Applied nutritional investigation

Moderate consumption of fatty fish reduces diastolic blood pressure in overweight and obese European young adults during energy restriction

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Abstract

Objective: Dietary intervention studies suggest that a daily fish meal can improve blood pressure (BP); however, such a dietary regimen might be difficult to sustain. The objective of the present study was to investigate whether salmon consumption three times per week improves BP during energy restriction in young adults.

Methods: In this 8-wk intervention, 324 subjects (20–40 y of age, body mass index 27.5–32.5 kg/m², from Iceland, Spain, and Ireland) were randomized to one of four energy-restricted diets (~30% relative to estimated requirements): salmon (150 g three times per week, resulting in a daily consumption of 2.1 g of ω-3 long-chain polyunsaturated fatty acids [ω-3 LC-PUFAs]), cod (150 g three times per week, 0.3 g of ω-3 LC-PUFAs per day), fish oil capsules (1.3 g of ω-3 LC-PUFAs per day), or control (sunflower oil capsules, no seafood). Body weight, diastolic BP (DBP), systolic BP (SBP), and docosahexaenoic acid (DHA) in erythrocyte membrane were measured at baseline and endpoint.

Results: Participants showed weight loss (~5.2 ± 3.2 kg, P < 0.001) and decreases in SBP (~4.4 ± 8.6 mmHg, P < 0.001) and DBP (~4.1 ± 7.4 mmHg, P < 0.001) after the intervention. The salmon (β = -2.71, P = 0.032) and fish oil (β = -2.48, P = 0.044) groups had significantly lower endpoint DBP than the cod group, but not significantly different from control. Lower baseline DHA (percentage) in erythrocytes was associated with greater DBP reductions (β = 0.576, P = 0.017).

Conclusion: Salmon consumption three times per week can decrease DBP similar to fish oil and significantly more than lean fish during an 8-wk dietary intervention providing fatty seafood. © 2010 Elsevier Inc. All rights reserved.

Keywords: Seafood; Fish; ω-3 Long-chain polyunsaturated fatty acid; Weight loss; Blood pressure; Young adults

Introduction

Hypertension is one of the causes of cardiovascular disease [1]. Diet plays an important role in the etiology of hypertension, because obesity and nutrient intake are known to affect blood pressure (BP). The BP-lowering properties of ω-3 long-chain polyunsaturated fatty acids (ω-3 LC-PUFA) from fish oil supplements have been thoroughly investigated and confirmed [2–5], with commonly used doses of 4–5 g of ω-3 LC-PUFAs per day leading to clinically significant reductions in BP. The largest effects are achieved in elderly hypertensives [4]. Several biological mechanisms have been suggested to explain the health benefits of ω-3 LC-PUFAs on BP, e.g., changes in phospholipid composition, platelet aggregation, and vasodilatation [6–11].

Without the use of seafood supplements (fish oil or marine algae), a ω-3 LC-PUFAs intake of 4–5 g/d can hardly
be achieved, even if one consumes a daily fish meal. There are relatively few dietary intervention trials that have investigated the effects of daily fish consumption (in contrast to fish oil ingestion) on BP, and some [12,13] but not all [14–16] have found BP reduction by fatty fish consumption. Not daily, but still frequent fatty fish consumption, e.g., three times a week, usually provides a daily amount of 1–1.5 g of ω-3 LC-PUFAs and might be sustained easier by less committed seafood eaters than a daily fish meal. It is an important question whether such a dietary regimen can improve BP.

In the present analysis, which was a part of the SEAFOODplus YOUNG study, we investigated the effects of regular fatty fish consumption (salmon three times per week) in comparison with lean fish (cod three times per week), fish oil (daily) and a control without seafood, in combination with energy restriction, on BP in young overweight and obese adults. The reason for also investigating lean fish, which does not provide high amounts of ω-3 LC-PUFAs, is that there is some preliminary evidence from animal studies suggesting that fish protein might also have BP-lowering effects [17,18]. We conducted a randomized, controlled dietary intervention trial in young overweight and obese, normo- and hypertensive individuals from three European countries. In terms of prevention, young adulthood might be a very critical time, with its changes in diet and physical activity linked with hypertension [19,20]. Results from the SEAFOODplus YOUNG study, e.g., on weight loss, have been published elsewhere [21].

