




10-2012

The Effects of Supplemental Fish Oil on Blood Pressure and Morning Cortisol in Normotensive Adults: A Pilot Study

Eric E. Noreen
Gettysburg College

Josef Brandauer
Gettysburg College

Follow this and additional works at: <https://cupola.gettysburg.edu/healthfac>

 Part of the [Cardiovascular Diseases Commons](#), [Chemicals and Drugs Commons](#), [Other Medicine and Health Sciences Commons](#), and the [Preventive Medicine Commons](#)

Share feedback about the accessibility of this item.

Noreen, E. E. and J. Brandauer. "The Effects of Supplemental Fish Oil on Blood Pressure and Morning Cortisol in Normotensive Adults: A Pilot Study." *Journal of Complementary and Integrative Medicine* 9.1 (2012): 1-10.

This is the publisher's version of the work. This publication appears in Gettysburg College's institutional repository by permission of the copyright owner for personal use, not for redistribution. Cupola permanent link: <https://cupola.gettysburg.edu/healthfac/35>

This open access article is brought to you by The Cupola: Scholarship at Gettysburg College. It has been accepted for inclusion by an authorized administrator of The Cupola. For more information, please contact cupola@gettysburg.edu.

The Effects of Supplemental Fish Oil on Blood Pressure and Morning Cortisol in Normotensive Adults: A Pilot Study

Abstract

Purpose: To determine the effects of 6wk of supplementation with fish oil (FO) on blood pressure and the morning salivary cortisol concentration in normotensive adults.

Methods: Testing was performed following an overnight fast. Subjects ($n=40$; 35 ± 13 y, mean \pm -SD) rested supine for 40 min, at which time blood pressure and heart rate were measured. Saliva was collected and analyzed for cortisol. Subjects were then randomly assigned to either: 4g/d of Safflower Oil (SO); or 4g/d of FO supplying 1,600mg/d eicosapentaenoic acid and 800mg/d docosahexaenoic acid. Testing was repeated following 6wk treatment.

Results: Compared to SO, there was a significant decrease in systolic blood pressure with FO (SO= 1.3 ± 5.8 mmHg; FO= -6.8 ± 10.2 mmHg; $p=0.004$), a significant reduction in pulse pressure with FO (SO= 0.2 ± 7.8 mmHg; FO= -6.4 ± 8.8 mmHg; $p=0.02$), and a tendency for a decrease in mean arterial pressure (SO= 1.2 ± 5.3 mmHg; FO= -2.5 ± 7.3 mmHg; $p=0.08$). There was a tendency for salivary cortisol to decrease with FO (SO= 0.005 ± 0.129 μ g/dL; FO= -0.068 ± 0.148 μ g/dL; $p=0.072$), however, this change was not significant; r correlated with the change in systolic blood pressure ($r=0.021$, $p=0.929$).

Conclusion: 6wk of supplementation with FO significantly decreases systolic blood pressure in normotensive adults and this change was not significantly correlated with a reduction in salivary cortisol.

Keywords

omega 3 fatty acids, pulse pressure, fish oil, dietary supplements, Eicosapentaenoic Acid, Docosahexaenoic Acid, automated oscillometric device

Disciplines

Cardiovascular Diseases | Chemicals and Drugs | Other Medicine and Health Sciences | Preventive Medicine

RapidX Upload

Rapid #: -7003232

CALL #: [http://ezproxy.bowdoin.edu/login?url=http://www.degruyter.co ...](http://ezproxy.bowdoin.edu/login?url=http://www.degruyter.co...)

LOCATION: **BBH :: EJournals :: De Gruyter Online**

TYPE: Article CC:CCG

JOURNAL TITLE: Journal of complementary & integrative medicine

USER JOURNAL TITLE: Journal of complementary & integrative medicine

BBH CATALOG TITLE: Journal of complementary & integrative medicine

ARTICLE TITLE: The effects of supplemental fish oil on blood pressure and morning cortisol in normotensive adults: a pilot study

ARTICLE AUTHOR: Eric Noreen and Josef Brandauer

VOLUME: 9

ISSUE: 1

MONTH: January

YEAR: 2012

PAGES: 1-18

ISSN: 1553-3840

OCLC #:

CROSS REFERENCE ID: [TN:235749][ODYSSEY:206.107.42.97/ILL]

VERIFIED:

BORROWER: **GDC :: Main Library**

PATRON:



This material may be protected by copyright law (Title 17 U.S. Code)
9/16/2013 8:13:10 AM

Journal of Complementary and Integrative Medicine

Volume 9, Issue 1

2012

Article 27

The Effects of Supplemental Fish Oil on Blood Pressure and Morning Cortisol in Normotensive Adults: a Pilot Study

Eric E. Noreen, *Gettysburg College*
Josef Brandauer, *Gettysburg College*

Recommended Citation:

Noreen, Eric E. and Brandauer, Josef (2012) "The Effects of Supplemental Fish Oil on Blood Pressure and Morning Cortisol in Normotensive Adults: a Pilot Study," *Journal of Complementary and Integrative Medicine*: Vol. 9: Iss. 1, Article 27.

