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ORIGINAL CONTRIBUTION

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Lack of effect of dietary n-6:n-3 PUFA ratio on plasma lipids and markers of insulin responses in Indian Asians living in the UK

Summary *Background* Indian Asians living in Western Countries have an over 50 % increased risk of coronary heart disease (CHD) relative to their Caucasians counterparts. The atherogenic lipoprotein phenotype (ALP), which is more prevalent in this ethnic group, may in part explain the increased risk. A low dietary long chain n-3 fatty acid (LC n-3 PUFA) intake and a high dietary n-6 PUFA intake and n-6:n-3 PUFA ratio in Indian Asians have been proposed as contributors to the increased ALP incidence and CHD risk in this subgroup. *Aim* To examine the impact of dietary n-6:n-3 PUFA ratio on membrane fatty acid composition, blood lipid levels and markers of insulin sensitivity in Indian Asians living in the UK. *Methods* Twenty-nine males were assigned to either a moderate or high n-6:n-3 PUFA (9 or 16) diet for 6 weeks. Fasting blood samples were collected at baseline and 6 weeks for analysis of triglycerides, total-, LDL- and HDL-cholesterol, non-esterified fatty acids, glucose, insulin, markers of insulin sensitivity and C-reactive protein. *Results* Group mean saturated fatty acid, MUFA, n-6 PUFA and n-3 PUFA on the moderate and high n-6:n-3 PUFA diets were 26 g/d, 43 g/d, 15 g/d, 2 g/d and 25 g/d, 25 g/d, 28 g/d, 2 g/d respectively. A significantly lower total membrane n-3 PUFA and a trend towards lower EPA and DHA levels were observed following the high n-6:n-3 PUFA diet. However no significant effect of treatment on plasma lipids was evident. There was a trend towards a loss of insulin sensitivity on the high n-6:n-3 PUFA diet, with the increase in fasting insulin ($P = 0.04$) and HOMA IR [(insulin x glucose)/22.5] ($P = 0.02$) reaching significance. *Conclusion* The results of the current study suggest that, within the context of a western diet, it is unlikely that dietary n-6:n-3 PUFA ratio has any major impact on the levels of LC n-3 PUFA in membrane phospholipids or have any major clinically relevant impact on insulin sensitivity and its associated dyslipidaemia.

Key words n-6:n-3 PUFA ratio – triglycerides – lipids – insulin – Indian Asians

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Introduction

In recent decades a marked increase in the incidence of the metabolic syndrome and its associated dyslipidaemia has been observed in western countries [1, 2]. This dyslipidaemia, which is referred to as the atherogenic lipoprotein phenotype (ALP), is characterised by elevated plasma triglyceride (TAG) levels, low HDL cholesterol levels and a predominance of the small dense putatively atherogenic LDL-3 particle [3, 4]. A higher prevalence of the ALP dyslipidaemia in migrant Indian Asians living in the UK is thought to be a major contributor to the 50 % higher incidence of coronary heart disease (CHD) observed in this ethnic group compared to their Caucasian counterparts [5–8].

Elevated TAG levels are thought to be the main determinant of the ALP dyslipidaemia [3, 4]. Through a system of neutral lipid exchange high TAG result in a reduction in overall HDL-C levels and a shift in the LDL

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density profile towards the denser LDL-3 particle. Increased eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) intake from oily fish/fish oils with its associated impact on tissue EPA and DHA content is arguably the most effective dietary hypotriglyceridaemic therapy [9–12]. A reversal of ALP characteristics following increased EPA plus DHA intake has frequently been observed [12].

However intake of oily fish in Indian Asians is low [13] and tissue long chain (LC) n-3 PUFA (EPA and DHA) are thought to be largely derived from the precursor n-3 PUFA alpha linolenic acid (ALNA) present in the diet. In mammals linoleic acid (LA) and ALNA are metabolised to their longer chain derivatives by a series of reactions catalysed by a common set of elongation and desaturation enzymes [14, 15]. There is growing evidence from studies using isotopically labelled ALNA to suggest that high intakes of LA inhibit conversion of ALNA to its long chain unsaturated products due to competition for the common delta-6 desaturase enzyme [15]. A typical Indian Asian diet in the UK is characterised by a high LA content [13, 16], resulting in a high dietary n-6:n-3 (LA:ALNA) PUFA ratio, which in combination with a low LC n-3 PUFA intake may be responsible for the low tissue EPA and DHA in this subgroup and may in part explain the high incidence of the deleterious ALP dyslipidaemia.

