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Case Report

CASE REPORT

Insomnia and exacerbation of anxiety associated with high-EPA fish oil supplements after successful treatment of depression

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Abstract

A 54-year-old male consulted his general practitioner for increasing general anxiety and mild panic attacks despite effective treatment for recurrent major depressive disorder, which included a fish oil supplement enriched in eicosapentaenoic acid (EPA). The patient would awaken suddenly at night with shortness of breath and overwhelming worry. During the daytime, he felt a general, nonspecific anxiety and frequently experienced sympathetic activation upon confronting routine challenges. He also experienced dyspnea-induced feelings of panic. He reported that he stopped taking the fish oil supplements after several more months of symptoms, and his anxiety and insomnia then largely disappeared. Several weeks later, he resumed consumption of high-EPA fish oil at the prior dosage for 2 days. On both nights, the patient reported nighttime awakening similar to the previous episodes, followed by daytime agitation. Since halting the fish oil supplements, the anxiety and insomnia have not returned and his depression remains in remission.

INTRODUCTION

Long-chain omega-3 polyunsaturated fatty acids (ω-3 PUFAs) are the key ingredient in fish oil nutritional supplements and evidence exists for their benefit to both cardiovascular and psychiatric health [1, 2]. Eicosapentaenoic acid (EPA), in particular, has been implicated in improving mood disorders [3] and EPA-enriched fish oil preparations are available. Sales in fish oil supplements are in the billions of dollars (US) annually and clinicians are increasingly likely to encounter patients who are regularly taking these supplements. Adverse events related to fish oil supplements are rarely reported and are described as mild to moderate [2, 4].

CASE REPORT

The patient is a 55-year-old male employed as a professor in the USA. At Age 42, he consulted his general practitioner for major depressive disorder and was prescribed fluoxetine, eventually titrated to 40 mg. Pharmacotherapy combined with psychotherapy generally relieved the worst episodes of depressive disorder, but occasional relapses occurred for the next 10 years or more. On at least three occasions, the patient discontinued the fluoxetine when the depression was in remission, but symptoms returned within a few months each time and he resumed taking the medication. When he was 46, his general practitioner suggested adding fish oil supplements to his regimen, particularly those that

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are enriched in EPA, at a dose of 2–3 g/day total lipids. He began taking with morning meals two 1-g softgels per day of fish oil that contained 6 : 1 EPA : DHA (docosahexaenoic acid, 500 mg EPA per softgel). The patient reported that the supplements seemed to noticeably relieve his depressive symptoms. He continued taking the same brand of high-EPA fish oil daily for 8 years (Metagenics 'EPA 500 Concentrate', formerly named 'EPA : DHA 6 : 1') and while the depressive episodes did not completely abate for several more years, they became shorter in duration and more manageable. At Age 54, he had not experienced a significant relapse for over a year so he once again tapered off the fluoxetine. Of note, until this time he had not reported any significant anxiety symptoms. The patient exercises regularly and is in excellent health. Other significant history includes asthma that is well controlled and a cerebral aneurysm successfully treated with endovascular coiling at Age 52. He uses an albuterol inhaler for rare exacerbations of asthma, usually during upper respiratory tract infections, and takes a daily multivitamin. He is medically literate and was cared for by two successive clinicians (including L.B.B.) in the same medical office for more than 20 years.

Six months after stopping the fluoxetine, the patient reported that he had recently begun experiencing gradually worsening insomnia and general anxiety. He often awakened after 2 or 3 h of sound sleep, sometimes with shortness of breath, and was then unable to stop ruminating about possible catastrophic scenarios. On some occasions, he felt so uncomfortable that he was forced to arise to take up reading for an hour or more until he could resume sleep. During the day, he sometimes felt overwhelmed and would experience a flush of alarm, during which his heart rate increased and he began to perspire. On several occasions, exercise-induced dyspnea triggered strong feelings of panic, most acutely when bicycling at high elevations.

The patient mentioned that he had recently run out of his fish oil supplements and seemed to feel better for the few days before he was able to purchase a new bottle. However, he felt that his remission from depression was due in part to these supplements so he continued to take them daily at the same dose. He was prescribed lorazepam for his anxiety. After 6 more months of the anxiety symptoms and insomnia, he stopped taking the fish oil supplements altogether. Within days he felt noticeable relief. He was much more at ease during the day and he could sleep through the night without significant awakenings. He stated that after he had been largely anxiety-free for several weeks, he experimented by resuming the supplements at the same dose as previously for two mornings. On both subsequent nights, and for one additional night, around 2 a.m. he suddenly became fully awake and could not resume sleep for at least an hour. While he did not experience feelings of doom on these awakenings, his thoughts were racing and he was again forced to arise and read for an hour or more. On the following days, he felt agitated and uneasy, which he said was typical when he did not get enough sleep. Two days after the trial ended, he was sleeping well again. At the time of this writing, the patient reports that he remains largely free of anxiety and insomnia. He also reports that he has not experienced significant depressive symptoms either.

DISCUSSION

There is mounting but somewhat conflicting evidence that fish consumption and a diet rich in long-chain omega-3 fatty acids may decrease the risk of depression and anxiety [2, 3, 5–8]. Interestingly, a large prospective cohort study found a U-shaped relationship between ω-3 PUFA consumption and mental disorders, with only the intermediate, but not the lowest and highest, levels of ω-3 PUFA intake reducing the risk of depression and anxiety [5]. In another study, a high-EPA regimen reduced depressive symptoms only in patients without comorbid anxiety [8]. The consumption of fish oil supplements (up to 2 g total EPA + DHA per day) has been recognized as safe and potentially beneficial by the American Heart Association and few adverse events have heretofore been associated with their consumption [9]. However, individual responses to any substance can vary from person to person. We provide here the first report known to us where omega-3 fatty acids are associated with an increase in insomnia and anxiety symptoms. Questions that arise from this case include why the apparent earlier benefits of the fish oil changed to deleterious effects after resolution of the depression and whether the latter effects were specific to high-EPA fish oil. Perhaps the patient's increasing age played a role in the change. Consumers and clinicians should be aware of potential idiosyncratic adverse events to any substance as widely consumed as ω-3 PUFAs.

CONFLICT OF INTEREST STATEMENT

None declared.

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