Materials and methods

Subjects

A total of 324 overweight individuals (138 men and 186 women) were included in the SEAFOODplus YOUNG study (www.seafoodplus.org) through advertisements, 140 from Iceland, 120 from Spain, and 64 from Ireland. All subjects were screened for inclusion and exclusion criteria. The inclusion criteria were a body mass index ranging from 27.5 to 32.5 kg/m², age 20–40 y, and waist circumferences ≥94 cm and ≥80 cm for men and women, respectively. Exclusion criteria were weight change (≥3 kg) due to a weight-loss diet within 3 mo before the start of the study, use of supplements containing ω-3 fatty acids, calcium, or vitamin D during the previous 3 mo, allergy to fish, drug treatment of diabetes mellitus, hypertension or hyperlipidemia, and pregnancy or lactation. Of the subjects 85.8% (n = 278) completed the intervention. The study was approved by the national bioethical committee in Iceland (04-031), the ethical committee of the University of Navarra in Spain (24/2004), and the clinical research ethics committee of the Cork University Hospital in Ireland. The study followed the Helsinki guidelines, and all participating subjects gave their written consent. The sample size calculations for the study were based on the estimation that an 80% completion rate allows detection of an approximately 3-mmHg difference in BP among the four diet groups, assuming a standard deviation of 6 mmHg, a significance P value <0.05, and a statistical power >0.8.

Study design

This study was a randomized, controlled dietary intervention trial, which was conducted at the Landspitali-University Hospital in Reykjavik, Iceland, the University College of Cork, Ireland, and the University of Navarra in Pamplona, Spain, from April 2004 to November 2005. The intervention lasted for 8 consecutive weeks, when the subjects were instructed to follow an energy-restricted diet, with 30% of the estimated energy expenditure given by Harris-Benedict equations [22,23], and physical activity level [24] (approximately 600 kcal/d, range 473–718 kcal/d). All participants were randomly assigned to one of four groups, which varied by dietary protein source and amount of ω-3 LC-PUFAs: control, no seafood (six sunflower oil capsules per day); lean fish (150 g of cod, three times per week); fish oil (six capsules per day); or fatty fish (150 g of salmon, three times per week).

Groups receiving sunflower or fish oil capsules were single blinded. All diets had an identical macronutrient composition: total fat (~30% of total energy), carbohydrate (~50% of total energy), protein (~20% of total energy), and dietary fiber (~20–25 g). Diets did not differ in the amount of sodium, potassium, and calcium provided; however, the salmon diet provided significantly more vitamin D. The cod diet provided ω-3 LC-PUFAs, which resulted in a daily consumption of ~0.3 g; the salmon diet provided ~2.1 g of ω-3 LC-PUFAs per day and fish oil capsules provided ~1.3 g of ω-3 LC-PUFAs per day. It has to be mentioned that the amount of ω-3 LC-PUFAs in salmon used in this study was considerable higher than the amount found in databases, e.g., the U.S. Department of Agriculture database. Other sources of ω-3 fatty acids were congruent among diet groups. The salmon diet and fish oil supplement were originally formulated to provide a similar amount of ω-3 fatty acids. However, the farmed salmon used in the present study contained twice the fat expected (as published in the U.S. Food Composition database [25]), leading to different ω-3 contents in the salmon diet and in the fish oil supplement.

