

A Prospective Observational Study on The Adverse Drug Reactions and Medication Adherence of Haloperidol And Risperidone in Treating Psychotic Disorders

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ABSTRACT

Introduction:

Pharmacovigilance, when used in psychiatry, can assist in the identification of adverse drug reactions (ADRs) and notify doctors about the possibility of these occurrences in their everyday work. Timely diagnosis of such reactions is largely dependent on the clinical chemists' regular monitoring and assessment of the prescriptions. Thus, all of the detected ADRs among hospitalised psychiatric patients receiving haloperidol and risperidone were analysed in the current study

Methods and Material:

The Present study was prospective, observational study conducted in Department of Psychiatry, Government Medical College Hospital, Tiruppur. This study was conducted on 180 patients. The patient's demographic information (age, weight, and sex), prescribed medications, and all study specific details are all included in the data collection form. Medication Adherence Rating Scale, Naranjo's Scale and Modified Kuppaswamy Scale were used in this study.

Results:

Study population consisted of 170 participants. We had collected around 107 cases of psychotic disorder patients. Out of which 7 patients were excluded. Out of 170 patients in our study, 54.7% of patients were male and 45.3% of patients were female. In our study about 120 (70.5%) patients had some form of Schizophrenia, 18 (10.5%) patients had Bipolar Affective Disorder, 21 (12.55%) patients had a history of Psychosis, 9 (5.29%) patients had Substance Induced Psychotic Disorder, and 1 person (0.58%) each had Mood Disorder and Schizoaffective Disorder.

Conclusion:

On evaluation we found the scores obtained from the Naranjo ADR Assessment showed that the majority of the cases were moderate. Most of the patients in our study were having moderate level of severity. The Majority of the patients who took part in this study belonged to the lower socioeconomic class. The study also revealed that Risperidone had better patient compliance and lesser side effects than Haloperidol.

Keywords: Haloperidol, risperidone, Naranjo scale, Medication Adherence.

INTRODUCTION

"A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or for modification of physiological function" is the definition of an adverse drug reaction (ADR), according to the World Health Organisation. Given the rise in morbidity and death, rising medical expenses, and low compliance, these reactions provide a serious issue. Few research have been done globally and in India to examine the pattern of adverse drug reactions (ADRs) from psychiatric medications and determine whether a certain medication is causally linked to these reactions. ^[1,2]

Since ancient times, mental diseases have been extremely common. In the late 1990s, medical intervention in the treatment of mental disease began. The therapies were experimental and had a dismal prognosis for results. Many mental and behavioural illnesses were once treated with lobotomies, a surgical procedure. Heavy sedation, isolation, and restraint were used to control the erratic behaviour of agitated patients. Each of these therapies proved effective in lessening mental disease symptoms. Treatment for chronic disorders must be ongoing, and understanding and managing acute and late side effects becomes crucial^[4,5]

In India, pharmacovigilance is yet in its infancy. The rising incidence and prevalence of psychiatric problems in our nation has led to an increase in the usage of psychotropic medicines. Antipsychotic medications have a wide range of adverse drug reactions (ADRs) because of their impact on several dopaminergic pathways. Data on the precise prevalence and scope of the issue in the Indian context are, however, lacking.

Information regarding the frequency of side effects associated with novel antipsychotic medications is scarce, particularly from the Indian subcontinent. This is a whole new field for pharmacological study and medication manufacture, and the occurrence of these ADRs would inform both clinical practice and research in this area.^[6,7]

Pharmacovigilance, when used in psychiatry, can assist in the identification of adverse drug reactions (ADRs) and notify doctors about the possibility of these occurrences in their everyday work. Timely diagnosis of such reactions is largely dependent on the clinical chemists' regular monitoring and assessment of the prescriptions. Thus, all of the detected ADRs among hospitalised psychiatric patients receiving haloperidol and risperidone were analysed in the current study.^[8]

Application of pharmacovigilance in psychiatry can help in the detection of ADRs and alert physicians regarding the likelihood of such events in their routine practice. Frequent monitoring and evaluation of the prescriptions by the clinical pharmacists have an essential impact on timely identification of such reactions (Voora L et al., 2020). Hence the present study was carried out to analyze all the identified ADRs among hospitalized psychiatric patients

AIM

To Study the adverse drug reactions and medication adherence of Haloperidol and Risperidone.

