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RESEARCH ARTICLE

LYBALVI (OLANZAPINE AND SAMIDORPHAN) IN THE MANAGEMENT OF SCHIZOAFFECTIVE DISORDER IN AN ADULT WITH PRADER-WILLI SYNDROME

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Abstract

Prader-Willi syndrome (PWS) is a neurodevelopmental genomic imprinting disorder characterized by obesity, behavioral issues, mental illness, and self-injury. Managing psychiatric symptoms in PWS is a clinical challenge because of significant weight gain associated with antipsychotic medications in an already obese patient population. We report a case of a patient with Prader Willi syndrome and schizoaffecti ve disorder (depressive type) treated with Lybalvi (olanzapine and samidorphan) and followed up after a month with a gradual increase in the dose of olanzapine, leading to the resolution of hallucinations without a significant increase in weight. This case highlights the potential use of Lybalvi for patients with psychiatric illnesses who are overweight, obese, or vulnerable to the hazardous effects of weight gain, including Prader-Willi syndrome. Further research into the use of Lybalvi in vulnerable populations is required to strengthen its association and benefits.

Introduction:-

Prader-Willi syndrome (PWS) is a complex neurodevelopmental disorder [1]. The incidence of Prader-Willi syndrome is 1:15,000 to 1:30,000 [2]. Birth hypotonia is followed by hyperphagia, obesity, and abnormal behavior in children [3]. Other features include developmental delay, learning problems, short stature, mild craniofacial dysmorphism, and endocrine disorders [4]. PWS is either due to a lack of expression of imprinted paternal genes or when both chromosome 15s are inherited from the mother [5]. Specific PWS genetic subtypes may be responsible for specific phenomenology of psychiatric symptoms and behavioral problems associated with the syndrome [5]. Prader-Willi syndrome is frequently characterized by co-occurring behavioral challenges [6]. Aggression, obsessive-

compulsive tendencies (e.g., hoarding food and other items, demanding the same routines and repetitive actions), skin excoriation, temper tantrums, and high risk of self-injury are the most common psychiatric conditions associated with PWS [7]. Individuals with maternal uniparental disomy (mUPD) had a higher incidence of psychiatric illnesses, i.e., about 6.7 per 100 person-years with frequent episodes and recurrences [8]. Psychiatric symptoms may be mood-related symptoms with or without psychotic features in all genetic subtypes of PWS [8]. Schizoaffective disorder (SAD) is a long-term psychiatric condition, often diagnosed in individuals who present with both mood-related and psychotic symptoms [9]. The diagnostic criteria of SAD require the following: 1. A period of illness with a major mood episode co-occurring with schizophrenia, 2. At least two weeks of delusions or hallucinations in the absence of a major mood episode during the lifetime duration of the illness, and 3. Mood symptoms that are present for the majority of the total active and residual illness duration [10].

The psychotic symptoms experienced by patients with PWS are often unusual in manner and difficult to categorize into the current diagnostic classification system [11]. Anxiety, movement disorders, confusion, hallucinations, persecutory delusions, sleep dysfunction, and mood swings are the most common presentations in individuals with PWS [11]. Antipsychotics, lithium, and benzodiazepines have been used to treat mental disorders in PWS patients [12]. SAD is a hybrid of the "schizophrenia spectrum or affective disorders" that clinicians often use to categorize the complex psychotic phenomena observed in patients with this condition [12]. The long-term management of schizoaffective disorder includes a combination of psychopharmacology, such as antipsychotics, mood stabilizers, or antidepressants, and psychotherapy, such as CBT [9]. Paliperidone, recently approved by the FDA, often helps patients operate alongside family therapy, vocational rehabilitation, and other supportive services [13]. Olanzapine has been widely used as an antipsychotic of choice for schizophrenia and other schizophrenia-like disorders, with a common and notorious side effect of weight gain [14]. Samidorphan acts as a modulator that reduces metabolic side effects, with somnolence, dizziness, and headache being common [15]. Here, we present a case of a 23-year-old female, Ms. P, diagnosed with Prader-Willi syndrome and schizoaffective disorder treated with Lybalvi, an olanzapine and samidorphan combination, leading to resolution of symptoms without any weight gain, which might suggest a possible use for this medication in this group of patients and similar ones.