In the current study the impact of the dietary n-6:n-3 PUFA ratio on membrane phospholipid fatty acid composition and on blood lipid responses and markers on insulin resistance were investigated in Indian Asians living in the UK. The current study forms part of a larger project which proceeds to examine the impact of a high or moderate n-6 PUFA intake on the responsiveness of fasting and postprandial triglycerides and insulin responses to fish oil intervention [17].

Data generated in the current study will also provide information applicable to the general Caucasian population, where an increased prevalence of ALP and dietary patterns characterised by a low oily fish and an increased consumption of n-6 PUFA as vegetable oils and vegetable oil based spreads are becoming increasingly evident.

Subjects and methods

Subjects

Twenty-nine healthy adult Indian (Sikh) Asian men, aged 35–70 years, were recruited from the Reading and Slough areas. Exclusion criteria for participation in the study included: evidence of cardiovascular disease including angina, diagnosed diabetes or blood glucose > 8.0 mmol/l, blood pressure > 180/110 mmHg, strenuous exercise more than 3 times per week, BMI > 35 or < 18 kg/m^2, total cholesterol > 8.0 mmol/l or triglycerides < 0.5 or > 4.0 mmol/l. Individuals on hypolipidaemic medication or taking fatty acid supplements on a regular basis were also excluded. Participants were required to be nonsmokers, to have been resident in the UK for at least 2 years and to consume at least one traditional ethnic meal per day. The study was approved by the University of Reading and the West and East Berkshire Health Authorities Ethics Committees and each participant gave written consent prior to commencing the study. The baseline characteristics of the study group are outlined in Table 1.

Dietary intervention

Participants were randomly assigned on the basis of age, BMI, and triglycerides to consume either a moderate or high n-6:n-3 PUFA ratio diet for a period of 6 weeks. Dietary treatment aimed to alter the background dietary n-6 PUFA intake to achieve the required n-6:n-3 PUFA ratios. The diets were chosen to approximately represent the total n-6 PUFA levels and the n-6:n-3 PUFA ratio of a typical Caucasian (moderate n-6:n-3 PUFA) and Indian Asian (high n-6:n-3 PUFA) diet [18, 19]. Variation in the ratio of the diet was achieved by varying the n-6 PUFA and MUFA content whilst maintaining equal n-3 PUFA intakes in the two dietary groups. The dietary targets were accomplished by replacing the cooking oils and spreads normally consumed as part of the diet with experimental cooking oils and spreads specially modified for the purpose of the study. These products provided by Van den Bergh Oils (Crawley, UK) included an

Table 1 Baseline characteristics of the group as a whole and following randomisation to either the moderate or high n-6:n-3 PUFA diets

	Total Group (n = 29)	Moderate n-6:n-3 PUFA diet (n = 15)	High n-6:n-3 PUFA diet (n = 14)	P[1]
Age (y)	48 ± 2	48 ± 3	48 ± 2	0.83
BMI (kg/m^2)	26.0 ± 0.5	26.4 ± 0.8	25.6 ± 0.6	0.75
TAG (mmol/l)	1.58 ± 0.12	1.47 ± 0.15	1.69 ± 0.20	0.36
TC (mmol/l)	4.96 ± 0.15	5.10 ± 0.24	4.80 ± 0.18	0.63
LDL-C (mmol/l)	3.10 ± 0.15	3.24 ± 0.24	2.95 ± 0.19	0.34
HDL-C (mmol/l)	1.13 ± 0.05	1.16 ± 0.05	1.11 ± 0.09	0.63
NEFA (μmol/l)	451 ± 31	462 ± 55	439 ± 29	0.34
Glucose (mmol/l)	5.31 ± 0.11	5.34 ± 0.19	5.28 ± 0.13	0.78
Insulin (pmol/l)	44.1 ± 3.4	45.5 ± 5.3	42.6 ± 4.3	0.68
CRP (mg/l)	1.67 ± 0.18	1.70 ± 0.21	1.62 ± 0.31	0.83

