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Chapter 16

PTSD and the Attenuating Effects of Fish Oils: Results of Supplementation After the 2011 Great East Japan Earthquake

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1. Introduction

1.1. Evidence of effects of omega-3 polyunsaturated fatty acids on depression and anxiety disorder

Omega-3 polyunsaturated fatty acids (omega-3 PUFAs) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are essential fatty acids that cannot be synthesized by humans de novo and must therefore be obtained through the diet. Omega-3 PUFAs are speculated to be beneficial against psychiatric disorders, especially depression, and an increasing growing number of randomized controlled trials (RCTs) have been carried out to verify their efficacy. In fact, a number of previous meta-analyses of RCTs support the positive effects of omega-3 PUFAs supplementation in reducing depressive symptoms [1-7]. However, a recent meta-analysis by Bloch and Hannestad in 2011 found that nearly all evidence of omega-3 PUFAs benefit was removed after adjusting for publication bias [8]. Their meta-analysis has subsequently been criticized by two papers published in quick succession [6, 7]. One of these papers, by Martins et al [6], pointed out methodological flaws with Bloch and Hannestad's analysis. For example, Bloch and Hannestad's analysis included the study examining individuals without formal psychiatric diagnosis, and 2 other studies satisfying their inclusion criteria were not included. Martins et al concluded that supplements containing EPA ≥60% of total EPA + DHA were effective against depression, a finding in agreement with

a meta-analysis by Sublette et al [5]. Taken together, then, the latest evidence does suggest the efficacy of omega-3 PUFAs containing EPA ≥60% against depression.

Several biological mechanisms potentially explain the effect of omega-3 PUFAs in depression and anxiety disorder [1]. To date, however, few RCTs have been carried out to investigate whether omega-3 PUFAs are effective against anxiety disorders. While one such study suggested that omega-3 PUFAs might not be effective for patients suffering from depression with comorbid anxiety disorder [9], some RCTs found that omega-3 PUFAs decreased hostility and aggression among patients with borderline personality disorder [10].

1.2. Omega-3 polyundasurated fatty acids and inflammation

A competitive interaction exists between omega-6 polyunsaturated fatty acids (omega-6 PUFAs) such as arachidonic acid (AA) and omega-3 PUFAs in regard to their shared enzymatic pathways. Compared with the eicosanoids produced from AA, such as prostaglandin E2 (PGE2), those produced from omega-3 PUFAs, such as prostaglandin E3 (PGE3), have little pro-inflammatory activity [11]. Therefore, it is speculated that the amounts of omega-6 eicosanoids released in response to depression-associated inflammation and cell apoptosis, are determined by the fatty acid composition of the cell membrane phospholipids [12]. On this basis, it is thought that increased levels of omega-3 PUFAs in the cell membranes reduces the release of AA-derived prostaglandins, thereby reducing inflammatory activity [13].

Naturally occurring depression-related cell apoptosis may be mediated by free radicals that appear in the brain during the process of inflammatory or ischemic damage. Inflammation and ischemia are known to increase the risk for clinically defined depression [14]. Taken into account that cytokines stimulate the intrinsic pathway of apoptosis and induce depression [15, 16], it is not altogether surprising to find frequent comorbidity of inflammation and depression. The interaction between omega-6 and omega-3 PUFAs eicosanoids, therefore, partly control inflammation, apoptosis and depression as a result [14].

1.3. Omega-3 polyunsaturated fatty acids and neurogenesis

The severity of depression is known to be associated with serum brain-derived neurotrophic factor (BDNF) [17], which exerts various effects on the nervous system, including neuronal outgrowth, differentiation, synaptic connectivity, and neuronal repair and survival [18-20]. Its severity is also associated with low levels of erythrocyte omega–3 PUFAs [21]. Short-term dietary supplementation with omega-3 PUFAs has been shown to up-regulate adult neurogenesis in lobsters [22]. In rats, dietary omega-3 PUFAs increased levels of BDNF, which promotes neuronal survival and growth [23].DHA extended neurites and branches of rat hippocampal neurons in vitro [24]. DHA supplementation to rats also promoted the maturation of neurons and hippocampal neurogenesis in vivo [25].. On the basis of these findings, omega-3 PUFAs supplementation can enhance the effect of BDNF-related synaptic plasticity and neurogenesis.

