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A Pilot Study on the Side Effects of Using Atypical Antipsychotics in Patients with Schizophrenia on Developing Obsessive-Compulsive Symptoms

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ABSTRACT

Aims: This study aimed to investigate the side effects of using Atypical antipsychotics in Patients with Schizophrenia on developing Obsessive-Compulsive symptoms.
Method: In this pre-experimental research, 90 hospitalized patients with Schizophrenia who received Atypical antipsychotics were studied. Yale-Brown Obsessive-Compulsive Scale(YBOCS) was used.
Results: The mean score of the YBOCS test at the first week (before using atypical antipsychotics), one month (after using Atypical antipsychotics), and two months (after using Atypical antipsychotics) was 12.13, 16.26, 22.64.
Obtained data indicates that using Atypical antipsychotics has a significant effect on developing obsessive-compulsive symptoms in patients with Schizophrenia.
Conclusion: Atypical antipsychotics can cause obsessive-compulsive symptoms in patients with Schizophrenia.

1. Introduction

Schizophrenia could be an ongoing condition characterized by positive, negative, and psychological features and symptoms. Schizophrenia could be a complicated, heterogeneous behavioral and psychological feature syndrome that appears to originate from disruption of genetic or environmental factors or cause brain development. (Owen et al., 2016).

Currently, atypical antipsychotics (AAP) are regarded as the most common therapy for Schizophrenia is due to its typical side effects and superior effectiveness. However, there are still some issues to be resolved. Approximately 80% of schizophrenia patients are resistant to treatment, which has led to a growing trend of using AAP Low-risk polypharmacy. (Jeon et al., 2017). In expansion to its impacts on treatment-resistant Schizophrenia, Clozapine has appeared to diminish suicidality, which happens at an expanded rate in patients with Schizophrenia. (Khokhar et al., 2018).

The heterogeneity of the pathophysiology of the different spaces of Schizophrenia requires different medications that are best met by the master utilize of AAPDs at the Current time.

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Pharmacogenetic endeavors are steady with modern proof that different qualities are included within the risk for Schizophrenia and the adequacy of AAPDs. (Meltzer H. Y. et al., 2017).

Psychoneurotic disorder (OCD) is probably related to antipsychotics. However, very little is understood concerning the comparative risks of antipsychotics. (Park et al., 2021).

Drug therapy is the primary treatment for Psychotic disorders such as Schizophrenia. In some cases, positive symptoms (such as delusions and hallucinations) may respond comparatively well to pharmacologic treatment. Negative symptoms typically do not reply to an identical degree. (Hieronymus et al., 2021). Negative symptoms of Schizophrenia include emotional distress, rigidity, alogia, unresponsiveness, and social withdrawal. (Leucht et al.,2017).

There are two types of antipsychotic drugs: typical and atypical, Dopamine D2 receptor antagonists are more potent than atypical agonists, and 5-hydroxytryptamine-A (5-HT2A) receptor antagonists are more potent than typical agonists. (Ballard and Howard, 2006). Risperidone is a receptor antagonist of serotonin, dopamine, and noradrenaline and is authorized to treat mania and bipolar disorders. (Davies et al., 2018).

The atypical antipsychotic olanzapine is approved for the treatment of Schizophrenia and bipolar disorder in adults. There has been evidence that controlling behavioral indications in dementia can be effective. (Calsolaro et al., 2019). Studies indicated that antipsychotic drugs (ADs) could impact oxidative stress estimated with various bio signs in patients with Schizophrenia is disputable and limited. (Dietrich-Muszalska et al., 2021)

Second-generation antipsychotics (SGAs) have been involved in the de novo development and worsening obsessive-compulsive side effects (OCS) in patients with Schizophrenia. Among SGAs, Clozapine, olanzapine, and risperidone are the foremost unmistakable specialists related to these sequelae, concurring with case reports. (Fonseka et al.,2014).

Clozapine can trigger serious OCS. Including aripiprazole with/without Clozapine, measurement diminishment may be a terrific elective to antidepressants for overseeing clozapine-associated OCS. Clinicians should be more watchful about these antagonistic impacts and regulate suitable medications. (Kim et al., 2020)

Atypical antipsychotics displayed a few side impacts, such as metabolic disorder (MetS) and corpulence, which are related to expanded cardiovascular illness risk for schizophrenia patients. In this way, the metabolic impacts of atypical drugs might be related to the untimely mortality watched in Schizophrenia. (Laursen et al., 2012; Mitchell et al., 2013).

