Available online at www.sciencedirect.com

SCIENCE DIRECT

Clinica Chimica Acta 367 (2006) 77 – 80

www.elsevier.com/locate/clinchim

Prognostic significance of ischemia modified albumin after percutaneous coronary intervention

Jaroslav Dušek [a,*], Josef Št'ásek [a], Miloš Tichý [b], Josef Bis [a], Jaroslav Gregor [c], Jan Vojáček [a], Vladimír Mašín [d], Pavel Polanský [e], Miroslav Brtko [e], Dušan Černohorský [f]

[a] *First Department of Internal Medicine, University Hospital Hradec Králové, Charles, University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic*

[b] *Department of Biochemistry, University Hospital Hradec Králové, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic*

[c] *Department of Pneumology, University Hospital Hradec Králové, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic*

[d] *Department of Medical Biophysics, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic*

[e] *Department of Cardiosurgery, University Hospital Hradec Králové, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic*

[f] *Department of Gerontology and Metabolism, University Hospital Hradec Králové, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic*

Received 5 November 2005; received in revised form 21 November 2005; accepted 21 November 2005
Available online 10 January 2006

Abstract

Ischemia modified albumin (IMA) is a new biochemical marker of ischemia. IMA levels rise in patients who develop ischemia during percutaneous coronary intervention (PCI). It is unclear whether IMA elevations correlate with PCI variables. The possible prognostic value of post-PCI IMA elevation has not yet to be studied.

Methods: We studied 60 patients (mean age 61 years; 51 male) who underwent successful elective single-vessel PCI for the management of stable angina pectoris. IMA levels were measured and compared with PCI variables and target lesion revascularization rate. The median post-PCI follow up is 46 months (CI 44.6 to 47.7).

Results: We found that the only variable related to post-PCI IMA levels was periprocedural dissection of target vessel (147.6 vs. 141.1 kU/l, $p=0.035$). No correlation between high and low balloon inflation pressure (143.6 vs. 141.6 kU/l, $p=0.64$), short and long inflation pressure (141.5 vs. 143.6 kU/l, $p=0.17$), with and without stent placement (143.7 vs. 141.3 kU/l, $p=0.93$) was found. IMA level more then 130 kU/l was associated with higher frequency of target lesion revascularization at nearly 4-years follow-up ($p=0.026$).

Conclusion: Post-PCI IMA elevation is associated with higher target lesion revascularization.

Keywords: Ischemia modified albumin; Angioplasty; Prognosis

1. Introduction

Ischemia modified albumin (IMA), as measured by the Albumin Cobalt Binding (ACB) Test, is a new marker of transient myocardial ischemia. The ACB test measures the binding capacity of exogenous cobalt to the N-terminus of human albumin. In the presence of myocardial ischemia, structural changes take place in the N-terminus of albumin that rapidly reduce its binding capacity for transition metal ions [1]. The exact mechanism of these changes in the N-terminus of human albumin is unclear. Contemporary presumption is that it is due to ischemia/reperfusion mediators, hypoxia, acidosis etc. [2,3]. There is no correlation between the Albumin Cobalt Binding (ACB) Test results and human serum albumin levels in normal range [2]. Recent studies [4,5] have substantiated previous findings [6,7] and shown that IMA is highly sensitive for the

* Corresponding author. First Department of Internal Medicine, University Hospital Hradec Králové, Sokolská 581, 500 05 Hradec Králové, Czech Republic. Tel.: +420 495 833 119; fax: +420 495 833 581.
E-mail address: dusek@fnhk.cz (J. Dušek).

0009-8981/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.cca.2005.11.020

identification of acute coronary syndromes and, in combination with the ECG and troponin, has both high sensitivity and negative predictive value. IMA has also been shown to be elevated in patients after percutaneous coronary intervention (PCI) as a result of ischemia reperfusion injury [8,9]. In present study, we compared the association between IMA levels and inflation pressure, duration of inflations in patients with coronary artery disease who underwent elective PCI, and if increased IMA improved risk stratification for target lesion revascularization (TLR).

