STUDY OF SERUM LEVELS OF CALCIUM IN CORONARY ARTERY DISEASE AND DIABETES MELLITUS

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ABSTRACT
In the present study Serum Calcium levels are estimated in patients of CAD with DM, CAD without DM, CAD with DM and other risk factors compared to healthy normal subjects. Sr Calcium was found to be significantly decreased in all the study groups as compared to normal subjects.

KEYWORDS: Coronary Artery Disease, Diabetes Mellitus, Calcium.

INTRODUCTION
Diabetes Mellitus (DM) is a common medical problem and a major risk factor for the development of atherosclerosis and Coronary Artery Disease (CAD). Hypertension is an asymptomatic and important disease of modern civilized life. The overall prevalence of hypertension has been reported to range from 6-32%. Essential hypertension is associated with disturbed calcium metabolism. The calcium ion plays major role as an intracellular second messenger in excitation contraction coupling in cardiac and smooth muscle cells. An increase in peripheral vascular resistance was a uniform finding in all types of established hypertension. The free intracellular calcium concentration determines...
the tension in vascular smooth muscle cells thereby resulting in peripheral vascular resistance. An increased calciuria could be a feature of the essential hypertensive patients.[2]

Abnormalities of calcium metabolism have been described in patients with essential hypertension. Zidek et al.[3] found an increased intracellular calcium activity in normotensive subjects with a familial hypertensive disposition in comparison with normotensives without family history of hypertension. Touyz et al.[4] showed significantly increased intracellular calcium levels in essential hypertensives. Some authors[5,6] have reported lower concentrations of serum calcium in the hypertensives than in normotensive subjects. In these investigations, serum calcium levels were studied in essential hypertensive and their first-degree relatives.

Since their introduction, calcium antagonists have been widely used for various cardiovascular diseases, particularly angina pectoris, arrhythmias and hypertension. Their beneficial effects are related to systemic vasodilation, caused by inward flow of calcium ions through the different calcium channels.

At present, several trials have proven that calcium antagonists reduce the risk of strokes, coronary artery disease, dementia and major fatal and non fatal cardiovascular events. Inspite of the abundant evidence already available, several questions remain unanswered and are being addressed by ongoing or planned trials. Some studies are being conducted to know whether specific calcium antagonists, over and above their blood pressure lowering effects, might exert a beneficial effect in specific subgroups of hypertensive patients.[7]

Diabetic subjects experience a disproportionately large number of coronary heart disease events. Although microvascular complications adversely affect quality of life, macrovascular complications are responsible for most cases of death and disability associated with diabetes. In particular, myocardial infarction, stroke, and sudden coronary death are of great importance.[1] Standard coronary risk factors appear to carry greater significance in those with diabetes[8,9] but risk stratification using other risk factors does not explain their excess risk.

Pathologic studies have demonstrated a strong correlation between the presence of coronary calcium and the amount of atheromatous plaque.[10,11] Furthermore, computed tomography (CT) calcium scanning has been shown to predict subsequent coronary events.[12-15]
However, few studies have examined the predictive accuracy of calcium measurement in diabetes.

The South Bay Heart Watch (SBHW) is a prospective cohort study designed to determine the relation between radiographically detectable coronary calcium and coronary outcomes in high-risk adults. This is a report of data obtained from the SBHW cohort to determine whether CT coronary calcium assessment is useful for prospectively discriminating diabetic subjects destined to suffer a coronary event.

Calcification is closely associated with atheromatous plaque, and is a recognized marker for coronary artery disease. Until recently, it was believed that calcium present in the atheromatous plaques is in the form of calcium phosphate, precipitated in a passive manner. However, recent findings indicate that calcification is an active process and calcium is deposited as hydroxyapatite, similar to that in active bone formation. It is known that the amount of calcium in the coronary arteries is better correlated with the amount of atherosclerosis in different individuals and, to a lesser extent, with the segments of the coronary tree in the same individual. There are numerous articles on the correlation of coronary calcium with angiographically proven coronary artery disease; however, there are no such large studies from India.

Significant associations between serum calcium and blood pressure have been demonstrated in several studies, and it has been hypothesized that serum calcium could play a major role in the development of hypertension. Associations have also been found between serum lipid levels and blood pressure. However, little is known about any possible association between serum lipids and serum calcium. In the report from the University of Ghent, Belgium, the researchers used data from a large nutrition survey to investigate the relationship between serum calcium and serum lipids in men and women.