It is accepted that second-generation antipsychotics (SGAs), most imperatively Clozapine, might develop or aggravate actuate onset OCS. A few epidemiological and pharmacological contentions believe in this suspicion. (Zink, 2014).

An expansive extent of symptoms of Obsessive-Compulsive Disorder may develop in schizophrenia patients treated with second-generation antipsychotics. However, there is only a little research on this comorbidity's effect. (Biria et al., 2019). One potential clarification of the need for clinical hazard components for developing OCD in antipsychotic-treated patients cases may have been misidentified. Obsessive-Compulsive Disorder (OCD) and Obsessive-Compulsive Symptoms (OCS) are assumed to be highly comorbid with bipolar disorder and Schizophrenia. Comorbid OCD/OCS ascendency the course of Schizophrenia and bipolar disorder. (Sharma, L. P et al.,2019). Obsessive-compulsive symptoms (OCS) are usual in Schizophrenia, with a prevalence ranging from 12 to 25%. Patients with comorbid OCS present more commonly resisting psychotic symptoms. Besides, the appearance and aggravation of OSC are more frequently reported with atypical antipsychotics. (Aissa et al., 2021).

2. Method

2.1. Participants and Procedures

The study was pre-experimental research. The statistical society in this research was all psychiatric hospitals in Tehran. Available sampling was used in this study, and Razi psychiatric hospital was selected as a statistical sample.

The sample size was 90 hospitalized patients with Schizophrenia between 18 and 40 years of age who received Atypical antipsychotics. Yale-Brown Obsessive-Compulsive Scale(YBOCS) was used. OCS symptoms of patients with Schizophrenia were evaluated with the YBOCS scale one week before consumption of antipsychotics and one month and two months after consumption of antipsychotics.

2.2. Measure

2.2.1. YBOCS Scale

The Yale-Brown Obsessive–Compulsive Scale (Y-BOCS) could be a broadly utilized clinician-rated meet to evaluate the existence and seriousness of obsessive-compulsive disorder (OCD). (Alić et al., 2022). The patient's report is used to complete a significant portion of it, and the final grading depends on the interviewer's clinical judgment. The interview is semi-structured and consists of ten items with scores ranging from zero to four. The patient's report and the interviewer's observations during the test determine the score.

Obsessions were assessed using the first five items on this scale.The following five items were used to assess practical obsessions. Unlike many other scoring systems, the YBOCS scale can assess disorder symptoms and obsessive-compulsive disorder severity.

The severity and variance of obsessive-compulsive symptoms were assessed using this scale. The reliability of the testers' scores in this test is assessed to be 0.72- 0.98. (Sajatovik & Ramirez, 2003). Obsessive-compulsive disorder is represented by cutting points 16 and up. (Koran,1999).

2.2.2. Results

The mean score of the YBOCS test at the first week (before using atypical antipsychotics), one month (after using Atypical antipsychotics), and two months (after using Atypical antipsychotics) was 12.13, 16.26, 22.64.

3. Results

3.1. Data Analysis

Table1.
Results one week before consumption of Atypical antipsychotics

Mean	Percent	N	YBOCS scores Test
	24.4	22	5-10
	70	63	10-15
	5.6	5	15-20
	0	0	X>20
12.13	100	90	sum

