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A Comparative Study: Aripiprazole versus Olanzapine in Treatment of Amphetamine-Induced Psychosis

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Abstract

Amphetamines are commonly used for attention deficit hyperactivity disorder and sleep disorders, but their overdose can be a serious problem. This study aimed to evaluate and compare the therapeutic effects of aripiprazole and olanzapine in reducing psychotic symptoms in patients experiencing amphetamine-induced psychosis.

In this comparative study, 48 patients were evaluated in two groups, with one group receiving olanzapine and the other receiving aripiprazole. The PANSS questionnaire was used to assess patients' psychosis before starting the medication and on the seventh and fourteenth days of treatment. Analytical data were analyzed using Kolmogorov-Smirnov tests to measure normality, independent t-tests or Mann-Whitney tests, Pearson or Spearman correlations, and Chi-square tests.

The results showed that both aripiprazole and olanzapine were effective in reducing positive symptoms and overall psychiatric symptoms in patients with amphetamine-induced psychosis. However, aripiprazole had fewer side effects compared to olanzapine. These findings suggest that aripiprazole may be a good alternative to olanzapine in the treatment of amphetamine-induced psychosis, potentially reducing mortality and morbidity associated with olanzapine use.

Keywords: Aripiprazole, Olanzapine, Psychosis, Amphetamine, Side effects, Treatment

Introduction

The history of amphetamine stimulant use goes back several centuries (1). Amphetamine was synthesized in Germany around 1887, and a few years later methamphetamine was developed in 1918 in Japan. Therapeutic use of amphetamines in Western medicine began in the 1930s when they were used as a bronchodilator for the treatment of asthma (2). Amphetamine is one of the most commonly used illicit drugs worldwide due to its widespread availability and low price (3). Amphetamine-related psychological symptoms are common and include irritability, anxiety, psychosis, and mood disorders (4). These symptoms and syndromes often lead to progressive social and occupational decline as well as poor treatment outcomes (5). The clinical diagnosis and understanding of psychosis in amphetamine users are quite challenging due to the different etiologies that lead to psychological symptoms among them (6). At the same time, psychological symptoms are known as possible consequences of amphetamine use regardless of any previous history of psychosis (7). Amphetamine use among people with a genetic vulnerability to psychosis or previous mental disorders, such as schizophrenia, may lead to the onset or worsening of their condition (8). Research into the relationship between amphetamine and psychosis has been ongoing for more than 40 years. However, many questions about the etiology, chronicity, and determinants of clinical course remain unanswered. Nevertheless, a combination of observational, laboratory, and clinical studies has improved our understanding of the clinical features, risk factors, and course of psychosis among amphetamine users. Olanzapine and aripiprazole are both second-generation antipsychotics with different mechanisms of action and side effects (9, 10). Aripiprazole is a newer second-generation antipsychotic drug used to treat psychosis. It is approved by the FDA for the treatment of schizophrenia, mania phase, and mixed bipolar disorder, and as adjunctive therapy in major depression (11). The difference between aripiprazole and olanzapine is that aripiprazole acts as a relative agonist on dopamine D2 receptors and 5-HT1A receptors, while it acts as an antagonist on the 5-HT2A receptor. The use of aripiprazole and other related dopamine agonists is a new strategy for normalizing neurotransmission (5). Possible revision: Aripiprazole may be a preferable alternative for controlling substance-induced psychosis due to its lower incidence of side effects compared to olanzapine. This could potentially result in reduced mortality and morbidity associated with the use of olanzapine.. Today, Amphetamine use has become an epidemic health concern among drug users in Iran (12). The use and abuse of amphetamine can lead to recurrent amphetamine-induced psychosis, which is recurrent (13). On the other hand, chronic amphetamine-induced psychosis is very similar to schizophrenia (14). Statistics indicate that amphetamine is the second or third most commonly used illegal drug in Iran. The number of patients admitted to psychiatric hospitals in Iran with amphetamine-induced psychosis is increasing (15). Currently, there is no FDA-approved drug for the treatment of amphetamine addiction or the psychosis it causes. Drug development for the treatment of addiction and amphetamine-induced psychosis is a relatively new area of research. Therefore, this study aimed to compare the efficacy of aripiprazole and olanzapine in the treatment of amphetamine-induced psychosis.

