ARACHIDONIC ACID SUPPLEMENTATION CAUSES AN INCREASED THROMBOXANE TO PROSTACYCLIN RATIO EVEN IN THE PRESENCE OF n-3 FATTY ACIDS

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There is significant interest in the interrelationship between long chain n-3 and n-6 fatty acids due to their ability to modulate eicosanoid production and therefore thrombosis tendency. In general, intake of arachidonic acid (AA) results in enhanced eicosanoid production, whereas n-3 fatty acids (FA) appear to modulate eicosanoid production by decreasing the prostacyclin to thromboxane ratio (Whelan et al. 1993).

This study was designed to investigate the consequences of ingestion of both AA and n-3 long chain FA on the production of thromboxane and prostacyclin in rats. In addition, we wanted to determine whether the inclusion of high levels of long chain n-3 FA would have any beneficial effect on eicosanoid production in the presence of increasing levels of dietary AA. Four groups of male Sprague-Dawley rats were fed a control diet enriched with eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (approximately 100 mg/day) for 24 days. During the last 10 days the four groups were orally supplemented with either 0, 30, 60 and 90 mg/day of ethyl arachidonate. A further group of rats was fed the control diet for 24 days. In vitro aortic prostacyclin (6-keto-PGF1α) production, serum thromboxane (TXB_2) production and plasma platelet and aortic phospholipid (PL) FA were measured.

Enriching the diet with n-3 FA resulted in significant reductions in tissue AA levels and an increase in the n-3 FA, particularly EPA. Despite these changes in FA, no changes were observed for in vitro eicosanoid synthesis compared with the control animals. The inclusion of AA in the diet resulted in dose-dependent increases in tissue AA levels with corresponding decreases in EPA (plasma, platelet and aortic FA PL) compared with the n-3 enriched-fed rats. These changes resulted in significant step-wise increases for both aortic prostacyclin and serum thromboxane production. The dietary AA caused a differential (two-fold) increase in thromboxane relative to prostacyclin for all three levels of AA supplementation. The major effect of AA supplementation on FA PL content was to displace EPA from the membrane PL. This was observed even with as little as 30 mg/day of AA. The increases in eicosanoid production are most likely due to a combination of increased AA content and a reduction in EPA (a cyclooxygenase inhibitor). The results indicated that in the combined presence of dietary AA and n-3 FA, the n-3 FA do not appear to exert a beneficial effect on the production of eicosanoids.

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