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COMPARATIVE STUDY OF OLANZAPINE AND OLANZAPINE AUGMENTATION ALONG WITH OMEGA3 FATTY ACIDS IN THE MANAGEMENT OF SCHIZOPHRENIA

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Abstract

Schizophrenia is a multifaceted and persistent mental health condition marked by hallucinations, delusions, and emotional and social disconnection. While antipsychotic medications have shown efficacy in managing symptoms, researchers continue to explore innovative treatment approaches. This study examined the potential advantages of combining olanzapine with **Ω**-3 fatty acids. Using a randomized controlled design, the research divided 45 individuals with schizophrenia, already stabilized on olanzapine, into three groups: one receiving olanzapine alone, another receiving olanzapine with **Ω** -3 supplements and a third group comprising healthy individuals prone to stress. By comparing the outcomes across these groups, this study aimed to shed light on the potential benefits of omega-3 fatty acids as an adjunct treatment for schizophrenia.This six-month study employed the PANSS scale for assessment, yielding remarkable outcomes. Regular follow-ups every four weeks revealed that the first group, receiving olanzapine alone, showed no significant improvement, with symptoms remaining stable but not worsening. In contrast, the second group, receiving olanzapine with **Ω**-3 supplements, demonstrated substantial progress, with notable improvements in both positive and negative symptoms, as well as general physiological symptoms. Seven out of 30 parameters showed significant results, as measured by the PANSS scale. The third group, comprising healthy individuals receiving **Ω**-3 fatty acids, exhibited satisfactory responses, with improvements in overall symptoms, and four parameters reflected significant responses. The study's preliminary findings suggest that the combination of olanzapine and **Ω**-3 fatty acids led to greater reductions in PANSS total scores compared to olanzapine alone, indicating a potential benefit of **Ω**-3 fatty acids in mitigating the severity of schizophrenia symptoms.The study's results support the possibility of **Ω**-3 fatty acids as a supplementary treatment to enhance the effectiveness of olanzapine in managing schizophrenia. Schizophrenia is a complex and chronic mental health condition characterized by hallucinations, delusions, and emotional and social disconnection. Although antipsychotic medications have shown promise in alleviating symptoms, researchers continue to seek innovative treatment approaches. This study explored the potential benefits of combining olanzapine

with **Ω**-3 fatty acids in a randomized controlled trial. Forty-five individuals with schizophrenia, already stabilized on olanzapine, were divided into three groups: one receiving olanzapine alone, another receiving olanzapine with **Ω**-3 supplements, and a third group consisting of healthy individuals prone to stress. Over six months, participants were assessed using the Positive and Negative Syndrome Scale (PANSS). The outcomes were notable, suggesting that **Ω**-3 fatty acids may be a valuable adjunct treatment for schizophrenia, enhancing the management of symptoms and improving overall well-being. However this is one of the preliminary studies on Omega-3 fatty acids for the management of schizophrenia, further studies are suggested for better insight.

Keywords: Schizophrenia, Hallucinations, Antipsychotic Medications, Olanzapine, Olanzapine Augmentation, **Ω**-3 Fatty Acid, PANSS.