Methods

Study design

The present study is a comparative study. This study was performed on men and women hospitalized in Ibn Sina Psychiatric Hospital in Shiraz during the years 2017-2018, which met the criteria for amphetamine-induced psychosis.

Sample size and study method

The study involved 48 men and women aged 15 to 65 years who were admitted to Ibn Sina Psychiatric Hospital in Shiraz, diagnosed with amphetamine-induced psychosis according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria (16). Participants were randomly and double-blindly divided into two groups of 24: one receiving olanzapine (starting dose of 10 mg) and the other aripiprazole (starting dose of 10 mg). The sample size of 24 per group was selected based on practical considerations, such as recruitment feasibility and available resources, and was considered sufficient to detect clinically meaningful differences, supported by prior studies and consistent with similar pilot research (17, 18). Informed consent was obtained, and psychosis severity was assessed using the PANSS questionnaire before treatment and on the 7th and 14th days (19). Doses were adjusted to the maximum allowed based on patient needs and psychosis severity, with no other antipsychotics permitted during the two-week treatment period. The study balanced statistical power and feasibility while recognizing the limitations of human subject research.

Inclusion and exclusion Criteria

Participants' inclusion criteria included men and women aged 15 to 65 years without physical or mental diseases disrupting the study, positive test results for the psychosocial diagnosis of amphetamine in the hospital laboratory on the day of hospitalization, and no use of other stimulant drugs that cause psychosis. Exclusion criteria were patients with physical problems interfering with antipsychotic therapy, including severe heart, kidney, or liver diseases, a history of allergy to olanzapine or aripiprazole in the past, patients who experienced severe side effects with olanzapine or aripiprazole during the study, homicidal or suicidal individuals and women who tested positive for pregnancy or had an infant (19, 20).

Statistical analysis

In this study, after collecting data, information was entered into SPSS software version 21. Subsequently, statistical analysis was conducted in two parts: descriptive and analytical. Descriptive data were analyzed using mean, standard deviation, frequency, and frequency percentage, while analytical data were assessed using Kolmogorov-Smirnov tests to measure normality, independent t-tests or Mann-Whitney tests, Pearson or Spearman correlation, and Chi-square tests.

Results

In the present study, 48 patients with amphetamine-induced psychosis were divided into two groups and treated with either olanzapine(starting dose of 10 mg) or aripiprazole (starting dose of 10 mg). The patients' condition was evaluated at the beginning of hospitalization, 7 days, and 14 days after treatment. Table 1 displays the demographic information of the patients, including sex, age, duration of infection, marital status, and city of residence. No significant relationship were found between these factors and the treatment groups. The Scale for the Assessment of Positive Symptoms (SAPS) was used to measure positive symptoms in both groups of patients before and after treatment. There was no significant difference in the scale of positive symptoms at the time of admission between the two groups (p-value=0.549). However, the scale of positive symptoms decreased significantly during treatment in both treatment groups (p-value <0.001).

The evaluation of the interaction between the Positive Symptom Scale and the drug used during treatment revealed that the rate of positive symptom scale changes during treatment was similar in both groups. Additionally, there was no significant difference observed in the effect of the two drugs on the positive symptom scale (p-value =0.135) (Figure 1).

One of the outcomes of this study was the comparison of the general psychiatric scale

between two groups of patients who showed no significant difference at the start of their hospitalization (*p*-value = 0.854). However, during the treatment period, the general psychiatric scale in both treatment groups decreased significantly (*p*-value <0.001). Further analysis of the interaction between the general psychiatric scale and the specific drug used during treatment revealed that the rate of change in the scale was similar in both groups (*p*-value = 0.333).

