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ORIGINAL RESEARCH

# Quetiapine versus Haloperidol in Controlling Conversion Disorder Symptoms; a Randomized Clinical Trial

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**Abstract:** **Introduction:** About 5% of visits to emergency departments are made up of conversion disorder cases. This study was designed with the aim of comparing the effectiveness of quetiapine and haloperidol in controlling conversion disorder symptoms. **Methods:** The present single-blind clinical trial has been performed on patients with conversion disorder (based on the DSM-IV definition) presenting to emergency department of 9-Day Hospital, Torbat Heydariyeh, Iran, from January 2017 until May 2018. **Results:** 73 patients were allocated to haloperidol and 71 to quetiapine group. Mean age of these patients was 32.03 ± 12.80 years (62.50% female). Two groups were similar regarding the baseline characteristics. Within 30 minutes, 90.41% of haloperidol cases and 91.55% of quetiapine cases were relieved (p=0.812). The most common side effects after 30 minutes were extrapyramidal symptoms (9.59%) in the haloperidol group and fatigue and sleepiness (7.04%) in the quetiapine group. Extrapyramidal symptoms was significantly higher than the quetiapine group (p=0.013). **Conclusion:** The results of the present study showed that although quetiapine and haloperidol have a similar effect in relieving the patients from conversion disorder symptoms, the prevalence of extrapyramidal symptoms is significantly lower in the group under treatment with quetiapine. Therefore, it seems that quetiapine is a safer drug compared to haloperidol.

**Keywords:** Conversion disorder; hysteria; dissociative disorders; quetiapine fumarate; haloperidol; emergency service, hospital



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## 1. Introduction

Conversion disorder is a type of disorder in physical function, which is not in conformity with anatomic and physiologic concepts of central or peripheral nervous system. This disorder occurs as a result of stress and helps alleviate the stress of the patient. This disorder happens in various ages and mostly in young women and individuals with a weakness in coping mechanism (1). Conversion disorder is often associated with simultaneous diagnosis of mood disorder, stress disorder, and schizophrenia and its prevalence among the relatives of those affected with these disorders is higher than the general population (2). A significant symptom of these disorders is involuntary loss of function or action disorder in

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the function of voluntary nervous system. Usually, the symptoms of this disease manifest suddenly and due to extreme and exciting conditions; including numbness or paralysis in hand and foot, fainting, etc. Sometimes the symptoms of hysteria disappear at the same speed they were manifested and they can usually be relieved or completely resolved via suggestion (3). Statistics indicate that about 5% of visits to emergency departments are made up of conversion disorder cases (4). There is no specific guideline for management of these patients in the emergency department. Anti-stress drugs lead to a decrease in stress of the patients and consequently cause improvement in conversion disorders (4-6). Haloperidol is a traditional anti-psychotic drug that is used for treatment of various psychiatric disorders (7, 8). Better effectiveness of this drug compared to diazepam in treatment of conversion disorder has been confirmed (9) but its side effects including extrapyramidal symptoms is a serious limitation for its application (10, 11) and therefore, researchers are looking for new drugs to replace it. Quetiapine is an atypical anti-psychotic drug used for treatment of schizophrenia, bipolar disorder, and prescribed in association with an antidepressant drug for treatment of depression disorder. Effectiveness of quetiapine in treating psychological disorders has been witnessed, especially in mood and anxiety disorders (12). This drug exerts its anti-psychotic effects via a direct antagonistic effect on dopaminergic and serotonin receptors. Therefore, it might be beneficial in treatment and control of conversion disorders. The present study was designed with the aim of comparing the effectiveness of quetiapine and haloperidol in controlling conversion disorder symptoms in patients presenting to the emergency department.

## 2. Methods

### 2.1. Study design and setting

The present single-blind clinical trial has been performed on patients with conversion disorder in 9-Day Hospital, Torbat Heydariyeh, Iran, from January 2017 until May 2018. Diagnosis of conversion disorder was done based on the 4th edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV- TR, 2000). Ethics committee of Torbat Heydariyeh University of Medical Sciences approved the protocol of the present study. This clinical trial has been registered on IRCT with following code: IRCT2015100712050N2. The researchers adhered to the principles of Helsinki declaration throughout the study period.

### 2.2. Participants

The studied participants included those affected with conversion disorder diagnosed by an emergency medicine physician based on DSM-IV definitions. Exclusion criteria are shown in table 1. Sampling was done via convenience method. Patients who had one of the following conditions were excluded from the study: no definite diagnosis of conversion disorder, patients with problems in vital signs, critically ill patients, those aged under 18 years and over 60 years, pregnant and lactating patients, addicts, those not participating or not tolerating oral medication, being affected with acute cardiopulmonary, liver, or kidney diseases, history of Parkinson, history of epilepsy or taking anti-epileptic drugs, history of hypothyroidism, hypokalemia, hypomagnesemia, familial long QT syndrome, simultaneous treatment with other neuroleptic drugs of drugs that elongate QT interval, allergy to neuroleptic drugs and benzodiazepines.