Additionally, in PTSD, the pathogenesis of which is characterized by excess consolidation of fear memory and failure of extinction learning [26], it might be possible to control fear memory

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by regulating hippocampal neurogenesis [27]. Indeed, in mice with active hippocampal neurogenesis, the period of hippocampus-dependent fear memory was found to be shorter [28]. Given the findings of animal research conducted to date, omega-3 PUFAs seem to be the most promising candidate for dietary intervention to facilitate adult hippocampal neurogenesis following a traumatic event [25, 29]. In fact, in an open label trial in patients with physically injury, we previously found that PTSD symptoms were significantly alleviated by taking DHA-rich fish oil [30].

1.4. Background of the study

On March 11, 2011, The Great East Japan Earthquake and tsunami devastated the northeastern coast of Japan. As of July 18th, 2012, 15,867 died and 2,906 were missing arrocding to the National Police Agency. Many rescue workers, as well as survivors, were exposed to traumatic experiences. A number of studies have reported adverse psychological outcomes among rescue workers. In a study of medical care personnel sent to aid trauma victims of an airline crash, 13.5% developed PTSD within 18 months of the crash [31]. Similarly, in a study of rescue workers deployed to the site of the September 11 terrorist attack in New York in 2001, 16.7% developed PTSD and 21.7% developed depression at 13 months after the attack [32]. Moreover, peritraumatic distress (distress during and right after a traumatic experience) and TV viewing for extended periods were shown to predict PTSD symptoms in rescue workers [33, 34]. PTSD is associated with higher psychiatric comorbidity, attempted suicide, and physical illnesses [35], as well as with high medical expenses [36]. An appropriate strategy for the prevention of PTSD in rescue workers is therefore clearly required, but as yet adequate measures have not been developed.

Against this background, we carried out a study to determine whether fish oil supplementation can attenuate PTSD symptoms among rescue workers after the Great East Japan Earthquake. The main findings have been breifly reported elsewhere [37] and here we present the overall findings of the study.

2. Methods

2.1. Participants

This trial named “Attenuating posttraumatic distress with omega-3 polyunsaturated fatty acids among disaster medical assistance team members after the Great East Japan Earthquake (APOP)” was a single-blind, randomized, parallel-group field trial administered by the National Disaster Medical Center (NDMC), Tokyo, Japan. The head office of the Disaster Medical Assistance Team (DMAT) is located at NDMC. DMAT members are doctors, nurses, and operational coordination staff (medical or clerical staff who are neither doctors nor nurses) who are dispatched as a mobile medical team with specialized training that is capable of acting during the acute phase of a large-scale disaster. DMAT activities commenced on the day of the Great East Japan Earthquake, March 11, and concluded on March 22.

The DMAT members recruited to the present trial met the following inclusion criteria: 1) aged 18 years or older; 2) a native Japanese speaker or non-native speaker with Japanese conversational abilities; and 3) physically and psychologically capable of understanding and providing consent for study participation. The exclusion criterion was regular intake of warfarin for at least 3 months before deployment, because Fish oil supplementation could have provided additional anticoagulation with warfarin.

2.2. Procedures

The detailed trial procedures have been reported elsewhere [38], but briefly a written guide to the study, including an explanation of the study and informed consent, was posted to the Emergency Medical Information System by DMAT head office and a mass email was sent to all DMAT members asking for their participation. The Peritraumatic Distress Inventory (PDI) [39, 40] was used to quantify peritraumatic distress. Other detailed baseline assessment has been reported elsewhere [38].

