Original Research Article

Comparative Study of Effectiveness in Haloperidol Versus Olanzapine in Schizophrenia

ABSTRACT

Aim: To compare the efficacy of oral Typical Antipsychotic drug [Haloperidol] Group A versus oral Atypical Antipsychotic drug [Olanzapine] Group B in patients who met the criteria for schizophrenia. This study includes observe and compare the positive symptoms and negative symptoms in Group A and Group B by using PSYRATS scale and Negative symptom Assessment Tool.

Study design: ProspectiveComparative Observational study

Place and Duration of Study: The study was carried from April 2023 – September 2023 at Psychiatric Outpatient Department in the Government Medical College and Hospital, Nagapattinam.

Methodology: The study sample comprised 60 patients [N=60], The 30 subjects were in Group A and 30 subjects were in Group B who met the SCID – DSM V criteria and also include criteria 1. Age between 22 – 65 years. 2. Subject should have Minimum Mental State Examination [MMSE] score between 25 – 30.

Result: Out of 60 patients Olanzapine was associated with a Mean baseline to endpoint improvement of (-22.77) versus a Mean change of (-14.39) in Haloperidol. Olanzapine [Group B] had higher mean difference than Haloperidol [Group A].

Conclusion: By using PSYRATS scale and Negative Symptom Assessment Tool, Olanzapine treated group were numerically better than the Haloperidol treated group in both Negative and Positive Symptoms

Comment [JE1]: Inferential statistics and its' summary should be included

Keywords: Schizophrenia; Haloperidol; Olanzapine; PSYRATS Scale; Negative Symptom Assessment Tool.

1.INTRODUCTION

Schizophrenia is a chronic mental health condition where a person separate from reality into a world of unknown. It defines that heterogenous syndrome of Disorganized & Bizarre thoughts, Delusion, Hallucinations inappropriate affect & impaired psychosocial functioning [1].It's classified into several types such as Paranoid, Hebephrenic, Catatonic, Undifferentiated, Residual and Simple. The exact cause of Schizophrenia isunknown. The combination of physical, genetics, psychological and environmental factors can make a person more likely to develop the condition.It is the most common functional psychosis and great variation occurs in clinical presentation. The first psychotic episodes can be sudden with onset symptoms of social withdrawal, trouble concentrating, temper flares, difficulty sleeping.The DSM – V classifies the symptoms of schizophrenia into three categories – Positive, Negative and Cognitive dysfunction [2].This dopamine hypothesis describes the positive

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symptoms occur due to excessive activation of D2 receptor via mesolimbic pathway, while low levels of dopamine in nigrostriatal pathway are reason to cause abnormal motor symptoms which affect extrapyramidal system.The positive symptomsincludedelusion, hallucination, disorganized thoughts and disorganized behaviour. Low mesocortical dopamine levels resulting from the mesocortical pathway are thought to elicit the negative symptoms of the disease. The Negative symptoms consist of five elementsare blunted affect, alogia, avolition, asociality and anhedonia. Cognitive dysfunction shows substantial impairment in overall cognitive performance include attention, working memory, verbal learning, memory and executive functions [3]. In worldwide people affected from schizophrenia where approximately 24 billion or 1 in 300 people (0.32%). In India, where about 1.1 billion people reside, the prevalence of schizophrenia is about 3/1000 in individual. It is more common in men and in terms of age of onset, men tend to be younger by an average of about 5 years than women when they develop schizophrenia. It is frequently associated with significant distress and impairment in personal, family, social, educational, occupational and other important areas of life [4]. Schizophrenia is treated with typical and atypical antipsychotic drugs. The first line agents are Risperidone, Olanzapine, Aripiprazole, Quetiapine, Haloperidol, Trifluoperazine [5]. This study aims to compare the effectiveness of oral antipsychotics, Typical [Haloperidol] versus Atypical [Olanzapine] in patients with Schizophrenia in outpatient Department of psychiatry in Government Medical College and Hospital.