Introduction: Schizophrenia is a complex psychiatric disorder with a strong genetic component, and its prevalence is increasing due to advances in molecular genetics technology (Legge, 2021). According to recent data, the incidence rate has risen to 15.2 per 100,000 individuals over the past seven to eight years, with a median male-to-female ratio of 1:1.4 (Sommer, 2020). Notably, gender differences play a significant role in the distribution and manifestation of this mental health condition. The onset and course of the disease vary between males and females, which may influence the underlying causes and symptoms. For instance, females are more likely to experience depressive symptoms, while males tend to exhibit more negative symptoms. Furthermore, females tend to respond better to treatment and have lower mortality rates, which may be attributed to differences in substance abuse patterns between genders.The distribution of schizophrenia incidence rates exhibits asymmetry, with a concentration of high rates causing a skewed distribution. Focusing on the middle 80% of rates, the incidence of schizophrenia varies across a fivefold range, spanning from 7.7 to 43.0 per 100,000 individuals. As a severe and chronic mental health condition, schizophrenia affects millions globally, causing significant distress and impairment in various aspects of life. It poses substantial challenges for individuals and their families. Pharmacological interventions, primarily antipsychotic medications, are the mainstay of treatment, aiming to manage symptoms and prevent relapse. Schizophrenia has emerged as a significant public health concern worldwide, with cases increasing daily, particularly among males (Dong, 2022). Additionally, research has linked schizophrenia to other non-motor complications, such as Parkinsonism (Cole D Sang, Aidan F Mullanin, 2022). Recent research has revealed that schizophrenia tends to affect young men more frequently and severely. Several risk factors contribute to this, including a family history of the disorder, complications during or after pregnancy, advanced parental age, urban upbringing, childhood trauma (such as bullying), substance abuse, and adult-life challenges (Simona A Stilo, 2022). Furthermore, schizophrenia is now recognized as an inflammatory disease, with numerous human and animal studies highlighting the central role of inflammation (Filiou, 2014). Elevated levels of pro-inflammatory markers, like cytokines, have been detected in the blood and cerebrospinal fluid of schizophrenia patients (Michaela). In terms of pathophysiology, Guillane Ford and Christophe Lancon (2020) suggested that inflammation plays a fundamental role in the onset and progression of this psychotic disorder. Notably, the peripheral blood profile of schizophrenia patients exhibits increased levels of both pro-inflammatory and anti-inflammatory cytokines, with Interleukin-6 being the most elevated. Other cytokines, such as Interleukin 1, Tumor Necrosis Factor-alpha, and IFN, also contribute to this inflammatory process.Schizophrenia is a chronic and debilitating mental health condition that can significantly impact an individual's thoughts, behaviors, emotional expressions, and relationships (Smitha Bhandari, MD, January 21, 2022). The disorder tends to affect males in their early teens and females in their twenties and thirties (Sanjana Gupta, April 2022). With a prevalence of less than 1% in the US population, schizophrenia's symptoms include delusions - false beliefs not based in reality (Cleveland Clinic, 2022) - and hallucinations, which are imaginary experiences that others cannot perceive. Hallucinations can be auditory, visual, olfactory, gustatory, tactile, or somatic, and may involve multiple senses. The main symptoms of schizophrenia are categorized into positive,

negative, and cognitive symptoms (Oepen G, 1994). Positive symptoms include hallucinations and delusions, while negative symptoms encompass blunted emotions, difficulty experiencing pleasure, and cognitive symptoms involve attention deficits (Mardor SR, J Clin, 1996).

Objectives of Research:

To optimize the benefits of omega-3 fatty acids in managing psychiatric conditions like schizophrenia and other mental health disorders, it is essential to improve access to these polyunsaturated fatty acids for underserved communities. Additionally, increasing awareness about the role of omega-3 fatty acids in reducing the risk of diabetes, infertility, and weight gain can lead to better health outcomes. As this research area remains unexplored in our country, this study aimed to bridge such gap and highlight the implications of omega-3 fatty acids in mental health treatment, paving the way for future research and interventions.

Material and Methods:Scales for Schizophrenia (PANSS Scale).

