Journal of Affective Disorders 129 (2011) 282–288

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Long chain n-3 fatty acids intake, fish consumption and suicide in a cohort of Japanese men and women — The Japan Public Health Center-based (JPHC) Prospective Study

Kalpana Poudel-Tandukar [a], Akiko Nanri [a], Motoki Iwasaki [b], Tetsuya Mizoue [a,*], Yumi Matsushita [a], Yoshihiko Takahashi [c], Mitsuhiko Noda [c], Manami Inoue [b], Shoichiro Tsugane [b,1] and for the Japan Public Health Center-based Prospective Study Group

[a] Department of Epidemiology and International Health, International Clinical Research Center, National Center for Global Health and Medicine, Japan
[b] Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Japan
[c] Department of Diabetes and Metabolic Medicine, National Center for Global Health and Medicine, Japan

ARTICLE INFO

Article history:
Received 28 December 2009
Received in revised form 30 June 2010
Accepted 17 July 2010
Available online 6 August 2010

Keywords:
Cohort study
Suicide
Fish consumption

ABSTRACT

Objective: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been implicated as protective against suicide. However, it is uncertain whether a higher intake of EPA and DHA or of fish, a major source of these nutrients, lowers suicidal risk among Japanese, whose fish consumption and suicide rate are both high. This study prospectively examined the relation between fish, EPA, or DHA intake and suicide among Japanese men and women.
Method: Subjects were 47,351 men and 54,156 women aged 40–69 years who participated in the JPHC Study, completed a food frequency questionnaire in 1995–1999, and were followed for death through December 2005. We used the Cox proportional hazards regression model to estimate the hazard ratio (HR) and 95% confidence interval (CI) for suicide by quintile of intake.
Results: A total of 213 and 85 deaths from suicide were recorded during 403,019 and 473,351 person-years of follow-up for men and women, respectively. Higher intakes of fish, EPA, or DHA were not associated with a lower risk of suicide. Multivariate HRs (95% CI) of suicide death for the highest versus lowest quintile of fish consumption were 0.95 (0.60–1.49) and 1.20 (0.58–2.47) for men and women, respectively. A significantly increased risk of suicidal death was observed among women with very low intake of fish, with HRs (95% CI) for those in 0–5th percentile versus middle quintile of 3.41 (1.36–8.51).
Conclusions: Our overall result does not support a protective role of higher intake of fish, EPA, or DHA against suicide in Japanese men and women.

1. Introduction

The long chain n-3 polyunsaturated fatty acids (PUFA) found in oily fish such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been suggested to be protective against suicide (Freeman, 2000). One explanation for this is that low plasma EPA and DHA may adversely impact serotonergic and corticotrophic functions in the brain (Arato et al., 1989; Mann et al., 1996; Hibbeln et al., 1997, 2004). In particular, an increased risk of suicide has been linked to low

* Corresponding author. Department of Epidemiology and International Health, International Clinical Research Center, National Center for Global Health and Medicine, Toyama 1-21-1, Shinjuku-ku, Tokyo 162-8655, Japan. Tel.: +81 3 202 7181; fax: +81 3 3202 7364.
E-mail addresses: mizoue@ri.ncgm.go.jp (T. Mizoue), stsugane@ncc.go.jp (S. Tsugane).
[1] Reprint requests: Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tsukiji 5-1-1, Chuo-ku, Tokyo 104-0045, Japan. Tel.: +81 3 547 8579; fax: +81 3 3547 8578.

0165-0327/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2010.07.014

concentrations of the serotonergic metabolite 5-hydroxyindoleacetic acid (5-HIAA) (Mann et al., 1996) and to high concentrations of corticotrophin-releasing factor in cerebral spinal fluid (Arato et al., 1989), both of which have been associated with low plasma EPA and DHA.

Studies have shown protective associations between the intake of fish, EPA, or DHA and suicide or suicidality (Hirayama, 1990; Huan et al., 2004). For example, suicide attempters consumed a smaller amount of fish (Li et al., 2009; Tanskanen et al., 2001) or polyunsaturated fatty acids (Zhang et al., 2005) and had lower levels of plasma EPA or DHA (Huan et al., 2004; De Vriese et al., 2004; Sublette et al., 2006) than non-attempters. One randomized-controlled trial (Hallahan et al., 2007) showed that EPA + DHA supplementation reduced suicidality. However, evidence for these associations in a population in which both the fish intake and suicide rate is high is limited (Hirayama, 1990; Hakkarainen et al., 2004). In a 17-year follow-up of 256,118 Japanese, those who ate fish daily had a lower risk of suicide compared to those who ate fish less than daily, albeit that this finding may have been limited by a lack of adjustment for confounding variables (Hirayama, 1990). This observation among Japanese was not corroborated in a Finnish cohort, in which the risk of suicide was not associated with the intake of fish, EPA or DHA (Hakkarainen et al., 2004).

