THE EFFECT OF DIETARY ARACHIDONIC ACID AND N-3 POLYUNSATURATED FATTY ACIDS ON EICOSANOID PRODUCTION IN HUMANS

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The aim of this study was to determine the effect of dietary arachidonic acid (AA) alone or in combination with long chain n-3 polyunsaturated fatty acids (PUFA) on thrombosis tendency in humans as measured by the ratio of thromboxane:prostacyclin (determined as urinary metabolites by GCMS). The major PUFA in the western diet is linoleic acid (LA), which is considered to be a major source of tissue AA. Since the in vivo desaturation and elongation process required for the synthesis of AA is slow in humans (Emken et al. 1987), it has been suggested that foods containing AA might also contribute to tissue AA pools (Sinclair et al. 1987). There is no quantitative data in humans which allows an estimate of the proportion of tissue AA which is derived from dietary LA compared with that derived from dietary AA. As AA is the predominant precursor of vaso-active eicosanoids, it follows that dietary AA could influence dramatically the bodies production of thromboxane (platelet aggregation and vaso constriction) and prostacyclin (inhibitor of platelet aggregation and vaso dilator). We have previously shown that oral administration of purified ethyl arachidonate to rats leads to an increase in systemic production of prostacyclin (PGI_2) (Mann et al. 1994). There is considerable evidence that the n-3 PUFA reduce thrombosis tendency, possibly mediated by a reduction in thromboxane A_2 (TXA_2) synthesis by platelets. Thus diets rich in foods containing AA alone may exert a different effect on eicosanoid production than diets containing raised levels of both AA and n-3 PUFA.

To study this aspect of thrombosis we carried out a dietary intervention study consisting of three distinct diets, each of three weeks duration (12 males, 12 females). The first week of each was a vegetarian period followed by two weeks of either white meat (turkey, AA:n-3 PUFA, 2.5:1), red meat (beef and lamb, AA:n-3 PUFA, 1:1) or fish (Atlantic salmon, AA:n-3 PUFA, 0.04:1). All 9 weeks on the diets were designed to have energy intake as fat restricted to 15% of energy and AA intake as a fixed proportion of dietary energy, ranging from 90mg/day (6048kJ/day diet) to 210mg/day (14625kJ/day diet). Each diet was followed by a three week wash out period.

No change was observed in AA level in platelet phospholipids (PL) at the end of the white meat or red meat diets. There was a small decrease in platelet PL AA on the fish diet along with a small, but significant increase in EPA and DHA levels. Serum PL levels of AA increased on the white meat and red meat diets but decreased on the fish diet, with a substantial increase in PL levels of EPA and DHA. Contrary to expectations, PGI_2 production decreased on both white and red meat diets despite the small rise in serum AA. On the fish diet there was also a decrease in PGI_2 production, but this paralleled the decrease in serum AA. A simultaneous rise in prostacyclin (PGI_3) derived from EPA was observed in this group, although the level of this eicosanoid remains minute compared with PGI_2 levels.

The failure to observe an increase in PGI_2 production on the white and red meat diets may be due to the dietary levels of AA being too low to raise tissue levels of AA significantly, this is despite subjects eating between 150-330g/day white meat and 270-530g/day red meat, depending on baseline energy intake. These amounts were at the limit of possible consumption for the subjects, indicating that the overall contribution of white and red meat to tissue levels of AA and subsequent PGI_2 production, is minimal in the short term.

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