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A Comparative Study on Relative Safety and Efficacy of Chlorpromazine and Risperidone in Schizophrenia patients

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ABSTRACT

Patient safety is the foremost concern in the healthcare system. However, only a few studies have been conducted regarding the safety and efficacy of antischizophrenic drugs in the south Indian population. The main objective is to study relative safety profile and efficacy between chlorpromazine and risperidone among schizophrenia patients in teaching hospital. Prospective, observational, comparative study conducted for six months among schizophrenia patients. The data was collected from 62 enrolled subjects with the help of questionnaires and scales, and data was analyzed by using a t-test and other relevant descriptive analysis by using the statistical software SPSS version 20.0. Out of a total of 70 patients, males were 39, and females were 31. Out of 70 patients, only 62 patients completed the study according to the inclusion criteria. The occurrence of schizophrenia was higher in the age of late adolescence and early adulthood. Risperidone was more effective in treating negative and general symptoms compare to chlorpromazine, but equally efficacious in treating positive symptoms. Poor medication adherence was found in patients receiving both drugs. Chlorpromazine is more effective in a patient with predominantly positive symptoms. Risperidone is more effective and should be preferred in patients with positive, negative, and general symptoms.

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INTRODUCTION

"Schizophrenia is a severe mental disorder, characterized by profound disruptions in thinking, affecting language, perception, and sense of self. It often includes psychotic experiences, such as hearing voices or delusions. It can impair functioning through the loss of an acquired capability to earn a livelihood, or the disruption of studies" (WHO, 2019). Several studies revealed that schizophrenic patients have two to threefold increased risk of dying. The prevalence of adult schizophrenic patients ranges from 1-17 per 1000 population, which is one of the challenging morbidity in society. The incidence is increasing in countries like

India as well. There is a risk of about 18 members to get affected by schizophrenia among 1000 population (Stroup *et al.*, 2011; Saha *et al.*, 2016). Several systemic reviews and meta-analysis suggest the 30%–40% higher risk of schizophrenia among the male population in developing countries (McGrath *et al.*, 2008; Thornley *et al.*, 2003; Murray, 2006). Positive, negative and cognitive symptoms are three broad categories of schizophrenic manifestations.

Pharmacological, as well as non-pharmacological modalities of management, including psycho social support, are some options available to slow down the progress of the disease. However, the accessibility of the general population and the awareness of patients is still challenging. Chlorpromazine was frequently chosen drug of choice by physicians despite its well-known side effects (Dolder *et al.*, 2002). After the late 1980s, risperidone evolved as first-line medication among Schizophrenic patients due to better tolerability and less incidence of extrapyramidal. This study aims to compare the relative safety and efficacy of chlorpromazine and risperidone.

MATERIALS AND METHODS

A prospective, observational, comparative study was conducted in the department of psychiatry at Vijayanagara Institute of Medical Sciences located in the Ballari district of southern India. The ethical approval was granted by the ethics committee of the institute (Reg. No. TVMCP/ IEC/V PD/ 2017-18/01) Informed consent was taken before enrolling the schizophrenic patients in the study. The sample size of 60 patients was finalized based on data available on the medical record department. A comparative study was carried out on hospitalized Schizophrenic patients above18 years of age of either sex prescribed with chlorpromazine or risperidone. The study was conducted for six months in the patients completing the follow up for the entire study duration.

Initially, a total of 70 patients were enrolled; eight patients were failed to follow up. Remaining 62 patients diagnosed with schizophrenia meet all inclusion criteria that were taken as sample size. A total of 62 patients was divided into an equal group of 31 patients, each taking chlorpromazine and risperidone during hospitalization. The dose considered for the comparison of both drugs was standardized at 100-400mg/day and 1-4 mg/day in divided dosage for chlorpromazine and risperidone, respectively. The patients were followed by and assessed for six months. The scoring was done starting from baseline (enrolling date) at an interval of 15 days for consecutive six visits. The scores obtained from follow up were recorded in the data collection form.

During the follow-up visit, Positive and Negative Syndrome (PANSS) score was used to assess the efficacy of the drug. Collected data were analyzed statistically to compare both drugs. Patient's drug compliance was also assessed by using DAI 10 questionnaire score and relative safety of the drugs was assessed by the number of side effects and adverse drug reaction occurred in the hospitalized patients as in Simpson Angus EPS scales. The mean and standard error of the mean was calculated; two-sample independent t-tests were used with a confidence interval of 95%, and p-value <0.05 was considered statistically significant using the SPSS software version 20.00.

RESULTS AND DISCUSSION

Age and gender-wise distribution

Out of 70 patients, dropouts in the chlorpromazine group were found to be 7(87.5%), and for risperidone group were found to be 1 (12.5%) Due to failure in their follow up. Patients included in our study were in the age group of 20 to 65 years, with the mean age of approximately 34 years in both groups receiving either chlorpromazine or risperidone. In our study, out of 70 patients, 39 were male, and the remaining was female. The incidence rate was not significantly differencing for schizophrenia. Details of age and gender are given in the Table 1 and Table 2.