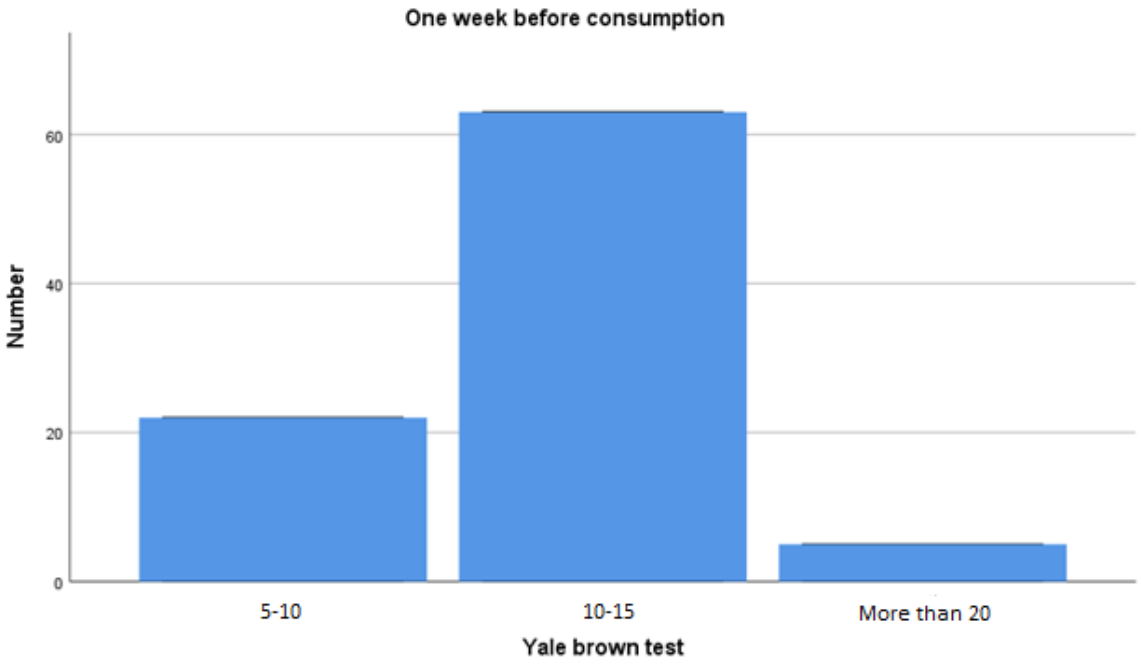

Figure 1. Yale brown test scores (one week before consumption of atypical antipsychotics)

Table 2.
Results of YBOCS test after one month after consumption of Atypical antipsychotics

Mean	Percent	N	YBOCS scores Test
	22	2	5-10
	35.6	32	10-15
	58.9	53	15-20
	3.3	3	X>20
16.26	100	90	sum

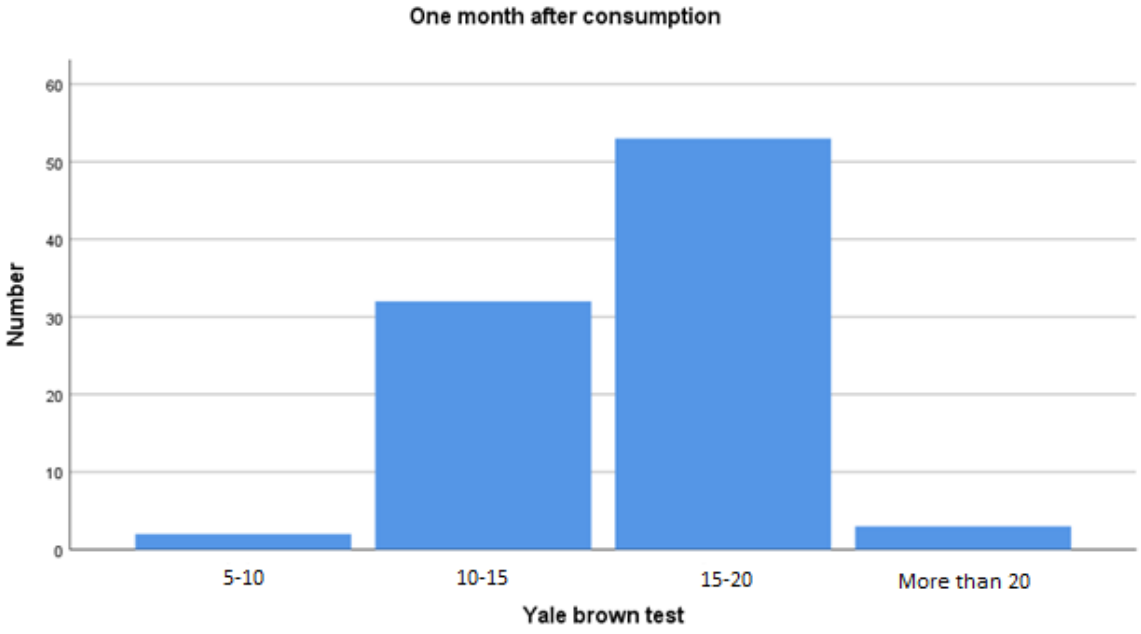

Figure 2. Yale brown test scores (one month after consumption of atypical antipsychotics)