The present study assessed the rate of psychosis in patients from both groups using the PANSS questionnaire before treatment, on the seventh day, and on the fourteenth day of drug treatment.

The initial total score of the PANSS questionnaire did not show a significant difference between the two groups of patients upon hospitalization (*p*-value = 0.803). However, during the treatment period, there was a significant decrease in the total score of the PANSS questionnaire in both treatment groups (*p*-value <0.001). The interaction between the total score of the PANSS questionnaire and the drug used during treatment showed that the rate of change in the total score of the questionnaire was similar in both groups (*p*-value = 0.239) (Table 2).

Discussion and Conclusion

This study aimed to compare the effectiveness of aripiprazole and olanzapine in treating amphetamine-induced psychosis in both men and women admitted to Ibn Sina Psychiatric Hospital in Shiraz. The results of the study showed that both olanzapine and aripiprazole significantly improved scores on the PANSS questionnaire over the 14-day treatment period. However, no significant differences were observed between the two drugs.

Although few studies, such as the present study, have been conducted comparing the two drugs on a case-by-case basis, the results of most similar studies have been consistent with the present study. Wani et al. conducted a study from 2011-2014, which demonstrated that patients with stable schizophrenia who switched from olanzapine to aripiprazole not only improved their metabolic syndrome but also showed no change in psychopathology measured by the total PANSS score during the 24 weeks of follow-up (21).

In another study in 2009, Wlodzimierz et al. found that aripiprazole was equally as effective as olanzapine in the long-term treatment of patients with persistent, chronic, and acute recurrent schizophrenia and, resulted in less weight gain (9).

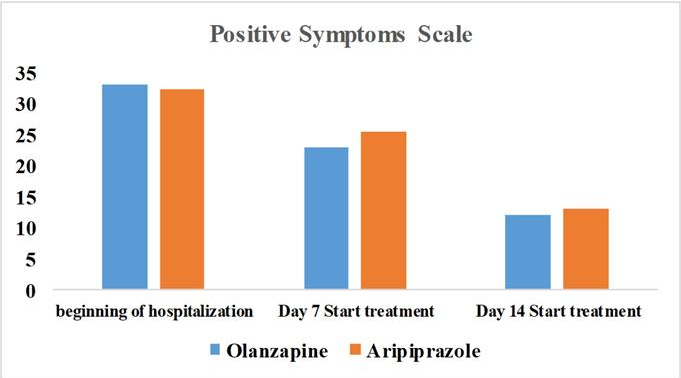

Figure 1. Effect of Olanzapin and Aripiprazol on the positive symptom scale

Table 1. Gender frequency, age, duration of illness, marital status, and city of residence of patients in the two groups of olanzapine and aripiprazole

Variable		Frequency of patients (%)	Patients of the olanzapine group	Patients in the aripiprazole group	P-value
Sex	Male	38 (79.2)	19 (79.2)	19 (79.2)	0.95
	Female	10 (20.8)	5 (20.8)	5 (20.8)	
Age	15-25 years	7 (14.6)	3 (12.5)	4 (16.7)	0.612
	26-35 years	16 (33.3)	9 (37.5)	7 (29.2)	
	36-45 years	13 (27.1)	8 (33.3)	5 (20.8)	
	46-55 years	10 (20.8)	3 (12.5)	7 (29.2)	
	More than 56 years	2 (4.2)	1 (4.2)	1 (4.2)	
Disease duration	Less than a month	3 (6.3)	2 (8.3)	1 (4.2)	0.592
	1-6 months	8 (16.7)	4 (16.7)	4 (16.7)	
	6-12 months	5 (10.4)	1 (4.2)	4 (16.7)	
	1-5 years	26 (54.2)	13 (54.2)	13 (54.2)	
	More than 5 years	6 (12.5)	4 (16.7)	2 (8.3)	
Marital status	Single	21 (61.8)	11 (55)	10 (71.4)	0.332
	Married	13 (38.2)	9 (45)	4 (28.6)	
City of residence	Shiraz	22 (61.1)	12 (60)	10 (62.5)	0.85
	Other Cities	14 (38.9)	8 (40)	6 (37.5)	