Efficacy Study Based on Symptoms

Comparison based on positive symptoms on each visit

During the baseline phase, the mean scores were found around 27 and 25, respectively. During the last visit, the mean scores were dropped by 12 and 11 and found to be 15 and 14, respectively. Details are shown in Table 3.

Chlorpromazine and risperidone were equally effective in controlling the positive symptoms in patients of schizophrenia.

Comparison based on negative symptoms on each visit

There was a significant reduction in the incidence of negative symptoms 44% due to risperidone, whereas the reduction of negative symptoms in patients receiving chlorpromazine was 17%. This shows better action of risperidone. Details are explained in Table 4.

Table 1: Mean age of the patients in both groups

	Age Wise Distribution				
	Patients	Mean	Std.	Min Age	Max Age
Chlorpromazine	38	32.44	8.97	20	55
Risperidone	32	37.71	12.19	23	65

Table 2: Sex-wise distribution in both groups

	Sex Wise Distribution		
Drugs	Male	Female	Total
Chlorpromazine	17	21	38
Risperidone	22	10	32
Total	39	31	70

Table 3: Comparison of positive symptoms on each visit

		Positive Symptoms				
Phase	Drug	No. Patients	Mean	Std.	SE	T-Test
0	Chlorpromazine	31	27.19	6.63	1.19	P=0.292
	Risperidone	31	25.35	6.97	1.25	
1	Chlorpromazine	31	26.06	6.35	1.14	P=0.449
	Risperidone	31	24.83	6.32	1.14	
2	Chlorpromazine	31	23.39	5.01	0.90	P=0.644
	Risperidone	31	22.77	5.36	0.96	
3	Chlorpromazine	31	21.22	4.77	0.86	P=0.230
	Risperidone	31	19.70	5.06	0.91	
4	Chlorpromazine	31	17.94	4.62	0.83	P=0.518
	Risperidone	31	17.19*	4.36	0.78	
5	Chlorpromazine	31	15.65	4.57	0.82	P=0.248
	Risperidone	31	14.35*	4.12	0.74	

Baseline visit -o phase time of patient recruited into the study; no- number of patients, mean- mean of positive symptoms of 31 patients in each visit; Std.- Standard Deviation; SE-Standard error of the mean

Table 4: Comparison of negative symptoms on each visit

		Negative Symptoms				
Phase	Drug	No. Patients	Mean	Std.	SE	T-Test
0	Chlorpromazine	31	25.65	4.00	0.74	P=0.867
	Risperidone	31	25.74	4.00	1.34	
1	Chlorpromazine	31	25.55	3.59	0.65	P=0.340
	Risperidone	31	21.58	5.70	1.17	
2	Chlorpromazine	31	23.55	3.23	0.58	P=0.101
	Risperidone	31	18.74	5.57	1.02	
3	Chlorpromazine	31	22.71	3.49	0.63	P=0.002*
	Risperidone	31	18.74	5.57	1.00	
4	Chlorpromazine	31	21.58	3.96	0.71	P=0.001*
	Risperidone	31	16.58	5.84	1.05	
5	Chlorpromazine	31	21.19	4.59	0.82	P=0.001*
	Risperidone	31	13.64	4.81	0.86	

*-statistically significant; baseline visit -o phase time of patient recruitedinto the study date; no- number of patients, mean- mean of negative symptoms of 31 patients in each visit; Std.- Standard Deviation; SE- Standard Error

Table 5: Comparison of general symptoms on each visit

		General Symptoms				
Phase	Drug	No. Patients	Mean	Std.	SE	T-Test
0	Chlorpromazine	31	49.90	10.72	1.92	P=0.828
	Risperidone	31	49.29	11.39	2.05	
1	Chlorpromazine	31	49.52	10.20	1.83	P=0.435
	Risperidone	31	47.39	11.12	2.00	
2	Chlorpromazine	31	43.42	8.86	1.59	P=0.305
	Risperidone	31	41.10	8.84	1.59	
3	Chlorpromazine	31	39.29	7.69	1.38	P=0.097
	Risperidone	31	35.84	8.45	1.52	
4	Chlorpromazine	31	35.48	7.31	1.31	P=0.008*
	Risperidone	31	30.26	7.90	1.42	
5	Chlorpromazine	31	32.29	6.89	1.24	P=0.003*
	Risperidone	31	26.58	7.61	1.37	

*P<0.05, Significant baseline visit -o phase time of patient recruited into the study date; no- number of patients, mean- mean of general symptoms of 31 patients in each visit; Std.- Standard Deviation; SE- Standard Error

Table 6: Comparative effect of drugs on patient's medication compliance on each visit

		Adherence				
Phase	Drug	No. Patients	Bold Mean	Std.	SE	T-Test
0	Chlorpromazine	31	9.032	1.354	0.243	P=1
	Risperidone	31	9.032	1.140	0.205	
1	Chlorpromazine	31	8.774	1.687	0.303	P=0.871
	Risperidone	31	8.839	1.416	0.254	
2	Chlorpromazine	31	8.677	2.242	0.402	P=0.482
	Risperidone	31	8.323	1.661	0.298	
3	Chlorpromazine	31	8.484	2.158	0.387	P=0.524
	Risperidone	31	8.161	1.791	0.321	
4	Chlorpromazine	31	8.258	2.129	0.382	P=0.671
	Risperidone	31	8.032	2.041	0.366	
5	Chlorpromazine	31	7.581	2.363	0.424	P=0.406
	Risperidone	31	8.032	1.853	0.333	

