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MEETING ABSTRACT

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Effect of plasma from high and low serum unconjugated bilirubin individuals on cholesterol efflux

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Background: Mildly elevated bilirubin levels, a characteristic of Gilbert Syndrome (GS), have been inversely correlated with cardiovascular disease onset and mortality. Protection of lipids, proteins and other macromolecules from oxidation by bilirubin represents the most commonly accepted mechanism contributing to cardiovascular protection [1]. A critical step of atherosclerosis pathogenesis is the formation of cholesterol-enriched pro-atherogenic foam cells. Therefore, increased macrophage cholesterol efflux is expected to result in an overall anti-atherosclerotic effect. However, there are no data on how high serum levels of unconjugated bilirubin (UCB) might affect macrophage cholesterol efflux.

Methods: In this study, THP-1-derived macrophages were differentiated by PMA treatment and then labelled with [^{3}H]cholesterol. Cholesterol efflux was assessed in presence of human plasma from 120 individuals for 4 h. The subjects were divided into two age- and gender-matched groups, with high and low serum UCB with a cut-off point at 17.1 µM. A paired *t*-test was performed to analyse the data for statistical significance.

Results: The cholesterol efflux mediated by serum from high- and low-UCB individuals was 5.45% and 5.83%, respectively. Individuals with higher serum UCB showed significantly lower cholesterol efflux capacity, even after correction for Apo-A1 or HDL levels in plasma ($p < 0.001$).

Discussion: A number of studies have shown that the risk of mortality from cardiovascular disease is remarkably reduced in GS individuals. This protection may be explained by bilirubin's ability to protect blood lipids and LDL from oxidation [1]. Some studies showed that the individuals with GS had significantly reduced levels of total cholesterol, low-density lipoprotein cholestrol (LDL-C), triacylglycerol (TAG), oxidized low-density lipoprotein (oxLDL), very-low-density lipoprotein (VLDL), small dense low-density lipoprotein (sd-LDL), and elevated HDL / LDL ratios in plasma [2]. However, our results showed that plasma with higher bilirubin levels, as found in GS, does not contribute to higher cholesterol efflux from macrophages, and even had an inverse effect. This suggests that different pathways might be involved in the cardiovascular protection by increased plasma bilirubin.

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