We hypothesized that a higher intake of fish, EPA or DHA is associated with a lower risk of suicide. We considered that an investigation in Japan, in which one person takes their own life every 15 min on average (Mc Curry, 2008) and where people consume an average of 5–8 times more EPA + DHA than people in the United States (Sugano and Hirahara, 2000; Kris-Etherton et al., 2000), might provide useful information about the role of these nutrients in mental health. Here, we investigated the association between fish, EPA, or DHA intake and suicide in a cohort of Japanese men and women.

2. Method

2.1. Study subjects

The Japan Public Health Center-based (JPHC) Study was prospectively conducted in Cohort I (1990) and Cohort II (1993) of Japanese residents in 11 public health centers areas. The study design has been described in detail previously (Tsugane and Sobue, 2001). Among the eligible study population at a 5-year follow-up survey (136,605), 103,768 responded to the survey, yielding a response rate of 76%. We excluded subjects who did not have information on diet or fatty acid intake (1197) and those who reported energy intake outside of the mean ± 3 SD by sex (1064). We included 101,507 subjects in our analysis.

2.2. Lifestyle, anthropometry and dietary assessment

The study participants completed a self-administered five-year follow-up questionnaire which included queries on diet, lifestyle and anthropometric parameters. A food frequency questionnaire (FFQ) was used to assess the intake of 147 foods, including 19 fish questions. Each participant was asked how often s/he had consumed each food during the previous year. For each food item, the subjects indicated their mean frequency of consumption in terms of the specified serving size by checking one of nine frequency categories ranging from "never," to "7 or more times/day." Portion sizes were specified into less than half, the same, and more than 1.5 times a normal serving. Consumption of each food was calculated by multiplying the frequency score of consumption by portion size. The average daily intake of nutrients was calculated by multiplying the frequency of consumption of each item by its nutrient content per serving and totaling the nutrient intake for all food items.

We assigned specific values for each of 19 fish to calculate dietary intake of n-3 PUFA (Kobayashi et al., 2003). For reproducibility, sex-specific Spearman correlation coefficients between the two FFQs administered one year apart in Cohorts I and II ranged from 0.34 to 0.54 for energy-adjusted total fish and n-3 PUFA intake (Sasaki et al., 2003a; Ishihara et al., 2003). The Spearman correlation coefficients between questionnaire and dietary records for energy-adjusted fish intake in men and women were 0.32 and 0.32, respectively, for cohort I (Sasaki et al., 2003b), and 0.27 and 0.23, respectively, for cohort II (Ishihara et al., 2003) and between dietary intake and serum concentrations for EPA and DHA were 0.44 and 0.32, respectively ($p \leq 0.01$) among subsamples of Cohort 1 (Kobayashi et al., 2003).

2.3. Follow-up and identification of suicide

Cohort I was followed from 1995 and Cohort II from 1998, until December 31, 2005. Changes in residence, including survival, were obtained annually using the residential registry. The status of subjects who had moved out of the study area was assessed through the municipal office to which they had moved. Mortality data for persons in the residential registry are forwarded to the Ministry of Health, Labour and Welfare (MHLW) and are coded for inclusion in the National Vital Statistics. Residential registration and death registration are required by the Basic Residential Register Law and Family Register Law, respectively, and the registries are thought to be complete.

Information on deaths for subjects who remained in their original area was obtained from their primary health center (PHC), and for subjects who died after moving from their original PHC area from death certificates maintained by the MHLW, Japan. Information on the cause of death was obtained from the death certificate, provided by the MHLW, Japan with the permission of the Ministry of Internal Affairs and Communications. Death from suicide was defined according to the International Classification of Diseases, 10th Revision (ICD-10), as codes X60–X84.

2.4. Statistical analyses

The number of person-years in the follow-up period was calculated from the response date to the five-year follow-up to the date of death or December 31, 2005, whichever came first. Hazard ratios and 95% confidence intervals (CI) were calculated for the categories of energy-adjusted fish, EPA, and DHA intake in quintiles, with the lowest consumption category as the reference, using Cox proportional hazards models and adjusting for confounding variables. Further, HRs (95% CI) were calculated for the lowest intake categories (0–5th percentile), with the middle quintile category as the reference. A regression