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Original Research

A study of carcinoembryonic antigen concentrations in patients with coronary artery disease

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Abstract

Background & aims: Carcinoembryonic antigen (CEA) is a tumour marker whose role is now being evaluated as a biomarker for early diagnosis of acute coronary syndromes. Its levels may rise even prior to rise of established biomarkers of myocardial necrosis.
Methods: Serum CEA concentrations were measured by double sandwich ELISA method in four groups of subjects with STEMI, NSTEMI/UA (24 patients of NSTEMI and 18 patients of unstable angina), stable angina and healthy controls with 42 males between 40 to 60 years of age in each group. Also qualitative Troponin T assay and CPK-MB concentrations measurement was done in groups with STEMI and NSTEMI/UA and correlations between CEA concentrations and Troponin T and CPK-MB were made.
Results: Mean serum CEA concentrations were 5.19 ± 0.39, 3.84 ± 0.34, 3.91 ± 1.40, 1.84 ± 0.35 and 2.12 ± 0.40 ng/ml respectively in groups with STEMI, NSTEMI/UA, UA alone, stable CAD and healthy controls respectively. STEMI, NSTEMI/UA and UA patients had significantly higher concentrations than stable CAD and healthy controls ($p < 0.001$). CEA concentrations were comparable in stable CAD and healthy controls ($p = 1.00$). Mean serum CPK- MB concentration in group with STEMI was significantly higher than in NSTEMI/UA group ($p < 0.001$). Highly significant positive correlation was obtained between mean CEA and CPK-MB concentrations in STEMI ($R = 0.866$, $p < 0.001$) and NSTEMI ($R = 0.950$, $p < 0.001$), STEMI and NSTEMI combined together ($R = 0.781$, $p < 0.001$) NSTEMI and UA together ($R = 0.648$, $p < 0.001$), but it was weak and statistically insignificant in UA patients ($R = 0.319$, $p = 0.197$). Mean serum concentration 4.69 ± 3.26 ng/ml of CEA in patients with ACS was significantly higher in troponin T positive patients as compared to 3.91 ± 1.40 ng/ml in Troponin T negative patients ($p < 0.001$).
Conclusions: CEA is a sensitive biomarker for early diagnosis of ACS. Its levels correlate with severity of ACS. It may play a crucial role in diagnosis of ACS in patients who present with atypical manifestations or when traditional biomarkers such as CPK-MB and Troponins are not raised.

Keywords: carcinoembryonic antigen; coronary artery diseases; acute coronary syndromes; cardiac biomarkers

1. Introduction

To predict the future has been the dream of human kinds for thousands of years. Although, clinical manifestations and pathognomonic ECG or echocardiographic findings have taken a big step forward in the treatment of ACS, there is still a no man's land in diagnosis when plasmin is struggling to solve clots secondary to plaque rupture. Any cost-effective method that can stratify the patients at this stage should be very welcome.

Rupture of unstable atherosclerotic plaque is a major mechanism of development of acute coronary syndrome (ACS) from stable CAD. Currently, creatinine phosphokinase-MB (CPK-MB) and cardiac troponins T and I are used to

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diagnose myocardial necrosis. Brain natriuretic peptide (BNP), myeloperoxidase, pregnancy associated plasma protein-A (PAPP-A) and metalloproteinase-9 are other reported useful markers for diagnosis of ACS. However, the availability of a sensitive and specific early bio marker of plaque instability, whose levels become elevated before or even in the absence of myocardial necrosis, should improve diagnostic and therapeutic decision making.

Carcinoembryonic antigen (CEA) is a tumour marker associated with various malignancies e.g. carcinoma colon, lung, breast, thyroid, stomach etc. Some non neoplastic conditions such as smoking, obesity, acute coronary syndromes, inflammatory bowel disease, liver and kidney disease also have been found to be associated with higher CEA concentrations.[1−3] Carcinoembryonic antigen (CEA) might be one such potential molecule which is being evaluated as a bio marker for early diagnosis of acute coronary syndromes (ACS). The hypothesis behind current study was that the transformation from stable to unstable plaque might be reflected by rise in concentrations of CEA.