Each subject received a detailed meal plan to follow, in addition to recipe booklets and instructions to minimize the difference among diets in sources of fat (other than ω-3 LC-PUFAs), fruit and vegetable consumption, and meal frequency. The participants’ physical activity level remained unchanged during the intervention. (For more information on the intervention, see Thorsdottir et al. [21].) A validated food-frequency questionnaire evaluated the consumption of fish and fish oil over the previous 4 wk and was completed by the participants at midpoint (4 wk) and endpoint (8 wk). It was asked whether the participants consumed the fish and capsules provided to them and did not consume any
additional fish or fish oil capsules during the study period. Consumption of fish and capsules was in good agreement with the study protocol [26,27].

Anthropometric measurements

All anthropometric measurements (body weight, height, waist circumference) were done at baseline and endpoint of the study using standard procedures as outlined in a research protocol approved and used by all countries participating in the study. Body weight was measured in light underwear on a calibrated scale (SECA 708, Hamburg, Germany). The subjects’ height was measured with a calibrated stadiometer.

Biochemical measurements

Subjects were told to avoid strenuous exercise and alcohol consumption the day before the blood samples were drawn at baseline and endpoint. The samples were analyzed for fatty acid composition in extracted erythrocyte membrane phospholipids by gas chromatography, following the conditions described by Bandarra et al. [28].

BP measurements

A strict routine for BP measurements was adhered to, as defined in the research protocol. First, the participant removed outer garments, and the shirtsleeve was rolled up. Then, the subject sat still and at rest, with no change of position for a few minutes before the measurement took place. The subject did not engage in conversation (total rest). The arm of the subject was allowed to rest on a desk to allow the antecubital fossa to be at the same level as the heart. The right arm was used for all subjects on all measurement days. Two readings were taken at intervals of 2 min, and the average of those readings represented the patient’s blood pressure. When the mercury difference between the first and second readings was >5 mm, an additional reading was obtained, and then the average of these three readings was used. The same person performed the measurements at baseline and endpoint for all subjects. Further instructions according to the user’s guide of the equipment used (Medissan) were followed. Hypertension was defined as systolic BP (SBP) ≥130 mmHg at baseline or diastolic BP (DBP) ≥85 mmHg at baseline [29].

Statistical analysis

The data were entered into SPSS 11.0 (SPSS Inc., Chicago, IL, USA). Data are described as mean ± standard deviation. Wilcoxon’s test was used to calculate whether there were significant changes in the variables between baseline and endpoint. Spearman’s correlation coefficient ($\rho$) was used to calculate bivariate associations between variables. Linear models were used to calculate the effects of diet groups and baseline $\omega$-3 LC-PUFAs on endpoint BP, the models also included the variables country, sex, and baseline BP. The results are shown as parameter estimates, where each of the three diet groups is compared with the control group. Variances were checked using Levene’s test of homogeneity, and residuals of the statistical models were checked for normality using the Kolmogorov-Smirnov test. $P \leq 0.05$ was regarded as statistically significant.

Results

The participants’ baseline values are listed in Table 1. Of the male participants, 55.8% had hypertension, but only 15.6% of female participants did. Baseline docosahexaenoic acid (DHA) content in erythrocytes correlated with baseline DBP ($\rho = -0.118$, $P = 0.050$) and with frequency of fish consumption ($\rho = 0.272$, $P < 0.001$).

During the intervention (Table 2) the intakes of energy, carbohydrates, protein, fat, saturated fat, calcium, sodium, and potassium decreased significantly, with the highest percentage of changes being in energy, fat, and saturated fatty acids. The absolute intake of PUFAs also decreased; however, PUFAs as a percentage of energy did not change significantly. Fiber intake increased. The changes were similar in all groups.