Table3.
Results of YOBCS scores two months after consumption of Atypical antipsychotics

Mean	percent	N	YBOCS scores Test
	7.8	7	10-15
	21.1	19	15-20
	71.1	64	X>20
22.64	100	90	sum

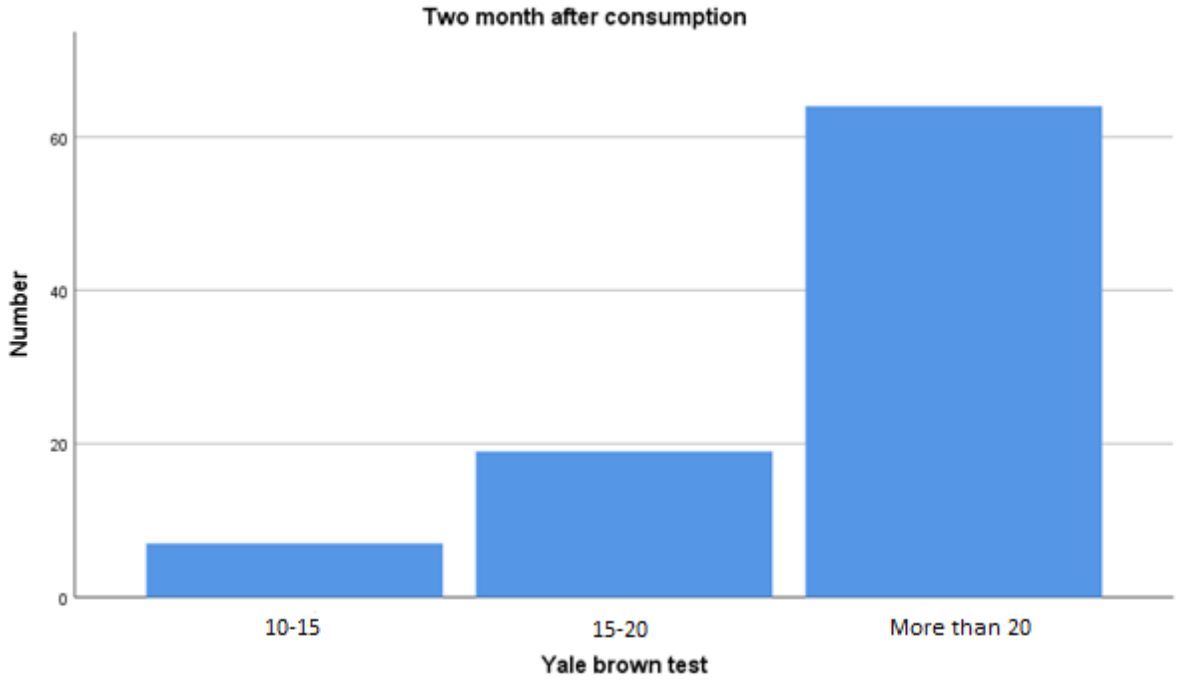

Figure 3. Yale brown test scores (two months after consumption of atypical antipsychotics)

