EFFECTS OF OXIDISED LDL ON NITRIC OXIDE AND ENDOTHELIN-1 PRODUCTION IN HUMAN MICROVASCULAR ENDOTHELIUM: ROLE OF THROMBOXANE A_2 RECEPTOR

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LDL particles modulate the release of NO and endothelin-1 by the endothelium. To what extent these effects depend on LDL concentration and degree of oxidation and eventually what is the role of tromboxane A_2 receptor is unknown.

HMEC-1 were exposed for 24-h to a) 3 concentrations (50, 100 and 200 μg/ml) of either native, low- or medium-oxidised LDL, b) 8-epi-$PGF_{2\alpha}$ (F_2–IP, 10^{-11}, 10^{-10}, 10^{-9}, and 10^{-8} M) either alone or with TXA_2 receptor blocker SQ 29.548 (10^{-6} M), c) native, low- and medium-oxidised LDL either alone or with SQ 29.548 (10^{-6} M). In all experiments intracellular eNOS, and NO_2/NO_3, endothelin-1 and interleukin-6 concentration in the medium were measured.

Both native and oxidised LDL induced a NO_2/NO_3 accumulation with dose and degree of oxidation acting synergistically; eNOS was stimulated only by oxidised LDL. F_2–IP, NO_2/NO_3 and eNOS with SQ 29.548 completely preventing these effects but only partially the effect of LDL. IL-6 was also synergistically stimulated by LDL dose and degree of oxidation but not by direct exposure to F_2–IP nor was affected by SQ 29.548. Both native and oxidised LDL stimulated endothelin-1 production independently of dose or degree of oxidation. F_2–IP had a modest stimulatory effect while the effect of SQ 29.548 was evident only with oxidised LDL.

In HMEC-1 LDL dose and degree of oxidation synergistically stimulate NO and IL-6 production and the effect on NO is largely mediated through the TXA_2 receptor. LDL simultaneously facilitate endothelin-1 production independently of the dose and degree of oxidation.