2.3. Ethics

The study protects the rights and welfare of participants in the spirit of ethical guidelines outlined under the Declaration of Helsinki, and further respects the ethical principles of the Ministry of Health, Labour, and Welfare of Japan. The study was approved by the Ethics Committee of the NDMC on April 1, 2011. Individual participants in this study gave written informed consent.

2.4. Interventions

For participants allocated to the fish oil plus psychoeducation group, seven capsules per day, each containing 320 mg of fish oil, were provided in line with previous research [41]. The fish oil composition of each capsule was 70% DHA and 7% eicosapentaenoic acid (EPA). Each capsule was placed in a brown 500-ml polyethylene container with a wide opening. Participants were instructed to take the capsules after eating and additionally told that they might take a full day's dosage at one time. For participants of both groups, a leaflet on psychoeducation about posttraumatic distress focusing on critical incident stress was provided.

2.5. Objectives

This study aimed to determine whether fish oil supplementation can attenuate the symptoms of PTSD and other posttraumatic distress such as depression among DMAT workers who were deployed during the acute disaster phase of the Great East Japan Earthquake.

2.6. Outcomes

The primary outcome was total score on the Impact of Event Scale-Revised (IES-R) at 12 weeks after shipment of the supplements on April 19, 2011. The IES-R, developed by Weiss, is a self-reporting questionnaire about PTSD symptoms and is the most widely used measure internationally in all forms of disaster-area research [42]. The IES-R is composed of 22 items on the

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three largest symptoms in the diagnostic criteria of PTSD, namely re-experiencing, avoidance, and hyperarousal. Respondents rate symptoms experienced in the previous week. The validity and reliability of the Japanese version of the IES-R has been confirmed [43].

Secondary outcomes were the total scores on each of the Kessler 6 Scale, the Center for Epidemiologic Studies Depression Scale (CES-D), and the shortened 14-item version of the Resilience Scale at 12 weeks after shipment of the supplements. the Kessler 6 Scale, developed by Kessler et al. [44], is a self-reporting questionnaire designed to screen for psychiatric disorders and mood and anxiety disorders; the CES-D, developed by Radloff [45], is a self-reporting questionnaire on depression; and the shortened 14-item version of the Resilience Scale, developed by Wagnild and Young [46], is a self-reporting questionnaire for quantitative evaluation of resilience. The Japanese version of each of these three scales has been validated [47-49].

Safety of the intervention was evaluated by the presence of adverse events during the observation period, by asking the participants about the presence of such events at 2, 4, 8, and 12 weeks after the start of fish oil supplementation. Whenever inquiries were received from participants, necessary information was provided to them.

2.7. Sample size

We estimated that the mean improvement in IES-R score as the primary outcome measure would be 10 (SD 15) for the fish oil plus psychoeducation group and 0 (SD 15) for the psychoeducation alone group [30]. We set α level at.05 and β at.10. This brought us to our required sample size estimation of 48 cases per group. Because the control group in this study received psychoeducation, we allowed up to 150 cases for the intervention group and 300 cases for the control group.

2.8. Randomization

Participants were randomly assigned to either the fish oil supplementation plus psychoeducation group or psychoeducation alone group. The trial statisticians (NN and TS) independently conducted randomization by the permuted block method using a four-person block, and concealed allocation mechanism until the study was finished. The participants were stratified by sex because previous studies showed that the prevalence of PTSD and of major depressive disorder was higher in women than in men [50].

2.9. Blinding

Because placebo capsules were not provided to psychoeducation alone group, participants could not be masked. Also, the researcher who provided necessary information regarding safety management to the participants (DN) could not be masked in just a few cases when participants inadvertently stated that they took the fish oils capsules. Other researchers were masked to allocation.

2.10. Statistical methods

All analyses were conducted according to the intention-to-treat principle. A sensitivity analysis was performed using a multiple imputation procedure with SAS version 9.1 (SAS Institute Inc, Cary, North Carolina) to impute each psychological variable end point for participants who did not have a follow-up psychological variable assessed.

