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Research Article

Exploring the Efficacy of Lurasidone as an Adjunct to Fluvoxamine in the Treatment of **Obsessive-Compulsive Disorder with Comorbid** Restrictive Anorexia Nervosa: A Case Report

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Abstract

Introduction: Eating Disorders (EDs) significantly impact quality of life and social functioning, with varying prevalence rates and a recent rise in diagnosis due to the COVID-19 pandemic. Anorexia Nervosa (AN) frequently co-occurs with Obsessive-Compulsive Disorder (OCD), and this comorbidity leads to more severe symptoms and poorer outcomes. Treatments like Cognitive Behavioural Therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) are commonly used, but tailored interventions are needed for patients with both conditions.

Material and Methods: The study utilized structured clinical assessment tools, psychometric scales, and psychopharmacological agents. Psychometric scales such as SCID-5-CV, EDI-3, EDE-Q, BUT, SCL-90, EDS, CIA, Y-BOCS-II, and CGI were employed for a comprehensive clinical evaluation at baseline and after six months. The assessment included information on the patient's medical and family history, onset of eating disorder symptoms, and details of OCD-related symptoms.

Case Description: This case report describes an 18-year-old woman with severe OCD and restrictive anorexia nervosa (ANr). Initially treated with sertraline and aripiprazole, her regimen was adjusted to include Fluvoxamine and Lurasidone to better manage symptoms. After six months of intensive monitoring and treatment, the patient showed significant improvement in both AN-r and OCD symptoms, achieving clinical remission and increased BMI.

Discussion: The co-occurrence of OCD and AN is complex and often more severe, requiring innovative treatment approaches. Lurasidone, though promising as an adjunctive treatment, needs further research to confirm its efficacy and develop comprehensive treatment guidelines for patients with this comorbidity.

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Introduction

Eating Disorders (EDs) encompass a group of psychiatric syndromes characterised by disordered eating behaviours and psychological disturbances that significantly impact individuals' quality of life and social functioning [1,2]. The reported prevalence of EDs in the general population has shown variability, ranging from 0.1% to 3.8%, with a recent increased incidence of new ED diagnoses, due to COVID-19 pandemic [3]. Anorexia Nervosa (AN) frequently co-occurs with Obsessive-Compulsive Disorder (OCD), with relative prevalence rates reaching up to 62% in subjects with AN. Conversely, 5%-10% of OCD patients report a lifetime history of AN [4-7].

Obsessive-Compulsive Disorder (OCD) is defined by recurrent, intrusive obsessions and compulsions that are time-consuming and not solely centred on concerns about weight and food [8]. Although individuals with Eating Disorders (EDs) may display some OCD-like symptoms, a separate diagnosis of OCD necessitates the presence of obsessions and compulsions unrelated to food, body shape, or weight. Research indicates markedly higher rates of OCD in individuals with EDs and vice versa compared to the general population [9,10].

However, some authors proposed that EDs, especially AN, may fall within the obsessive-compulsive spectrum disorders according to DSM-5 criteria [11,12]. Thus, the relationship between OCD and EDs appears bidirectional, with symptoms of OCD serving as predisposing factors for EDs and vice versa [13]. Both disorders often exhibit worries related to orderliness, excessive compliance, rigidity, and difficulties with set-shifting [14]. The presence of OCD symptoms in comorbidity with EDs is associated with a worse disease outcome, greater severity of symptoms, and longer hospital stays [15,16].

Effective treatments for OCD and EDs include Cognitive Behavioural Therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs). However, clinical trials often exclude individuals with both conditions, highlighting the need for combined treatments. Recent international guidelines recommend CBT as the initial treatment for mild-to-moderate OCD symptoms [17,18]. In more severe cases, adding selective serotonin reuptake inhibitors (SSRIs) to CBT is advised as the first-line treatment [19]. However, a significant proportion of patients may not respond adequately to either CBT or SSRIs alone or in combination. For treatment-resistant OCD (TR-OCD), guidelines suggest a trial of SSRIs for 8–12 weeks before considering a change in drug strategy; if SSRI treatment proves ineffective, the addition of antipsychotics is preferred over switching to a different SSRI [20].