DOI: 10.1515/1553-3840.1467

©2012 De Gruyter. All rights reserved.

The Effects of Supplemental Fish Oil on Blood Pressure and Morning Cortisol in Normotensive Adults: a Pilot Study

Eric E. Noreen and Josef Brandauer

Abstract

PURPOSE: To determine the effects of 6wk of supplementation with fish oil (FO) on blood pressure and the morning salivary cortisol concentration in normotensive adults. **METHODS:** Testing was performed following an overnight fast. Subjects ($n=40$; 35 ± 13 y, mean \pm -SD) rested supine for 40min, at which time blood pressure and heart rate were measured. Saliva was collected and analyzed for cortisol. Subjects were then randomly assigned to either: 4g/d of Safflower Oil (SO); or 4g/d of FO supplying 1,600mg/d eicosapentaenoic acid and 800mg/d docosahexaenoic acid. Testing was repeated following 6wk of treatment. **RESULTS:** Compared to SO, there was a significant decrease in systolic blood pressure with FO (SO=1.3 \pm -5.8 mmHg; FO=-6.8 \pm -10.2 mmHg; $p=0.004$), a significant reduction in pulse pressure (SO=0.2 \pm -7.8 mmHg; FO=-6.4 \pm -8.8 mmHg; $p=0.02$), and a tendency for a decrease in mean arterial pressure (SO=1.2 \pm -5.3 mmHg; FO=-2.5 \pm -7.3 mmHg; $p=0.08$). There was a tendency for salivary cortisol to decrease with FO (SO=0.005 \pm -0.129 μ g/dL; FO=-0.068 \pm -0.148 μ g/dL; $p=0.072$), however, this change was not significantly correlated with the change in systolic blood pressure ($r=0.021$, $p=0.929$). **CONCLUSION:** 6wk of supplementation with FO significantly decreases systolic blood pressure in normotensive adults and this change was not significantly correlated with a reduction in salivary cortisol.

KEYWORDS: eicosapentaenoic acid, docosahexaenoic acid, omega 3 fatty acids, pulse pressure, automated oscillometric device

Author Notes: Support for this study was provided by a Gettysburg College Research and Professional Development Grant. The fish oil and safflower oil capsules used in this study were generously donated by Genuine Health Corporation.

INTRODUCTION

It is generally acknowledged that an increased dietary intake of fish, or fish oil that is rich in long chain omega 3 fatty acids, results in a modest, yet significant reduction in blood pressure (Appel, Miller, Seidler, & Whelton, 1993; Geleijnse, Giltay, Grobbee, Donders, & Kok, 2002; Morris, Sacks, & Rosner, 1993). However, the majority of the studies examining the effects of fish oil on blood pressure have been performed in individuals with either primary or secondary hypertension, and/or in individuals with a known disease. Currently very little is known about the effects of fish oil on blood pressure in healthy, normotensive subjects. While a few studies have examined the effects of fish oil on blood pressure in subjects with untreated borderline hypertension, the results have been equivocal. Prisco, et al. (1998) observed a significant 6mm Hg decrease in systolic blood pressure and a significant 5mm Hg decrease in diastolic blood pressure following 2 months of fish oil treatment, however, Sacks et al. (1994) found no effect of 6 months of fish oil treatment on blood pressure in borderline hypertensives. Similarly, the results of fish oil treatment in healthy normotensive adults have also been equivocal. Mortensen et al. (1983) observed a significant decrease in systolic blood pressure of ~ 4mm Hg following 4wks of fish oil treatment. Conversely, other studies have found no effect of fish oil on blood pressure in normotensive subjects (Bruckner, Webb, Greenwell, Chow, & Richardson, 1987; Prisco et al., 1998; Ryu, Lerner, & Sullivan, 1990). Flaten et al. (1990) similarly concluded that there was no effect of fish oil on blood pressure in normotensive subjects following 6wks of treatment. They did observe a significant decrease in systolic blood pressure of ~ 4mm Hg following 6wks of treatment with fish oil, but they largely dismissed this change since they also observed a similar change in the group that received the olive oil “placebo.” However, recent work has shown that olive oil can lower blood pressure when it is given to subjects who do not routinely consume an olive oil rich diet (Bondia-Pons et al., 2007; Perona et al., 2009). This strongly suggests that caution should be used when interpreting results from studies that have used olive oil as the placebo treatment.

The exact mechanism(s) by which dietary long chain omega 3 fatty acids reduce blood pressure are not fully understood. One potentially novel mechanism explaining the hypotensive effect of dietary omega 3 fatty acids could be a reduction in blood pressure secondary to a reduction in cortisol. The effects of dietary fish oil on cortisol concentration are poorly understood, however, there is limited evidence that an increased consumption of fish oil results in a reduction in cortisol concentration (Delarue et al., 2003; Eguchi et al., 2011; Michaeli, Berger, Revelly, Tappy, & Chioloro, 2007).

