THE EFFECT OF DIETARY ARACHIDONIC ACID ON EICOSANOID PRODUCTION IN HUMANS

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The major polyunsaturated fatty acid (PUFA) in the western diet is linoleic acid (LA, 18:2n-6), which is considered to be the major source of tissue arachidonic acid (AA, 20:4n-6), the principal precursor for the vaso-active eicosanoids thromboxane (TXA_2) and prostacyclin (PGI_2). However, dietary AA may itself, contribute significantly to tissue levels of AA in humans. The aims of this study were to determine the extent to which dietary AA contributed to PGI_2 and TXA_2 production in vivo and whether dietary long chain (LC) n-3 PUFA have a modulating influence on the metabolism of AA to these vaso-active eicosanoids.

Initially we determined the concentration of AA, eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3) in a range of common food items and applied these results to previously determined food intakes of Australian adults (National Dietary Survey of Adults 1986), it was thus estimated that the AA intake of Australian adult males was 130 mg/day and females 96 mg/day. A small scale dietary study was then conducted in which subjects (n=10) consumed foods rich in AA and/or LC n-3 PUFA. At an intake level of 500 mg of AA/day, both PGI_2 and TXA_2 production increased, with a small shift in the PGI_2:TXA_2 balance, favouring TXA_2. However, when the diet also contained 500 mg/day of DHA and a smaller amount of EPA (~200 mg/day), PGI_2 production increased, with no change in TXA_2, thus shifting the PGI_2:TXA_2 balance in favour of PGI_2. In a second study (n=7), subjects consumed 500 g/day of lean kangaroo meat (~300 mg AA, ~260 mg LC n-3 PUFA) for one week. Serum phospholipid (PL) levels of AA, LC n-3 PUFA and in vivo PGI_2 production all increased during this period, while TXA_2 production remained static. We then conducted a larger dietary intervention study (n = 23-25), to determine the effect on in vivo eicosanoid production of diets rich in lean white meat (AA/EPA = 140:1), lean red meat (AA/EPA = 2:1) and fish (AA/EPA = 0.2:1). The daily AA intake was 140 ± 33 mg (mean ± SD), in each study. The white meat diet increased serum PL AA, but not in vivo PGI_2 or TXA_2. Red meat increased serum PL AA, DHA and docosapentaenoic acid (DPA, 22:5n-3), but had no effect on in vivo PGI_2 or TXA_2. Fish consumption decreased AA in serum PL, but increased serum PL EPA and DHA, which coincided with a decrease in in vivo TXA_2 ($P<0.05$ for all significant changes).

Therefore, diets rich in lean meats can raise plasma AA levels, but do not effect TXA_2 production, hence are not pro-thrombotic. Diets rich in LC n-3 PUFA can raise plasma EPA and DHA levels, lower TXA_2 production and are anti-thrombotic. Diets which combine equal quantities of AA and LC n-3 PUFA may be able to increase PGI_2 production while keeping TXA_2 production constant, but the dietary levels of these fatty acids would need to be higher than the current Australian consumption levels and certainly higher than could be consumed in red or white meat by most people. Finally, dietary LC n-3 PUFA seems to have a modulating effect on the platelet production of TXA_2, (but not on endothelium production of PGI_2). This phenomena provides us with an insight into the improved haemostatic function and reduced thrombosis risk amongst hunter-gatherer groups (including Eskimos and Australian Aborigines), who consume diets rich in both AA and LC n-3 PUFA.

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