Values represent mean ± SEM

[1] Statistical significance between the moderate and high n-6;n-3 dietary group at baseline. *BMI* body mass index; *TAG* triglycerides; *TC* total cholesterol; *LDL-C* low density lipoprotein cholesterol; *HDL-C* high density lipoprotein cholesterol; *NEFA* non-esterified fatty acids; *CRP* C-reactive protein

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olive oil based spread and olive oil which contained 71 and 79 g/100 g MUFA and 6 and 6 g/100 g n-6 PUFA respectively (moderate n-6:n-3 PUFA diet), or a corn oil based spread and corn oil which provided 30 and 32 g/100 g MUFA and 46 and 53 g/100 g PUFA respectively (high n-6:n-3 PUFA diet). The use of the olive oil and corn oil based products resulted in dietary n-6:n-3 PUFA ratios of 9 and 16 respectively, as assessed by diet diary (see below). The levels of total fat, saturated fatty acids, trans fatty acids and n-3 PUFA were comparable between the two diets (Table 2). A more detailed description of the dietary manipulation has been previously reported [16].

Study design

The study was a randomised double blind parallel study, with participants consuming either the moderate or high n-6:n-3 PUFA diets to which they were assigned for a period of 6 weeks. Achievement of the dietary targets was assessed by a 3d estimated diet diary (2 week days and 1 weekend day), with the dietary information analysed using the nutritional database computer programme, Foodbase (version 2.0, Institute of Brain Chemistry and Human Nutrition). The detailed fatty acid composition of the oils and spreads and a range of recipes for dishes typically consumed by Indian Asians were added to Foodbase prior to dietary analysis in order to improve the accuracy of the assessment. Platelet membrane phospholipid fatty acid composition was also monitored to determine compliance with the dietary treatments.

At the beginning and end of the 6-week intervention period participants were asked to attend the Nutrition Unit in a fasted state to provide a blood sample and have weight and blood pressure measured. Fasting blood samples were analysed for triglycerides (TAG), total- (TC), LDL- (LDL-C), and HDL-cholesterol (HDL-C), glucose, insulin, non-esterified fatty acids (NEFA), C-reactive protein (CRP) and platelet membrane phospholipid fatty acid levels. In addition, insulin and glucose concentrations were used to derive an estimate of insulin resistance from the HOMA IR model [($insulin_0$ x $glucose_0$)/22.5] [20] and the revised QUICKI (RQUICKI) model [1/(log NEFA + log glucose + log insulin)] [21].

Table 2 The fatty acid composition of the diet for the moderate and high dietary n-6:n-3 PUFA dietary groups

	Moderate n-6:n-3 PUFA diet		High n-6:n-3 PUFA diet		P[1]
	(g/day)	% en[2]	(g/day)	% en	
Total fat	101 ± 9	39	95 ± 8	37	0.72
SFA	26 ± 3	9	25 ± 7	10	0.59
MUFA	43 ± 5	15	25 ± 3	10	0.00
n-6 PUFA	15 ± 1	5	26 ± 3	10	0.00
n-3 PUFA	2 ± 0	0.7	2 ± 0	0.7	0.96
trans fatty acids	2 ± 0	0.5	2 ± 0	0.7	0.65
n-6:n-3	9 ± 1		16 ± 2		0.00

PUFA polyunsaturated fatty acids
[1] independent student t-test
[2] % of total energy

Biochemical analysis

All blood samples were collected into potassium EDTA tubes. The samples were centrifuged at 1600 g for 10 minutes and the plasma collected. For HDL-C analysis dextran sulfate and magnesium chloride was added to a subsample of plasma in order to precipitate the apolipoprotein B-containing lipoproteins [22] and the supernatant together with the remaining plasma used for determination of TC, TAG, CRP, glucose, insulin and NEFA concentrations was stored at –20°C.