The Positive and Negative Syndrome Scale (PANSS) is the gold standard for evaluating the effectiveness of antipsychotic treatments. Schizophrenia is such a complex neuropsychiatric disorder which is attributed by the symptoms like hallucinations & delusions, as well as emotional blunting and disinterest in one's surroundings. The PANSS scoring system enables clinicians to differentiate between positive and negative symptoms, facilitating a more accurate diagnosis and prognosis. While antipsychotic medications can effectively manage positive symptoms, negative symptoms are more resistant to treatment and often lead to long-term morbidity and functional impairments in individuals with schizophrenia. The PANSS scale, developed by Victor Peralta and Manual J. Cuesta 1994, independently assesses positive and negative symptoms, allowing researchers to measure and monitor their severity. Its reliability and validity have made it a widely used tool in research settings (Journal of Addiction Research and Therapy 8, 2017 by SunetaKumari, Mansoor Malik, Christina Florival, PartanManalai).Sofia Papa conducted a study in 2023 to assess the efficacy of antipsychotic medications in reducing pessimistic symptoms, utilizing the Positive & pessimistic Syndrome Scale (PANSS). This assessment tool consists of 30 items, each with a precise definition and a 7-point rating scale that ranged them from 1 to 7 indicating absent to Extreme. The PANSS extensively validated as a reliable instrument for evaluating schizophrenia symptoms, encompassing positive, negative, and psychopathological features. This comprehensive interview-based assessment evaluates the existence and brutality of positive & negative manifestations, in addition to general psycho-pathology in the individuals having schizophrenia. The 30 items were subdivided into 3 subclasses: 7 of them had positive symptoms as well as 7 have negative symptoms while 16 items contain general psycho-pathological symptoms. Symptom severity was based on the 7-point scale, with probable ranges from 7-49 for positive & negative scales and for general psycho-pathological manifestations it were 16-112. The predominance of one syndrome over the other can be determined using bipolar indexing, which yields a range of -42 to +42.

Diagnosis of schizophrenia:

According to the American Psychiatric Association, there is no single definitive test for diagnosing schizophrenia. Instead, a comprehensive diagnostic approach involves:

Clinical histories & physical exam

Scheduled blood test

Imaging technological studies (such as CT or MRI scans)

Cerebrospinal fluid (CSF) analysis (in severe cases)

Brain activity testing, like electroencephalography (EEG)

These tests can help support a diagnosis and rule out other conditions with similar symptoms.

Results:
A paired t-test was employed for this comparative study. The 30 parameters of the PANSS scale were analyzed for all three groups. For the first group, data analysis revealed that all parameters remained stable, with no worsening of symptoms. In contrast, the second group showed significant improvements in 7 out of 30 parameters (P2, P3, N1, N2, N3) after receiving olanzapine with omega-3 fatty acids, whereas olanzapine alone did not yield significant improvements. Notably, the control group exhibited significant responses to omega-3 fatty acids in parameters P3, P6, P7, N3, N4, and all G. Following the post-hoc Turkey test, significant results were observed in patients receiving both olanzapine and omega-3 fatty acids, as well as those receiving omega-3 fatty acids alone. However this is the preliminary study on Omega-3 fatty acids in the treatment of schizophrenia and further studies are suggested for better insight.

DISCUSSION

The prevalence of mental health issues is escalating daily, significantly impacting our daily lives, thought patterns, relationships, emotions, and overall well-being. Adverse social, environmental, financial, and emotional factors contribute to the development of mental disorders. A range of mental health issues exist, including anxiety, depression, and bipolar disorders. Schizophrenia, a severe, chronic, and complex mental health condition, is a growing concern that many psychiatrists encounter in their clinical practice. This debilitating condition affects individuals' thoughts, emotions, and behaviors, causing significant distress. Positive symptoms include delusions, hallucinations, hostility, and grandiosity, while negative symptoms encompass social and emotional withdrawal, communication difficulties, and cognitive impairment. General psychopathological features include tension, anxiety, guilt, lack of cooperation, and social withdrawal. The Positive and Negative Syndrome Scale (PANSS) is a diagnostic tool used to assess the efficacy of treatments for schizophrenia and other mental health conditions.In the realm of treatment modalities, a combination of psychotherapy, rehabilitative services, and atypical antipsychotics like olanzapine has proven effective due to its relatively low incidence of extra pyramidal effects. Olanzapine's mechanism of action involves targeting both dopamine and serotonin receptors. However, it also has several adverse effects, including weight gain, which increases the risk of developing diabetes mellitus and infertility. On the other hand, omega-3 fatty acids, which are essential but not produced by the body, offer numerous benefits when obtained through supplementation or dietary sources like fish (tuna, salmon, trout), seeds (flax, rapeseed, walnut, chia, hemp), and soybean oil. These polyunsaturated fatty acids boast anti-inflammatory properties, immune-boosting effects, and support brain function and development. Additionally, they are rich in calcium, promoting bone health and reducing the likelihood of osteoporosis and arthritis. The anti-inflammatory role of omega-3 fatty acids significantly contributes to the treatment and prevention of various psychiatric disorders. This research aimed to explore the potential of omega-3 fatty acids in enhancing the treatment of schizophrenia while mitigating the adverse effects associated with atypical antipsychotics like olanzapine.This research aimed to raise awareness about the remarkable benefits of essential fatty acids, which should be considered for daily supplementation. The rising prevalence of mental health disorders and psychosis, combined with the beneficial effects of these fatty acids, make them an excellent treatment option for psychiatric conditions. For this study, outpatient department cases of schizophrenia were selected. A sample size of 45 patients was chosen, comprising 15 males and females diagnosed with schizophrenia, with no history of co-morbidities, aged between 18 and 45. From January 2023 to June 2023, one group received 10mg of olanzapine orally once daily, with regular four-week follow-ups for six months. Another group, meeting the same criteria, received 10mg of olanzapine orally once daily, along with 500mg of omega-3 fatty acids (Cap Normega) twice daily, with regular four-week follow-ups for six months. Both groups were assessed using the Positive and Negative Syndrome Scale (PANSS) scoring scale.