Table 1
Baseline data of participants ($n = 324$)*

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Cod</th>
<th>Salmon</th>
<th>Fish oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>32.1 ± 5.3</td>
<td>31.3 ± 5.7</td>
<td>31.3 ± 5.3</td>
<td>31.0 ± 5.3</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>87.7 ± 10.1</td>
<td>89.5 ± 9.4</td>
<td>90.4 ± 11.4</td>
<td>85.0 ± 9.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.0 ± 1.5</td>
<td>30.2 ± 1.4</td>
<td>30.4 ± 1.4</td>
<td>29.9 ± 1.5</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>95.2 ± 7.4</td>
<td>96.8 ± 6.7</td>
<td>96.9 ± 7.9</td>
<td>94.0 ± 6.7</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>127 ± 11</td>
<td>125 ± 12</td>
<td>127 ± 13</td>
<td>124 ± 12</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73 ± 7</td>
<td>73 ± 8</td>
<td>72 ± 8</td>
<td>71 ± 7</td>
</tr>
<tr>
<td>EPA (%)</td>
<td>1.62 ± 1.28</td>
<td>1.10 ± 0.50</td>
<td>1.07 ± 0.51</td>
<td>1.14 ± 0.71</td>
</tr>
<tr>
<td>DHA (%)</td>
<td>5.97 ± 1.56</td>
<td>5.54 ± 1.22</td>
<td>5.72 ± 1.27</td>
<td>5.88 ± 1.59</td>
</tr>
<tr>
<td>Female participants</td>
<td>60%</td>
<td>56%</td>
<td>50%</td>
<td>64%</td>
</tr>
</tbody>
</table>

BMI body mass index; DBP, diastolic blood pressure; DHA, docosahexaenoic acid in erythrocyte phospholipids; EPA, eicosapentaenoic acid in erythrocyte phospholipids; SBP, systolic blood pressure

* Mean ± SD.
During the intervention, the absolute and relative intakes of energy, fat, saturated fatty acids, and monounsaturated fatty acids and absolute intakes of PUFAs, sodium, calcium, and potassium were not significantly different among groups (corrected for sex and country); however, relative intake of PUFAs was significantly higher in the fish oil group than in the control (1.0% difference, \( P = 0.001 \)), cod (1.5% difference, \( P < 0.001 \)), or salmon (0.9% difference, \( P = 0.003 \)) group.

After the intervention, the body weight of subjects decreased (\(-5.2 \pm 3.2\) kg, \( P < 0.001 \); for more information, see Thorsdottir et al. [21]). Waist circumference, SBP, and DBP also improved in the participants (all \( P_s < 0.001 \)). These changes are presented in Table 3. Reductions in BP did not correlate with changes in sodium, potassium, or calcium intake. No side effects were reported by the groups that had received the fish oil or sunflower oil capsules.
Linear models were used to calculate the effects of diet groups, baseline DHA content in erythrocytes, and weight loss on BP reduction during the 8-wk intervention (Table 4). The salmon and fish oil groups had insignificantly lower endpoint DBPs than the control group. The cod group tended to have higher DBP than the control group (2.2 mmHg, $P = 0.065$). Endpoint DBP in the salmon or fish oil group was significantly lower compared with the cod group (−2.9 mmHg, $P = 0.022$, and −2.5 mmHg, $P = 0.042$, respectively). Lower baseline DHA in erythrocyte membranes was significantly associated with lower endpoint DBP (corrected for baseline DBP). Each kilogram of weight loss was associated with an endpoint DBP reduction of −0.24 mmHg; however, this did not reach statistical significance. Exclusion of weight loss in the linear model did not change the overall model, but it reduced the effect size of cod from −2.2 to 2.0 mmHg compared with the control group, possible related to the lower weight loss observed in the control group compared with the other groups. Sex-by-diet group interactions were not significant. Neither baseline DHA nor diet group was a significant predictor for endpoint SBP (model not shown).

### Discussion

In this study we investigated the effects of different diets on BP reduction during an 8-wk weight-loss diet in young overweight and obese European adults. Subjects in the four groups received salmon (fatty fish), cod (lean fish), fish oil capsules, or placebo capsules, but otherwise the same percentage energy restriction, and were recruited to diets prescribing identical macronutrient composition. During these 8 wk, mean body weight, SBP, and DBP decreased significantly in the participants. The main results of our study are that moderate consumption of fatty fish during an 8-wk energy restriction results into a lower endpoint DBP compared with lean fish intake, and that a low content of DHA in erythrocyte membrane at baseline is associated with greater DBP reductions at endpoint.