Platelets were extracted from whole blood according to the methods of Indu and Ghafoorunissa [23] (300xg for 18min followed by 1700 g for 10min), and stored at –80 °C for platelet phospholipid fatty acid analysis.

Plasma samples were analysed for TG, TC, HDL-C, CRP, glucose and NEFA (Wako NEFA C kit; Alpha Laboratories, Warrington, Ches., UK) using a Monarch Automatic Analyser (Instrumentation Laboratories Ltd, Warrington, UK) and enzymatic colorometric kits (Instrumentation Laboratories Ltd). LDL-C was calculated using the Friedwald formula [24]. Insulin concentrations were determined using a commercially available ELISA kit (Dako Ltd, High Wycombe, Bucks, UK). The mean intra- and inter-assay CVs, respectively, for TC, TAG, glucose, insulin, NEFA and CRP were 2.1 %, 1.4 %, 1 %, 4 %, 1.1 %, 1.2 % and 4 %, 3.1 %, 3.7 %, 5.5 %, 1.8 %, and 4.4 % respectively.

The phospholipid fatty acid composition of platelet membrane was determined using gas liquid chromatography (GLC) as has been previously described [23, 25]

Statistical analysis

Group results are expressed as mean values with their standard error (mean ± SEM). The data were checked for normality and all skewed variables were log_{10} transformed prior to statistical analysis. The significance of baseline differences between the two dietary groups was analysed using independent student t-tests and Mann-Whitney tests. The impact of the intervention on the biochemical outcomes and platelet fatty acid composition was assessed using two-way ANOVA with time (0, 6 weeks) and treatment (moderate n-6:n-3 PUFA diet,

high n-6:n-3 PUFA diet) as the independent variables. Linear associations between outcome measures were evaluated by testing Spearman's correlation coefficients.

Results

The group (n = 29) had a mean age, BMI, TC and TAG of 48 y, 26.0 kg/m^2, 4.96 mmol/l and 1.58 mmol/l respectively. There was no significant difference between the two dietary groups for any of the biochemical parameters following randomisation to dietary group at baseline (Table 1).

Dietary changes

As expected, the two diets resulted in significant differences with respect to MUFA (43 versus 25 g/day) (P = 0.00) and n-6 PUFA (15 versus 26 g/day) (P = 0.00) intakes between the two groups. The dietary n-6:n-3 PUFA ratios also differed with ratios of 9 and 16 in the moderate and high n-6 PUFA diets respectively (P = 0.00). There was no difference between the two diets with respect to total fat, SFA, n-3 PUFA or trans fatty acids intakes (Table 2).

Platelet membrane fatty acid composition

Absolute values (% of total fatty acids) of the platelet membrane fatty acid composition for the two dietary treatment groups are given in Table 3 and Fig. 1. There was no significant effect of either of the diets on the SFA content of the membranes. A significant time*diet effect for MUFA (P = 0.02) was observed, with a modest increase evident in the moderate n-6:n-3 PUFA group. No significant effect of dietary treatment on the total n-6 PUFA content of the platelet phospholipids was observed. However, a significant between group effect of treatment over time was evident for total n-3 PUFA (P = 0.00), with an increase of 5 % of total fatty acids on the moderate diet reaching borderline significance (P = 0.06) and a significant 6 % decrease on the high n-6:n-3 PUFA diet (P = 0.01). These alterations in PUFA composition resulted in a significant effect of diet on the n-6:n-3 PUFA ratio of the membrane (P = 0.00), with the 6 % increase in the ratio on the high n-6:n-3 PUFA diet reaching significance (P = 0.03). Although no significant changes in membrane AA (P = 0.53) were observed, there was a non-significant trend towards an increase in membrane EPA and DHA on the moderate n-6 PUFA