Analysis of covariance (ANCOVA) was used to investigate the significance of the differences in the initial values as well as those of the net changes after the intervention among the 2 groups, 95% confidence interval values, and P values. Covariates for ANCOVA were sex, age, and each psychological variable score at baseline. In addition, we examined the impact of sex difference for fish oil supplementation on posttraumatic distress. A two-tailed test was used, with the α level set at 0.05.

3. Results

3.1. Participants flow and recruitment

Figure 1 shows the trial profile. Of the 1,816 DMAT workers deployed to the disaster areas, 172 were enrolled and randomly allocated to the fish oil plus psychoeducation group or psychoeducation alone group between April 2 and 12, 2011 (Figure 1). The mean duration from baseline assessment to follow-up assessment was 14.2 weeks (SD 0.9), and from shipment of the supplements to follow-up assessment was 12.6 weeks (SD 0.8). Only 1 participant in the psychoeducation alone group was lost to follow-up.

3.2. Baseline data

The two groups were well balanced with respect to baseline characteristics, except that the IES-R total and intrusion subscale scores were relatively high in the intervention group (Table 1). The mean term of the deployment was 4.1 days (SD 2.0). Two participants (1%) were injured during deployment, 11 (6%) saved children, 24 (14%) had contact with corpses, and the median of the PDI was 12.5 (range 0-42). These variables, identified as risk factors for PTSD in previous research [31, 51], did not differ significantly between the two groups. The PDI scores were comparable to those in accident survivors (Median 15.0, range 0-40] [52, 53].

3.3. Numbers analyzed

Eighty-six participants were assigned to each group. Primary outcome data were available for all participants, except one. All participants constituted the intention-to-treat population. The imputation technique assigned changes in the effectiveness end point for the noncompleter based on the participant's baseline characteristics and baseline psychological variables.

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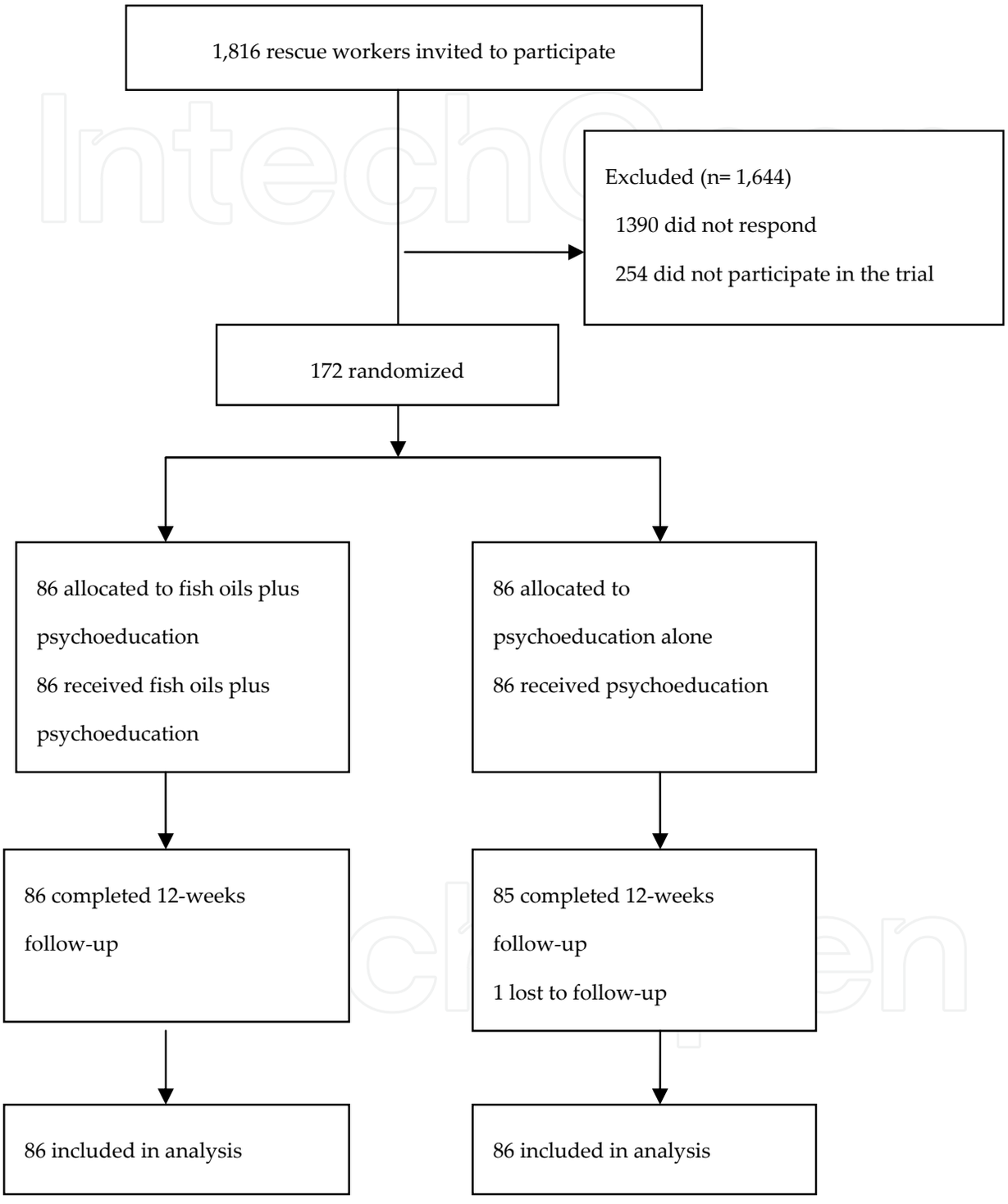