MATERIALS AND METHODS
The present study was carried out in the Department of Biochemistry, Dr. D. Y. Patil Education Society’s Medical College and Hospital, Kolhapur. This study was approved by Institutional ethical committee. In this study a total number of 200 subjects between age 40 yrs to 60 yrs matched with age and sex were included. They were distributed in controls and four groups.
All controls were from the same age groups as patients, not showing any clinical signs and symptoms suggestive of CAD. They were having normal blood pressure (BP), ECG, blood sugar level and apparently no other cardiac risk factors. Group-I contained patients diagnosed to have CAD (based on angiography) with confirmed DM and were receiving treatment for the same. Group-II contained patients with CAD but no DM. Group-III contained Type II DM patients receiving treatment for DM, and had normal ECG and BP. Group-IV contained patients with CAD and DM along with other risk factors (such as smoking, hypertension, family history of CAD, obesity etc.) Used for the estimation of Calcium. Calcium was estimated by OCPC method, End Point. O-Cresolphthalain V/V Colorimetric.\cite{17}

**Inclusion Criteria**

A) Control group: 100 age matched healthy subjects were included in the control group. The subjects were selected after screening for any prior history of cardiovascular disease or any other disease. B) CAD Patients: Angiographically proven patients by the cardiologists with relevant coronary artery disease showing greater than 50% stenoses in at least one major coronary artery at the time of diagnostic catheterization were enrolled in this study. Each subject was screened by a complete history, physical examination and laboratory analysis. C) Diabetic Patients with CAD: Clinically diagnosed patients whose fasting blood glucose level was above 125 mg/dl.

**Exclusion Criteria**

The patients with hemodynamically significant valvular heart disease undergoing catheterization, surgery or trauma, known cardiomyopathy, known cancer, abnormal hepatic and renal function, past or concurrent history of any disease and taking any medication that could influence the oxidant and antioxidant status and endothelial functions were excluded from the study group.
RESULT

Showing the levels of Calcium in (mg/dl) in control subjects and different study groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Calcium (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9.3 ± 1.58</td>
</tr>
<tr>
<td>Group I (CAD with DM)</td>
<td>7.1 ± 1.1 *</td>
</tr>
<tr>
<td>Group II (CAD with out DM)</td>
<td>7.1 ± 1.47 * #</td>
</tr>
<tr>
<td>Group III (DM with out CAD)</td>
<td>7.5 ± 1.50 * ♣</td>
</tr>
<tr>
<td>Group IV (CAD with DM with other risk factors)</td>
<td>7.6 ± 7.71 * ♠</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD

* P<0.001 all four study groups as compared to controls
# P<0.05 Group II as compared to Group I
♣ P<0.05 Group III as compared to Group I
♠ P<0.05 Group IV as compared to Group I

In the present study sr. Calcium was found to be significantly decreased in all the study groups as compared to control group. Similarly significant fall in the serum calcium level was observed when Gr. II, III and IV were compared with Gr.I

DISCUSSION

Significant associations between serum calcium and blood pressure have been demonstrated in several studies, and it has been hypothesized that serum calcium could play a major role in the development of hypertension.[18]

Calcification is closely associated with atheromatous plaque, and is a recognized marker for coronary artery disease.[19] Pathologic studies have demonstrated a strong correlation between the presence of coronary calcium and the amount of atheromatous plaque.[10,11]

In the present study sr. calcium was found to be significantly decreased in all the four study groups as compare to control group. Similarly significant fall in the serum calcium level was observed when Gr. II, III and IV were compared with Gr.I. Abnormalities of calcium metabolism have been described in patients with hypertension.[3] Some authors have reported lower concentrations of sr. calcium in the hypertensives than in normotensive subjects. Our results are in accordance with these workers. Coronary calcification is closely associated with atheromatous plaque and is a recognised marker for CAD.[19] Recent findings indicate that calcification is an active process and calcium is deposited as hydroxypatite, similar to that in active bone formation.[20] It is possible that due to extraction of calcium from the plasma.
there is lowering of sr. calcium. Fu. Y., Wang, Touyz, R. M. et al (5,6) has observed significantly reduced serum calcium in hypertensives and the results are in close agreement with that of others who also found a significant decrease in serum calcium in patients with essential hypertension. Reichel et al[21] also reported reduced calcium in males with elevated diastolic blood pressure.

Abnormal cellular ion transport resulting in altered membrane control over intracellular calcium may be related to essential hypertension. Changes in magnesium levels may contribute to altered cell membrane calcium binding in essential hypertension.[22]

The free intracellular calcium concentration determines the tension in vascular smooth muscle cells, thereby resulting in peripheral vascular resistance. Calcium has direct effect on peripheral vascular tone.[23] Alterations in intracellular calcium are thought to be involved in the common pathway mediating the secretion and action of many hormones, including the pressor action of catecholamines and angiotension II. Calcification is not found in normal coronary arteries. The atherosclerotic process starts in the second decade of life, when calcium deposition begins. The calcium deposition increases with age, and with progression of atherosclerotic lesions. Coronary artery calcification is temporally related to vascular inflammation and the demise of lipid-laden macrophages.[24,25] The exact mechanism is unclear, and may be due to the deposition of extracellular calcium from dying cells, or the formation of bone-like structure by calcifying cells.[26,27] Since calcium is deposited only in the atherosclerotic plaques and not in the normal vessels, and since atherosclerosis is a diffuse process, a high coronary calcium burden reflects the presence of more extensive coronary atherosclerosis. Hence, higher Coronary calcium scores (CCSs) are associated with the presence of significant CAD.

CONCLUSION
Coronary calcification is closely associated with atheromatous plaque and is a recognised marker of CAD. Recent findings indicate that calcification is a active process and calcium is deposited as hydroxyapatite, similar to that in active bone formation. It is possible that due to extraction of calcium from the plasma there is lowering of Sr. Calcium.

REFERENCES


