

Methamphetamine-Associated Psychosis and Treatment With Haloperidol and Risperidone: A Pilot Study

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Abstract

Background: Different studies have suggested that antipsychotic medications of the first generation have better effectiveness for the treatment of psychotic symptoms compared with antipsychotic medications of the second generation.

Objectives: The current study was the first pilot study in Iran that compared Haloperidol with Risperidone in the treatment of positive symptoms of psychosis among a group of methamphetamine-dependent patients.

Materials and Methods: This randomized clinical trial was designed and conducted in 2012. Overall, 44 patients who met the diagnostic and statistical manual of mental disorders, fourth edition-text revised (DSM-IV-TR) criteria for methamphetamine-associated psychosis (MAP) and were hospitalized at Razi psychiatric hospital in Tehran were selected. Patients (1:1) were randomly divided to two groups. Overall, 22 subjects received Haloperidol (5 - 20 mg) and 22 subjects received Risperidone (2 - 8 mg). All subjects were assessed at baseline, during three consecutive weeks of treatment and one week after treatment (i.e., follow-up). Scale of assessment of positive symptoms (SAPS) was completed for each subject.

Results: The study findings indicated that both Haloperidol (< 0.05) and Risperidone (< 0.05) were similarly applicable in the treatment of MAP but no differential effectiveness was found between the two medications. The treatment effects of both medications increased in the first two weeks of treatment and remained stable in the second two weeks.

Conclusions: Risperidone and Haloperidol are two effective antipsychotic medications for the treatment of positive symptoms of MAP but other aspects of these two neuroleptic medications such as the long-term treatment effects should be studied. Further studies with more samples and longer follow-ups are suggested.

Keywords: Haloperidol, Methamphetamine, Psychosis, Risperidone, Treatment

1. Background

As an addictive psychostimulant drug, methamphetamine use is a new health concern in Iran but a few studies have targeted treating methamphetamine-associated psychosis (MAP) with antipsychotic medications in Iran and around the world (1-25).

2. Objectives

In the recent years, MAP has impacted the healthcare system of Iran (2).

3. Materials and Methods

3.1. Participants and Eligibility Criteria

The current pilot study had a randomized clinical trial design. The study was conducted in 2012. Patients who

were hospitalized at Razi psychiatric hospital in Tehran and at the same time, were diagnosed with MAP based on the diagnostic and statistical manual of mental disorders, fourth edition-text revised (DSM-IV-TR) criteria, were eligible to enter the study. Other inclusion criteria included age range of 18 - 60 years, and the chronicity and severity of positive symptoms. Exclusion criteria included meeting Axis I psychiatric comorbidity especially Schizophrenia, co-use of other types of substances like opioids within the past month prior to recruitment, current neurological disorders, mental retardation, and taking medications such as other antipsychotic and Benzodiazepines before starting the study.

3.2. Study Measures

Details of baseline demographics such as gender, age, history of psychiatric disorders, history of drug use and

current methamphetamine use were recorded using a checklist. By the assistance of the psychiatrist of Razi hospital, the clinical files of the patients were also reviewed to complete the data collection. The Persian validated version of the scale of assessment of positive symptoms (SAPS) was completed for each patient to assess positive symptoms of psychosis amongst the patients. It should be noted that we did not use the scale of assessment of negative symptoms (SANS) to assess negative symptoms of psychosis among our sample because negative symptoms do not emerge in MAP.

Scale of assessment of positive symptoms was developed by Andersen to assess positive symptoms of psychosis. The assessed positive symptoms include hallucinations, delusions, deviant behaviors and disrupted concrete thinking. Scale of assessment of positive symptoms includes 30 questions. Each question has six scores ranging from 0 to 5. The total scores range between 0 and 150 (26). It has high reliability and validity to assess negative symptoms of psychosis. Internal consistency of the Persian validated version was 83%, and pre-test and posttest reliability was 88% (25). In this study, internal reliabilities via Cronbach alpha coefficients for positive symptoms were 92% indicating high reliability to meet the study aims.

3.3. Ethical Considerations

Participation was confidential and voluntary. Consent forms were obtained from the caregivers. The protocol of the study was approved by the ethical committee of University of Social Welfare and Rehabilitation Sciences in Tehran, Iran.

