

O4: STUDIES OF OXIDATIVE STRESS INDUCED DAMAGE ON LIPOPROTEINS IN β -THALASSEMIA/HEMOGLOBIN E.

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ABSTRACT

Atherogenic-related vascular complications commonly occur in β -thalassemia/Hemoglobin E patients (β -thal/HbE). It is believed that oxidative modification of LDL could be a contributing cause of atherosclerosis. This study was designed to study the changes that occurred to plasma lipoproteins of β -thal/Hb E, under the profound environment of oxidative insults from iron overloading in patients. The markers of oxidative stress were monitored in 30 β -thal/Hb E patients and compared with 10 healthy volunteers. It was the varying degrees of iron-overloading in the patients that rendered oxidative insult to the body tissue/organ, resulting in a precipitous drop of plasma and tissue vitamin E, a major hydrophobic chain breaking antioxidant with accompanying accumulation of TBARs, the oxidized products of lipids in the plasma and lipoproteins of the β -thal/Hb E.

The plasma profile of lipids, namely cholesterol (C) and cholesteryl esters (CEs) in both LDL and HDL were separated and characterized using an HPLC. The characteristic changes in lipid compositions of the LDL and HDL of the patients were markedly different from that of normal individuals. The ratios of some cholesterol esters (CEs) over the total cholesterol (TC), namely the cholesteryl linoleate (CL) to TC in the LDL ($p < 0.001$) and HDL ($p < 0.05$) were lowered in the β -thal/Hb E with less effect observed on free cholesterol (FC), suggesting that CEs, located at the core of the lipoproteins were prone to more oxidative damage than those FC located at the periphery. This finding was further supported by the elevated ratios of free cholesterol over total cholesterol (FC/TC ratios) in both LDL ($p < 0.05$) and HDL ($p < 0.001$). The lower ratios of cholesteryl linoleate to cholesteryl oleate (CL/CO ratio) noted a significant correlation with clinical severity suggesting that CL/CO ratios could be used as a clinical marker/index of severity in the β -thal/HbE patients. A closed relationship of non-transferrin bound iron (NTBI) and TBARs ($r = 0.925$, $p < 0.0001$) in LDL of these β -thal/Hb E patients with also a CL/CO ratio of less than 2 in lipoproteins ($n = 10$) strongly support the contention that non-chelatable NTBIs initiate lipid peroxidation in the β -thal/HbE.

This study demonstrated that cholesteryl linoleate is the primary target of oxidative damage in lipoproteins, which was induced by NTBIs in β -thal/Hb E. It thus suggested that cholesteryl linoleate could be used as an indicative marker of clinical severity in thalassemia.

Key words: lipoprotein, β -thalassemia/hemoglobin E, oxidative stress, cholesteryl linoleate, cholesterol, NTBI.