Figure 1. Flow diagram of the study

	Fish oil plus psychoeducation group (n=86)	Psychoeducation alone group (n=86)	P value*1
Demographic data			
Age in years (mean±S.D.)	37.9 ± 7.4	37.4 ± 7.4	0.62
Women (%)	27.9	26.7	0.86
BMI (mean±S.D.)	22.7 ± 2.8	23.0 ± 3.0	0.50
Occupation (%)			0.87
Medical Doctor	26.7	24.4	
Nurse	46.5	45.4	
Other	26.7	30.2	
Years of occupational experience (mean±S.D.)	14.5 ± 7.2	13.2 ± 7.3	0.24
Previous disaster operation experience (%)	27.9	26.7	0.86
Married (%)	67.4	72.1	0.51
Has a child (or children) (%)	57.0	61.6	0.53
Education (%)			
University or higher	47.7	53.5	0.45
Current smoker (%)	29.1	23.3	0.39
Current drinker (%)	80.2	83.7	0.55
Has past history of any physical disaeses*2 (%)	0.0	0.0	-
Has past history of depression (%)	0.0	4.7	-
Psychological data			
IES-R (mean±S.D.)			
IES-R-Total	14.5 ± 15.1	10.7 ± 11.5	0.07
IES-R-Intrusion	6.5 ± 6.6	4.7 ± 5.1	0.05
IES-R-Avoidance	4.0 ±5.2	3.0 ± 4.2	0.16
IES-R-Hyperarousal	3.9 ± 4.6	2.9 ± 3.6	0.12
K6 (mean±S.D.)	4.5 ± 5.0	3.4 ± 4.2	0.13
CES-D (mean±S.D.)	13.6 ± 9.1	11.6 ± 8.1	0.13
RS-14 (mean±S.D.)	65.5 ± 10.3	67.1 ± 9.9	0.31

Abbreviations: IES-R, Impact of Event Scale-Revised; K6, Kessler 6 Scale; CES-D, Center for Epidemiologic Studies Depression Scale; RS-14, Resilience Scale 14-item version

*1) Student's t test or Chi-square test

*2) Physical disease defined as cancer, cardiovascular disease, stroke, chronic renal disease, chronic liver disease, and accidental injury.