3.4. Study Procedure

After meeting all eligibility criteria and obtaining consent forms, 44 patients with current psychiatric diagnosis of MAP were recruited. Patients were randomly divided to two groups based on a given random code including 22 patients in the Haloperidol group and 22 patients in the Risperidone group. This was done by a well-trained psychiatrist. Group 1 received Haloperidol (5 to 20 mg, per day, starting with 5 to 10 mg per day and raised gradually every three to four days up to 20 mg according to the symptoms) and group 2 received Risperidone (2 - 8 mg, per day, starting with 2 to 4 mg per day and raised gradually every three to four days up to 8 mg according to the symptoms) at baseline and for three consecutive weeks. Patients were followed after one week. Scale of Assessment of Positive Symptoms was completed on a weekly basis for each patient. The duration of study was one month because studies showed that the required time for showing treatment failure with antipsychotic medications was four to

six weeks. Furthermore, based on the DSM-IV-TR criteria, the psychiatric diagnosis of MAP will be wrong if it takes more than one month. During one month, symptoms of MAP were assessed weekly. In this study, assessment of SAPS included hallucinations, delusions, deviant behaviors positive concrete thinking and the total score of SAPS.

3.5. Data Analysis

Data was analyzed by performing descriptive methods of statistics, independent t-test and variance analysis with repeated measures, using the SPSS version 19 software.

4. Results

Overall, 54.6% of the subjects were male in the Haloperidol group (group 1) and 86.4% of the subjects were male in the Risperidone group (group 2). The mean age of group 1 was 35.3 ± 7.9 years and the mean age of group 2 was 34.6 ± 7.9 years. Overall, 68% of the subjects in group 1 and 82% of subjects in group 2 were currently single. In total, 72.7% of the subjects in group 1 and 59.1% of the subjects in group 2 were unemployed (See Table 1).

The table below shows the mean scores of the two groups in hallucination. As Table 2 shows the mean scores of hallucination in the two groups were reduced from 13.5 (SD = 6.3) in the Haloperidol group and 15 (SD = 4.9) in the Risperidone group at baseline to 0.14 (SD = 0.4) and 0.27 (SD = 0.76) on the third week of treatment, respectively. The mean scores of delusion in the two groups were reduced from 17 (SD = 7.8) in the Haloperidol group and 15.7 (SD = 7.4) in the Risperidone group at baseline to 0.14 (SD = 0.64) and 0.73 (SD = 1.5) on the third week of treatment, respectively. The P value for all items was < 0.05 , which was significant (See Table 2).

The table below shows the mean scores of the two groups in bizarre behavior. As the table shows the mean scores of bizarre behavior in the two groups was reduced from 8.5 (SD = 4) in the Haloperidol group and 7.7 (SD = 3.3) in the Risperidone group at baseline to 0.00 (SD = 0) and 0.27 (SD = 0.63) on the third week of treatment, respectively. The P value for all items was < 0.05 , which was significant (See Table 3).

The mean scores of hallucination in the Haloperidol group and Risperidone group were (13.5 (SD = 6.3) and 15.09 (SD = 4.9), $t = 0.8$), respectively. The mean scores of delusion in Haloperidol group and Risperidone group were 17.0 (SD = 7.8) and 15.7 (SD = 7.0), $t = 0.5$, respectively. The mean scores of bizarre behavior in the Haloperidol group and Risperidone group were 8.5 (SD = 4.0) and 7.6 (SD = 3.3), $t = 0.7$, respectively. The mean scores of concrete thinking in the Haloperidol group and Risperidone group were 5.7 (SD = 2.8) and 8.9 (SD = 4.0), $t = 3.0$, respectively.

Table 1. Details of Demographics Among the Patients in the Two Groups (n = 44)

	Group 1	Group 2	P Value
Gender			
Male	12 (54.6)	19 (86.4)	0.03
Female	10 (45.4)	3 (13.6)	0.06
Mean age, y	35.3 (SD ± 7.9)	34.6 (SD ± 7.9)	
Education status			
Less than 12 years	19 (86.4)	20 (90.9)	
12 years	3 (13.6)	2 (9.1)	
Age range, y			
21 - 33	10 (45.4)	9 (41)	0.09
34 - 46	10 (45.4)	11 (50)	0.08
47 - 59	2 (10.2)	2 (9)	0.02
Marital status			
Currently single	7 (31.2)	4 (18)	
Currently married	6 (27.3)	9 (40.9)	0.08
Job status			
Currently has a job	15 (68.2)	18 (82)	
Currently unemployed	16 (72.7)	13 (59.1)	0.065
Duration of current hospitalization (days)	3 (SD ± 3.9)	2 (SD ± 5.8)	
Duration of methamphetamine use (Months)	7 (SD ± 4.7)	9 (SD ± 6.9)	0.08

