Elevated plasma levels of $F_{2\alpha}$ isoprostane in cystic fibrosis

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Cystic fibrosis (CF) is associated with chronic lung infection and chronic inflammation. Neutrophil activation and subsequent release of reactive oxygen species contribute to cellular damage and reduced lung function while lipid peroxidation is the central feature of oxidant injury. While many authors have reported elevated indices of oxidative stress in CF including lipid peroxidation, the reliability of existing methods has been questioned. Recently, isoprostanes have been shown to be a reliable in vivo marker of oxidant injury. They are prostaglandin-like compounds, produced in in large quantities by free-radical catalysed peroxidation of arachidonic acid with 8-iso-$PGF_{2\alpha}$ being the most abundant. 8-iso-$PGF_{2\alpha}$ has been shown to be an antagonist of platelet thromboxane receptors in the pulmonary bed in rats and rabbits and to cause airflow obstruction and plasma exudation in guinea pig lung. The present study was designed to examine the relationship between 8-iso-$PGF_{2\alpha}$ levels, plasma antioxidant and clinical status in CF. We hypothesised that plasma 8-iso-$PGF_{2\alpha}$ levels would be higher in subjects with CF compared to healthy controls.

Plasma 8-iso-$PGF_{2\alpha}$ levels were measured in 22 subjects with CF and 9 healthy controls using an 8-Isoprostane enzyme immunoassay kit along with plasma vitamins A, E and β-carotene. Plasma 8-iso-$PGF_{2\alpha}$ levels were shown to be significantly elevated in the CF subjects compared to controls (319.6 ± 52.6 pg/mL versus 145.0 ± 21.0 pg/mL, P = 0.005). Plasma levels of vitamins A & E for the CF subjects were significantly lower than for the controls with mean plasma β-carotene below the laboratory normal range. There were no significant correlations between plasma 8-iso-$PGF_{2\alpha}$ levels and clinical status or plasma antioxidant levels.

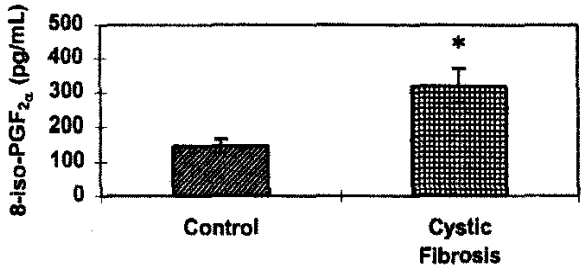

Figure. 8-iso-$PGF_{2\alpha}$ levels were significantly higher in subjects with CF compared to controls, even after adjustment for variation in body surface area.

In conclusion, this study has found significantly elevated lipid peroxidation in subjects with CF. Current antioxidant supplementation in CF is not sufficient to reduce lipid peroxidation to comparable levels in healthy control subjects. While the optimum antioxidant supplementation regime for people with CF is yet to be determined, future intervention trials, targeting reduced 8-iso-$PGF_{2\alpha}$ will help to determine the role oxidative stress plays in the progression of lung disease in CF.