A recent study observed a significant increase in antipsychotic use among youth with AN over the years, rising from 0% in 1992 to 20% in 2015; Olanzapine emerged as the most commonly prescribed antipsychotic, reflecting a preference among clinicians. Efforts to evaluate the efficacy of Olanzapine in the treatment of AN reveal mixed results. While previous meta-analyses have highlighted the uncertainty due to study limitations [21,22], a recent metaanalysis by Han et al [23] indicates that Olanzapine significantly boosts BMI compared to placebos in adult AN cases. However, the efficacy for adolescents remains uncertain due to limited study participants. Obstacles to definitive evidence on Olanzapine's efficacy in AN include scant patient numbers, potential selection biases, and short-term study durations, leaving its long-term effectiveness unclear.

Patients receiving antipsychotics tended to be younger and exhibited more severe illness characteristics, including lower admission BMI and increased comorbidities [24]. Moreover, evidence for Olanzapine's significant impact on AN-psychopathological features, such as excessive concerns about weight gain and obsessiveness, is conflicting [25,26]. In conclusion, current scientific evidence on SE-AN treatments are unfortunately still limited. The aim of this case report is to describe a different treatment that has been proposed to date and their effectiveness on restrictive anorexia nervosa (AN-r) related outcomes. This case report details the treatment of an 18-year-old woman with severe OCD and comorbid restrictive anorexia nervosa (AN-r), who received an SSRI treatment augmented with a low-dose second-generation antipsychotic drug, for six months. The report adheres to the CARE Statement [27].

Materials and Methods

The study has involved the use of structured clinical assessment tools, psychometric scales, and psychopharmacological agents as part of the materials utilised. A comprehensive clinical evaluation was conducted using the following psychometric scales at baseline and after six months: Structured Clinical Interview for DSM-5 Disorders Clinical Version (SCID-5-CV) [28], Eating Disorder Inventory-3 (EDI-3) [29], Eating Disorder Examination Questionnaire (EDE-Q) [30], Body Uneasiness Test (BUT) [31], Symptom Checklist-90 items (SCL-90) [32], Exercise Dependence Scale (EDS) [33], Clinical Impairment Assessment Questionnaire (CIA) [34], Yale-Brown Obsessive Compulsive Scale (Y-BOCS-II) [35], and Clinical Global Impressions Scale (CGI) [36]. The patient's medical history, family history, onset of eating disorder symptoms, and details of symptoms related to OCD were documented.

Case Description

An 18-year-old Caucasian woman with a previous diagnosis of AN-r and OCD due to her severe symptomatological condition

(characterised by severe malnutrition, marked dietary restriction, physical hyperactivity, amenorrhoea for about 2 years, BMI=14.5 Kg/m2), started a residential rehabilitation program at the Regional Residential Centre for Eating Disorders 'Mariconda' in Salerno, Italy. A comprehensive clinical assessment was administered at the beginning of the rehabilitation process; the psychometric scales used were described above (Table 1).

The symptomatology presented by the patient met the DSM-5-TR criteria [37,38] for an OCD [300.3; F42.0] and AN-r [307.1; F50.01]. During the initial assessment, the patient denied having any past or current medical condition, but a severe bradycardia was revealed from cardiology consultation. She also reported not using any medications or tobacco/substances. Her family history was negative for psychiatric illnesses. The onset of her ED was reported at 14 years old, primarily characterised by restrictive behaviours. Her lowest Body Mass Index (BMI) reached 14.8 kg/m2 at the age of 17. The patient, in addition to AN-specific symptoms, described the presence of obsessions and compulsions as extremely distressing, time-consuming and impairing social, family and school functioning, resulting in avoidant behaviour. Such symptomatology was not exclusively related to food as she reported obsessions about study, contamination, self-aggression, fear of feeling inappropriately embarrassed, fear to be responsible for something terrible to happen, fear of losing things, magical thoughts and superstitious obsessions, excessive concerns with illness or disease, intense doubts of not saying the "right thing", intrusive images, words and numbers, She also reported specific compulsions such as excessive or ritualised washing and cleaning, checking (associated with ideas of contamination and fear of making mistakes), rereading, erasing and rewriting, counting, ordering and arranging, excessive list making and mental rituals. The most severe and frequently reported obsessions were those about intrusive images and somatic obsession, the most severe compulsions were body checks, general checking, ordering and arranging.