The mean scores of psychotic symptoms in the Haloperidol group and Risperidone group were 45.7 (SD = 14.4) and 45.4 ((SD = 12.2), $t = 0.42$), respectively. Although, the mean scores of the two groups improved in hallucination, delusion, bizarre behavior, concrete thinking and psychotic symptoms yet there was not significant difference between the two groups. In this study, the P value for all items was < 0.05 , which was significant (See Table 4).

As Table 3 shows the mean scores of concrete thinking in the two groups were reduced from 5.7 (SD = 2.8) in the Haloperidol group and 8.9 (SD = 4.0) in the Risperidone group at baseline to 0.05 (SD = 0.21) and 0.36 (SD = 0.72) on the third week of treatment, respectively. The P value for all items was < 0.05 , which was significant (See Table 3).

As Table 3 shows the mean scores of psychotic symptoms in the two groups were reduced ranging from 45.7 (SD = 14.4) in the Haloperidol group to 47.4 (SD = 12.2) in the Risperidone group at baseline and from 0.27 (SD = 10.07) to 1.6 (SD = 2.9) on third week of treatment, respectively (See

Table 2. Mean Scores of Hallucination/Delusion (n = 44)

Psychiatric Medication, n = 22	Treatment Stage	Mean Scores /SD
Haloperidol	Baseline/hallucination	13.5 (6.3)
	Week 1	3 (4.1)
	Week 2	0.91 (2.3)
	Week 3	0.14 (0.4)
Risperidone	Week 4	0.00 (0)
	Baseline	15 (4.9)
	Week 1	4 (4.3)
	Week 2	0.64 (1.4)
Haloperidol	Week 3	0.27 (0.76)
	Week 4	0
	Baseline/Delusion	17 (7.8)
	Week 1	5 (5.3)
Risperidone	Week 2	0.86 (2.2)
	Week 3	0.14 (0.64)
	Week 4	0.00 (0)
	Baseline	15.7 (7.4)
Haloperidol	Week 1	6.2 (6.6)
	Week 2	2.6 (4.7)
	Week 3	0.73 (1.5)
	Week 4	0.00 (0)

Table 3).

5. Discussion

Over the past decade, a growing body of evidence suggests that second-generation antipsychotics such as Risperidone are effective in the treatment of patients with psychosis (27). Current research evidence strongly suggests a relationship between methamphetamine use and the development of acute psychosis. First, early studies demonstrated that methamphetamine could trigger acute psychosis in healthy individuals (28).

The positive symptoms of methamphetamine psychosis are similar to those of paranoid schizophrenia, consisting mainly of delusions and hallucinations. The recurrent nature of methamphetamine psychosis is also suggested as another apparent similarity, as recurring methamphetamine psychosis could be similar to schizophrenia (29).

The current pilot study is one of the few studies in Iran that considered MA psychosis treatment with Haloperidol

Table 3. Mean Scores of Bizarre Behaviors/Concrete Thinking (n = 44)

Psychiatric Medication, n = 22	Treatment Stage	Mean Scores/SD
Haloperidol	Baseline/Bizarre behaviors	8.5 (4)
	Week 1	0.5 (1.3)
	Week 2	0.1 (0.4)
	Week 3	0
	Week 4	0
Risperidone	Baseline	7.7 (3.3)
	Week 1	1.7 (2.5)
	Week 2	0.4 (0.9)
	Week 3	0.2 (0.6)
	Week 4	0.5 (0.2)
Haloperidol	Baseline/Concrete Thinking	5.7 (2.8)
	Week 1	1.3 (1.2)
	Week 2	0.2 (0.5)
	Week 3	0.5 (0.2)
	Week 4	0
Risperidone	Baseline	8.9 (4.0)
	Week 1	2.6 (3.1)
	Week 2	1.09 (1.5)
	Week 3	0.3 (0.7)
	Week 4	0
Haloperidol	Baseline/Psychotic Symptoms	45.7 (14.4)
	Week 1	10.05 (8.9)
	Week 2	2.05 (4.7)
	Week 3	0.27 (1.07)
	Week 4	0
Risperidone	Baseline	47.4 (12.2)
	Week 1	14.5 (13.9)
	Week 2	2.6 (4.5)
	Week 3	1.6 (2.9)
	Week 4	0