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Comment [JE5]: Replace with "were"

Comment [JE6]: Replace with "0.3%"

Comment [JE7]: Replace with "Prevalence is higher in males than females"

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2. MATERIAL AND METHODS

2.1 Study Site and Study Design

The study was carried out in the psychiatric outpatient Department of Government Medical College and Hospital,Nagapattinamover a period of six months (April 2023- September 2023). It is aProspective Comparative Observational study.

2.2 Study Population

This study included 60 patientsand they were divided into two groups, Group A patients received Oral Typical Antipsychotic [Haloperidol] and Group B patients received Oral Atypical Antipsychotic [Olanzapine].

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2.3 Study Criteria

Inclusion Criteria: Patients of either sex and age group between 22- 65 were included in study and those who had been newly diagnosed with schizophrenia according to SCID based on the 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders. Patients who were included in study should have Minimum Mental State Examination [MMSE] score between 25- 30.

Exclusion Criteria: Patient with schizophrenia who were untreated for 2 years and also patient with multiple episodes of schizophrenic attack were excluded from study. Patient with co-morbidities of diabetes mellitus and who has presence of Extrapyramidal Symptoms, also those who are with Body Mass Index above 30 were excluded from the study.

2.4 Data Collection and Analysis

Patients who are clinically diagnosed with schizophrenia during the study period was enrolled in the study. Prior to the study, details about the study were explained to patient in vernacular language and written informed consent was obtained. Sixty cases were selected., and they were divided into two groups. Group A patients received, Initial starting dose of Haloperidol1.5mg/day with increase in dose of 2 mg/day to a maximum of 30mg/day. Group B patients received, Initial starting dose of Olanzapine5mg/day with increase in dose of 2.5 mg/day to a maximum of 20mg/day. Comprehensive data were collected which includes demographical details, past medical and medication history, social history, family history, allergy history using Standard Data Collection form. A predesigned pro – forma PSYRATS scale [17items, 0 – 4 severity scale] and Negative Symptom Assessment Tool [5 items, 0 – 4 severity scale] was used to observe and compare the effectiveness of Haloperidol and Olanzapine in Positive and Negative symptoms.The effectiveness was calculated by comparing the scores from baseline and after the follow up for up to 3 months and Endpoint effective analysis was done.IBM SPSS STATISTICS 29.0.1.0 was used to perform statistical analysis. Data was gathered in MS EXCEL and it was transferred to spreadsheet of SPSS. Descriptive data was presented as mean and standard deviation. To compare the positive symptoms and negative symptoms from baseline to

Comment [JE11]: State your sampling technique and include it here

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endpoint between patients who received haloperidol [Group A] and olanzapine [Group B] was analysed usingPaired samplet test.For all statistical analysis, the *P* value<0.05 was considered as statistically significant.

Comment [JE15]: Independent t test would have been better than Paired Sample test, as the latter test for same group, whereas in this case are different groups.

I will recommend you use Propensity Score Matching, controlling for confounders such as age, sex and other variables, then get the Average Treatment Effect (ATE). This a powerful tool and will work well if you can also increase the sample size of the study.

3. RESULT AND DISCUSSION

3.1 Demographics

3.1.1 Gender wise distribution

In gender wise distribution out of 60 patients with schizophrenia, 31(51.60%) was found to be male and 29(48.40%) were female. The male had higher predominance over female patients (Table 1).

Table 1. Gender distribution in study subjects

Gender	Group A (n= 30)	Group B (n= 30)	Total (n= 60)	Percentage
Male	12	19	31	51.60%
Female	18	11	29	48.40%

n- number of study subjects.

3.1.2 Age wise distribution

In age wise distribution among 60 patients who are enrolled in study, the maximum number of subjects 31(52%) belongs to the age group of 22- 35 years (Table 2).

Table 2. Age distribution in study subjects

Age	Male	Female	Total	Percentage
22 – 35	17	14	31	52%
36 – 45	9	7	16	27%
46 – 55	4	6	10	16%
56 – 65	1	2	3	5%

3.1.3 Marital status

The marital status of study subjects revealed that out of 60 patientsthe majority 28(46%) were unmarried and 25(42%) were married and about 4(7%) were divorced, 3(5%) was found to be widow (Figure 1).

