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Toll like receptor 4 in acute myocardial infarction

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Background: Toll-like receptor 4 (TLR 4) have been identified as central for innate immune receptors. Previous studies were done for local (at plaque rupture site) and systemic expression of TLR 4 from mononuclear concentrate (MNC) and on subgroup of lymphocyte population in acute myocardial infarction (AMI) and heart failure (HF) patients. TLR inhibition is considered as a emerging new therapeutic modality for LV remodeling in HF. We want to study difference of expression of TLR4 on MNC and plasma, even though for TLR 4 protein detection in plasma probably requires higher concentration on the lymphocytes and to be secreted into plasma, but still if plasma detected TLR 4 has same prognostification importance as from TLR 4 of MNC then, TLR 4 detection from plasma may be used at bed side.

Material and methods: We recruited acute MI patients who presented with in 48 hrs of onset of chest pain. 10 ml of venous blood for TLR 4 and for other biochemical tests was collected within 24 hrs of admission. Group 1 are AMI patients in whom TLR 4 concentration measured from MNC (Ficoll paque method) and Group 2 are AMI patients in whom TLR 4 concentration measured from plasma. Two groups of Controls were taken. Contols A consisted of volunteers without known CAD and coronary risk factors. In these controls TLR 4 detection was done from MNC and plasma. Control B consisted of patients with obvious sepsis, where we used plasma for TLR 4 concentration. TLR 4 was estimated using Human Toll-like receptor 4 (TLR4) ELISA kit from Cusabio Company. According to that kit standards TLR 4 concentration < or=0.03 ng/dl is considered as negative. Killips class, adverse events in hospitals (including recurrent angina, Left ventricular failure, ventricular arrhythmias and death) and CPK levels were correlated with TLR 4 levels.

Results: We studied 40 AMI patients and 20 controls .Group 1 had 26 AMI subjects, Group 2 had 14 AMI patients. 15 persons in Control A and 5 patients in Control B. Average age of AMI patients were 54.1±11.6 yrs and 8 were female patients. Patients with inferior MI (including RV MI, posterior MI, infero-lateral) were 11 (27.5%), anterior (including septal, antero-lateral MI) MI were 26 (65%) and extensive MI were 3 (7.5%). Hypertension was present in 21 (52.5%) and Diabetes mellitus in 10 (25%) patients. Average Killips class was 1.7±0.9 and CPK levels were 1652.2±1294.6 units/l. 14 patients undergone primary PCI. Mean TLR 4 concentration was 0.7±0.4 ng/dl.TLR 4 was positive in 14 patients of Group 1, 2 patients of Group 2, none in Control A & all 5 in Control B. In group 1 average Killips class was 2.4±0.8 in TLR 4 positive cases vs 1.17±0.4 in TLR 4 negative cases (p=<0.001). Mean TLR 4 concentration was 0.8±0.7 ng /dl. Average CPK level was 1760.4±875.4 units/l in TLR 4 positive cases vs. 1994±986.3 units/l in TLR 4 negative case. One patient had primary ventricular tachycardia (VT), had negative TLR 4 levels (0.05 ng/dl). One patient developed cardio-genic shock in hospital on IABP, died on day 3 in this group, he had high TLR 4 values (1.5 ng/dl). There is no correlation to TLR 4 concentration and occurrence of primary VT and CPK levels but strong association with Killips class and death. In group 2, average Killips class was 3±1.4 in TLR 4 positive cases vs. 1.3±0.5 in TLR 4 negative case (p=0.001). Average CPK level was 1348 ±439.3 units/l in TLR 4 positive cases vs. in 1537±45.7 units/l in TLR 4 negative case. Mean TLR 4 concentration was 0.5±0.2 ng/dl. One patient who had primary VT had negative TLR 4 levels (0.03 ng/dl). One patient with extensive anterior MI with severe LV dysfunction in hospital had LVF and shock, in Killips class 4 on ventilator and IABP with tight LMCA stenosis and additional LAD diffuse disease died, had high TLR 4 values (0.2 ng/dl). Even though TLR 4 detection was significantly less in this group patients as anticipated, like in Group 1 , in this group 2 also there is no correlation to TLR 4 concentration and occurrence of primary VT and CPK levels but strong association with Killips class and death.

Conclusion: Plasma TLR 4 detection was given same correlation with Killips class and prognostication of the patient with AMI like the TLR 4 detected from MNC. Therefore, kits to design for using plasma of the AMI patients for detection of TLR at bedside, may be useful in prognostification. Targeted TLR inhibition therapy may improve the mortality in future studies.