and Risperidone among a group of patients, who were hospitalized at Razi psychiatric hospital. A few studies from Iran have targeted treating MAP. The study findings suggested that both Haloperidol and Risperidone were effective for the treatment of MAP yet there was no significant difference between the two antipsychotic medications. A few studies in other countries have addressed the treatment of MAP with antipsychotic medications. The findings of the current study are in contrast with the study find-

ings of Green et al. (2002) (30), who found that Haloperidol was more effective in treating psychosis in comparison with Risperidone.

In another study, it was found that making a treatment transition from Haloperidol to Risperidone among Schizophrenic patients reduced the scores of subscales of positive, negative and general psychosis symptoms (31). Zhang et al. (2001) (32) found that the general symptoms of psychosis in the Risperidone group were significantly improved compared with the Haloperidol group. A study found that Risperidone was superior in the treatment of symptoms of psychosis compared with Haloperidol (33).

The reported changes in these studies can be the result of several factors. First, the dose of use may impact the treatment effects. In fact, there is still no agreement on the dose required to treat positive symptoms of MAP, especially for Risperidone. There are no studies that have examined the best dosage. There is only evidence that higher doses of antipsychotic medications have better effectiveness compared with lower ones. Further studies of this issue are still required.

It should be noted that positive symptoms of MAP are associated with considerable health service utilization and increased psychiatric symptoms over time (34). Little is known about the pharmacological therapies of patients with MAP in Iran. In addition, the most effective regime for stabilizing patients with MAP still needs to be studied in Iran. Methamphetamine users are vulnerable to MAP, either as a result of exacerbation of symptoms of underlying psychotic disorders (35) or emerging new psychotic symptoms during intoxication and withdrawal stages (36); recurrence can occur in response to psychological stressors even in the absence of methamphetamine use (37).

Recently, however, the picture of success for these antipsychotic medications has become somewhat vague. Patients diagnosed with positive symptoms of MAP should be monitored more closely, in particular for signs of a chronic development.

5.1. Limitations and Suggestions

The current study also had some limitations as follows: the study sample was limited to only one psychiatric center. Therefore, data generalization is difficult. Because of a number of problems such as difficulty in sample recruitment, the sample size was small. Further studies with more representative numbers of samples are suggested. Because of psychiatric treatment of patients, it was difficult to have further follow-ups. Therefore, designing and conducting research studies with more follow-up sessions are suggested. In this study, we compared the therapeutic effectiveness of Haloperidol with Risperidone in the treatment of MAP yet further studies with Placebo groups are

Table 4. The Differences Between the Two Groups in Treatment of Positive Symptoms of Methamphetamine-Associated Psychosis (n = 44)

Group	PS	Mean/SD	F	Mean/SD	df	t	P
Haloperidol Risperidone	Hallucination	13.5 (6.3) (15.0 (4.9))	0.32	1.05 (1.7)	42	0.8	0.22
Haloperidol Risperidone	Delusion	17.0 (7.8) (15.7 (7.0))	0.15	1.27 (2.3)	42	0.5	0.22
Haloperidol Risperidone	Bizarre behaviors	8.5 (4.0) (7.6 (3.3))	0.48	0.48 (0.8)	12	0.7	0.12
Haloperidol Risperidone	Concrete thinking	5.7 (2.8) (8.9 (4.0))	0.47	(3.18 (1.04))	42	3.3	0.12
Haloperidol Risperidone	Psychotic symptoms	(45.7) (14.4) (45.4 (12.2))	1.22	1.73 (0.67)	42	0.4	0.11

Abbreviation: PS, Psychotic symptoms.

still suggested. However, the current study is one of the few studies in Western Asia, especially the Persian Gulf region, which targeted treating MAP with antipsychotic medication.

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Footnotes

Authors' Contribution: Mercedeh Samiei, Mohammad Vahidi and Reza Daneshmand designed the study. Mohammad Vahidi, Azadeh Yaraghchi and Omid Rezaee conducted the study. Reza Daneshmand performed the data analysis. All authors contributed to writing the manuscript and reading and approving the final version.

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