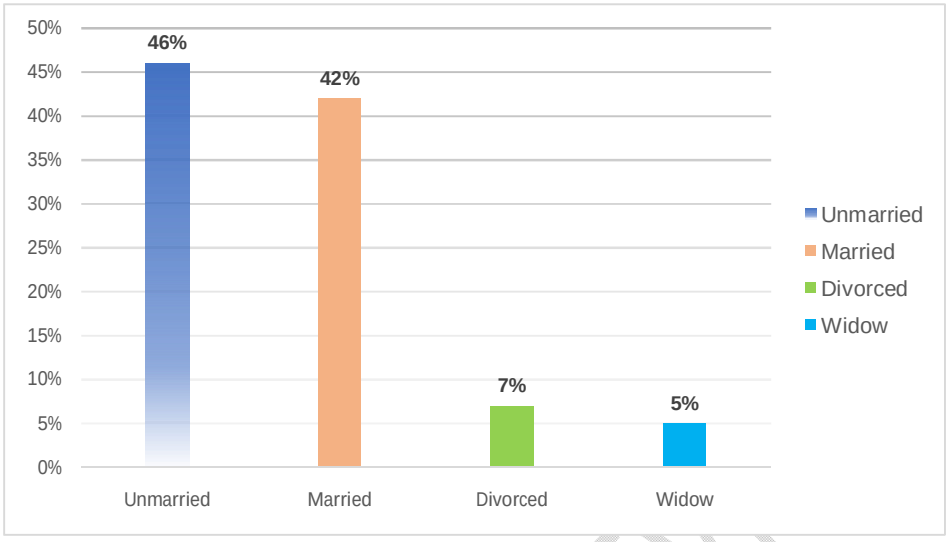

Fig. 1. Marital status of study subjects

3.1.4 Occupational status

Among 60 patients with schizophrenia majority of subjects remind unemployed 35(58.40%) and 25(41.60%) was employed (Figure 2).

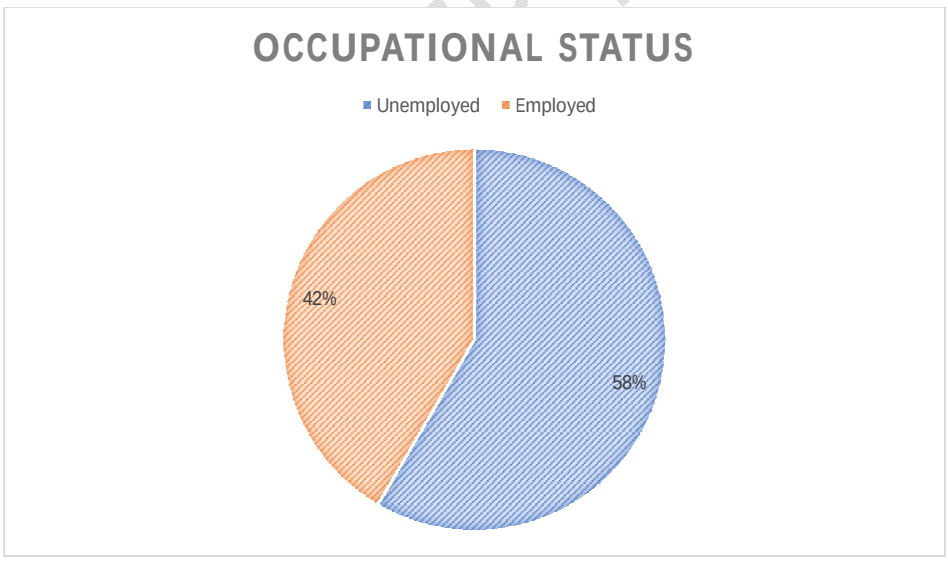

Fig. 2. Occupational status of study subjects

3.2 Comparison of positive symptoms in Group A & Group B using PSYRATS scale

By evaluating the positive symptoms in study subjects with schizophrenia by using PSYRATS scale from baseline to the endpoint, Group A patients who received haloperidol had a mean difference of [28.86 ± 11.56(baseline)] to [17.50 ± 9.13(endpoint)]. Significant mean difference of -11.36 was observed. It was found to be statistically significant using paired t test (*P*= 0.0017) (Table 3).