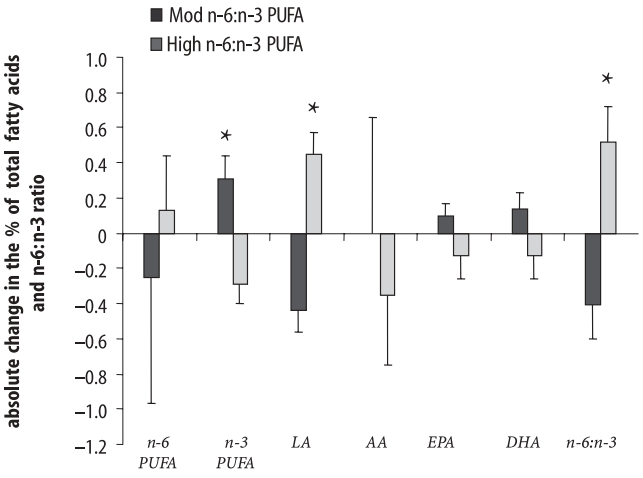

Fig. 1 Absolute change in the % of the total fatty acid and n-6:n-3 PUFA ratio of platelet membrane phospholipids in response to the moderate and high n-6:n-3 PUFA diets
* significant between group differences as determined by two way ANOVA with time and treatment as variables
LA linoleic acid; *AA* arachidonic acid; *EPA* eicosapentaenoic acid; *DHA* docosahexaenoic acid; *n-6:n-3* n-6:n-3 PUFA ratio

Table 3 Platelet membrane fatty acid composition in the moderate and high n-6:n-3 PUFA treatment groups at baseline and after 6 weeks of dietary intervention

	Moderate n-6:n-3 group (n = 15)			High n-6:n-3 PUFA group (n = 14)			P[2] (Between Group)
	0wk	6wk	P[1]	0wk	6wk	P[1]	
SFA	34.3±0.5	33.6±0.3	0.16	33.5±0.3	33.9±0.32	0.25	0.06
MUFA	15.7±0.5	16.3±0.3	0.08	15.5±0.27	15.3±0.18	0.25	0.02
n-6 PUFA	44.5±0.9	44.2±0.3	0.10	45.7±0.4	45.8±0.4	0.36	0.06
n-3 PUFA	5.6±0.2	5.9±0.2	0.06	5.2±0.3	4.9±0.2	0.01	0.00
n-6:n-3 PUFA	8.1±0.3	7.7±0.3	0.06	9.0±0.4	9.5±0.4	0.03	0.00
AA	34.5±0.7	34.5±0.4	0.23	35.6±0.4	35.3±0.4	0.73	0.53
EPA	1.8±0.1	1.9±0.09	0.1	1.5±0.09	1.4±0.08	0.18	0.12
DHA	3.0±0.17	3.1±0.18	0.23	2.9±0.20	2.8±0.18	0.03	0.14

Values represent means ± SEM and the % of total fatty acids in the sample
Abbreviations as per Table 2 plus *AA* arachidonic acid, *EPA* eicosapentaenoic acid, *DHA* docosahexaenoic acid
[1] Within group changes analysed using paired t-tests
[2] Between group changes analysed by two way ANOVA with time and treatment as independent variables

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Table 4 Changes in fasting lipids, insulin and glucose levels over the 6-week dietary intervention periods for the moderate and high n-6:n-3 PUFA groups

	Moderate n-6:n-3 PUFA diet (n = 15)			High n-6:n-3 PUFA diet (n = 14)			P[2] (Between group)
	0wk	6wk	P[1]	0wk	6wk	P[1]	
TAG (mmol/l)	1.47±0.15	1.51±0.19	0.96	1.69±0.20	1.61±0.21	0.32	0.77
TC (mmol/l)	5.10±0.24	4.92±0.20	0.10	4.80±0.18	4.69±0.19	0.36	0.88
LDL-C (mmol/l)	3.24±0.24	2.99±0.16	0.08	2.95±0.19	2.88±0.14	0.76	0.62
HDL-C (mmol/l)	1.16±0.05	1.25±0.07	0.07	1.11±0.09	1.08±0.09	0.42	0.45
NEFA (μmol/l)	462±55	573±49.1	0.08	439±29	425±33	0.71	0.16
Insulin (pmol/l)	45.5±5.3	48.8±5.0	0.45	42.6±4.3	55.7±6.3	0.04	0.37
Glucose (mmol/l)	5.34±0.19	5.60±0.19	0.01	5.28±0.13	5.40±0.14	0.13	0.68
HOMA IR	1.84±0.24	2.08±0.26	0.26	1.66±0.16	2.24±0.28	0.02	0.51
RQUICKI	0.41±0.01	0.39±0.01	0.02	0.41±0.01	0.40±0.01	0.12	0.67
CRP (mg/l)	1.70±0.21	1.83±0.29	0.50	1.62±0.31	1.70±0.41	0.99	0.90