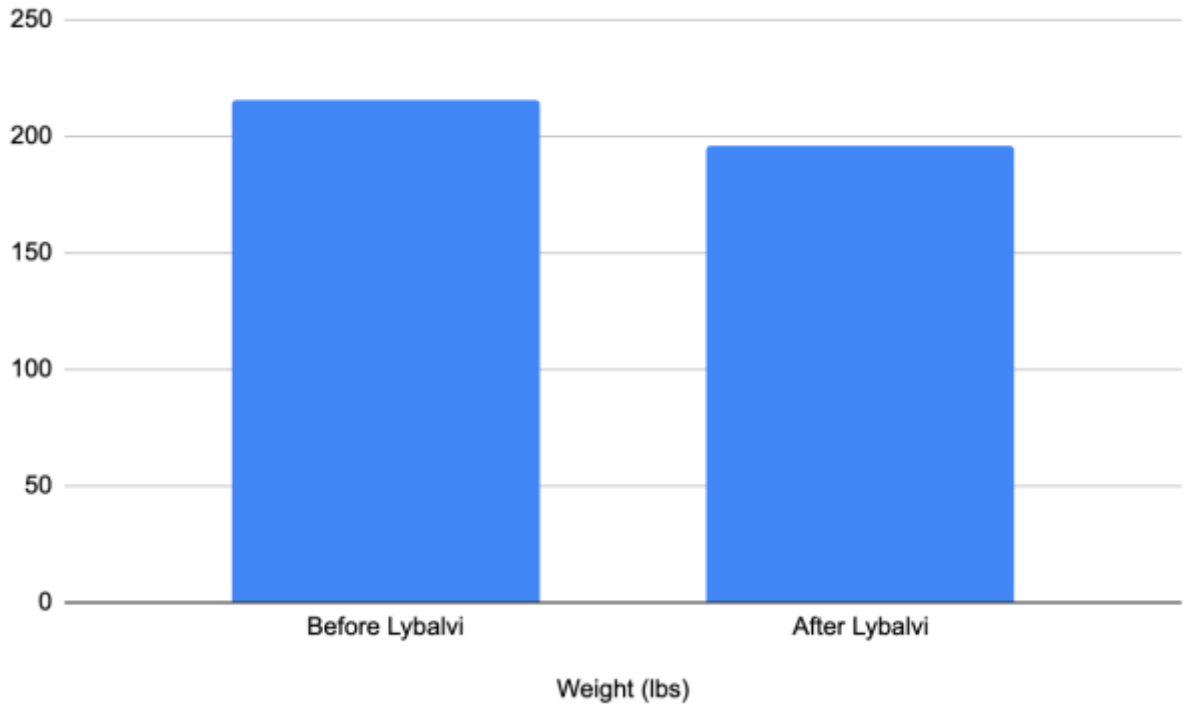
Case Presentation:

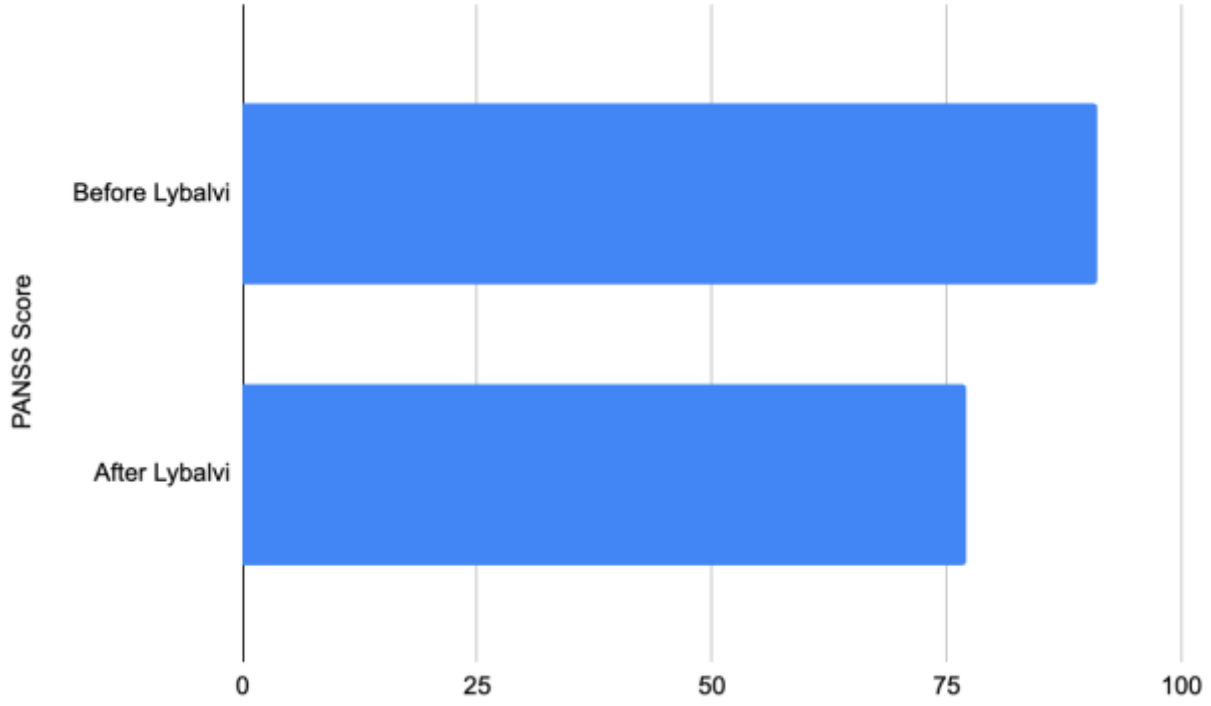
We present a 23-year-old female, Ms. P, with a history of Prader-Willi syndrome diagnosed at 14 months of age, with complaints of hearing voices unheard by others, delusions that she is in immediate danger, and fluctuating episodes of elevated and depressed moods for the past nine to ten years. Her symptoms were acute in onset and episodic in course. It was associated with a decreased need for sleep, followed by decreased interest in her regular activities at home during the episodes. Hallucinations and delusions were present even without mood symptoms for at least a month, and mood symptoms prevailed for the entire course of her illness. Ms. P reported no history of suicidal or homicidal ideation. On a mental status examination, Ms. P appeared older than her stated age, with physical features of PWS. She was cooperative but mildly distracted with slow speech. She described her mood as feeling sad, tearful, crying, and angry. Her affect was restricted. She heard different types of voices all the time, which bothered her even in her sleep. She also reported obsessive and intrusive thoughts and behaviors. She felt helpless, worthless, and hopeless. Insight was poor, and she did not acknowledge her mental illness.