Table 3. Statistical analysis of positive symptoms in Group A

Positive symptoms [score= 68]	Group – A(n= 30)		*P* value
	Mean	SD	
Baseline	28.86	11.56	
Endpoint	17.50	9.13	0.0017
Mean difference	-11.36		

n- number of study subjects.

On the other hand, Group B patients who received olanzapine had a greater mean difference of [27.36 ± 13.46(baseline)] to [10.23 ± 8.42(endpoint)]. Here, the mean difference was found to be -17.13 which is comparatively greater than that of Group A patients who received haloperidol. It is also statistically significant by paired t test (*P* = 0.0015) (Table 4).

Table 4. Statistical analysis of positive symptoms in Group B

Positive symptoms [score= 68]	Group – B(n= 30)		*P* value
	Mean	SD	
Baseline	27.36	13.46	
Endpoint	10.23	8.42	0.0015
Mean difference	-17.13		

n- number of study subjects.

Therefore, with implies olanzapine [Group B] had greater effectiveness in reducing the positive symptoms of schizophrenia compared to haloperidol [Group A].

3.3 Comparison of negative symptoms in Group A & Group B using Negative symptom assessment tool [BNSS]

In our study, the negative symptoms in patients with schizophrenia was analysed using the Negative symptom assessment tool, the score was calculated from baseline to the end point, Group A patients who received Haloperidol had a mean difference of [3.80 ± 2.60(baseline)] to [2.33 ± 2.29(end point)]. Mean difference of about -1.47 was observed. Paired t test was found to be statistically significant(*P* = 0.0019) (Table 5).

Table 5. Statistical analysis of Negative symptoms in Group

Negative symptoms [score= 20]	Group – A (n= 30)		*P* value
	Mean	SD	
Baseline	3.80	2.60	0.0019
Endpoint	2.33	2.29	
Mean difference	-1.47		

n- number of study subjects.

However, Group B patients who received Olanzapine had a considerable mean difference of[9.60 ± 6.09(baseline)] to of [3.30 ± 3.43(end point)]. The mean difference was observed to be - 6.3 which is comparatively high than Group A who received Haloperidol. Furthermore, it was found to be statistically significant by using paired t test (*P* = 0.0011) (Table 6).

Table 6. Statistical analysis of Negative symptoms in Group B

Negative symptoms [score= 20]	Group – B (n= 30)		*P*value
	Mean	SD	
Baseline	9.60	6.09	0.0011
Endpoint	3.30	3.43	
Mean difference	-6.3		

n- number of study subjects

Thereby, it shows that Olanzapine[Group B] showed better effectiveness in reducing negative symptoms of schizophrenia compared to Haloperidol [Group A].

3.4 End point effective analysis

By calculating the end point effectiveness altogether, Olanzapine was found to be better effective than Haloperidol in treatment of Schizophrenia as it marks to be effective in reducing both positive and negative symptoms. Also, a significant mean difference was observed (Table 7).

Table 7. End point effective analysis.

Positive& Negative symptoms	Group A [Haloperidol]		Group B [Olanzapine]	
	Mean	SD	Mean	SD
Baseline	32.9	12.12	35.63	13.04
End point	18.51	10.13	12.86	9.76
P Value	0.0019		0.0018	
Mean Difference	-14.39		-22.77	

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3.6 Discussion

A Prospective Comparative Observational study was conducted for a period of 6 months to evaluate the effectiveness of Haloperidol and Olanzapine as the candidate drug in our study as they are the most used drugs in our government tertiary care hospital.

In that, out of 60 patients who were enrolled in the study, male patients 31(51.60%) had higher predominance over female patients 29(48.40%). This study results concur with the studies conducted by Vinod K Mathew et al. Epidemiology of schizophrenia in an Indian hospital who stated that males predominantly had schizophrenia with 59.1% males and 40.59% females [6].