Table 2. The total score of the PANSS questionnaire in the two groups

The Total Score of The Panss Questionnaire	Beginning Of Hospitalization	Day 7 Start Treatment	Day 14 Start Treatment	*P*.Value
Olanzapine	101.7 ± 13.5	78.8 ± 10.9	54.0 ± 9.6	<0.001
Aripiprazole	101.6 ± 13.5	84.5 ± 17.8	54.5 ± 14.2	<0.001
***P*.Value**	0.803	0.239	0.239	

Sulaiman et al. conducted a study to evaluate the effect of aripiprazole on amphetamine-induced psychosis. The study found that aripiprazole improved the symptoms of amphetamine-induced psychosis and was a safe drug with tolerable side effects (22). Other studies have also shown that aripiprazole has fewer metabolic side effects and extrapyramidal symptoms compared to olanzapine. For instance, Henderson et al. demonstrated that in patients with schizophrenia, adding aripiprazole to olanzapine improved the patients' metabolic factors compared with placebo (23). In 2003, Lieberman et al. conducted a study comparing olanzapine with haloperidol in the treatment of first-episode psychosis.

The results of this study showed that both drugs improve the symptoms of psychosis, but olanzapine is less likely to be continued in treatment for patients due to extrapyramidal side effects (10).

A 2008 study by Kinon et al. found that aripiprazole and olanzapine were effective in reducing restlessness in schizophrenic patients, but the aripiprazole-treated group experienced a smaller increase in glucose, fats, and prolactin (24). In another study, Chrzanwski et al. in 2006, examined the long-term effects of

aripiprazole and olanzapine in the treatment of schizophrenic patients. The results of this study showed that both drugs were effective in the treatment of schizophrenia, but aripiprazole is better because it does not cause weight gain (9).

The results of the present study showed the effectiveness of two drugs, aripiprazole, and olanzapine, in the treatment of amphetamine-induced psychosis. No significant difference was observed during the 14-day treatment period with these drugs. The therapeutic effect of aripiprazole and olanzapine on amphetamine-induced psychosis is similar. However, as aripiprazole has fewer side effects than olanzapine, it can be a good alternative. On the other hand, mortality and morbidity due to replacing olanzapine with aripiprazole will likely be less in the future.

While previous studies have explored the effects of aripiprazole and olanzapine in various contexts, our research uniquely focuses on amphetamine-induced psychosis specifically. Most existing literature has primarily examined these medications in the context of schizophrenia Additionally, unlike many studies that report on long-term effects or metabolic side effects, our study emphasizes the immediate therapeutic outcomes within a 14-day timeframe while assessing both efficacy and side effects. This direct comparison in a specific patient population allows for a clearer understanding of how these treatments function in the context of amphetamine-induced psychosis. More detailed studies with larger sample sizes are recommended to confirm the results of this study.

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Author contributions

Data collection was led by E.MS. and L.RJ while M.A-A was responsible for drafting and editing the manuscript. M.M-B. designed the study, supervised the data collection, R.T, E.A and S.S. carried out a thorough review of the manuscript. All authors have read and approved of the final manuscript.

Conflicts of Interest and Source of Funding

This work was supported by Shiraz University of Medical Sciences and the Institutional Review Board .The authors declare no competing interests.

Data availability statement

The dataset used and analyzed during this study is available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with ethical guidelines (IR.SUMS.MED.REC.1396.98 ethic cod). The research protocol was approved by Shiraz University of Medical Sciences. All subjects provided written informed consent following the Declaration of Helsinki.

Consent for publication

All authors have agreed to the submission and publication of the manuscript.

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