Although the adrenal hormone cortisol is essential for maintaining normal blood pressure, an excess of cortisol results in hypertension (Whitworth, Mangos, & Kelly, 2000; Whitworth, Williamson, Mangos, & Kelly, 2005). The exact mechanism(s) by which an excess of cortisol results in hypertension is unclear, but research has pointed to an inhibition of the vasodilator nitric oxide (Kelly, Tam, Williamson, Lawson, & Whitworth, 1998), and/or an increase in the concentration of the vasoconstrictor erythropoietin (Kelly, Martin, & Whitworth, 2000). Historically, cortisol induced hypertension was thought to be clinically relevant only to patients with Cushing's disease, or those using exogenous glucocorticoid therapy (Whitworth, et al., 2000). However, it has been suggested by some researchers that elevated cortisol may also contribute to essential hypertension (Soro, Ingram, Tonolo, Glorioso, & Fraser, 1995; Walker, Best, Shackleton, Padfield, & Edwards, 1996). In support of this, several studies have found a correlation between elevated morning cortisol levels and hypertension (Bose, Olivan, & Laferrere, 2009; Filipovsky et al., 1996; Kidambi et al., 2007; Phillips et al., 2005; Schoorlemmer, Peeters, van Schoor, & Lips, 2009). However, the relationship between morning cortisol levels and blood pressure in normotensive individuals has not been clearly established.

Therefore, the purpose of this pilot study was to assess the effects of fish oil on blood pressure and morning cortisol concentrations, as well as the relationship between changes in morning cortisol concentrations and blood pressure in healthy normotensive adults following 6wk of an increased dietary intake of fish oil.

METHODS

Prior to all testing, approval for the study was obtained from the institutional review board at Gettysburg College, and written informed consent was obtained from all subjects.

Healthy adults (19-55y) were recruited through word of mouth and flyers posted at Gettysburg College and the surrounding community. Subjects were healthy and active, but not engaged in consistent, systematic exercise training. Individuals who ate fatty fish at least 3 times a month, or were supplementing their diet with omega 3 fatty acids were excluded from the study. Subjects were also excluded if they had a doctor diagnosed metabolic or endocrine disorder, or if they were taking any prescription medications, with the exception of birth control hormones and allergy or asthma medications. Individuals with a baseline systolic blood pressure measurement greater than 140 mmHg, or a diastolic blood pressure measurement greater than 90 mmHg were excluded from the study. In total, 40 individuals volunteered to participate (Table 1). Subjects were asked to maintain their current diet and exercise practices throughout the study. Additionally,

subjects were instructed to keep a diet and activity log for the 24h period prior to the baseline testing and to duplicate these for the 24h period prior to the post testing.

Experimental Protocol

Subjects reported to the laboratory first thing in the morning immediately after waking. Subjects were not allowed to eat or drink anything other than water starting 10h before their scheduled testing time. This included the use of mouthwash or toothpaste in the morning since this could interfere with the salivary cortisol measurements. Upon arrival at the laboratory, subjects were asked to void if they could, and then they rested quietly in a supine position for 40 minutes in a darkened room, after which blood pressure and heart rate were measured using an automated oscillometric device (Omron HEM-907, Omron Healthcare, Kyoto Japan) that automatically took the average of two readings. Following these tests, a saliva sample was taken via passive drool and later analyzed for cortisol content (see below for details). Subjects were then randomly assigned in a double blind manner to one of two groups based on the order of entrance into the study.

The two groups were:

Safflower oil (SO): 4g/d of safflower oil (Genuine Health Corporation, Toronto, Ontario, CA) administered in 4 enteric coated capsules. Each capsule provided 1g of cold pressed, high linoleic acid, safflower oil. See appendix A for a breakdown of fatty acids found in the safflower oil capsules. Safflower oil is a rich source of long chain polyunsaturated omega 6 fatty acids. Since the average western diet contains considerable amounts of omega 6 fatty acids, the safflower oil is believed to be a good placebo.

Fish oil (FO): 4g/d concentrated fish oil (omega 3 extra strength, Genuine Health Corporation, Toronto, Ontario, CA) administered in 4 enteric coated capsules. Each capsule provided 400mg eicosapentaenoic acid and 200mg of docosahexaenoic acid. See appendix A for a breakdown of the fatty acids found in the fish oil capsules.

Subjects were instructed to take 2 capsules with breakfast and 2 capsules with dinner for a 6wk period. Subject compliance was monitored by asking the subjects to return any left over pills at the completion of the study. Subjects were also asked to write down any possible side effects noted during the 6wk treatment.

Subjects were instructed to maintain their normal diet and exercise patterns during the treatment period. All testing was repeated following 6wk of treatment.