OBJECTIVES:

1. To evaluate the socio-demographic profile of individuals affected with psychotic disorders.
2. To study the adverse drug reactions of Haloperidol and Risperidone.
3. To study the medication adherence in patients who undergo treatment for psychotic disorders.
4. To provide alternative treatment regimen for patients suffering from adverse drug reactions from their existing drug regimen.

METHODOLOGY:

Ethical Approval: The study is initiated after the clearance of institutional ethics committee

Study Site: Department of Psychiatry, Government Medical College Hospital, Tiruppur

Study Duration: The study conducted for 6 months.

Sample Size: 170 subjects

Study Design: Prospective Observational study

Study Criteria

Inclusion criteria:

1. Age: Between 18 years to 60 years.
2. Patients who have been diagnosed with psychotic disorder and are undergoing treatment.
3. Patients who have been prescribed First (Haloperidol) or Second Generation (Risperidone) Antipsychotics.

Exclusion criteria:

1. Critically ill patients.
2. Pregnant and lactating mothers.
3. Age group below 18 years of age and above 60 years of age.
4. Individuals with severe comorbidities such as Cerebrovascular Accident (CVA) and seizures.
5. Individuals who have developmental or congenital disorders.

Data Collection

To collect data from patients and medical records, a valid and reliable form tailored to each patient was developed. Student investigators constructed the profile form, which was validated through many standard publications. The patient's demographic information (age, weight, and sex), prescribed medications, and all study

specific details are all included in the data collection form. Medication Adherence Rating Scale, Naranjo's Scale and Modified Kuppuswamy Scale were used in this study.

Statistical Analysis

The data were entered into Microsoft Excel Spreadsheet and Statistical analysis was performed by simple statistical methods to generate Frequencies, Percentages.

RESULTS

Study population consisted of 170 participants. We had collected around 107 cases of psychotic disorder patients. Out of which 7 patients were excluded.

1. Modified Kuppuswamy Socioeconomic scale

Modified Kuppuswamy Socioeconomic scale		Score
Education of Head of Family	Professional degree	7
	Graduate or postgraduate	6
	Intermediate or post high school diploma	5
	High school certificate	4
	Middle school certificate	3
	Primary school certificate	2
	Illiterate	1
Occupation of head of family	Professional (white collar)	10
	Semi-professional	6
	Clerical, shop-owner / Farm	5
	Skilled worker	4
	Semi-skilled worker	3
	Unskilled worker	2
	Unemployed	1
Monthly Income of Family	≥52,734	12
	26,355 - 52,733	10
	19,759-26,354	6
	13,161-19,758	4
	7,887-13,160	3
	2,641-7,886	2
	<2640	1

Out of 170 patients in our study, 100% of patients come under the lower socioeconomic class (n=170). As such, there is a direct correlation between the lower socioeconomic class and cases of psychotic disorders.

2. Subject Characteristics

Subject Characteristics		No, of Patients (n=170)
Gender	Male	93 (54.70)
	Female	77 (45.29)
Age	Adult (18 - 35)	52 (30.5)
	Middle Age (35 - 55)	96 (56.5)
	Senior (> 55)	22 (13)
History Of Substance	Present	51 (30)

Abuse	Absent	119 (70)
Family History of Psychiatric Disorders	Present	44 (22.88)
	Absent	126 (74.11)

Out of 170 patients in our study, 54.7% of patients were male and 45.3% of patients were female. 52 (30.5%) of patients were Adults aged between 18 - 35, 96 (56.5%) of patients were Middle aged between 35-55 and 22 (13%) of patients were senior citizens aged above 55 years of age. Patients. 51 (30%) had a history of substance abuse (Alcohol, Tobacco and Cannabis) and 119 (70%) of the patients did not have a history of substance abuse. From this, we can infer that substances may not be a strong indicator of Psychotic disorders. .88% had prior family history of Psychotic Disorders and 126 (74.1%) had no family disorders of Psychotic Disorders

