Use of Omega-3 Polyunsaturated Fatty Acids as Augmentation Therapy in Treatment-Resistant Schizophrenia

To the Editor: Fish oil supplements containing omega-3 fatty acids are among the most commonly used nutraceuticals,[1] and while their role as augmentation therapy has been studied in schizophrenia, their benefits are not as clear in treatment-resistant cases. We present a case report of a treatment-resistant patient with schizophrenia who achieved remission with omega-3 fatty acid supplementation.

Case report. Mr A is a 52-year-old Mexican man of white ancestry diagnosed with schizophrenia during his early 20s. According to his family and historical records, he struggled during the initial 5 years of his schizophrenia diagnosis with poor response to several trials of typical antipsychotics and 2 complete trials of electroconvulsive therapy in the context of numerous inpatient treatments. He achieved partial remission with clozapine for approximately 15 years with no blood count abnormalities or impairing side effects. However, negative symptoms presented insidiously, and he became severely impaired, meriting institutionalized care for the next 5 years.

We received an interconsultation 3 years ago after he suffered an acute pulmonary embolism secondary to deep vein thrombosis that required a 5-day stay in the intensive care unit (Brief Psychiatric Rating Scale[2] [BPRS] score = 76). Clozapine 600 mg was suspended, and Mr A was switched to haloperidol 20 mg with partial response in hallucinatory behavior and disorganization (BPRS score = 62) but poor response to negative symptoms and extrapyramidal side effects. Several treatment strategies were implemented, including switching to amisulpride 800 mg (8 weeks), asenapine 20 mg (8 weeks), and risperidone 6 mg. The latter was better tolerated, and after 8 weeks of treatment, we started a flupentixol 20-mg augmentation trial; this last option proved the most beneficial (BPRS score = 44).

A year ago, we started omega-3 fatty acid supplementation (eicosapentaenoic acid [EPA] 2,936 mg/day, docosahexaenoic acid [DHA] 1,068 mg). After 4 weeks, we observed an important increase of speech quantity and content. After a 10-week period, Mr A started taking care of himself with little help, drawing, having complex conversations, having more of an appetite, and visiting church and restaurants with help (BPRS score = 20). He presently remains in this state. Mr A and his family agreed to share his case.

Omega-3 polyunsaturated fatty acids (PUFAs) are essential substrates of neuronal membrane metabolism and redox regulation.[3] Abnormalities in omega-3 PUFA concentrations contribute to increased inflammatory states in response to psychological stress, potentially contributing to psychiatric disorders.[4,5]

Omega-3 PUFA supplementation in schizophrenia has shown positive results in 3 clinical trials.[6–8] In contrast to Mr A's case, patients were not treatment-resistant and were younger with significantly shorter illness duration.[6–8] Our observation of beneficial effects of omega-3 PUFAs in residual symptoms also contrasts with negative findings by Fenton and colleagues[9] in a randomized, double-blind, placebo-controlled clinical trial of supplementation for cognitive impairment and residual symptoms. Studies by Bentsen et al[10,11] may hold the key to this discrepancy, as they found a bimodal distribution of omega-3 PUFAs in patients with schizophrenia and different response to supplementation depending on baseline measures. We hypothesize that some, but not all, treatment-resistant patients with omega-3 PUFA deficiencies may benefit greatly from its supplementation. Unfortunately, we did not measure baseline levels in our patient.

The most promising use of omega-3 PUFAs in recent schizophrenia literature explores augmentation therapy in individuals at ultra–high risk for psychosis[12–15] or after a first-episode psychosis[16,17] with predominantly positive results. Successful preventive measures in patients prone to psychosis will hopefully reduce our need to study treatment-resistant patients like Mr A.

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