Additionally, 15 individuals were selected who didn't have a schizophrenia diagnosis but struggled with stress and anxiety, which significantly impacted their daily life activities. This group, with the

same age range and no history of co-morbidities, received Cap Normega with the same dosage. They were monitored every four weeks for six months. The results, analyzed using the paired t-test, were intriguing. The first group, taking olanzapine alone, showed stagnant or non-significant improvements in symptoms when assessed using the PANSS scale. While the standard medication, used for generations, didn't worsen symptoms, it was surprising to see minimal or no improvements. Notably, 7 out of 15 female patients experienced weight gain (as reported by Eric Prommer, MD, in April 2012), but negative and other pathophysiological features remained stable, without worsening.Regarding the second group, which received olanzapine and omega-3 fatty acids for six months with regular four-week follow-ups, the results were noteworthy. Using the PANSS scale, significant improvements were observed in positive symptoms (P2, P3, N1, N2, N3) and general pathophysiological features. Notably, this group did not experience significant weight gain, consistent with Amyrichper's findings (January 2023), which highlighted the benefits of omega-3 fatty acids in promoting brain health and mitigating chronic mental disorders. Similarly, (Mei-Chi Hsu, Young-Sheng Huang, and Wen-Sheng OuYang 2020) demonstrated that omega-3 fatty acid supplementation reduced the conversion rate to psychosis and improved both positive and negative symptoms, with overall general features showing significant improvement in schizophrenia patients. In my research, 21 out of 30 PANSS scoring parameters showed significant results, while 9 parameters did not respond significantly, indicating the crucial role of omega-3 fatty acids in psychiatric and mood disorders, as previously established by (Malcom Peet 2008). Unlike previous studies, which employed meta-analysis and molecular-level approaches with large sample sizes, my study offers a distinct perspective. The third group, comprising 15 individuals with no history of schizophrenia, received only omega-3 fatty acids as a placebo. Surprisingly, they exhibited remarkable results. Since they didn't have schizophrenia, their positive and negative symptom scales were minimal or absent. However, the results revealed significant improvements in negative symptoms (N3, N4) and general pathophysiological features (G). Out of 30 parameters, 19 showed significant results, supporting Urvi Dalal's findings (2021) that omega-3 fatty acids possess unique properties that energize our bodies and mood. Similarly, Puri and Serfaty have also discussed the benefits of omega-3 fatty acids.

Conclusion:

In conclusion, Omega-3 fatty acids have emerged as a crucial component in the management of schizophrenia, a chronic and debilitating mental health condition that is increasingly affecting young adults. While antipsychotic medications are a mainstay of treatment, combining them with omega-3 fatty acids has been shown to reduce symptoms while minimizing the adverse effects of these drugs, as demonstrated by this study. Moreover, these essential fatty acids have proven to be highly effective in promoting mental well-being in healthy individuals, enhancing mood and reducing stress and depression.

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