Salivary Analysis

Subjects rinsed their mouth with water prior to all saliva collections to minimize contamination of the samples. Saliva was collected in a polypropylene vial via passive drool through a short straw and stored at -80 °C until analyzed. Prior to analysis, samples were thawed and centrifuged at 10,000g for 20 minutes to remove mucins and analyzed in duplicate for cortisol concentration using a commercially available enzyme immunoassay kit (Salimetrics, State College, PA, USA). Salivary cortisol is a sensitive marker of activation the hypothalamus-pituitary-adrenal system's response to stress, which correlates very well to plasma cortisol concentrations (Hellhammer, Wust, & Kudielka, 2009). The normal morning salivary cortisol concentrations range from 0.094 – 1.551 µg/dL for healthy adults in the age range used in this study (Aardal & Holm, 1995).

Blood Pressure Variables

Heart rate, systolic and diastolic blood pressure were automatically determined by the Omron HEM-907 automated oscillometric device. Pulse pressure was calculated as the difference between systolic and diastolic blood pressure, and the mean arterial pressure (MAP) was calculated as $(2/3 * DBP + 1/3 * SBP)$.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences version 13 (SPSS Inc., Chicago, IL). Salivary cortisol concentrations were not normally distributed so they were log transformed prior to analysis. A group by time, repeated measures ANOVA was used to evaluate significant differences, and a standard Pearson's r was used to evaluate correlations. For all analysis, the alpha level was set at $p \leq 0.05$. All values are presented as mean \pm standard deviation.

RESULTS

Blood Pressure

The results from the blood pressure measurements are presented in Table 2. There were no significant differences between groups at baseline for any values. A group by time repeated measures ANOVA revealed a significant decrease in

systolic blood pressure (Table 2: SO = 1.3 ± 5.8 mmHg; FO = -6.8 ± 10.2 mmHg; $p=0.004$), and pulse pressure (Table 2: SO = 0.2 ± 7.8 mmHg; FO = -6.4 ± 8.8 mmHg; $p=0.02$), following fish oil treatment. Although MAP decreased following fish oil treatment, this change was not significant (SO = 1.2 ± 5.3 mmHg; FO = -2.5 ± 7.3 mmHg; $p=0.08$). There were no significant differences observed between the groups for heart rate or diastolic blood pressure.

Salivary Cortisol Concentrations

Salivary cortisol concentrations decreased following fish oil treatment, however the change was not significant (Table 2: SO = 0.005 ± 0.129 $\mu\text{g/dL}$; FO = -0.068 ± 0.148 $\mu\text{g/dL}$; $p=0.072$).

Correlations

There were no significant relationships observed between the baseline morning salivary cortisol concentration and the blood pressure variables (Table 3). Following treatment, there were no significant relationships observed in the FO group between the change in salivary cortisol concentration and any of the blood pressure variables (Table 4).

Subject Compliance and Side effects

No subject in either group returned any unused pills, suggesting 100% compliance. It should be noted, however, that all of the subjects were friends, colleagues, or students of the researchers. This could have given them an increased incentive to follow the study guidelines, or alternatively it may have served to decrease the likelihood that the subjects would admit to missing doses. Both treatments were very well tolerated, with no major side effects noted for either treatment. Of particular note, no one in the fish oil group reported experiencing “fishy” reflux, which is a common side effect noted in studies that have used a non-enteric coated fish oil capsule.

DISCUSSION

The main finding of this study was a significant decrease in systolic blood pressure following 6wks of consumption of a fish oil that is rich in long chain omega 3 fatty acids (Table 2). While this finding is in agreement with previous studies (Flaten et al., 1990; Mortensen, Schmidt, Nielsen, & Dyerberg, 1983), other studies have failed to observe a significant effect of fish oil on blood pressure in normotensive subjects (Bruckner, et al., 1987; Prisco, et al., 1998;

Ryu, et al., 1990). Unfortunately, differences in study design, such as the dose of fish oil used and the duration of treatment, limits direct comparison between the different studies that have examined the effects of fish oil on blood pressure in normotensive subjects. More work is needed to clearly define the effects of fish oil supplementation on blood pressure in healthy normotensive subjects.

The clinical significance of the hypotensive effect observed in this study is also unknown. Previous work has shown that decreasing blood pressure in normotensive individuals with known coronary disease results in a reduction in negative cardiovascular events (Nissen et al., 2004). Although no study to date has directly determined if a similar protective effect exists when blood pressure is reduced in normotensive subjects without coronary disease, epidemiologic data reveal a decreased risk of cardiovascular events and all cause mortality in individuals who have a resting systolic blood pressure below the accepted value of 120mm Hg (Stamler, Stamler, & Neaton, 1993). Therefore the results of the present study indicate that the increased consumption of fish oil may serve as a prophylactic means of reducing the risk of cardiovascular disease in healthy normotensive individuals, but more work is needed to clearly establish this.