Her perinatal history is significant to her vulnerability to her disorders: her mother's age was 43 at the time of her birth. There is no known family history of psychiatric or any other genetic conditions. Given the characteristic limitations of PWS, Ms. P's mother is her legal guardian and provides essential support for all activities of daily living and vocational needs. During childhood and adolescent years, she presented difficulties adapting to school, displaying frequent tantrums, being oppositional and defiant, having learning difficulties, and having a significant lack of social skills and attention span. She was never diagnosed with attention deficit disorder or psychiatric conditions of the same vein, nor did she receive any treatment in her early years for any associated behavioral problems. She gives no history of substance use.

At the age of 14, she presented with an episode of "weird" behavior while she was at a school camp, where the patient reported hearing voices, not remembering who she was, and claiming that she was in danger, with agitation and aggressiveness. She was initially diagnosed with bipolar disorder at that time and hospitalized for treatment. She was treated with several medications over the years, including lamotrigine 100 mg/day combined with valproate 500 mg/day for almost two years, with no consistent improvement. Topiramate 100 mg/day and lithium 300 mg/day were also tried together after this for more than 4 years, with inconsistent control of her symptoms. Although the mood symptoms were partially controlled, hallucinations and delusions remained persistent.

Before she presented to us, she was on clonazepam, 2 mg/day for more than a year, and lurasidone, 100 mg/day, which she had been using for the past 3 years. She weighed 216 pounds with a BMI of 32 and a PANSS score of 91. After she presented to us, based on the history and examination, schizoaffective disorder was then suspected, and a trial with Lybalvi (olanzapine-samidorphan) was begun, starting on 5-10 mg daily, which showed only mild improvement of her positive symptoms. The dose was then increased to 10-10 mg and, one month later, to 15-10 mg. By the end of the first week of treatment, she reported no hallucinations or delusions. By the second week, the patient displayed a significant improvement in her vocational functioning as well as psychotic symptoms. The parents reported that she was sleeping better without an increase in her appetite. Within a month, her PANSS score improved to 77, and her weight is 196 pounds with a BMI of 31. The patient was followed up monthly for the next three months, showing in all of the visits a consistent absence of positive symptoms (hallucinations) with no change in her weight but a significant reduction in her appetite.





Discussion:-

Prader-Willi Syndrome (PWS) is a severe genetic disorder [4]. It is caused by the loss of paternal gene expression due to paternal gene deletion in the chromosome 15 region (q11-13), maternal uniparental disomy (UPD), or imprinting defects [7]. PWS is the most common cause of life-threatening obesity, in which the patients present with behavioral symptoms including aggression and obsessive-compulsive actions and habits (e.g., skin picking) [12]. Genetic subtypes in PWS affect the behavioral manifestations and their severity [5]. A study showed that patients with paternal gene deletion were more likely to demonstrate predominantly depressive symptoms without psychosis [11]. In contrast, patients with mUPD presented with features of bipolar affective disorder with psychotic features [16].