She early started psychotherapy and psychopharmacological support.

Prior to admission, the patient was already on sertraline and aripiprazole, at a dosage of 100 mg/day and 5 mg/day, respectively; doses were increased up to 200 mg/day and 10 mg/day, respectively, during the first month of hospitalisation. To closely monitor the intensive treatment course, weekly psychiatric, and nutritional visits were scheduled. Once a week, she also started a CBT psychotherapy. Due to the marked physical hyperactivity and the presence of significant brooding thoughts, it was deemed

necessary to modify the pharmacological therapy.

Following a comprehensive clinical and laboratory evaluation, Fluvoxamine, an SSRI of choice for OCD treatment, was initiated. The dosage was gradually titrated up to 100 mg, daily. However, due to persistent physical hyperactivity and incomplete control of OCD symptoms, a further increase to 150 mg was applied. Medical staff avoid suggesting the prescription of clomipramine due to its serious side effects such as irregular heart rhythms.

When Olanzapine was proposed as an adjunctive medication, the patient refused for the potential weight gain, sedation and drowsiness. As an alternative, Lurasidone was prescribed as add-on therapy, given its lower risk of weight gain with respect to Olanzapine. Furthermore, Lurasidone is considered to have a more favourable cognitive side effect profile compared to many other antipsychotic medications. Due to the individual's low weight, a dosage of 37 mg per day was chosen for administration, right after the evening meal. This detailed monitoring allowed a comprehensive assessment of the patient's progress, capturing changes in OCD and AN-r symptoms over time. Such a thorough evaluation provided valuable insights into the effectiveness of the treatment regimen and underlines the importance of a multidimensional assessment in complex cases of psychiatric comorbidity.

Results

After six months of inpatient treatment, a clinical response to AN-r and obsessive thoughts and compulsions was observed; symptoms that improved more significantly were drive for thinness, bulimia, eating disorder risk, interpersonal insecurity, interpersonal alienation, interoceptive deficits, dysregulation, fear of maturity, interpersonal problems, emotional problems, general adaptation, avoidance, compulsive, selfmonitoring, depersonalization, global severity index, obsessive compulsiveness, interpersonal hypersensitivity, anxiety and relational distress (Table 1). At the follow-up visit, a full clinical remission, defined as having mild to no symptoms on the CGI-S, associated with a Y-BOCS score of ≤ 14, was achieved. This improvement was further supported by a significant increase in her BMI, indicating a reversal of the malnutrition she was experiencing upon admission. The patient, indeed, entered the treatment with a weight of 37 Kg and a BMI of 14.8 Kg/m² (amenorrhea, lasting 9 months, started at a weight of 45 Kg), while she recovered her menstrual cycle after three months of treatment, at a weight of 41.5 Kg and a BMI of 16.6 Kg/m². At the time of discharge, she reached her natural weight of 47 Kg, with a BMI of 18.9 Kg/m² (Figure 1).

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	T0	T1	Items improved more significantly
EDI- 3	98	61	• drive for thinness
			• bulimia
			• eating disorder risk
			• interpersonal insecurity
			• interpersonal alienation
			• interoceptive deficits
			• emotional dysregulation
			• fear of maturity
			• interpersonal problems
			• emotional problems
			general adaptation
EDE-Q	5,2	2	all except "concern for the body"
BUT	5	3,6	• avoidance
			• compulsive self-monitoring
			depersonalization
			• global severity index
SCL-90	75	44	obsessive compulsiveness
			• interpersonal hypersensitivity
			• anxiety
			relational distress
EDS	5	1	
CIA	47	13	
Y-BOCS-II	32	14	
CGI	4	2	

Table 1: Psychometric evaluations.