### 2.3. Intervention

Patients underwent treatment with haloperidol or quetiapine via block randomization with size 6 blocks (using a computer program). IV haloperidol with 5mg dose (manufactured by Caspian Company, Rasht, Iran) and rapid-releasing oral quetiapine with 50 mg dose (manufactured by Tehran Shimi, Tehran, Iran) were prescribed. The present study was designed as a single-blind one in which the patient was blind to the drug prescribed. Drugs were prepared as colorless and anonymous packs and injected to the patients.

### 2.4. Outcome

The evaluated outcomes included being relieved from conversion disorder symptoms and presentation of side effects. Side effects were reported in 4 groups of extrapyramidal symptoms, fatigue and sleepiness, headache, and other. Patients were evaluated 30 minutes and 24 hours after drug prescription.

### 2.5. Data gathering

For gathering data, a pre-designed checklist consisting of demographic data, history of mental diseases, symptoms on admission, response to treatment, and side effects 30 minutes and 24 hours after treatment was used. An emergency medicine specialist was responsible for data gathering.

### 2.6. Statistical Analysis

Sample size was calculated based on treatment success of haloperidol (28%) and quetiapine (55%) in alleviating psychotic symptoms (13). Therefore, considering $\alpha$=0.05 and $\beta$=0.1, the required sample size in each group was considered 68 patients. Data were analyzed via STATA 14.0 software and with intention to treat analysis approach. Results were reported as mean ± standard deviation or frequency and percentage. T-test was applied for comparing quantitative data, and chi-square or Fisher's exact tests were used to compare the frequency between the 2 groups. In all analyses, $p<0.05$ was considered as level of significance.

## 3. Results

### 3.1. Baseline characteristics of the patients

Throughout the study period, 144 patients were evaluated. 73 patients were allocated to haloperidol group and 71 patients were in the quetiapine group. Mean age of these patients was 32.03 ± 12.80 years and 62.50% of the patients were female. Age (p=0.654) and sex (p=0.414) distribution were not different between the 2 groups. 12 (16.44%) patients in the haloperidol group and 6 (8.45%) patients in the quetiapine group had a history of psychotic disorders (p=0.147). The most common presentation of the patients on admission to emergency department were non-paralysis (25.69%) and epileptic seizure (9.72%) (p=0.584). Table 1 depicts the distribution of baseline characteristics of the patients in the 2 treatment groups.

### 3.2. Outcomes

Within 30 minutes after prescription of haloperidol and quetiapine, respectively, 90.41% and 91.55% of the patients in each group were relieved of conversion disorder symptoms (p=0.812). It should be noted that 30 minutes (p=0.412) and 24 hours (p=0.940) after prescription of drugs the overall prevalence of side effects was not different between the 2 groups (table 2). The most common side effects after 30 minutes after prescription of the drugs were extrapyramidal symptoms (9.59%) in the group under treatment with haloperidol and fatigue and sleepiness (7.04%) in the group treated with quetiapine (table 3). Analyses showed that prevalence of extrapyramidal symptoms as side effects in haloperidol group was significantly higher than the group treated with quetiapine at this time (p=0.013). Although 24 hours after drug administration the prevalence of extrapyramidal symptoms in haloperidol group was still higher than quetiapine group (8.22% vs. 1.41%), this difference was not significant (p=0.116).

## 4. Discussion

The results of the present study showed that although quetiapine and haloperidol have a similar effect in relieving the patients from conversion disorder symptoms, the prevalence of extrapyramidal symptoms is significantly lower in the group under treatment with quetiapine. Therefore, it seems that quetiapine is a safer drug compared to haloperidol.

Effectiveness and safety of quetiapine have been evaluated in controlling the symptoms of various mental diseases, but to the best our knowledge, the role of this drug in controlling conversion disorder is evaluated in the present study for the first time. However, there are studies available that have assessed the effectiveness of quetiapine and haloperidol in controlling the symptoms of other mental diseases. For example Arvanitis et al. showed that quetiapine is superior to haloperidol in 150 to 750 mg/day doses compared to placebo and haloperidol in treating acute exacerbation of schizophrenia (14). In addition, in their study, Velligan et al. showed that quetiapine is more effective than haloperidol in improving the cognitive function of schizophrenia patients (15). However, Delmonte et al. showed that haloperidol is more effective in treating severe mania compared to quetiapine (16). Yet, Verachai et al. express that the effectiveness and side effects of haloperidol and quetiapine in treatment of methamphetamine-induced psychosis are similar (17). On the other hand, Emsley et al. express that quetiapine has both more effectiveness and less extrapyramidal side effects in controlling the symptoms of schizophrenia compared to haloperidol (18). As can be seen, the effectiveness of quetiapine and haloperidol varies in treatment and control of different mental disease symptoms and there is a lot of disagreement between the studies.

In one of the studies performed with the aim of comparing prescription of quetiapine and venlafaxine in treating the symptoms of somatization, it was determined that although quetiapine leads to improvement of these symptoms, it has a lower effectiveness compared to venlafaxine (19). In addition, Jin-long et al. showed that low doses of quetiapine are effective in treatment of somatization disorder. The researchers mentioned safety and rapid effect as the pros of this drug (20). Since conversion disorder is one of the subsets of somatization disorders it can be said that the 2 mentioned studies are in line with the present study.