3.2. Findings and Conclusions

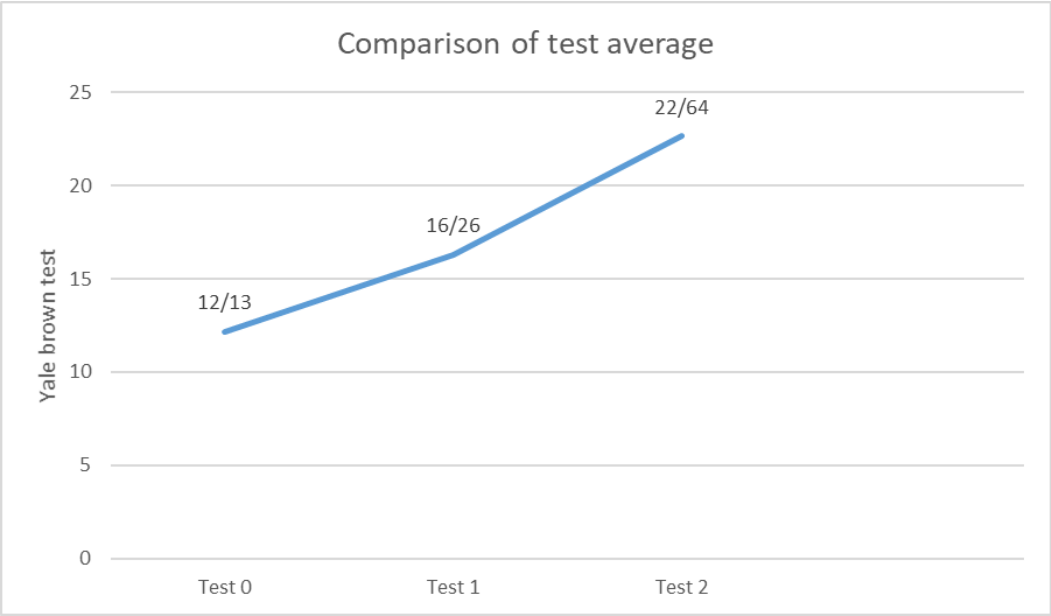

Figure 4. Comparison of the test average

By comparing the Mean scores of the test stages, it is clear that the mean increases in each stage. However, it remains to be seen whether this increase can be generalized to the whole community or is due to sampling error.

To determine whether a community was typical or not, I performed a normality test (Shapiro-Wilk) with 95% accuracy (α = 0.05): The assumption was that society is normal.

The assumption was that society was normal.

Table 4.
Comparison of mean scores

sig	**test**
0.154	One week before consumption
0.072	One month after consumption
0.094	Two months after consumption

Given that sig was more significant than 0.05 in all cases, the assumption was not rejected. I assumed that society was normal and used parametric tests. To determine the significance of the difference between the means of the tests, I used the test of the dependent means with 95% accuracy.

3.3. (Paired-Samples T-Test)

The assumption in all cases was that the means do not differ significantly at different stages.

Table 5.
Paired T-Test (one week before consumption of antipsychotics and one month after consumption of antipsychotics)

results	**Pairs of test results compared**
T=11.59 Sig=0.000 Difference between Means=4.13	One week before consumption - one month after consumption

Given that sig was less than 0.05, the assumption was incorrect and that the difference in Means was significant at this stage. That is, drug treatment between these two tests increased the mean score of the Yale-Brown test.

Table 6.
Paired T-Test (one month after consumption of antipsychotics and two months after consumption of antipsychotics)

results	**Pairs of test results compared**
T=12.02 Sig=0.000 Difference between Means=6.37	one month after consumption -two months after consumption

Given that sig was less than 0.05, the assumption was incorrect, and the difference in Means at this stage was significant. That is, drug treatment between these two tests increased the mean score of the Yale-Brown test.

Table 7.
Paired T-Test (two months after consumption of antipsychotics and one week before consumption of antipsychotics)

results	Pairs of test results compared
T=21.79 Sig=0.000 Difference between Means=10.51	One week after consumption-two, months after consumption

Given that sig was less than 0.05, the assumption was incorrect, and the difference in Means at this stage was significant. That is, drug treatment between these two tests increased the mean score of the Yale-Brown test.

4. Conclusion

According to the test results, it was clear that the mean difference between the different stages of the test was not accidental or due to testing error, and drug treatment had an effect on increasing this Mean. The drug's effect in the second month was slightly more significant than in the first month.

Obtained data indicated that patients did have no significant OCS symptoms before treatment and before using Atypical antipsychotics, but after treatment with atypical antipsychotics, OCS symptoms appeared. Moreover, these findings prove the side effects of using Atypical in patients with Schizophrenia.

5. Discussion

This study aimed to investigate the side effects of using Atypical Antipsychotics on developing Obsessive-Compulsive disorder in patients with Schizophrenia.

Results indicate that using Atypical antipsychotics can cause Obsessive-Compulsive symptoms in patients with Schizophrenia. Several studies support this assumption. Clinical research is increasingly demonstrating the efficacy of glutamate receptor antagonists in treating pharmacoresistant OCD. Research that demonstrated an increase in obsessive-compulsive disorder scores after taking olanzapine.

According to Kang (2020), It is believed that Clozapine initiates obsessive-compulsivebehavior in patients with Schizophrenia.

In a prospective study by De Haan (2002) that compared two groups of patients receiving antipsychotic treatment with risperidone and olanzapine, patients were assessed using the YBOCS scale at the start of treatment and the end of the sixth week.Both medicines exacerbated obsessive-compulsive symptoms.