3. Types of Psychotic Disorders:

Type Of Psychotic Disorder	No. Of Patients	Percentage
Schizophrenia	120	70.5%
Bipolar Affective Disorder	18	10.5%
Psychosis	21	12.55%
Mood Disorder	1	0.58%
Substance Induced Psychotic Disorder	9	5.29%
Schizoaffective Disorder	1	0.58%

Out of 170 patients in our study 120 (70.5%) of patients had Schizophrenia, 18 (10.5%) of patients had Bipolar Affective Disorder, 21 (12.55%) of patients had a history of Psychosis, 9 (5.29%) of patients had Substance Induced Psychotic Disorder, 1 (0.58%) patient had Mood Disorder and 1 (0.58%) patient had Schizoaffective Disorder.

4. Assessment Of ADRs in Patients Administered with Haloperidol

Side Effects	Doubtful (0 or less)	Possible (1-5)	Probable (5-9)	Definite (9-14)
Weight Gain		1	18	1
Tremors		4	27	9
Slowness		1	32	2
Rigidity/Immobility		1	11	1
Sedation		1	9	
Joint Pain			14	
Micturition Problems			2	
Altered Appetite			3	
Dyspnoea			1	
Sleep Disturbance			4	
Tardive Dyskinesia			2	
Hypersalivation			3	
Digestion Issues			2	
Tachycardia			1	
Menstrual Issues			1	
Weight Loss		1		

Fatigue		1	4	
Akathisia			1	
Blurred Vision			1	
Muscle Spasm		1	1	

Out of 170 patients, 50% (n=85) were administered Haloperidol - A First Generation Antipsychotic Drug. The most prominent ADRs were found to be Tremors (n=40, possible = 4, Probable =27, definite=9), Bradykinesia/Slowness of activity (n=35, possible=1, probable=32, definite=2), Weight Gain (n=20, possible=1, probable=18, definite=1), Rigidity/Immobility (n=13, possible=1, probable=11, definite=1), Sedation (n=10, possible=1, probable=9) Joint Pain (n=14) and other lesser reported ADRs were found to be Micturition Problems (n=2), Altered Appetite (n=3), Dyspnoea (n=1), Sleep Disturbances (n=4), Tardive Dyskinesia (n=2), Hypersalivation (n=3), Digestive Issues (n=2), Tachycardia (n=1), Menstrual Issues (n=1), Weight Loss (n=1), Fatigue (n=5), Akathisia (n=1), Blurred Vision (n=1), Muscle Spasm (n=2)

Side Effects	Doubtful (0 or less)	Possible (1-5)	Probable (5-9)	Definite(9-14)
Weight Gain		1	49	1
Tremors		1	27	
Slowness		1	21	1
Fatigue			11	
Headache			1	
Shortness of Breath			1	
Sedation			12	1
Back Pain			3	
Joint Pain			21	
Altered Appetite			7	
Dyspnoea			1	
Sleep Disturbance			6	
Tardive Dyskinesia				1
Edema			1	
Hypersalivation			2	
Immobility			2	
Micturition Problems			2	
Muscle Stiffness			1	
Lower Abdominal Pain			1	
Digestion Issues			5	
Memory Loss			2	
Dizziness			4	
Genital Issues			1	

Dry Mouth			2	
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5. Assessment Of ADRs in Patients Administered with Risperidone

Out of 170 patients, 50% (n=85) were administered Risperidone - A Second Generation Antipsychotic Drug. The most prominent ADRs were found to be Weight Gain (n=51, possible=1, probable=49, definite=1), Tremors (n=28, possible=1, probable=27), Bradykinesia/Slowness of Activity (n=23, possible=1, probable=21, definite=1), Fatigue (n=11), Sedation (n=13), Joint Pain (n=21), Altered Appetite (n=7) and lesser reported ADRs include Headache (n=1), Shortness Of Breath (n=1), Back Pain (n=1), Dyspnea (n=1), Sleep Disturbance (n=6), Tardive Dyskinesia (n=1), Edema (n=1), Hyper salivation (n=2), Immobility (n=2), Micturition Problems (n=2), Muscle Stiffness (n=1), Lower Abdominal Pain (n=1), Digestive Issues (n=5), Impaired Memory (n=2), Dizziness (n=4), Genital Issues (n=1), Dry Mouth (n=2).