Table 1. Characteristics of the study population at randomization

3.4. Outcomes and estimation

ANCOVA adjusted for sex and age showed a significant reduction in IES-R intrusion and hyperarousal subscale scores in the fish oil plus psychoeducation group. When adjusted for the scores at baseline, however, no significant difference in primary outcome was seen between the two groups when adjusted for the scores at baseline (-0.9, 95% CI, -3.0 to 1.2; P = 0.39) and no significant differences were seen in any of secondary outcomes (Table 2).

Variables	Baseline (mean±S.D.)	After 12 weeks (mean±S.D.)	Net change 1 (95% CI)	P value	Net change 2 (95% CI)	P value
IES-R-Total						
Fish oils group	14.5 ± 15.1	9.0 ± 9.5	-2.7	0.06	-0.9	0.39
Control group	10.7 ± 11.5	7.9 ± 10.0	(-5.5, 0.1)		(-3.0, 1.2)	
IES-R-Intrusion						
Fish oils group	6.5 ± 6.6	3.3 ± 3.4	-1.5	0.03	-0.5	0.28
Control group	4.7 ± 5.1	3.1 ± 3.7	(-2.8, -0.2)		(-1.3, 0.4)	
IES-R-Avoidance						
Fish oils group	4.0 ± 5.2	3.3 ± 4.4	-0.04	0.94	0.3	0.44
Control group	3.0 ± 4.2	2.4 ± 3.7	(-1.0, 0.9)		(-0.5, 1.1)	
IES-R-Hyperarousal						
Fish oils group	3.9 ± 4.6	2.3 ± 2.7	-1.1	0.03	-0.6	0.11
Control group	2.9 ± 3.6	2.5 ± 3.5	(-2.1, -0.1)		(-1.4, 0.1)	
K6						
Fish oils group	4.5 ± 5.0	2.9 ± 3.4	-0.4	0.52	0.2	0.62
Control group	3.4 ± 4.2	2.2 ± 3.7	(-1.5, 0.8)		(-0.6, 1.1)	
CES-D						
Fish oils group	13.6 ± 9.1	10.8 ± 6.3	-1.5	0.20	-0.3	0.73
Control group	11.6 ± 8.1	10.3 ± 7.2	(-3.9, 0.8)		(-2.1, 1.5)	
RS-14						
Fish oils group	65.5 ± 10.3	67.2 ± 11.3	2.7	0.09	2.2	0.15
Control group	67.1 ± 9.9	66.1 ± 13.3	(-0.4, 5.8)		(-0.8, 5.2)	

Abbreviations: IES-R, Impact of Event Scale-Revised; K6, Kessler 6 Scale; CES-D, Center for Epidemiologic Studies Depression Scale; RS-14, Resilience Scale 14-item version; CI, confidence interval

Net change 1: Analysis of covariance (ANCOVA) adjusted for sex and age

Net change 2: Analysis of covariance (ANCOVA) adjusted for sex, age and each psychological variable score at baseline

Table 2. Change in IES-R, K6, CES-D and RS-14 scores of participants in the fish oils and control groups

Because previous studies showed that the prevalence of PTSD and of major depressive disorder was higher in women than in men [50], subgroup analysis by sex was pre-specified. In women, the IES-R total mean score was reduced from 15.7 (SD 14.9) at baseline to 9.3 (SD 8.8) at follow-up in the fish oil plus psychoeducation group, compared to that from 11.2 (SD 13.0) to 10.4 (SD 12.3) in the psychoeducation alone group. In men, the IES-R total score was reduced in both groups, from 14.0 (SD 15.3) to 8.9 (SD 9.9) in the fish oil plus psychoeducation group and from 10.5 (SD 11.1) to 6.9 (SD 9.0) in the psychoeducation alone group. Remarkably, even when adjusted for age and IES-R scores at baseline, change in the IES-R score of women in the two groups from baseline to 12weeks was -3.9 (95% CI, -7.5 to -0.3; P = 0.04) (Table 3).