The repeated measures ANOVA showed a tendency for salivary cortisol concentrations to decrease in the fish oil group (SO = 0.005 ± 0.129 $\mu\text{g/dL}$; FO = -0.068 ± 0.148 $\mu\text{g/dL}$; $p=0.072$). However, when a two tailed dependent t test was performed on the Pre and Post scores of each group independently, the SO change was not significant ($p=0.93$), but the Post score was significantly lower than the Pre score in the FO group ($p=0.05$). It is very likely that the reduced statistical power of the omnibus F used in the repeated measures ANOVA resulted in a type II error, and the reduction in salivary cortisol concentrations following fish oil supplementation is a real effect. In support of this, the 95% confidence interval of the Pre- Post difference in salivary cortisol concentration for the fish oil group (Table 2) does not contain the null value of zero, but rather contains only negative values (-0.132 to -0.004 $\mu\text{g/dL}$). In contrast, the 95% confidence interval for the safflower oil group is centered on a mean difference value of essentially the null value of zero (-0.124 to 0.134 $\mu\text{g/dL}$). Taken together, these additional statistics suggest a reduction in salivary cortisol concentration in the subjects taking the fish oil. Although there is a very limited amount of data examining the effects of dietary fish oil on cortisol levels, this finding is in agreement with other studies that have shown a reduction in cortisol levels following fish oil treatment (Delarue, et al., 2003; Eguchi, et al., 2011; Michaeli, et al., 2007). However, it should be pointed out that these studies measured cortisol concentration following a stressor, whereas the present study measured morning cortisol concentration in a rested state.

An increased consumption of fish oil resulted in a reduction in blood pressure as well as a reduction in morning salivary cortisol concentrations.

Despite this, there was no significant correlation observed in the fish oil group between the change in blood pressure and the change in salivary cortisol concentrations following treatment (Table 4). This would suggest that the reduction in blood pressure observed following fish oil treatment in normotensive subjects is not a result of a reduction in cortisol levels. In the present study, the subjects had normal values for morning salivary cortisol concentrations, as well as normal resting supine blood pressure values. Therefore, it still remains a possibility that a reduction in cortisol may relate to a reduction in blood pressure in individuals that have an elevated blood pressure as a result of elevated levels of cortisol. In support of this, it has been shown that the administration of the cortisol suppressing drug dexamethasone lowers blood pressure in hypertensive, but not normotensive subjects (Whitworth, Gordon, McLachlan-Troup, Scoggins, & Moulds, 1989). Hence, dietary fish oil may have a more pronounced effect in individuals who have an elevated blood pressure as a result of increased cortisol levels since the hypotensive effect from a reduction in cortisol may be additive to the direct hypotensive effects of fish oil consumption.

Since the reduction in cortisol concentration does not appear to explain the observed reduction in blood pressure in the present study, the mechanism(s) responsible for the reduction in blood pressure remain unclear. Other studies have suggested a variety of potential mechanisms by which fish oil consumption can decrease blood pressure, including an increased large artery vasodilation (Engler & Engler, 2000; Johansen, Seljeflot, Hostmark, & Arnesen, 1999), a reduced reactivity of vessel vascular smooth muscle (Chu, Yin, & Beilin, 1992), an inhibition of hemostasis and platelet aggregation (Rogers et al., 1987; Vericel, Calzada, Chapuy, & Lagarde, 1999), and an enhanced endothelium dependent vasodilation (Shah et al., 2007; Shimokawa & Vanhoutte, 1989). It is likely then, that one, or a combination, of the factors listed was responsible for the reduction in blood pressure following fish oil treatment observed in the present study.

In addition to the modest sample size used, there are other limitations to the present study. The main limitation of this study was the collection of data at only one time point pre and post treatment. It is generally recognized that blood pressure measurements should be made several times over the course of the day to accurately determine a true average blood pressure (Powers et al., 2011). Given the dynamic nature of blood pressure control, it remains a possibility that fish oil treatment only lowers systolic blood pressure under the specific conditions used for measurement in the present study, and the effect would be lost if 24h ambulatory measurements were used. Similarly, cortisol excretion has a pronounced diurnal rhythm, and a series of measurements over 24h would be more likely to capture the true effect of dietary fish oil on cortisol excretion. There are a multitude of lifestyle choices that can influence resting blood pressure. Although the subjects were instructed not to change their diet or activity

level during the course of the study, no attempts were made to control for these variables.

The present study is the first to examine the relationship between morning cortisol levels and blood pressure following fish oil treatment in healthy normotensive adults. Although there was a significant reduction in systolic blood pressure following fish oil treatment, this was not correlated with the reduction in salivary cortisol concentrations observed. However, it remains a possibility that a reduction in cortisol following fish oil treatment may be related to a reduction in blood pressure in individuals that have hypertension as a result of elevated cortisol levels. Future research should evaluate the effects of fish oil treatment on individuals with elevated cortisol levels and hypertension. The clinical significance of lowering systolic blood pressure in already normotensive adults is unclear; more studies are needed to determine if this change results in a decrease in long-term morbidity and mortality rates.

