Long-Chain Omega-3 Fatty Acids Eicosapentaenoic Acid and Docosahexaenoic Acid and Blood Pressure: A Meta-Analysis of Randomized Controlled Trials

Miller, P. E., Van Elswyk, M., & Alexander, D. D. (2014). Long-chain omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid and blood pressure: a meta-analysis of randomized controlled trials. American journal of hypertension, 27(7), 885–896.

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BACKGROUND

- Thirty-one percent of Americans are hypertensive, 30% are prehypertensive, and approximately 20% are hypertensive yet unaware of their status.
- The active ingredients in fish oil considered responsible for its antihypertensive effect are the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).
- Previous research shows that diet and lifestyle modifications, including physical activity, sodium reduction and fish oil supplementation, can reduce blood pressure (BP), enhance antihypertensive drug efficacy and decrease cardiovascular disease (CVD) risk.

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AIM

The aim of this meta-analysis was to examine the effect of EPA+DHA, without upper dose limits and including food sources, on blood pressure in randomized controlled trials (RCTs).

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METHODS

Studies inclusion/ exclusion criteria:

- Included studies were RCTs that examined the effect of EPA+DHA on BP in non hospitalized adults (aged ≥18 years). Eligible outcomes were systolic and diastolic BP values (SBP and DBP, respectively).

- Studies were excluded if:
  - Included hypertensive subjects treated with BP lowering medications
  - Treatment duration < 3 weeks
  - Cross over RCTs with < 4 weeks washout period
  - Provided no information on the amount of EPA+DHA
  - Conducted in non representative general adult population [i.e. pregnant and nursing women, individuals with pre-existing CVD or significant diseases (renal disease or cancer) or secondary hypertension].

A comprehensive literature search was conducted using Ovid/Medline, Embase and the Cochrane Library.

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RESULTS I

- 70 RCTs met all eligibility criteria and were included in the meta-analysis
  - Mean study duration: 69 days; mean EPA+DHA dose: 3.8g/ day
  - Sources of EPA+DHA: different types of seafood, EPA+DHA fortified foods, and supplements containing fish oil, algal oil, purified ethyl esters.
- Overall meta-analysis model: both SBP and DBP significantly decreased by 1.52 mmHg and 0.99 mmHg respectively, after EPA+DHA provision, compared with placebo.
- Meta-analysis of hypertensive subjects: both SBP and DBP significantly decreased by 4.51 mmHg and 3.05 mmHg respectively, following EPA+DHA provision, compared to placebo.
- Meta-analysis of normotensive subjects: both SBP and DBP significantly decreased by 1.25 mmHg and 0.62 mmHg respectively, following EPA+DHA provision, compared to placebo.
- Relatively few studies evaluated EPA+DHA as individual fatty acids, hence there was insufficient statistical power to detect a meaningful difference between EPA and DHA separately on lowering either SBP or DBP.

Results II

- No clear pattern of dose response between EPA+DHA and SBP was observed.
  - Significant reductions on SBP were observed with doses of 1 to <2 g/d (-1.81 mmHg) and 3 to <4 g/d (-3.85 mmHg).
  - There was a trend for SBP reduction for a dose of 0 to <1 g/ day.
- No apparent effect on DBP was observed for dose levels <2 g/day.
  - Significant reductions on DBP were observed for 2 to <3 g/day (-1.09 mmHg) and 3 to <4 g/day (-1.86 mmHg).
  - There was a trend for DBP reduction for a dose of ≥5 g/ day.

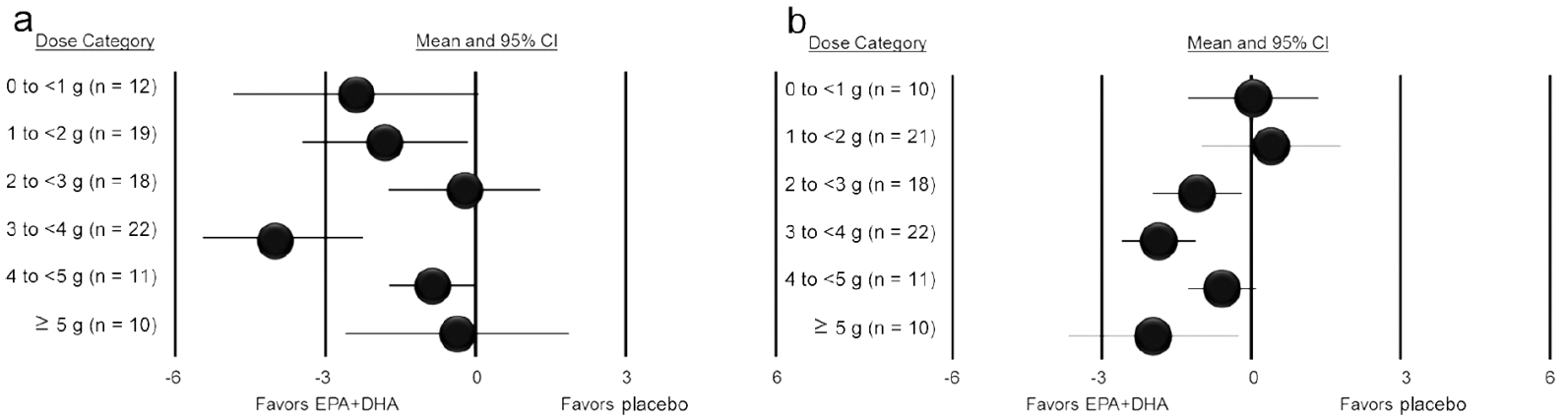

Figure 3. Results from meta-analyses of randomized controlled trials examining eicosapentaenoic and docosahexaenoic acids (EPA+DHA) and (**a**) systolic blood pressure and (**b**) diastolic blood pressure by EPA+DHA dose category. The circle represents the pooled summary estimate across all studies within each dose category, with 95% confidence intervals (CIs). n indicates the number of data points in each dose category, which may be greater than the number of individual studies.