6. Average Naranjo Scale Score (Male Vs Female) _ T test

FEMALE		MALE		T - TEST VALUE	P- VALUE
MEAN	STD DEV	MEAN	STD DEV		
7.34	0.65	7.07	0.88	0.2700	0.0264

T - test revealed that there exists a significant statistical difference in average Naranjo scale score of both females and males which indicates the hypothesis is false and hence it was concluded that there is significant difference in average Naranjo scale score of both females and males. So the severity of adverse events is different in females and males, and severity is more in female when compared to males.

7. Average Naranjo Scale Score (Haloperidol group Vs Risperidone group)_ T test

HALOPERIDOL		RISPERIDONE		T - TEST VALUE	P- VALUE
MEAN	STD DEV	MEAN	STD DEV		
7.27	0.89	7.07	0.69	0.2000	0.1034

T - test revealed that there exists no significant statistical difference in Average Naranjo scale score of both Haloperidol group and Risperidone group which indicates the hypothesis is true and hence it was concluded that there is no significant difference in Average Naranjo scale score of both Haloperidol group and Risperidone group. So the severity of adverse events is same in Haloperidol group and Risperidone group.

8. Medication Adherence profile of Haloperidol

Medication Adherence	No. of Patients	Percentage
Good Adherence	39	45.9%
Poor Adherence	46	54.1%

Using the Medication Adherence Rating Scale, the adherence of patients undergoing therapy with Haloperidol was assessed and patients who had good adherence was estimated to be 45.9% (n=39) and patients who had poor adherence was estimated to be 54.1% (n=46)

9. Medication Adherence profile of Risperidone

Medication Adherence	No. of Patients	Percentage
Good Adherence	44	51.8%
Poor Adherence	41	48.2%

Using the Medication Adherence Rating Scale, the adherence of patients undergoing therapy with risperidone was assessed and patients who had good adherence was estimated to be 51.8% (n=44) and patients who had poor adherence was estimated to be 48.2% (n=41).

10. Medication Adherence Score (Male Vs Female) _ T test

FEMALE		MALE		T - TEST VALUE	P- VALUE
MEAN	STD DEV	MEAN	STD DEV		
4.38	2.34	4.56	2.33	-0.1800	0.6171

T - test revealed that there exists no significant statistical difference in medication adherence score of both females and males which indicates the hypothesis is true and hence it was concluded that there is no significant difference in medication adherence score of both females and males. So both female and male patients are equally adherent to medications use.

11. Medication Adherence Score (Haloperidol group Vs Risperidone group)_ T test

HALOPERIDOL		RISPERIDONE		T - TEST VALUE	P- VALUE
MEAN	STD DEV	MEAN	STD DEV		
4.30	2.37	4.65	2.29	-0.3500	0.3289

T - test revealed that there exists no significant statistical difference in medication adherence score of both Haloperidol group and Risperidone group which indicates the hypothesis is true and hence it was concluded that there is no significant difference in medication adherence score of both Haloperidol group and Risperidone group. So both groups patients are equally adherent to medications use.

DISCUSSION

In our study, 170 patients were interviewed out of which 93 were male and 77 were female. The age range of the patients in the study varied greatly. The adult population between the ages of 18 - 35 was 52 (30.5%) patients. Middle Aged patients between the ages of 35 -55 formed the majority of the study population coming at 96 (56.5%) and Senior population (above 55 years old) comprised of 22 (13%) patients. This is similar to a study conducted by Mehta et al^[10].

In our study about 120 (70.5%) patients had some form of Schizophrenia, 18 (10.5%) patients had Bipolar Affective Disorder, 21 (12.55%) patients had a history of Psychosis, 9 (5.29%) patients had Substance Induced Psychotic Disorder, and 1 person (0.58%) each had Mood Disorder and Schizoaffective Disorder which is somewhat similar to the study conducted by Mehta et al^[10].

Our study revealed that men (n=93, 54.70%) were more likely to be affected by psychotic disorders than women (n=77, 45.29%). Which is congruent to a study conducted by Ochoa S, Usall J et al^[11].