Table 1
Subject Characteristics

	Safflower Oil		Fish Oil	
	Pre	Post	Pre	Post
Sex				
Male (n)	8		6	
Female (n)	12		14	
Age (y)	36±14y (29,41)		35±13y (29,41)	
Weight (kg)	71.2±15.9 (63.8,77.5)	71.5±16.0 (64.0,79.0)	72.3±14.8 (65.4,79.2)	72.3±14.1 (65.7,78.9)
		0.3±0.8 (-0.1,0.7)		0.0±0.9 (-0.4,0.4)

Data are expressed as means ± SD (95% confidence interval).

Table 2
Pre and Post values following 6 weeks of treatment with 4g/d of safflower oil, or 4 g/d of fish oil

	Safflower Oil			Fish Oil		
	Pre	Post	Post-Pre Difference	Pre	Post	Post-Pre Difference
Salivary Cortisol (µg/dL)	0.316±0.242 (0.203,0.429)	0.320±0.319 (0.171,0.469)	0.005±0.129†† (-0.124,0.134)	0.275±0.186 (0.188,0.362)	0.207±0.137 (0.138,0.276)	-0.068±0.148†† (-0.132,-0.004)
Heart Rate (BPM)	65±10 (60,70)	67±12 (62,72)	2±7 (-1,5)	62±12 (56, 68)	61±10 (56, 66)	-1±9 (-3,3)
Systolic BP (mmHg)	108.4±10.9 (103.3,113.5)	109.7±12.5 (103.8,115.6)	1.3±5.8* (-1.4,4.0)	111.3±9.9 (106.7,115.9)	104.6±8.9 (100.4,108.8)	-6.8±10.2* (-11.6,-2.0)
Diastolic BP (mmHg)	67.2±8.2 (63.3,71.1)	68.3±9.0 (64.1,72.5)	1.1±6.7 (-2.1,4.3)	68.8±6 (66.0,71.6)	68.5±6.7 (65.3,71.7)	-0.4±7.4 (-3.8,3.0)
Pulse Pressure (SBP-DBP)	41.2±6.5 (38.1,44.3)	41.4±8.8 (37.3,45.5)	0.2±7.8** (-3.5,3.9)	42.5±10.3 (37.7,47.3)	36.1±6.4 (33.1,39.1)	-6.4±8.8** (-10.5,-2.3)
MAP (mmHg)	80.9±8.7 (76.8,85)	82.1±9.4 (77.7,86.5)	1.2±5.3† (-1.3,3.7)	83.0±5.8 (80.3,85.7)	80.5±6.9 (77.3,83.7)	-2.5±7.3† (-5.9,0.9)

Data are expressed as means ± SD (95% confidence interval). Data were analyzed using a treatment X time repeated measures ANOVA. BPM = beats per minute. BP = blood pressure. Pulse pressure = Systolic blood pressure – diastolic blood pressure. MAP=mean arterial pressure (2/3 * DBP + 1/3 * SBP) * significant treatment X time interaction, p=0.004, ** significant treatment X time interaction, p=0.02, † treatment X time interaction, p=0.08, †† treatment X time interaction, p=0.072

Table 3. Relationship between baseline salivary cortisol and blood pressure variables

		HR	DBP	SBP	PP	MAP
Salivary Cortisol	Pearson Correlation	0.046	0.052	0.156	0.146	0.107
	Sig. (2-tailed)	0.780	0.750	0.338	0.369	0.511
	N	40	40	40	40	40

HR = heart rate. DBP = diastolic blood pressure. SBP = systolic blood pressure. PP = pulse pressure. MAP = mean arterial pressure

Table 4. Relationship between the change in salivary cortisol and the change in blood pressure variables following 6 wk of fish oil treatment

		Δ HR	Δ DBP	Δ SBP	Δ PP	Δ MAP
Δ Salivary Cortisol	Pearson Correlation	-.046	-.067	.021	.081	-.035
	Sig. (2-tailed)	.847	.779	.929	.734	.883
	N	20	20	20	20	20

Δ = change in variable following treatment.

Appendix A. Fatty acid profile of fish oil and safflower oil capsules.

Fatty Acid	Fish Oil (%)	Safflower Oil (%)		Fatty Acid	Fish Oil (%)	Safflower Oil (%)
14:0	0.00	0.00		20:1w11	0.00	0.00
14:1	0.00	0.00		20:1w9	2.05	0.00
15:0	0.00	0.00		20:1w7	1.02	0.00
15:1	0.00	0.00		21:0	0.00	0.00
16:0	0.33	7.00*		20:2w6	0.00	0.00
16:1	0.39	0.00		20:3w6	0.35	0.00
16:2w6	0.00	0.00		20:4w6	2.74	0.00
17:0	0.00	0.00		20:3w3	0.00	0.00
17:1	0.00	0.00		20:4w3	1.82	0.00
16:4w3	0.00	0.00		20:5w3	44.42	0.00
18:0	1.10	2.00*		21:5w3	2.67	0.00
18:1w9	1.84	13.0*		22:0	0.47	0.00
18:1w7	0.7	0.00		22:1w11	2.61	0.00
18:2w6	0.00	78.0*		22:1w13	0.00	0.00
18:2w4	0.00	0.00		22:1w7	0.41	0.00
18:3w6	0.00	0.00		22:1w9	0.74	0.00
18:3w3	0.00	0.00		22:4w6	0.61	0.00
18:4w3	0.36	0.00		22:5w6	1.03	0.00
19:0	0.00	0.00		22:5w3	8.97	0.00
19:1	0.00	0.00		24:0	0.00	0.00
20:0	0.48	0.00		22:6w3	23.69	0.00
				24:1w9	0.89	0.00