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CONCLUSION I

The SBP reduction observed in hypertensive subjects following EPA+DHA provision, could prevent an individual from requiring antihypertensive medication, or could help maintain an individual in a lower stage of progressive hypertension.

The SBP reduction observed in normotensive subjects following EPA+DHA provision, translates to a delay of age related SBP increase by 2 years and progression from prehypertensive to hypertensive status.

CONCLUSION II

"Collectively, the evidence from RCTs indicates that provision of ≥2 g/d EPA+DHA may reduce both SBP and DBP, with the strongest benefits observed among hypertensive individuals who are not on antihypertensive medication".

Long-Chain Omega-3 Fatty Acids Eicosapentaenoic Acid and Docosahexaenoic Acid and Blood Pressure: A Meta-Analysis of Randomized Controlled Trials

Paige E. Miller,[1] Mary Van Elswyk,[2] and Dominik D. Alexander[3]

BACKGROUND
Although a large body of literature has been devoted to examining the relationship between eicosapentaenoic and docosahexaenoic acids (EPA+DHA) and blood pressure, past systematic reviews have been hampered by narrow inclusion criteria and a limited scope of analytical subgroups. In addition, no meta-analysis to date has captured the substantial volume of randomized controlled trials (RCTs) published in the past 2 years. The objective of this meta-analysis was to examine the effect of EPA+DHA, without upper dose limits and including food sources, on blood pressure in RCTs.

METHODS
Random-effects meta-analyses were used to generate weighted group mean differences and 95% confidence intervals (CIs) between the EPA+DHA group and the placebo group. Analyses were conducted for subgroups defined by key subject or study characteristics.

RESULTS
Seventy RCTs were included. Compared with placebo, EPA+DHA provision reduced systolic blood pressure (−1.52 mm Hg; 95% confidence interval (CI) = −2.25 to −0.79) and diastolic blood pressure (−0.99 mm Hg; 95% CI = −1.54 to −0.44) in the meta-analyses of all studies combined. The strongest effects of EPA+DHA were observed among untreated hypertensive subjects (systolic blood pressure = −4.51 mm Hg, 95% CI = −6.12 to −2.83; diastolic blood pressure = −3.05 mm Hg, 95% CI = −4.35 to −1.74), although blood pressure also was lowered among normotensive subjects (systolic blood pressure = −1.25 mm Hg, 95% CI = −2.05 to −0.46; diastolic blood pressure = −0.62 mm Hg, 95% CI = −1.22 to −0.02).

CONCLUSIONS
Overall, available evidence from RCTs indicates that provision of EPA+DHA reduces systolic blood pressure, while provision of ≥2 grams reduces diastolic blood pressure.

Keywords: blood pressure; docosahexaenoic acid; eicosapentaenoic acid; fish oil; hypertension; meta-analysis; omega-3; randomized controlled trials; systematic review.

doi:10.1093/ajh/hpu024

Thirty-one percent of Americans are hypertensive, 30% are prehypertensive, and approximately 20% are hypertensive yet unaware of their status.[1,2] Only 47% of those with hypertension are adequately controlled.[1] Prior research shows that diet and lifestyle modifications, including physical activity, sodium reduction, and fish oil supplementation, can reduce blood pressure (BP), enhance antihypertensive drug efficacy, and decrease cardiovascular disease (CVD) risk.[3]

The active ingredients in fish oil considered responsible for its antihypertensive effect are the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA; 20:5 n-3) and docosahexaenoic acid (DHA; 22:6 n-3). Although previous meta-analyses of fish oil supplementation and BP have been published,[4–7] none have been designed with inclusion criteria sufficient to examine the extensive scope of literature available in this active area of investigation. For example, the most recently published meta-analysis excluded trials that examined food sources of EPA and DHA (herein referred to as EPA+DHA) and those that were less than 8 weeks in duration.[7] Therefore, our main objective was to update the state of the science by conducting the most comprehensive meta-analysis of its kind of randomized controlled trials (RCTs) that examined EPA+DHA in relation to BP.

Correspondence: Paige E. Miller (pmiller@exponent.com).

Initially submitted November 17, 2013; date of first revision December 24, 2013; accepted for publication January 19, 2014; online publication March 6, 2014.

[1]Center for Epidemiology, Biostatistics, and Computational Biology, Exponent, Inc, Chicago, Illinois; [2]Van Elswyk Consulting, Inc, Longmont, Colorado; [3]Center for Epidemiology, Biostatistics, and Computational Biology, Exponent, Inc, Boulder, Colorado.

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