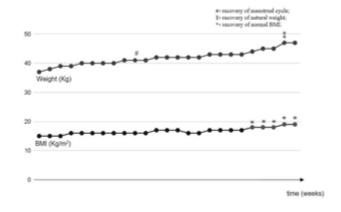


Figure 1: Weight Monitoring.

Discussion

OCD and AN often co-occur at rates higher than expected by chance, with studies indicating that 10% to 40% of individuals with one condition also experience the other [39]. When OCD and AN coincide, research suggests that the combined presentation can be more severe and pose greater challenges for treatment. Obsessive thought patterns and compulsive behaviour can significantly hinder recovery from AN. In the field of OCD treatment, Lurasidone has emerged as a promising avenue of exploration, albeit with significant limitations. Traditional therapies like SSRIs and cognitive behavioural therapy may not always suffice for individuals with OCD. Lurasidone presents a potential alternative, particularly for those who have not experienced sufficient relief with standard treatments.

Lurasidone, a medication primarily used for schizophrenia and bipolar disorder [40,41], has emerged as a potential treatment option for OCD (20). While it lacks official approval for OCD treatment, its mechanism of action and some positive results in specific patient groups warrant further exploration. Unlike some other antipsychotics, Lurasidone minimally affects receptors linked to drowsiness, weight gain, and cognitive impairment. This is beneficial for patients, especially those with OCD, as it reduces bothersome side effects that often lead to discontinuation of treatment. By avoiding significant sedation, weight gain, and cognitive impairment, Lurasidone improves treatment adherence and overall quality of life, making it an attractive option for longterm therapy. Several case studies have hinted at its efficacy, especially as an adjunct therapy for individuals resistant to SSRIs alone. However, substantial gaps in knowledge persist. The absence of large-scale studies specifically designed to evaluate the efficacy of Lurasidone in people with OCD and AN makes it difficult to establish treatment guidelines. Additionally, understanding the long-term safety profile of Lurasidone, particularly when used in conjunction with other medications, is crucial.

While Lurasidone shows promise as an additional treatment for OCD, particularly in refractory cases, further research is mandatory. In line with our case report, Orsolini et al. [20] examining the augmentation of Lurasidone with Fluoxetine in a patient diagnosed with Obsessive-Compulsive Disorder (OCD) and Anorexia Nervosa-restricting subtype (AN-r), revealed promising outcomes [20]. This two case report, emphasize the necessity for larger-scale investigations to substantiate the effectiveness of this therapeutic strategy across diverse patient groups. The combination of Lurasidone and Fluoxetine demonstrated encouraging results in alleviating symptoms associated with OCD and AN-r in the reported case. However, the study's single-case design inherently limits its ability to generalise findings to a wider patient population. Individual variations in response to treatment, as well as specific characteristics of the patient in the study, such as age, gender, and

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severity of symptoms, may influence outcomes and efficacy.

Conclusion

In light of the challenging comorbidity between OCD and AN, the study highlights the potential advantages of incorporating Lurasidone as an adjunct therapy, especially in cases resistant to standard treatments like SSRIs. While Lurasidone shows promise in treating OCD symptoms, further research and large-scale clinical trials are imperative to validate its efficacy and safety profile, particularly in individuals with comorbid conditions such as AN. By establishing broader applicability and understanding potential nuances in treatment response, the study can inform clinical practice and enhance treatment guidelines for individuals dealing with the complexities of coexisting OCD and AN. This case report emphasises the necessity for further research to establish comprehensive treatment guidelines and enhance outcomes for individuals facing these challenging mental health conditions.

Conflict of interest: The authors declare no conflicts of interest in relation to the research study conducted, the analysis presented, and the interpretation of the results.

Ethical Guidelines: Informed consent was obtained from all participants, and their rights, well-being, and confidentiality were prioritised throughout the study. All data collected and reported in this study adhere to ethical standards, and any potential conflicts of interest have been disclosed transparently.

Conflict of interest: None of the Authors declare that they have conflicts of interest

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