*P<0.05, Significant; baseline visit -o phase time of patient recruited into the studydate; no- number of patients, mean- mean of bold answers 31 patients in each visit; Std.- Standard Deviation; SE- Standard Error

Comparison based on general symptoms on each visit

The baseline score of schizophrenia was about 49 for both treatment groups. During follow up, the scores fall to 32 for chlorpromazine and 27 for risperidone during the final visit, which was statistically significant (p=0.003). The details are shown in Table 5.

Adherence

Adherence was studied by using drug attitude inventory ten questionnaires, where individual patient's attitude towards each question was collected. Mean at the base-line visit was around nine for both groups, ongoing treatment of the patients of both group adherences decreases but was not a statistically significant difference. The details are shown in Table 6.

Safety

The baseline observations mean score of Simpson Angus EPS scales of chlorpromazine and risperidone groups was found to be around 5 and 8, respectively. In subsequent visits, the scores were gradually increased and found to be 15 for chlorpromazine and 12 for the risperidone, which was statistically significant. The details are shown in Table 7.

Medication-related adverse drug reactions were in increasing order in each ongoing visit, but chlorpromazine was significantly causing more extra pyrami-

Table 7: Comparative side effects of drugs on patients on each visit

			EPS			
Phase	Drug	No. Patients	Mean	Std.	SE	T-Test
0	Chlorpromazine	31	5.16	3.804355	0.683	P=0.029*
	Risperidone	31	7.58	4.660287	0.837	
1	Chlorpromazine	31	6	3.587014	0.644	P=0.076
	Risperidone	31	7.90	4.62857	0.831	
2	Chlorpromazine	31	7.81	4.166688	0.748	P=0.657
	Risperidone	31	8.32	4.92874	0.885	
3	Chlorpromazine	31	10.35	4.461303	0.801	P=0.341
	Risperidone	31	9.16	5.28581	0.949	
4	Chlorpromazine	31	12.26	4.932665	0.886	P=0.112
	Risperidone	31	10.13	5.439007	0.976	
5	Chlorpromazine	31	14.68	4.975856	0.893	P=0.033*
	Risperidone	31	11.81	5.393943	0.968	

*P<0.05, Significant; baseline visit -o phase time of patient recruited into the study date; no- number of patients, mean- mean score of Simpson Angus EPS scalesof 31 patients in each visit; Std.-Standard Deviation; SE- Standard Error

dal symptoms than risperidone.

A total number of 70 patients were enrolled in the study. Among them, 62 patients completed the study. The means age was 34 years, which is similar to a study conducted by (Tamrakar *et al.*, 2006) and the incidence was similar in both males and females; this is similar to the study conducted by (Mamarde *et al.*, 2011) From baseline to the scores obtained during the fifth visit shows a decrease in the symptoms in both of the groups, which shows that both drugs were quite effective in controlling the positive symptoms of the schizophrenia, which was supported by studies conducted by (Mamarde *et al.*, 2011; Tamrakar *et al.*, 2006).

In the present comparative study, risperidone was found more promising in controlling the negative symptoms (44%) compare to that of chlorpromazine (17%). Similarly, it was found more promising in general symptom also risperidone (64%) and chlorpromazine (53%) during the last visit which was in accordance with the study conducted by (Kennedy *et al.*, 1998; Rabinowitz and Davidson, 2001; Li *et al.*, 2015) It was found that the mean Simpson Angus EPS Scales score for EPS symptoms increased for chlorpromazine to 9 while the mean Simpson Angus EPS Scales score for EPS symptoms increased for risperidone to 4 from baseline to the fifth visit. This suggests the increased ADRs in the patients receiving chlorpromazine than the patient receiving risperidone. Our study found that Typical Antipsychotic is having more EPS than Atypical Antipsychotic (risperidone), which is similar to the study of (Mamarde *et al.*, 2011; Tamrakar *et al.*, 2006).

In the present study, the medication adherence score was around nine for both groups of patients; during ongoing treatment, the patients of both group adherence decrease significantly, but no statistically significant difference was obtained between two groups, which were similar to the study conducted by (Mamarde *et al.*, 2011) But found to be contrary to the study conducted by (Dolder *et al.*, 2002).

CONCLUSIONS

Our study reveals the more promising findings of risperidone over chlorpromazine in terms of safety and efficacy, whereas medication adherence remains almost the same. Risperidone was more effective in treating positive, negative, and general symptoms of schizophrenia and have fewer incidences of adverse drug reactions also. Chlorpromazine was also found to be equally effective in controlling positive symptoms of schizophrenia. The overall study suggests that risperidone has a broader spectrum in controlling the symptoms and found to be safer than chlorpromazine. Hence, our study suggests the risperidone over chlorpromazine.

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