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Systematic review and meta-analysis of omega-3-fatty acids in elderly patients with depression



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ABSTRACT

One of the typical symptoms of a psychological crisis is depression, an increasing concern in the elderly population. Although omega-3-polyunsaturated fatty acids (PUFAs) are reported to be promising nutrients for treating depression, currently, there are no systematic reviews or meta-analyses of randomized control trials that provide critical evidence regarding the potential benefits of omega-3 fatty acids in elderly patients with depression. This analysis was conducted to provide evidence for the clinical application of omega-3 fatty acids in the treatment of depressive symptoms of elderly subjects older than 65 years. Seven databases were searched from their inception date until September 2016. Following this search, 6 studies were selected, which included 4605 patients (mean age, 76.97 years; male-female ratio = 3752:853; mean dose of omega 3 intake, 1.3 g/d). These results were divided into 2 categories: well-being mental health group and depressive group. In the well-being mental health group, the Hedges q was 0.12 (95% confidence interval, -0.05 to 0.29), which indicated no significant effect of n-3 PUFA supplementation on depressed mood compared with placebo. In the depressive group, the pooled Hedges g was -0.94 (95% CI, -1.37 to -0.50]) for the random-effects model, which indicated a large effect of n-3 PUFA supplementation on those with depressed mood compared with placebo. Although this review shows that omega-3 fatty acids are effective in the treatment of elderly depressed patients, the benefits of omega-3 fatty acid supplementation were significant only in the elderly patients with mild to moderate depression.

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Abbreviations: ALA, α -linolenic acid; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GDS, Geriatric Depression Scale; PUFAs, polyunsaturated fatty acids; RCT, randomized control trial.

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1. Introduction

Psychological crises have emerged as serious social problems in elderly individuals, likely due to increased life expectancy and social changes, such as the increased prevalence of living alone. One of the symptoms of a psychological crisis is depression. Omega-3-polyunsaturated fatty acids (omega-3 PUFAs), which cannot be synthesized efficiently in the human body, are reported to be promising nutrients for treating depression [1]. The omega-6 series PUFAs are derived from linoleic acid (18:2), and the omega-3 series are derived from α -linolenic acid (ALA; 18:3) [2]. The omega-3 PUFAs eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are abundant in flaxseed oil, perilla oil, purslane, and fish oils and are major constituents of all cell membranes. Depleted omega-3 fatty acid levels in red blood cell membranes, particularly DHA, which accounts for 40% of membrane phospholipids in the brain, have been reported in patients with depression [3,4]. The possible mechanisms for the neuroprotective effect and therapeutic value of omega-3 fatty acids in depression include their modulation of brainderived neurotrophic factor and their cAMP-response element binding protein expression, which occurs by suppressing proinflammatory cytokines [5]. Furthermore, omega-3 fatty acids enhance serotonergic and dopaminergic neurotransmitter release and also decrease production of inflammatory eicosanoids [6]. Omega-3 fatty acids have been effective in randomized control trials (RCTs) focusing on patients with bipolar disorder, whereas no efficacy was found for those who have depressive symptoms in young populations and perinatal depression [7]. The biological mechanism in which omega-3 fatty acids influence depression is reported to be the potential interaction with the serotoninergic and dopaminergic transmission, including uptake and receptor function. The membrane change induced by omega-3 fatty acids may affect the actions of neurotransmitters, thus altering the regulation of dopaminergic and serotonergic neurotransmission, which is

dysfunctional in depressed patients [8]. Furthermore, the antiinflammatory effect of omega-3 fatty acid has been long recognized in that the eicosanoids produced from omega-3 fatty acids play a role in inflammation and regulation of immune function. Omega-3 fatty acids may exert significant influence in major depression via cytokine modulation. Cytokines, including interleukin-1 β and interferon- γ , as well as tumor necrosis factor- α , can have direct and indirect effects in the central nervous system [9]. An animal study showed that dietary omega-3 fatty acids regulate signal transduction and gene expression and also protect neurons from apoptosis by reducing oxidative stress [10]. Several studies have shown an association between omega-3 PUFAs and depression in elderly subjects [11-14]. However, despite the fact that RCTs and systematic meta-analyses have shown the potential application of omega-3 PUFAs in different populations, including children and pregnant women with depression, the data available regarding the association between depression and elderly individuals older than 65 years are still inadequate [15-18].

There are several studies reporting that omega-3 fatty acids can contribute to the treatment of depression in elderly individuals and that supplementation with omega-3 PUFAs reduces the occurrence of depressive symptoms in elderly female patients [11,19]. However, the depressive symptoms in elderly patients who had experienced a myocardial infarction and consumed EPA, DHA, and/or ALA did not differ significantly from those who received a placebo [20], and supplementation with fish oil did not increase the general psychological wellbeing of an older population [21]. No systematic reviews or meta-analyses of RCT studies have provided critical evidence regarding the potential benefits of omega-3 fatty acids in elderly patients with depression. This review was conducted to provide evidence on the clinical application of omega-3 fatty acids in the treatment of depressive symptoms in elderly subjects older than 65 years and to compare these results with those of placebo. We included RCTs that used the Geriatric Depression Scale (GDS) to measure depressive symptoms (Table 1).

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