ABSTRACT

Massive platelet aggregation occurs on the site where plaques rupture on the coronary artery. This is delineated to cause both acute myocardial infarction (AMI) and acute coronary syndromes (ACS). Acetylsalicylic acid some time become resistant to inhibit platelet aggregation in AMI as it is the cornerstone therapeutic approach. It was found that the concentration of dermcidin was many folds higher in AMI circulation than that of the normal. Dermcidin (0.4 μM) incubated normal plasma manifested the binding of the protein to platelets moreover, the protein incubated with platelets reverses the effect of aspirin in AMI. In contrast, dermcidin antibody was able to reinstate the sensitivity of the platelets to aspirin effect. It was discerned that in AMI, aspirin (15 μM) induced NO which removed the bound dermcidin from its high-affinity binding sites, and further the addition of 10 μM aspirin was able to inhibit the platelet aggregation completely. In the case of other peripheral vascular disorders like cerebrovascular accident, the phenomena are the same. The role of insulin in both ischemic stroke (IS) and hemorrhagic stroke (HS) was determined because insulin is supposed to have an anti-thrombotic property and diabetes mellitus is a risk factor for strokes. Normal platelet-rich plasma PRP (10^8platelets/ml) in the presence of 15μUnits insulin/ml produced 1.41 nmol NO instead IS and HS victims produced 0.38 nmol NO and 0.08 nmol NO respectively. Like AMI, the low-dose of aspirin followed by insulin sensitized the platelets again. DCN2 (0.14 μM) which is found in stroke patients, when incubated with hepatocyte cell, abolished glucose activated nitric oxide synthase (GANOS) activity which could be reversed by using 15 μM aspirin. Chest pain is the distinctive feature in AMI or ACS and organic nitro-compounds are often given to that patients, these compounds (nitroglycerine, isosorbide di-nitrate or aspirin or insulin even glucose can express nitric oxide generating protein di-sulfide isomerase (PDI) in goat arterial endothelial

cells which can up-regulate NO. So, NO is involved in the pain regulation and dermcidin is also indicated with NO. So, dermcidin may impart in the development of pain in ACS or AMI. Dermcidin is a stress induced protein. It is also found to express in hypoxia and in the presence of aqueous extract of tobacco leaves. When this protein was injected to the mice, it was found to develop hyperglycemia in mice where it was found that the protein impaired insulin induced glucose uptake in muscle cells. From the FRET analysis, it was found that DEA-NONOate induced NO is inhibited by dermcidin protein and it was measured by cGMP by using cGI-500 sensor. And we wanted to neutralize the hyperglycemic condition, from that basis we experimented with oral insulin preparation to avoid painful daily injection and to increase the rate of bioavailability even at its lower dose.Which actually was able to neutralize the alloxan induced hyperglycemia in mice via NO and GLUT4 regulations as noticed in our different experimentation.. So, the stress-induced dermcidin protein might play a crucial role in platelet aggregation and in the inhibition of NO. This protein actually is the cause of resistance to the aspirin effect. Herein we showed the specific and unique dose of aspirin/or insulin can neutralize the dermcidin effect in vascular disease and also might inhibit the dermcidin induced hyperglycemia or endothelial dysfunction.