Although life expectancy for PWS is rising, mortality often occurs in the 30s due to cardiorespiratory complications and the persistent difficulty of managing severe obesity [2]. Patients with PWS often have a reduced quality of life due to the associated behavioral patterns and comorbid psychiatric illnesses [17]. Mental disorders associated more frequently with this condition are schizophrenia, mood disorders, and obsessive-compulsive disorders [18]. Schizophrenia typically begins in the 20s, and symptoms typically involve a combination of hallucinations (often hearing voices), delusions (false, fixed beliefs), and disorganized thinking or behavior. These symptoms are categorized into positive (added behaviors), negative (diminished functioning), and cognitive (impaired thinking, attention, memory/focus). Key signs include social isolation, amotivation, and apathy [10]. More than 50 percent of persons with PWS and psychiatric symptoms had a depressive disorder with psychotic features [19]. The majority of PWS patients with psychiatric illness have atypical mood disorders with or without psychotic features, and fewer have schizophrenia spectrum disorders [16]. In our case, the patient was diagnosed with “schizoaffective disorder, depressive type” with PWS, which is only reported in one other publication [12].

Psychiatric and behavioral conditions associated with PWS often lead to caregiver burden because of their symptoms and management, and there are currently no guidelines about the use of psychotropic medications in these cases [20]. Antipsychotics (e.g., risperidone and aripiprazole), antidepressants (e.g., fluoxetine and sertraline), and mood stabilizers have been implemented in pharmaceutical treatment plans; however, there is limited research regarding the use of psychiatric medications in PWS [21] [22]. Only a few case reports have been documented regarding the use of antipsychotic drugs in PWS [7] [19]. First- and second-generation antipsychotics are being prescribed, but because their safety profiles are overlooked, high rates of extrapyramidal symptoms (EPS), weight gain, and hormonal imbalances have been reported [17]. The use of risperidone and olanzapine has been reported in the literature in the management of a 37-year-old woman with PWS and psychosis, which led to hypothermia [23].

The use of olanzapine as monotherapy or with samidorphan in PWS has not been systematically studied yet, and our case is the first-ever report of such.

Atypical antipsychotics (second-generation) are newer psychiatric medications used to treat schizophrenia, bipolar disorder, depression, and irritability in autism and work primarily by balancing dopamine and serotonin levels, offering a lower risk of movement-related side effects compared to older drugs [24]. Commonly used atypical antipsychotics are Risperdal (risperidone), Abilify (aripiprazole), Latuda (lurasidone), and Zyprexa (olanzapine) [1]. Atypical antipsychotics such as olanzapine lead to weight gain, type 2 diabetes mellitus, and obesity [14]. The early-onset hyperphagia in PWS causes obesity in these patients [18]. The presentations pose a challenge when treating PWS associated with psychiatric illnesses, such as schizoaffective disorder, as presented in our case with atypical antipsychotics. The Clinical Antipsychotic Trials of Intervention Effectiveness (CAITE) study found that olanzapine had a significant improvement in psychiatric symptoms, a longer period of effective treatment, and the lowest discontinuation rate in the management of psychotic symptoms; however, there are concerns about the association of olanzapine with weight gain and metabolic issues [24]. Olanzapine and samidorphan may provide an effective treatment for schizophrenia with a decreased risk of weight gain and other metabolic adverse effects [25].

Samidorphan is a drug that blocks mu-opioid receptors and helps reduce weight gain [26]. It is used in combination with the antipsychotic olanzapine to treat schizophrenia and bipolar I disorder while mitigating associated weight gain [27]. It acts as a modulator with a better safety profile, with somnolence, dizziness, and headache being its commonest side effects [15]. In our case, we were challenged with prescribing an effective antipsychotic medication without increasing the patient's weight. After the failure of the antipsychotic trial with lurasidone, treatment with olanzapine and samidorphan (Lybalvi) was started. Control of symptoms without a significant increase in weight was achieved with this combination. With intrinsic limitations coupled with expectations of the medication's pharmacokinetic profile and behavior, further clinical trials and investigations are recommended to provide reliable evidence that this intervention can help at-risk patients.

Ethical review and consent:
Formal ethical approval was not required for this study under local and institutional regulations. Written informed consent was obtained from the patient to publish this case.

Conflict of interest statement:
The authors have no conflicts of interest to disclose.

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Conclusion:-
This case illustrates the difficulties in diagnosing and treating mental illnesses in the setting of Prader-Willi syndrome. The co-occurrence of PWS and schizoaffective disorder, depressive type, is an uncommon and rarely reported clinical entity, and the lack of treatment guidelines puts psychiatrists in a dilemma. The metabolic profile of PWS, characterized by hyperphagia and a strong predisposition toward obesity, renders the use of conventional antipsychotics particularly hazardous. In this context, the olanzapine and samidorphan combination has emerged as an effective and rational therapeutic choice, providing adequate psychotic coverage while significantly reducing the metabolic risk associated with olanzapine therapy. Our patient's positive outcome contributes to the scientific literature that supports the use of olanzapine and samidorphan in metabolically vulnerable individuals. Further studies are recommended, as case reports such as ours face intrinsic and significant limitations, to establish clear evidence-based recommendations for the use of psychotropic drugs in patients with PWS, with a focus on both efficacy and side effect profiles.

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