Regarding adherence, 7 out of 86 participants (8%; 6 male, 1 female) in the fish oil plus psychoeducation group took fish oil supplements 2 days or less per a week.

3.5. Adverse events

The occurrence rate of adverse events was not significantly different between the two groups, with 32 participants (37%) in the fish oil plus psychoeducation group reporting at least one adverse event versus 22 (26%) of the psychoeducation alone group doing so. Of these events, none were regarded as serious or led to withdrawal. The main adverse events included loose bowel (21 (24%) in the fish oil plus psychoeducation group versus 15 (17%) in the psychoeducation alone group) and belching (12 (14%) in the fish oil plus psychoeducation group versus 7 (8%) in the psychoeducation alone group).

4. Discussion

4.1. Interpretation

This trial regretfully did not show the superiority of fish oil supplementation plus psychoeducation over psychoeducation alone for the prevention of PTSD and depressive symptoms among rescue workers. Even though a relatively good improvement was seen in IES-R score in the fish oil plus psychoeducation group, the improvement did not reach statistical significance. Furthermore, we recorded no significant differences between the two groups for the 3 secondary outcomes.

One of the possible reasons for not detecting the effectiveness of fish oil supplementation was that posttraumatic distress was reduced in both groups. A previous study of disaster workers at the September 11 terrorist attack sites showed that depressive symptoms were increased from 7 months after the disaster to 13 months after, while PTSD symptoms were reduced from 1 week to 13 months afterward [32]. In the present study, all psychological variables were reduced to some extent in both groups. Participants in both groups were contacted at 2, 4, 8, and 12 weeks for safety management and necessary information was provided to them upon request for ethical reasons: such contact might have been supportive for both groups of participants. Psychoeducation provided before the baseline assessment also might affect the results.

Variables		Net change (95% CI)	P value
IES-R-Total			
	Women	-3.9 (-7.5, -0.3)	0.04
	Men	0.2 (-2.2, 2.7)	0.86
IES-R-Intrusion			
	Women	-1.3 (-2.9, 0.4)	0.12
	Men	-0.1 (-1.1, 0.8)	0.78
IES-R-Avoidance			
	Women	-0.4 (-1.9, 1.1)	0.58
	Men	0.6 (-0.4, 1.6)	0.23
IES-R-Hyperaruosal			
	Women	-1.9 (-3.4, -0.5)	0.009
	Men	-0.1 (-1.0, 0.8)	0.77
K6			
	Women	0.1 (-1.9, 2.1)	0.90
	Men	0.2 (-0.7, 1.2)	0.61
CES-D			
	Women	-2.8 (-6.4, 0.8)	0.13
	Men	0.5 (-1.5, 2.6)	0.60
RS-14			
	Women	3.7 (-1.5, 9.0)	0.16
	Men	1.7 (-2.0, 5.4)	0.36

Abbreviations: IES-R, Impact of Event Scale-Revised; K6, Kessler 6 Scale; CES-D, Center for Epidemiologic Studies Depression Scale; RS-14, Resilience Scale 14-item version; CI, confidence interval

Net change: Analysis of covariance (ANCOVA) adjusted for age and each psychological variable score at baseline

Table 3. Change in IES-R, K6, CES-D and RS-14 scores of participants in the fish oils and control groups stratified by sex

The fish oil capsules used in this study contained 1,568 mg DHA and 157 mg EPA per day. Based on previous studies [25, 29], DHA rather than EPA appeared to facilitate adult hippocampal neurogenesis. However, there is evidence to support the effectiveness of EPA monotherapy or a combination of EPA and DHA for depressive disorders [1]. A recent review showed that a 2:1 EPA:DHA ratio might be optimal for the treatment of depressive disorders [54]. In fact, our open label trial in physically injured patients failed to alleviate depressive symptoms, while alleviating PTSD symptoms [30]. To our knowledge, no previous studies have examined the effectiveness of fish oils to prevent PTSD. The appropriate composition of fish oil capsules to prevent PTSD warrants attention.