Recently CEA has been reported to be associated with abdominal visceral fat in Korean non-smoker females. Visceral fat is a powerful risk factor for atherosclerosis.[4]

Only scanty data is available in literature highlighting role of CEA in CAD. A study, conducted on Japanese men, reported significantly higher concentrations of CEA in patients with carotid atherosclerosis as compared to healthy controls.[5] However, another study reported higher concentrations of CEA in patients with ACS but not in those with stable CAD.[6] However, in this study patients with NSTEMI/UA were not separately analysed. Moreover, correlation with CPK-MB and Troponin T was not assessed. In view of above controversies we planned this study.

2. Material and method

This analytical cross sectional study was carried out at a tertiary hospital in north India between years 2011 to 2013 and comprised of four groups with 42 male subjects, between 40-60 years of age, in each group. These four groups namely- A, B, C and D comprised of patients with STEMI, NSTEMI/UA, stable angina and age and sex matched healthy controls. Out of total 42 patients include in NSTEMI/UA group 24 patients had NSTEMI while remaining 18 were diagnosed to have unstable angina (UA). Patients with STEMI and NSTEMI were diagnosed on the basis of 2007 American heart association universal definition of acute myocardial infarction.[7] Patients included in stable angina group were those who were already diagnosed chronic stable angina after appropriate clinical and laboratory investigations and were already in follow up in coronary clinic or newly diagnosed patients of stable angina based on clinical history and stress tests such as treadmill test (TMT), thallium scan, stress echocardiography or coronary angiography. Control group included healthy attendants of patients.

After obtaining written consent, a detailed history and thorough physical examination were performed on all subjects. Various anthropometric parameters like height, weight and waist circumference were recorded. Patients with any acute or chronic inflammatory conditions, past or present malignancy, acute or chronic liver disease, chronic kidney disease (Serum creatinine >1.5 mg/dl), multiorgan dysfunction syndromes, inflammatory bowel disease, smokers with history of smoking for more than 50 pack years (1 bidi considered equivalent to 1 cigarette) or those with positive test for stool for occult blood were excluded from the study.

Routine laboratory investigations including complete blood counts, blood sugar (fasting and postprandial), kidney function tests such as serum blood urea, creatinine, liver function test such as serum proteins, bilirubin, alkaline phosphatase, ALT (alanine aminotransferase) and AST (aspartate aminotransferase), serum lipid parameters and 12 lead ECG were performed on all subjects. Those with any evidence of liver or kidney disease on investigations were excluded from study.

For routine haematological investigations, after overnight fasting blood samples were collected in EDTA vial for blood counts and plain vial for serum related investigations. Stool sample for occult blood was also collected in the morning.

Special Investigations included Serum CEA concentrations estimation (for all groups), for which 2 ml blood was taken in plain vial as early as possible after presentation but not beyond 24 hours after onset of chest pain in groups A and B. In groups C and D sample was at the time of recruitment. Vials were transported to department of Biochemistry and stored in deep freezer at −80°C for further processing. Commercially available kits using double sandwich ELISA (Weldon Biotech, India) for quantitative assessment of CEA levels were used for estimation of its concentrations.

Qualitative cTn T test was done in groups A and B using commercially available kit. Serum CPK-MB concentrations were measured in groups A and B by immunoenzymatic method[8] using commercially available kit. Blood samples for both Troponin T and serum CPK-MB levels were taken as soon as possible after admission, but not beyond 24 hours of onset of chest pain.

3. Statistical analysis

Software SPSS 17.0 was used to analyse the data. One way Analysis of variance (ANOVA) was used to compare means across the groups. Post-hoc Tukey's test was used for multiple comparisons. Spearman's rank order correlation was used for correlation between CEA and CPK-MB concentrations (quantitative data) in groups A and B separately. Unpaired t-test was used to compare mean CEA concentrations in Troponin T positive patients and Troponin T negative patients separately in groups A and B. A p-value <0.05 was considered statistically significant and <0.001 as highly significant.

4. Results

There was a trend towards higher BMI, waist circumference, waist hip ratio, blood sugar with increasing severity of CAD i.e. highest values were found in STEMI followed by