Quetiapine results in less extrapyramidal side effects compared to haloperidol in controlling the effects of conversion disorder. This is one of the strong points of this drug because extrapyramidal symptoms are the most important side effect that limits the use of haloperidol. Dyskinesia, dystonia, akinesia, and neuroleptic malignant syndrome are among the side effects that require emergency care (21) and if a drug is available that reduces these symptoms, it will be very useful in clinic. In the present study, only 1 case of extrapyramidal side effects was observed in the quetiapine group, while there were 13 patients who were affected by these side effects as a result of consuming haloperidol. This significant difference results in quetiapine being introduced as a proper replacement for haloperidol.

## 5. Limitation

Among the limitations of the present study is the absence of placebo arm. Since from an ethical point of view it is not possible to leave a group of patients untreated, this could not be done. Among other limitations of this study was the short duration of follow-up for the patients. Since the half-life of

**Table 1:** Baseline characteristics of conversion disorder patients

| Variable | Haloperidol n=73 | Quetiapine n=71 | Total n=144 | P |
|---|---|---|---|---|
| **Age (mean, SD; years)** | 31.56±12.18 | 32.52±13.47 | 32.03±12.80 | 0.654 |
| **Sex (n, %)** | | | | |
| Male | 25 (34.25) | 29 (40.85) | 54 (37.50) | 0.414 |
| Female | 48 (65.75) | 42 (59.15) | 90 (62.50) | |
| **Psychotic disorders' History (n, %)** | | | | |
| No | 61 (83.56) | 65 (91.55) | 126 (87.50) | |
| Yes | 12 (16.44) | 6 (8.45) | 18 (12.5) | 0.147 |
| **Presentation on admission (n, %)** | | | | |
| Non-epileptic seizure | 6 (8.22) | 8 (11.27) | 14 (9.72) | |
| Speech disorder | 8 (10.96) | 4 (5.63) | 12 (8.33) | 0.584 |
| Paralysis | 17 (23.29) | 20 (28.17) | 37 (25.69) | |
| Other | 42 (57.53) | 39 (54.93) | 81 (56.25) | |

**Table 2:** Success of haloperidol and quetiapine in alleviating conversion disorder symptoms

| Variable | Haloperidol n=73 | Quetiapine n=71 | Total n=144 | P |
|---|---|---|---|---|
| **Response to treatment (n, %)** | | | | |
| No | 7 (9.59) | 6 (8.45) | 13 (9.03) | 0.812 |
| Yes | 66 (90.41) | 65 (91.55) | 131 (90.97) | |
| **Side effect (n,%)** | | | | |
| 30 min | | | | |
| No | 65 (89.04) | 66 (92.96) | 131 (90.97) | 0.412 |
| Yes | 8 (10.96) | 5 (7.04) | 13 (9.03) | |
| 24 hours | | | | |
| No | 64 (87.67) | 62 (87.32) | 126 (87.50) | 0.950 |
| Yes | 9 (12.33) | 9 (12.68) | 18 (12.50) | |

**Table 3:** Comparison of haloperidol and quetiapine side effects in alleviating conversion disorder symptoms

| Variable | Haloperidol n=73 | Quetiapine n=71 | Total n=144 | P* |
|---|---|---|---|---|
| **30 min (n, %)** | | | | |
| Extrapyramidal symptoms | 7 (9.59) | 0 (0.00) | 7 (4.86) | 0.013 |
| Fatigue and sleepiness | 3 (4.11) | 5 (7.04) | 8 (5.46) | 0.491 |
| Headache | 2 (2.74) | 1 (1.41) | 3 (2.08) | >0.999 |
| Other | 3 (4.11) | 0 (0.00) | 3 (2.08) | 0.245 |
| **24 hours (n, %)** | | | | |
| Extrapyramidal symptoms | 6 (8.22) | 1 (1.41) | 7 (4.86) | 0.116 |
| Fatigue and sleepiness | 6 (8.22) | 6 (8.45) | 12 (8.33) | >0.999 |
| Headache | 2 (2.74) | 2 (2.82) | 4 (2.78) | >0.999 |
| Other | 1 (1.37) | 0 (0.00) | 1 (0.69) | >0.999 |

* , Based on Fisher's exact test

haloperidol in body is 48 hours, 48-hour follow-up of the patients might present different results.

## 6. Conclusion

The results of the present study showed that although quetiapine and haloperidol have a similar effect in relieving the patients from conversion disorder symptoms, the prevalence of extrapyramidal symptoms is significantly lower in the group under treatment with quetiapine. Therefore, it seems that quetiapine is a safer drug compared to haloperidol.

## 7. Appendix

### 7.1. Acknowledgements

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### 7.2. Author contribution

All the authors of this article met the standard criteria of authorship based on the recommendations of international committee of medical journal editors.

### 7.3. Funding/Support

None.

### 7.4. Conflict of interest

Hereby, the authors declare that there is no conflict of interest regarding the present study.

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