Intervention studies investigating the effects of $\omega$-3 LC-PUFA supplementation on BP, commonly using doses of 4–5 g of $\omega$-3 LC-PUFAs a day, provide convincing evidence that $\omega$-3 LC fatty acids in form of fish oil can reduce BP [3–5]. Dietary intervention trials that have investigated the effects of fish consumption (in contrast to fish oil ingestion) on BP are few. An intervention study by Vandongen et al. [14] failed to show a significant effect of fish consumption (providing $3.65$ g of $\omega$-3 fatty acids per day) on BP compared with control [14]; however, a similar intervention study by the same study group showed significant independent and additive effects of fish consumption and weight loss during a calorie-restricted weight-loss program [13]. An early experimental study could not find a significant difference in BP changes between a fish group (providing $4.5$ g of $\omega$-3 LC-PUFAs per day) and a control group [15]; however, the groups were small, and the power of this study might have been a limiting problem. Von Houwelingen et al. [16] found no effect of 100 g of mackerel daily for 6 wk compared with meat in a study in The Netherlands and Norway. A recent study by Lara et al. [12] showed significant improvements of BP due to daily salmon consumption. Although these studies do not give a clear picture, a BP-reducing effect of fatty fish consumption is likely, considering 1) its $\omega$-3 LC-PUFA content, 2) the available evidence for the beneficial effects of $\omega$-3 LC-PUFAs on BP from fish oil supplements, and 3) the documented bioavailability of $\omega$-3 LC-PUFAs from fatty seafood [27]. Possible reasons for the disagreement among studies might be found in the difficulty to obtain compliance to such dietary regimens, low statistical power, especially of older studies, and possible variance of baseline BP of the participants.

### Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Cod</th>
<th>Salmon</th>
<th>Fish oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>−4.4 ± 2.8</td>
<td>−5.4 ± 2.7</td>
<td>−5.5 ± 3.3</td>
<td>−5.4 ± 3.2</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>−4.0 ± 2.4</td>
<td>−5.0 ± 2.9</td>
<td>−5.4 ± 3.3</td>
<td>−5.1 ± 3.1</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>−5.1 ± 8.1</td>
<td>−3.1 ± 8.1</td>
<td>−5.3 ± 9.4</td>
<td>−3.9 ± 8.5</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>−4.2 ± 7.5</td>
<td>−3.7 ± 8.3</td>
<td>−4.7 ± 7.6</td>
<td>−3.6 ± 6.3</td>
</tr>
<tr>
<td>EPA (%)</td>
<td>−0.44 ± 1.35</td>
<td>−0.06 ± 0.64</td>
<td>0.69 ± 0.75</td>
<td>0.62 ± 0.98</td>
</tr>
<tr>
<td>DHA (%)</td>
<td>−0.36 ± 1.80</td>
<td>0.51 ± 1.37</td>
<td>1.40 ± 1.64</td>
<td>0.68 ± 1.57</td>
</tr>
</tbody>
</table>

DBP, diastolic blood pressure; DHA, docosahexaenoic acid in erythrocyte phospholipids; EPA, eicosapentaenoic acid in erythrocyte phospholipids; SBP, systolic blood pressure

*Mean ± SD.

### Table 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>B</th>
<th>95% CI</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cod$^1$</td>
<td>2.234</td>
<td>−0.142 to 4.610</td>
<td>0.065</td>
</tr>
<tr>
<td>Salmon$^1$</td>
<td>−0.637</td>
<td>−3.042 to 1.769</td>
<td>0.603</td>
</tr>
<tr>
<td>Fish oil$^1$</td>
<td>−0.257</td>
<td>−2.608 to 2.093</td>
<td>0.829</td>
</tr>
<tr>
<td>DHA at baseline (%)$^1$</td>
<td>0.572</td>
<td>0.100 to 1.043</td>
<td>0.018</td>
</tr>
<tr>
<td>Weight loss (kg)$^1$</td>
<td>−0.237</td>
<td>−0.480 to 0.005</td>
<td>0.055</td>
</tr>
</tbody>
</table>

CI, confidence interval; DHA, docosahexaenoic acid in erythrocyte phospholipids

* The statistical model also contained diastolic blood pressure at baseline, country, sex, and age.