* average value

REFERENCES

- Aardal, E., & Holm, A. C. (1995). Cortisol in saliva--reference ranges and relation to cortisol in serum. *European journal of clinical chemistry and clinical biochemistry : journal of the Forum of European Clinical Chemistry Societies*, 33(12), 927-932.
- Appel, L. J., Miller, E. R., 3rd, Seidler, A. J., & Whelton, P. K. (1993). Does supplementation of diet with 'fish oil' reduce blood pressure? A meta-analysis of controlled clinical trials. *Arch Intern Med*, 153(12), 1429-1438.
- Bondia-Pons, I., Schroder, H., Covas, M. I., Castellote, A. I., Kaikkonen, J., Poulsen, H. E., et al. (2007). Moderate consumption of olive oil by healthy European men reduces systolic blood pressure in non-Mediterranean participants. *The Journal of nutrition*, 137(1), 84-87.
- Bose, M., Olivian, B., & Laferrere, B. (2009). Stress and obesity: the role of the hypothalamic-pituitary-adrenal axis in metabolic disease. *Curr Opin Endocrinol Diabetes Obes*, 16(5), 340-346.
- Bruckner, G., Webb, P., Greenwell, L., Chow, C., & Richardson, D. (1987). Fish oil increases peripheral capillary blood cell velocity in humans. *Atherosclerosis*, 66(3), 237-245.
- Chu, Z. M., Yin, K., & Beilin, L. J. (1992). Fish oil feeding selectively attenuates contractile responses to noradrenaline and electrical stimulation in the perfused mesenteric resistance vessels of spontaneously hypertensive rats. *Clin Exp Pharmacol Physiol*, 19(3), 177-181.
- Delarue, J., Matzinger, O., Binnert, C., Schneiter, P., Chioloro, R., & Tappy, L. (2003). Fish oil prevents the adrenal activation elicited by mental stress in healthy men. *Diabetes Metab*, 29(3), 289-295.
- Eguchi, R., Scarmagnani, F. R., Cunha, C. A., Souza, G. I., Pisani, L. P., Ribeiro, E. B., et al. (2011). Fish oil consumption prevents glucose intolerance and hypercorticotestonemia in footshock-stressed rats. *Lipids in health and disease*, 10, 71.
- Engler, M. B., & Engler, M. M. (2000). Docosahexaenoic acid--induced vasorelaxation in hypertensive rats: mechanisms of action. *Biol Res Nurs*, 2(2), 85-95.
- Filipovsky, J., Ducimetiere, P., Eschwege, E., Richard, J. L., Rosselin, G., & Claude, J. R. (1996). The relationship of blood pressure with glucose, insulin, heart rate, free fatty acids and plasma cortisol levels according to degree of obesity in middle-aged men. *J Hypertens*, 14(2), 229-235.
- Flaten, H., Hostmark, A. T., Kierulf, P., Lystad, E., Trygg, K., Bjerkedal, T., et al. (1990). Fish-oil concentrate: effects on variables related to cardiovascular disease. *The American journal of clinical nutrition*, 52(2), 300-306.