The study population revealed that 126 (74.11%) had no prior family history of psychotic disorder and 44 (25.88%) patients were found to have a family history of Psychotic Disorders

The Naranjo ADR Rating Scale is a causality assessment rating scale that has been used in this study to evaluate the various ADRs which have been reported by patients who participated in this study. There are 10 questions on the ADR Probability Scale, and the answers might be "Yes," "No," or "Do not know." A distinct point value (-1, 0, +1, or +2) is assigned to each response. Depending on the score, the relationship between the drug and the ADR can be classified into doubtful (0 and below), possible (1 - 4), probable (5 - 9) and definite (9 -13).

Haloperidol is a First Generation Antipsychotic Drug which is used widely in the treatment of psychotic disorders. Out of 170 patients, 50% (n=85) were administered Haloperidol - A First Generation Antipsychotic Drug. The most prominent ADRs were found to be Tremors (n=40, possible = 4, Probable =27, definite=9), Bradykinesia/Slowness of activity (n=35, possible=1, probable=32, definite=2), Weight Gain (n=20, possible=1, probable=18, definite=1), Rigidity/Immobility (n=13, possible=1, probable=11, definite=1), Sedation (n=10, possible=1, probable=9) Joint Pain (n=14). The results derived are very similar to a study conducted by Kurz M, Mummer M et al^[12].

Risperidone is a Second Generation Antipsychotic Drug which is used widely in the treatment of various Psychotic Disorders. Out of 170 patients, 50% (n=85) were administered Risperidone - A Second Generation Antipsychotic Drug. The most prominent ADRs were found to be Weight Gain (n=51, possible=1, probable=49, definite=1), Tremors (n=28, possible=1, probable=27), Bradykinesia/Slowness of Activity (n=23, possible=1, probable=21, definite=1), Fatigue (n=11), Sedation (n=13), Joint Pain (n=21), Altered Appetite (n=7). This is very similar to a study conducted by Alladi CG, Mohan A et al.^[13]

The Medication Adherence Rating Scale by Thompson et al^[9] was used to assess the Medication adherence profiles of patients who were administered Haloperidol and Risperidone. Our study shows that Risperidone shows much lesser Extrapyramidal Adverse Events and ADRs in general than Haloperidol. Another point to be noted is that patients administered with Risperidone show a greater degree of patient adherence (51.8%) than patients who were administered with Haloperidol (45.9%). This is supported by a study done by Davies A et al^[14] which more or less confirms that Risperidone is marginally safer than First Generation Antipsychotics such as Haloperidol.

CONCLUSION

Various scales used in assessment of multiple criterias such as Medication Adherence, Adverse Drug Reactions and Socioeconomic status. The Medication Adherence Rating Scale provides a questionnaire - higher scores indicate better compliance. Naranjo's ADR Causality Assessment Scale was used to assess ADRs. Depending upon the scores of the questionnaire, the causal relationship between the ADR and the drug can be assessed as doubtful (0 and below), possible (1-4), probable (5-9) and definite (9-14). Higher scores indicate a greater degree of causal relationship. Modified Kuppuswamy Scale was used to assess the socioeconomic profiles of the various participants of the study and it is based on the Education of the head of the family, Occupation of the head of the family and monthly income of the family. Depending upon the scores, the socioeconomic classes of the participants can be divided into Lower (score 1-4), Lower-Middle (5-10), Middle (5-10), Upper-Middle (16-25) and Upper (26-29) higher scores indicate a higher standard of living.

On evaluation we found the scores obtained from the Naranjo ADR Assessment showed that the majority of the cases were moderate. Most of the patients in our study were having moderate level of severity.

The Majority of the patients who took part in this study belonged to the lower socioeconomic class. The study also revealed that Risperidone had better patient compliance and lesser side effects than Haloperidol.

The patients who underwent severe ADRs were given alternative treatments which would help better the therapeutic outcome. Drugs such as Trihexyphenidyl (Antimuscarinic), Sodium Valproate (Antiepileptic / mood stabilizer), Diazepam (Benzodiazepine) and Vitamin Supplements were provided to lessen ADRs.

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