$^1$ Estimated differences in endpoint diastolic blood pressure compared with the control group.

$^1$ Estimated effects on endpoint diastolic blood pressure.
All of these cited studies prescribed daily fish consumption trying to reach sufficient ω-3 LC-PUFA intakes; however, daily intake of fish might be difficult to sustain for many individuals. An important question is whether a lower but still frequent fish intake, e.g., three times a week, can also affect BP. In the present study the salmon group consumed three fish meals a week (providing ~2.1 g of eicosapentaenoic acid and DHA per day). The salmon group had an endpoint DBP similar to the fish oil group and significantly lower than the cod group. The effect seen in our study (2.7-mmHg difference compared with cod) is smaller compared with other studies [12,13], possibly because our participants were younger (mean 30.4 y) and only 32.1% of them were classified as hypertensive. Higher baseline BP and older age have been associated with greater BP reduction by ω-3 LC-PUFAs [4]. Interestingly, the endpoint DBP of the control group was not significantly different from that of the salmon or fish oil group. This finding was unexpected, because we expected the endpoint DBP of the control group to be closer to that of the cod group, because both diets provided no or only small amounts of ω-3 LC-PUFAs. According to the food records, dietary intake of relevant nutrients (calcium, potassium, sodium) was not significantly different among groups, and, because the control group received capsules daily, a certain placebo effect cannot be excluded.

Our study also shows that baseline DHA content of erythrocyte membrane phospholipids is associated with DBP reduction after 8 wk, whereas a lower baseline DHA predicts a greater DBP reduction. This finding might be partly explained by the weak negative correlation ($r = -0.118$, $P = 0.050$) between DBP and DHA at baseline. However, because our statistical model corrected for baseline DBP, a lower baseline DHA might identify infrequent fish eaters, which is confirmed by a significant correlation between the frequency of fish consumption and DHA at baseline ($r = 0.272$, $P < 0.001$). Based on this finding, it can be considered that infrequent fish eaters benefit more from a dietary intervention providing fatty seafood in terms of DBP reduction than frequent fish consumers. According to the linear model an increase of baseline DHA by one standard deviation decreases the DBP reduction by 0.81 mmHg.

Limiting evidence from animal studies has suggested that fish protein has BP-lowering effects [17,18]. Our study does not support a beneficial effect of lean fish consumption on BP. Future research has to clarify whether BP reduction during weight loss can be improved with the inclusion of lean seafood.

According to the linear model each kilogram of weight loss was associated with a DBP reduction by 0.24 mmHg, although this was only borderline significant. Activation of the renin–angiotensin system in adipose tissue may represent an important link between obesity and hypertension, with angiotensin-converting enzyme activity suppressed most dramatically with weight loss [30]. A BP reduction of similar range has been reported by other intervention trials with modest weight loss; however, we could not find a significant effect of weight loss on SBP, whereas other studies have (reviewed by Mertens and Van Gaal [31].

A limitation of each dietary intervention trial is the uncertainty of whether the subjects’ dietary intake during the study period was as reported or prescribed. Because there was intense support of the study participants by our staff, including frequent telephone contact and personal visits, this risk was minimized.

**Conclusions**

Salmon consumption decreases DBP similar to fish oil consumption and more than lean fish consumption during an 8-wk diet in young overweight individuals. Lower DHA content in erythrocyte membrane at baseline, which might indentify infrequent fish eaters, is associated with greater DBP reduction during an 8-wk dietary intervention providing seafood.

**Acknowledgments**

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**References**