- Geleijnse, J. M., Giltay, E. J., Grobbee, D. E., Donders, A. R., & Kok, F. J. (2002). Blood pressure response to fish oil supplementation: metaregression analysis of randomized trials. *J Hypertens, 20*(8), 1493-1499.
- Hellhammer, D. H., Wust, S., & Kudielka, B. M. (2009). Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology, 34*(2), 163-171.
- Johansen, O., Seljeflot, I., Hostmark, A. T., & Arnesen, H. (1999). The effect of supplementation with omega-3 fatty acids on soluble markers of endothelial function in patients with coronary heart disease. *Arterioscler Thromb Vasc Biol, 19*(7), 1681-1686.
- Kelly, J. J., Martin, A., & Whitworth, J. A. (2000). Role of erythropoietin in cortisol-induced hypertension. *J Hum Hypertens, 14*(3), 195-198.
- Kelly, J. J., Tam, S. H., Williamson, P. M., Lawson, J., & Whitworth, J. A. (1998). The nitric oxide system and cortisol-induced hypertension in humans. *Clin Exp Pharmacol Physiol, 25*(11), 945-946.
- Kidambi, S., Kotchen, J. M., Grim, C. E., Raff, H., Mao, J., Singh, R. J., et al. (2007). Association of adrenal steroids with hypertension and the metabolic syndrome in blacks. *Hypertension, 49*(3), 704-711.
- Michaeli, B., Berger, M. M., Revelly, J. P., Tappy, L., & Chiolero, R. (2007). Effects of fish oil on the neuro-endocrine responses to an endotoxin challenge in healthy volunteers. *Clin Nutr, 26*(1), 70-77.
- Morris, M. C., Sacks, F., & Rosner, B. (1993). Does fish oil lower blood pressure? A meta-analysis of controlled trials. *Circulation, 88*(2), 523-533.
- Nissen, S. E., Tuzcu, E. M., Libby, P., Thompson, P. D., Ghali, M., Garza, D., et al. (2004). Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study: a randomized controlled trial. *JAMA : the journal of the American Medical Association, 292*(18), 2217-2225.
- Perona, J. S., Montero, E., Sanchez-Dominguez, J. M., Canizares, J., Garcia, M., & Ruiz-Gutierrez, V. (2009). Evaluation of the effect of dietary virgin olive oil on blood pressure and lipid composition of serum and low-density lipoprotein in elderly type 2 diabetic subjects. *Journal of agricultural and food chemistry, 57*(23), 11427-11433.
- Phillips, D. I., Bennett, F. I., Wilks, R., Thame, M., Boyne, M., Osmond, C., et al. (2005). Maternal body composition, offspring blood pressure and the hypothalamic-pituitary-adrenal axis. *Paediatr Perinat Epidemiol, 19*(4), 294-302.
- Powers, B. J., Olsen, M. K., Smith, V. A., Woolson, R. F., Bosworth, H. B., & Oddone, E. Z. (2011). Measuring blood pressure for decision making and quality reporting: where and how many measures? *Annals of internal medicine, 154*(12), 781-788.

- Prisco, D., Paniccia, R., Bandinelli, B., Filippini, M., Francalanci, I., Giusti, B., et al. (1998). Effect of medium-term supplementation with a moderate dose of n-3 polyunsaturated fatty acids on blood pressure in mild hypertensive patients. *Thrombosis research*, *91*(3), 105-112.
- Rogers, S., James, K. S., Butland, B. K., Etherington, M. D., O'Brien, J. R., & Jones, J. G. (1987). Effects of a fish oil supplement on serum lipids, blood pressure, bleeding time, haemostatic and rheological variables. A double blind randomised controlled trial in healthy volunteers. *Atherosclerosis*, *63*(2-3), 137-143.
- Ryu, J., Lerner, J., & Sullivan, J. M. (1990). Unresponsiveness of forearm hemodynamics to omega-3 polyunsaturated fatty acids and aspirin. *Prostaglandins*, *39*(3), 339-347.
- Schoorlemmer, R. M., Peeters, G. M., van Schoor, N. M., & Lips, P. (2009). Relationships between cortisol level, mortality and chronic diseases in older persons. *Clin Endocrinol (Oxf)*, *71*(6), 779-786.
- Shah, A. P., Ichijui, A. M., Han, J. K., Traina, M., El-Bialy, A., Meymandi, S. K., et al. (2007). Cardiovascular and endothelial effects of fish oil supplementation in healthy volunteers. *J Cardiovasc Pharmacol Ther*, *12*(3), 213-219.
- Shimokawa, H., & Vanhoutte, P. M. (1989). Dietary omega 3 fatty acids and endothelium-dependent relaxations in porcine coronary arteries. *Am J Physiol*, *256*(4 Pt 2), H968-973.
- Soro, A., Ingram, M. C., Tonolo, G., Glorioso, N., & Fraser, R. (1995). Mildly raised corticosterone excretion rates in patients with essential hypertension. *J Hum Hypertens*, *9*(6), 391-393.
- Stamler, J., Stamler, R., & Neaton, J. D. (1993). Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. *Arch Intern Med*, *153*(5), 598-615.
- Vericel, E., Calzada, C., Chapuy, P., & Lagarde, M. (1999). The influence of low intake of n-3 fatty acids on platelets in elderly people. *Atherosclerosis*, *147*(1), 187-192.
- Walker, B. R., Best, R., Shackleton, C. H., Padfield, P. L., & Edwards, C. R. (1996). Increased vasoconstrictor sensitivity to glucocorticoids in essential hypertension. *Hypertension*, *27*(2), 190-196.
- Whitworth, J. A., Gordon, D., McLachlan-Troup, N., Scoggins, B. A., & Moulds, R. W. (1989). Dexamethasone suppression in essential hypertension: effects on cortisol and blood pressure. *Clin Exp Hypertens A*, *11*(2), 323-335.

- Whitworth, J. A., Mangos, G. J., & Kelly, J. J. (2000). Cushing, cortisol, and cardiovascular disease. *Hypertension*, 36(5), 912-916.
- Whitworth, J. A., Williamson, P. M., Mangos, G., & Kelly, J. J. (2005). Cardiovascular consequences of cortisol excess. *Vasc Health Risk Manag*, 1(4), 291-299.