Iodide as a potential therapeutic in atherosclerosis

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Myeloperoxidase (MPO) is an enzyme released at sites of inflammation which generates powerful oxidants. It is strongly associated with atherosclerosis, a chronic inflammatory disease of the arteries. Both MPO and its reaction products are present in human atherosclerotic plaques, and MPO is an independent prognostic marker in patients with coronary artery disease as well as healthy individuals. Inhibition of oxidant formation by MPO may therefore have therapeutic potential in preventing atherosclerosis. MPO generates the oxidant hypochlorous acid (HOCl) from chloride (Cl^-), but it can also use the alternative substrates iodide (I^-) and thiocyanate (SCN^-) to form less damaging species. We hypothesize that I^- alone, or in combination with SCN^-, might reduce atherosclerotic plaque development by decreasing oxidative damage and inflammation. Apolipoprotein E deficient ($ApoE^{-/-}$) mice were fed a western-type diet for 16 weeks with concomitant supplementation with I^- (18 μM) and/or SCN^-(10 mM) in drinking water. Atherosclerotic plaque burden was evaluated in the aortic arch by en face analysis, whereas the plaque size and composition of lipid and collagen in the aortic valves were examined and quantified by histological staining. Treatment with I^- decreased the atherosclerotic plaque burden in the aortic arch but not the aortic valves. Both I^- and SCN^-, alone or in combination, significantly reduced plasma cholesterol levels. Quantification of plasma thyroid hormone levels indicated that treatment did not affect basic metabolism. In conclusion, I^- appears to have positive effects in reducing atherosclerosis. Whether the reduction in plaque burden seen with I^- is due to changes in lipid metabolism or a decrease in MPO-induced oxidative damage has yet to be determined. However, I^- supplementation has potential as a cheap, safe, and widely applicable primary prevention strategy to address the increasing global burden of atherosclerosis.