According to Sugnyani (2015), obsessive-compulsive symptoms regularly happen in many patients with Schizophrenia.Clozapine is known to initiate or aggravate OCS in patients with Schizophrenia. (Sharma & Reddy, 2019).

Grillaut Lauroche (2016) indicated that there is a higher recurrence of OCS in Antipsychotic-treated patients with Anti-serotoninergic primary profiles against those with the central dopaminergic blockade.

According to Grover (2019), accurate evaluation is essential to OCS management. In case the OCS/OCD is related to utilizing a specific antipsychotic, starting effort must be made to decrease the number of antipsychotics. However, If this is not effective, then the insertion of a specific serotonin reuptake inhibitor (SSRIs) must be considered. Szmulewicz (2015)

indicated that a subgroup of patients develops this symptomatology after starting with second-generation Antipsychotics (SGA). Moreover, there is proof of a causal relationship for this association, especially for Clozapine.

Fernandez-Egea et al. (2018) indicated that by employing a large cohort of clozapine-treated patients, they distinguished several variables that might confound earlier thoughts. They found rising OCD predominance and checking compulsion related to expanding an extended treatment time.

According to Lykouras (2003), obsessive-compulsive symptoms after taking atypical antipsychotics may be one of the side effects of these medications. Psychotic patients who acquire obsessive-compulsive symptoms while on atypical antipsychotics may biologically predisposed to obsessive-compulsive disorder. (Hwang et al., 2000).

Several studies have found that SGAs have important pharmacodynamic qualities, such as adjusted antidopaminergic and antiserotonergic capabilities, which outperform the low serotonergic receptor harmony of first-generation antipsychotics. (Meltzer, 2012). Additionally, differences in GABAergic and glutamatergic neurotransmission need to be considered. (Lopez-Gil et al., 2010). The theory of SGA-induced OCS as a side-effect (Lykouras et al., 2003; Kwon et al., 2009) was first created after the pioneer perceptions of Baker et al. (1992) and de Haan et al. (2009). Then several types of research indicate a transparent relationship and interaction between SGA-treatment, especially CLZ. (Schirmbeck and Zink, 2012), and the de novo event of OCS (de Haan et al., 2004; Reznik et al., 2004; Schirmbeck et al., 2011). Clozapine and quetiapine are powerless D2 antagonists, whereas second-generation antipsychotics such as risperidone, ziprasidone, paliperidone, and aripiprazole are D2 antagonists. Moreover, these antipsychotics have different properties, such as antagonism of 5-HT2A and agonism of 5-HT1A. (Burry et al., 2018; Severance et al., 2018; Desai et al., 2018).

According to Tezenas du Montcel (2019), nearly 30% of patients with Schizophrenia show OCS.

CLZ must be considered a crucial portion of antipsychotic drugs. (Joober and Boksa, 2010; Kang and Simpson, 2010; Kane, 2011; Meltzer, 2012), Particularly in schizophrenia cases. (Kane et al., 1988). Several studies indicated the efficacy of antipsychotics in the treatment of psychosis and also their side effects. (Gupta and Daniel, 1995; Still et al., 1996; Kelly et al., 2003). Subsequently, CLZ is considered the first choice in treating resistant psychosis. Moreover, there is a significant anti-suicidal impact on mortality rates of CLZ-treated schizophrenia patients (Tiihonen et al., 2009). However, aggravation of obsessive-compulsive symptoms under antipsychotic treatment in schizophrenia patients has been observed with CLZ. (Asenjo Lobos et al., 2010),

OCS and OCD prevalence is higher in schizophrenia patients under atypical antipsychotic treatment than in general. (Grillault Laroche & Gaillard, 2016).

Cheng (2019) reported high comorbidity between OCD and Schizophrenia patients.
According to Brakoulias and Stockings (2019), In a few patients, antipsychotics are utilized to increase the activity of serotonin reuptake inhibitors (SRIs), especially when there is a partial reaction to treatment.

Family history is essential in diagnosing obsessive-compulsive symptoms in patients. (Nicolini et al., 2009).

In this study, atypical antipsychotic side effects were found to be the source of OCS in Patients with Schizophrenia. Even people with Schizophrenia who do not have a family history of OCD has developed OCS after taking an atypical antipsychotic.

According to the findings of this study, atypical antipsychotics can raise the YBOS score scale. Moreover, According to these findings, atypical antipsychotics can cause Obsessive-Compulsive symptoms in patients with Schizophrenia.

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