcium balance (e.g., after calcium intake >1400 mg/day).¹⁰

METHODS

This was a retrospective study of 225 patients with cerebrovascular disease from December 2016 to December 2017 conducted at Rizal Medical Center, Department of Health, Philippines. Clinical data, including serum ionized calcium and cranial CT scan results, were retrieved from Medical records section and Department of Laboratory Medicine. The confidentiality of all the patients were protected throughout the data collection. The inclusion criteria were 18 years and older, all patients with a discharge/death diagnosis of cerebrovascular disease admitted to Intensive care unit. Serum Calcium was measured within 1-2 hours of sample collection. The primary end points were overall death or discharged with the diagnosis of cerebrovascular disease. The main outcome variable was all-cause mortality. The correlations-predictive power of Serum Calcium and hazard ratios were determined. To facilitate analysis, serum calcium values were categorized into three category-low,normal and high. All data were managed using Microsoft Excel for Windows and All clinical analysis and comparisons were executed using SPSS Software Version 23.

RESULTS

A total of 225 subjects above 18 years of age were studied where the mean age of patients who have had infarction was higher compared to those who had haemorrhage (59.77±13.29 vs. 54.85±11.74 , p value=0.097). Among them 208 subjects were diabetic and 176 were hypertensive. Similary among all of the participants Diabetis Milletus was present in very few participants i.e 6.2 % of total participants with infraction and 1.3% of total participants with haemorrhage. Similarly previous history of CVD were absent in 52% of pattient with infraction and 40% of patient with haemorrhage. Significant correlation was noted between hypertension and cerebrovascular disease (Table 1).

Table 1. Clinico-Demographic Profile of Participants

Categories	Infarction(%)	Bleeding(%)	Total(%)	P value*
Age				
Mean±SD	59.77±13.29	54.85±11.74	-	0.097
Sex				
Male	74(32.9)	65(28.9)	139(61.8)	0.128
Female	55(24.4)	31(13.8)	86(38.2)	
Hypertension				
Absent	15(6.7)	34(15.1)	49(21.8)	0.000
Present	114(50.7)	62(27.6)	176(78.2)	
Diabetes Mellitus				
Absent	115(51.1)	93(41.3)	208(92.4)	0.040
Present	14(6.2)	3(1.3)	17(7.6)	
Previous History of CVD				
Absent	117(52)	90(40)	207(92)	0.464
Present	12(5.3)	6(2.7)	18(8)	

*p-value significant at ≤ 0.05

Significant difference between sex and type of cerebrovascular accidents was not established (p value =0.128) (Table 1).Significant correlation was noted among those with low serum calcium levels and mortality in patients with cerebral infarction and haemorrhage. (Table 2.1 and 2.2). Correlation was noted between serum calcium level and clinical outcome of cerebral infarction patients (p value=0.023). CVD infarct patients who have normal calcium levels have more favourable clinical outcome than those with low levels. The Mean± SD of patients who died (n=13) averaged 1.25±.175 which is higher compared to the Mean± SD of patients who were discharged(n=116) that averaged 1.23±0.96, p value = 0.023.

Table 2.1. Serum Calcium and Clinical Outcome of Cerebral Infarction

Categories	Died	Alive	Total	P-value
Serum Calcium				0.023*
Mean±SD	1.25±.175	1.23±.096	-	
Low	3(2.3)	14(10.9)	17(13.2)	
Normal	5(3.9)	86(66.7)	91(70.5)	
High	5(3.9)	16(12.4)	21(16.3)	

*p-value significant at ≤ 0.05

Table 2.2. Serum Calcium and Clinical Outcome of Cerebral Haemorrhage Stroke Patients

Categories	Died	Alive	Total	P-Value
Serum Calcium				.570*
	1.23±.194	1.20±.138	-	
Low	7(7.3)	16(16.7)	23(24)	
Normal	19(19.8)	41(42.7)	60(62.5)	
High	6(6.3)	7(7.3)	13(13.5)	

*p-value significant at ≤ 0.05

DISCUSSION

In this retrospective study, CVD infarct patients who have normal level of serum calcium have more favorable clinical outcome than those who have low serum calcium level in patients. The Mean+SD of patients who died (n=13) averaged 1.25±.175 which is higher compared to the Mean+SD of patients who were discharged (n=116) that averaged 1.23±.096, p value 0.023<0.05. These results were similar to the findings of a prospective study done in the year 2007, where patients with normal serum calcium were more likely to survive a CVD infarct compared to those who have low serum calcium level.¹¹ In the present study, serum calcium level did not influence CVD outcomes through hypertension. These findings are parallel to a prospective cohort study done at an academic medical centre, where significant association between calcium level and BP on admission was not observed.¹² Serum calcium was not correlated with CVD outcomes in patients with diabetes, and this is similar to the findings of cohort studies conducted to see the association of CVD patients with serum calcium through diabetes.^{13,14}

CONCLUSION

Serum calcium was found to be associated with clinical outcome among stroke patients found to have infarction. The data suggest that high incidence of favourable clinical outcome among those who have normal level of serum calcium compared to those who have low serum calcium level. Clinical outcome of stroke patients were correlated. Specifically cases of haemorrhagic stroke were more likely related with poor clinical outcome as compared to cases of cerebral infarction. The study recommends that management for cases of CVD regardless of the type should be prompt and immediate. Intake of calcium rich diet may be considered among patients at higher risk.

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