In our study, the age group of 22-30 years were most affected with schizophrenia. Our study results are relevant to the findings of Vinod K Mathew et al. Epidemiology of schizophrenia in an Indian hospital. The study states that highest number 318(34.98%) of patients belonged to the age group 21-30 years [6].

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Our study reports for marital status of patient with schizophrenia shows that 42% were married, 46% were unmarried, 5% were widow, 7% were divorced. A majority were unmarried compared with other marital status which is similar to a study by Bawo O. James, Felicia I. Thomas et al. Barriers to care among people with schizophrenia attending a tertiary psychiatric Hospital in Nigeria. This study shows that majority of patients with schizophrenia were single (n= 119;73.9%) [7].

Among the study populationunemployed patients (58.40%) were predominant than employed patients (41.60%)they are similar to the findings of Bawo O. James, Felicia I. Thomas et al. Barriers to care among people with schizophrenia attending a tertiary psychiatric Hospital in Nigeria. They reported that maximum number of study subjects were unemployed (n= 97; 60.2%) [7].

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By evaluating the positive symptoms in study subjects with schizophrenia by using PSYRATS scale from baseline to endpoint, Group B patients who received olanzapine had greater mean difference(-17.13) compared to Group A patients who received haloperidol (-11.36) and it was found to be statistically significant. Our study results are relevant to the findings of Todd M. Sanger, Jeffery A. Lieberman, Mauricio Tohen, et al. Olanzapine versus Haloperidol treatment in first episodes Psychosis[8].

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Further, the negative symptoms in patients with schizophrenia was analysed using Negative Symptom Assessment Tool, the score was calculated from start of treatment to endpoint, Group B patients who received olanzapine had considerable mean difference (-6.3) which is comparatively higher than Group A patients who received haloperidol (-1.47) and it was found to be statistically significant. Our study results are relevant to the findings of Todd M. Sanger, Jeffery A. Lieberman, Mauricio Tohen, et

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al. Olanzapine versus Haloperidol treatment in first episodes Psychosis. In that olanzapine showed superior treatment effectiveness, consisting of both safety and efficacy advantages, when compared to the conventional neuroleptic haloperidol [8].

By calculating the endpoint effectiveness altogether, patients treated with haloperidol [Group A] had a mean difference of-14.39 and Group B patients who received olanzapine had superior mean difference of -22.77. So, it signifies in reducing both positive and negative symptoms which is corresponding to the result of Juan-Carlos Gomez, Ann Marie K. Crawford et al. Superior Efficacy of Olanzapine over Haloperidol: Analysis of Patients with Schizophrenia from a Multicentre International Trail [9].

They revealed that olanzapine was more effective than haloperidol in treating a varied spectrum of patients with schizophrenia, including patients with positive, negative, or mixed symptom profiles and either a chronic or sub chronic course of illness and olanzapine-treated patients exhibited statistically significantly greater improvements from baseline (last observation carried forward) on all efficacy measurements.

4. CONCLUSION

Based on the outcome of the study, the patients with age group between 22- 35 were most commonly affected with schizophrenia. Among them maximum number of subjects was found to be unmarried and they are mostly associated with social withdrawal. In patients suffering with schizophrenia, subjects treated with olanzapine had a better overall clinical response to treatment than haloperidol. In treating patients with positive symptomsolanzapine was comparably effective alike haloperidol though olanzapine outperforms haloperidol in treating patients with negative symptoms. This study highlights that olanzapine treated group had numericallybetter score than the haloperidol treated group. The score was calculated by using PSYRATS and Negative Symptom Assessment Tool.As they are the most used oral antipsychotics in our government hospital, these study results will provide insight for clinicians in treating patients with schizophrenia.

CONSENT AND ETHICAL APPROVAL

.Institutional review ethics Committee of Government medical college, Nagapattinam.. All subjects informed consent and approval were obtained before the participation in research. Each participant was also required to sign the consent form after procedure explanation to subjects in local language.

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REFERENCES

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