2. Methods

2.1. Patients and study design

Our cohort consists of 60 consecutive patients who underwent elective single-vessel PCI for the management of stable angina pectoris between February 2000 and March 2001. None of the patients had a recent myocardial infarction, unstable angina pectoris, abnormal renal function, stroke, transient ischemic attack, or symptomatic peripheral vascular disease. Serum albumin measurements were within the normal range in all patients. All patients gave written informed consent to participate in the study after thorough explanation of the study protocol. This investigation was approved by the local research ethics committee.

All patients were on standard medical treatment before and after PCI and decisions regarding the number of balloon inflations and the use of stent were at the discretion of the interventional cardiologist. Blood samples were drawn from a cubital median vein 2 h for IMA measurement and 12 h for CK MB and cTnT measurement after the last balloon inflation. Blood (10 ml) was drawn into tubes, centrifuged and samples were frozen at −70 °C within 2 h and stored until measurement. Specimens handled in this way showed no significant difference in assay results compared to fresh specimens. Repeat freeze–thaw cycles were avoided. Clinical follow-up was performed by either telephone contact or office visit every 6 months.

All patients received 100 mg/day aspirin, and patients who underwent stenting were treated concomitantly with either 500 mg/day ticlopidine or 75 mg/day clopidogrel for 4 weeks per routine protocol. Glycoprotein IIb/IIIa inhibitors were not used. The occurrence of major late clinical events was recorded, including death, myocardial infarction, and target lesion revascularization (whether surgical or percutaneous).

2.2. Albumin cobalt binding test for measurement of IMA

IMA was measured by the Albumin Cobalt Binding (ACB®) Test, Ischemia Technologies INC, Denver, CO, USA, Dimension AR analyzer (DADE-Behring). The ACB Test measures the cobalt binding capacity of albumin in a serum sample. The analytical sensitivity of the ACB Test was calculated to be 10.6 U/ml. The IMA upper limit of normal, 85 kU/l (95th percentile of a population of 283 apparently healthy individuals), was used as a cut-off point for myocardial ischemia in the study, according to the recommendation of manufacturer [9,10].

2.3. Cardiac troponin T and CK MB testing

Cardiac troponin T (cTnT) concentrations were measured by an electrochemiluminescence assay on the Elecsys 2010 analyzer (Roche diagnostics, Lewes, Sussex, UK). CTnT concentrations >0.01 ng/ml were considered to represent a positive result per our institutional criteria. CK MB concentrations were measured by the DADE-Behring assay set on the DIMENSION AR analyzer. The CK MB upper limit of normal, 0.50 μkat/l, was used as a cut-off point.

2.4. Statistical analysis

Statistical analysis was performed with the NCSS 6.0 statistical software package. Results for normally distributed continuous variables are expressed as the mean value (standard deviation) and continuous variables with non-normal distribution are presented as the median value. Categorical data are shown as number (percentage). The unpaired Wilcoxon's *t* test or Fisher's exact test was used to analyze the difference between medians in groups. Differences were considered to be statistically significant if the null hypothesis could be rejected with >95% confidence intervals ($p<0.05$). The median value for the inflation pressure was 14 atm and the median value for the duration of inflations was 90 s. These values were used as a cut-off point to recode the inflation pressure and duration of inflations into a binary variable comparing these characteristics. The Fisher's exact test was used for statistical analysis of various IMA levels as predictors TLR.

3. Results

Table 1 shows demographic and baseline clinical characteristics. The vessel treated was the left anterior descending coronary artery in 27 patients (45%); the left circumflex in 12 patients (35%); and the right coro-

Table 1
Clinical characteristics of the study group

Age (yrs)	60±8.5
Men	51
Systemic hypertension	38 (63%)
Smoker	45 (75%)
Hypercholesterolemia (>5 mmol/l)	54 (90%)
Diabetes mellitus	14 (23%)
Family history of ischemic heart disease	6 (10%)
Previous myocardial infarction	32 (53%)
Previous angioplasty	13 (22%)

Data are expressed as mean±SD, or number (percentage).