Values are given as mean ± SEM; *TAG* triglycerides; *TC* total cholesterol; *LDL-C* low density lipoprotein cholesterol; *HDL-C* high density lipoprotein cholesterol; *NEFA* non-esterified fatty acids; *HOMA IR* homeostasis model = [insulin (μU/ml) x glucose (mmol/l)]/22.5; *RQUICKI* revised QUICKI = [1/(log glucose (mg/dl) + log insulin (μU/ml) + log NEFA (mmol/l)]; *CRP* C reactive protein

[1] Within group changes analysed using paired t-tests/Wilcoxon signed rank test

[2] Between group changes analysed by two way ANOVA with time and treatment as independent variables

diet and a trend towards a decrease on the high n-6:n-3 PUFA diet (P = 0.12–0.14), with the within treatment decrease in DHA on the high n-6:n-3 PUFA diet reaching significance (P = 0.03).

Plasma lipids, glucose, insulin and CRP

There was no significant impact of diet on TAG, TC, LDL-C, HDL-C, NEFA, insulin, glucose, HOMA IR, RQUICKI or CRP over time (Table 2). However a significant within group increase in insulin (P = 0.04) and HOMA IR (P = 0.02) was evident in individuals following a high n-6:n-3 PUFA diet. Although no significant between treatment effect was observed for fasting glucose (P = 0.68) or RQUICKI (P = 0.670), a modest, but significant, increase in glucose levels (P = 0.01) and decrease in RQUICKI were observed following the moderate n-6:n-3 PUFA diet (P = 0.01).

Correlation between lipid and insulin sensitivity indices and fatty acid composition at baseline

Using Spearman's correlation analysis no significant association between membrane fatty acid composition and lipid, glucose, insulin, HOMA IR or RQUICKI was evident at baseline.

Discussion

Premature coronary heart disease (CHD) mortality is about 2-fold higher, whilst CHD incidence in all ages is about 50 % more in UK Indian Asians compared with white Europeans [5–7]. Conventional risk factors such as BMI, hypercholesterolaemia and smoking status do not account for this increased CHD incidence [26]. Recent evidence suggests that a higher prevalence of the metabolic syndrome including a centralised fat topography and its associated insulin resistance, ALP dyslipidaemia and proinflammatory profile including increased CRP levels, may in part explain the increased risk [5, 6, 26–28]. These components of the metabolic syndrome are integrally linked.

There is substantial evidence to suggest than increased intake and membrane EPA plus DHA has a positive impact on fat metabolism (with a more peripheral fat distribution) and insulin sensitivity in experimental animals [29–31]. However many of these studies have used diets with extreme fatty acid intakes and compositions (e.g. n-6:n-3 ratios of 1–100), levels which are in no way representative of a typical western human diet. Studies in humans have proved less clear cut, with the supplementation of the diet with up to 4 g EPA plus DHA per day having little impact on fat topography or insulin sensitivity [32, 33]. However the hypotriglyceridaemic effect of increased fish oil intake has been repeatedly demonstrated in humans, with a meta-analysis published in 1997 concluding that an intake of fish oils equivalent to 3–4 g EPA plus DHA per day results in a 25–30 % reduction in TAG levels [10]. In a recent trial conducted in our laboratory, the impact of chronic fish oil supplementation in ALP individuals was specifically examined [12]. The consumption of 3 g EPA plus DHA per day for 6 weeks resulted in a 35 %, 26 % and 26 % reduction in fasting TAG, postprandial TAG and % LDL-3 respectively. Previous work has indicated that the TAG

reduction in response to increased tissue EPA plus DHA is largely attributable to the cell signalling properties of these fatty acids, with modifications in the gene expression of proteins involved in fatty acid oxidation and TAG secretion by the liver [32].

