Trans, and n-3 polyunsaturated fatty acids and vascular function—A yin yang situation?

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Abstract

Trans fatty acids (TFA) and n-3 polyunsaturated fatty acids (n-3 PUFA) have opposite effects on several biological functions. We report a study on the effects on risk markers for cardiovascular disease. Eighty-seven healthy males were randomly assigned to 8 weeks of daily intake of either 20 g of industrially produced TFA (IP-TFA), 4 g n-3 PUFA, or control fat, incorporated in bakery products as part of the daily food.

High-density lipoprotein cholesterol decreased in the TFA-group, triglycerides and mean arterial blood pressure decreased in the n-3 group. Heart rate variability (HRV), arterial dilatory capacity, flow mediated vasodilation, compliance, and distensibility were unchanged.

Post hoc, we did a subgroup analysis of the results from the subjects with normal initial HRV. In these, 24-h heart rate (HR) was significantly increased by approximately three beats/min in the TFA group, with a decrease of the same magnitude in the n-3 group. A high HR is associated to an increased mortality and vice versa.

Our results thus support the notion that IP-TFA and n-3 PUFA affect risk for cardiovascular mortality via mechanisms not only related to changes in plasma concentrations of lipids and lipoproteins.

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1. Introduction

The magnitude of increased risk for coronary heart disease, associated with the intake of industrially produced TFA (IP-TFA) is, as estimated from prospective epidemiological and intervention studies, substantially greater than the risk accounted for by the effect of IP-TFA on blood lipids and lipoproteins [1,2]. In the same way, the findings of a decreased cardiovascular mortality after supplementation with n-3 PUFA is not only related to effects on blood lipids [3]. IP-TFA and n-3 PUFA have effects on many biological functions in ways that often are opposing (Fig. 1). To add to the clarification of any hitherto unnoticed effect(s), we performed a controlled dietary intervention trial comparing the effect of IP-TFA and long chain n-3 PUFA on risk markers for cardiovascular disease.

2. Methods

The study was a randomised, double blind, parallel, 8 weeks dietary intervention trial, which has been described in detail previously [4]. Eighty-seven healthy males aged 20-60 years were enrolled and block-randomised to three study groups. During the intervention period the study participants were supervised by a dietician and given a diet in which bread and cakes included in the normal diet, isocalorically were exchanged with bakery products containing a daily amount of 33 g of experimental fat. The experimental fat in the bakery products given to the three groups differed, sup-
Fig. 1. Opposing risk associations and biological effects of a diet rich in trans fatty acids and n-3 PUFA.

Implementing the participants in the TFA-group with a daily amount of 20 g IP-TFA and 13 g control fat, the n-3 PUFA group with 12 g of fish oil containing 4 g n-3 PUFA and 21 g control fat, and the control group with 33 g of control fat. Middle fractions of palm oil were used for the control fat, corresponding to 20 g saturated fat per day in the control group. The fatty acid composition of the experimental fats is given in Table 1.

All examinations were performed after 10 h of fasting at baseline and after the intervention period. The following variables were measured: body weight, blood pressure, blood lipids, platelet fatty acid composition, 24-h Holter recording of heart rate variability (HRV), flow-mediated arterial dilation (FMD), nitroglycerine-induced arterial dilation (NID), arterial compliance (AC), and arterial distensibility (AD). A total of 79 participants completed the 8 weeks intervention period.

Table 1
Fatty acid composition of the experimental fats

<table>
<thead>
<tr>
<th></th>
<th>TFA</th>
<th>n-3 PUFA</th>
<th>Control Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated</td>
<td>19.2</td>
<td>47.1</td>
<td>60.5*</td>
</tr>
<tr>
<td>n-6</td>
<td>18.6</td>
<td>27.6</td>
<td>30.3</td>
</tr>
<tr>
<td>Trans-unsaturated</td>
<td>55.1</td>
<td>4.6</td>
<td>3.2</td>
</tr>
<tr>
<td>18:1</td>
<td>18.3</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>59.9*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poly-unsaturated</td>
<td>n-6</td>
<td>0.2</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>n-3</td>
<td>13.5*</td>
<td>3.0</td>
</tr>
<tr>
<td>Total</td>
<td>0.2</td>
<td>16.2</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Values are per cent of total fatty acids.
* Bold figures indicate the characteristic fatty acid composition of the experimental fats.

3. Results

Analysis of platelet fatty acid composition showed a good compliance to the diets, with an increase in TFA in the TFA group from 1.2% to 4.6%, an increase in n-3 PUFA in the n-3 group from 4.7% to 8.0%, and no noticeable alterations of the fatty acid pattern in the control group. A significant increase in HDL-cholesterol (HDL-C) was observed in the n-3 group, whereas the HDL-C decreased in the TFA group (Fig. 2). In the n-3 group plasma triglycerides decreased significantly with approximately 20% compared to the control group. A significant fall in mean arterial blood pressure on 4–5% was observed in the n-3 group. No alterations in HRV, FMD, NID, AC or AD were found.

A post hoc analysis of heart rate (HR), a major risk factor for sudden cardiac death, was performed in subjects with initial normal HRV values, after exclusion of participants with extreme high HRV (n = 19). We found in this analysis a fall on approximately three beats per minute (BPM) in HR in the n-3 group and an increase of corresponding magnitude in the TFA group (Fig. 3).
4. Discussion

Great care should be taken when addressing the results of post hoc analysis. When considering the present results on HR it is interesting that a recent meta-analysis on the effect of fish oil on HR finds that fish oil reduces HR by 2.5 BPM in randomised controlled trials in humans [5]. These results support the findings in our post hoc analysis and thereby indirectly the results in the TFA group. An increase in HR by 3 BPM may seem small but corresponds to approximately 4000 beats per 24 h, a burden that is associated with increased cardiovascular risk including risk of sudden death [6]. Even a small increase in HR significantly increases the risk of sudden cardiac death [7].

5. Conclusion

The present results suggest that intake of industrially produced TFA may increase 24 h heart rate thereby increasing the risk of sudden death. Further studies in this area are however needed. If the findings are confirmed, they could provide a model for identifying the chemical basis for some of the negative health effects of TFA.

References