Remarkably, fish oil supplementation plus psychoeducation significantly lowered the IES-R total and hyperarousal subscale scores in women, despite the small sample size of women. To our knowledge, this is the first randomized controlled trial to show that fish oil reduced PTSD symptoms in women. While this outcome could be caused by chance because this was a secondary analysis, our finding coincides with that of previous longitudinal studies in Finland, Spain, and the United States [55-57] showing dietary intake of fish decreased the risk of developing depression in women, but not in men. Moreover, in Japan, a very low intake of fish was found to be associated with increased risk of suicidal death in women [58]. Although the difference in depressive symptoms assessed by the CES-D did not reach statistical significance among women in the present study, further studies with a large sample size may prove the effectiveness of fish oil supplementation for attenuating depressive symptoms in women. Also, our finding that women who took the fish oil supplements had a significant reduced score on the hyperarousal subscale is also partly consistent with a previous study showing that DHA intake prevented aggression from increasing at times of mental stress [41]. It is unclear why fish oils play an important role for regulating psychological well-being only in women, but it could be explained by the fact that estrogens cause higher DHA concentrations in women than in men [59]. Future studies should determine the effect of the sex difference in the effectiveness of fish oil supplementation for PTSD and posttraumatic depressive symptoms.

In addition to the possibility that fish oils do attenuate PTSD symptoms in women, it is well known that fish oils are effective for the secondary prevention of cardiovascular disease. An ecological study revealed that the availability of omega 3 PUFAs was inversely related with disease rates in 12 risk models, such as mortality from stroke and cardiovascular disease, as well as depression [60]. Given these positive effects on physical health and low rates of severe adverse events, fish oil supplementation could be a safe and novel strategy for the prevention of PTSD in women.

4.2. Generalizability

As shown in the figure 1, 1,390 out of 1,816 rescue workers invited to participate did not respond, which could limit the external validity of the findings. This might be because many rescue workers committed themselves to important roles at their own hospitals immediately after their deployment and could hardly afford to participate in this study.

4.3. Limitations

This study has some strengths. The participants are representative of all DMAT workers in that they are based across Japan. Baseline assessments were conducted within 1 month after the earthquake, which would minimize recall bias, and the attrition rate (<1%) was extremely low.

However, the study also has some limitations. First, this study was not a placebo controlled, double-blind trial. Because this study was implemented at a time of crisis, we could not prepare placebo capsules. It might be possible that we found a placebo effect acted more strongly in women who took the fish oil supplements. We are currently implementing a double-blind, placebo control trial of fish oils for the prevention of PTSD in physically injured patients (ClinicalTrials.gov Identifier: NCT00671099]. Second, this study relied on self-reports of adherence to the protocol, rather than biomarkers. We are currently measuring fatty acid composition of red blood cell membranes in a double-blind controlled trial mentioned above. Third, the finding of efficacy for women is driven by the significant reduction in hyperarousal cluster symptoms. Hyperarousal cluster symptoms are not PTSD-specific and are similar to the symptoms of other anxiety and mood disorders. Because assessment of PTSD is a self-report screening instrument rather than a structural interview, this study could not rule out an alternative explanation of the positive finding for women that attributes that difference to changes that are not related to PTSD.

5. Conclusion

This trial did not show the effectiveness of fish oil supplementation for the prevention of PTSD and depressive symptoms in rescue workers. However, the supplements did reduce PTSD symptoms significantly in women. Due to limitations mentioned above, the result of this study is a preliminary and should be accepted cautiously, but at the same time it is an encouraging finding. Not only rescue workers but large numbers of people were traumatized by natural disasters such as the Great East Japan Earthquake, and psychiatric resources to support them have been limited. Against this background, daily life-based intervention for the prevention of PTSD is preferable. Fish oil supplementation may offer a safe strategy for preventing PTSD in women, and thus is an important topic that should be further explored in disaster mental health care.

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