In the current study it was hypothesised that despite a naturally low EPA plus DHA dietary intake in Indian Asians living in the UK, membrane levels could be increased by lowering the n-6:n-3 PUFA ratio of diet, which would be associated with an increased conversion efficiency of ALNA to its long chain n-3 PUFA products. Any such changes in tissue fatty acid composition would be expected to result in an improvement of the ALP profile in our study group. The dietary intervention resulted in relatively small changes in fatty acid composition, which were generally in line with the predictions. Relative to the moderate n-6:n-3 PUFA diet the high n-6:n-3 PUFA group showed significant reductions in total n-3 PUFA, and trends for a reduction in LC n-3 PUFA and an increase in the n-6:n-3 PUFA ratio. However the extent of these changes was small and it is not possible to state with certainty that the high levels of n-6 PUFA intake in this study will have adverse effects on tissue and whole body LC n-3 PUFA status long term. Although there were no effects of the intervention diets on circulating lipid concentrations, fasting insulin and HOMA IR were increased on the high n-6:n-3 PUFA diet in line with predictions for adverse effects on insulin sensitivity.

The dietary information collected in the form of 3-day dietary records indicates that the dietary goals were achieved with total n-6 PUFA (g/d), MUFA (g/d) and n-6:n-3 PUFA ratios of 15, 43, and 9 and 26, 25, and 16 respectively. However, despite large changes in fat composition only modest changes in the fatty acid profile of the membranes were observed. From the current study it is evident that the effect of the dietary n-6 PUFA and n-6:n-3 PUFA ratio is small relative to the changes in membrane long chain n-3 PUFA that are observed following direct feeding of EPA and DHA. In a recent investigation conducted in our group increases in EPA and DHA from 0.53 to 3.13 mol/l and 2.50 to 3.61mol/100 mol were observed following the consumption of 3 g EPA plus DHA per day [25]. In a subsequent study the feeding of only 0.8 and 1.7 g of EPA plus DHA per day for 6 months resulted in large highly significant 45 % and 56 % increases in membrane long chain n-3 PUFA content respectively [35].

The two test diets were designed to represent the fatty acid profiles and the extremes of n-6:n-3 PUFA ratios consumed by individuals living in the UK. Total n-6 PUFA intakes of 15 g/d (modest n-6 PUFA diet) and 26 g/d (high n-6 PUFA diet) are comparable to the intakes of 12 g/d and 20 g/d previously reported by our group for representative Caucasian and Sikh populations [19]. The 'Total Diet Study' (1995) indicates that the average n-6 PUFA intake in the UK populations is 10.2 g/d [18]. The chosen n-6 PUFA levels yielded dietary n-6:n-3 ratios of 9 and 16 for the modest and high n-6 PUFA diets respectively. The modest diet is marginally higher than the ratio of 6–7 evident in a typical Caucasian diet [18, 19], but is lower than the ratio of approximately 12 evident in a Sikh subgroup [19]. A dietary n-6:n-3 PUFA ratio of 16 is not atypical for individuals following a traditional ethnic Indian Asian diet.

To the best of our knowledge the current study is the first intervention trial to investigate the impact of realistic alterations in dietary n-6:n-3 PUFA ratio on membrane fatty acid composition and the ALP dyslipidaemia and markers of insulin resistance. No clinically significant effect of dietary n-6:n-3 PUFA ratio on any of the outcomes was evident. However it should be noted that the current study was of relatively short duration and not specifically designed to examine insulin sensitivity. Further investigations, using longer intervention periods and more sensitive diagnostic methods for assessing insulin sensitivity, are warranted in order to draw firm conclusions regarding the long-term impact of dietary n-6:n-3 PUFA ratio on insulin action.

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