Original Research Article

Comparative Study of Effectiveness Of Haloperidol Versus Olanzapine Among patients with 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.Paired and Unpaired t test was performed to observe statistical significance.

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.

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

1.INTRODUCTION

Schizophrenia is a chronic mental health condition where a person separate from reality into a world of unknown. It is defined as a heterogenous syndrome of disorganized andbizarre thoughts, delusion, hallucinations inappropriate affect, and 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 Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM – V) classifies the symptoms of schizophrenia into three categories – Positive, Negative and Cognitive dysfunction [2].This dopamine hypothesis describes the positive 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 elementswhich are 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 were 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 0.3%. Prevalence is higher in males than females 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. This mental disorderis 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 medications are Risperidone, Olanzapine, Aripiprazole, Quetiapine, Haloperidol, Trifluoperazine [5]. This study aims to compare the effectiveness of oral antipsychotics, Typical [Haloperidol] versus Atypical [Olanzapine]among patients withSchizophrenia in outpatient Department of psychiatry in Government Medical College and Hospital.

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

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 selectedby using simple random sampling, 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 has strong inter-rater reliability and good validity[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 end point effective analysis was done.IBM SPSS

STATISTICS 29.0.1.0 was used to perform statistical analysis. Data was gathered in Microsoftexcel 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 endpoint between patients who received haloperidol [Group A] and olanzapine [Group B] was analysed using Paired samplet test and Unpairedt test.For all statistical analysis, the *P* value<0.05 was considered as statistically significant.

2.5 Consentand Ethical approval

All authors declared that written informed consent was obtained from the patient for publication of this research articleand all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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).

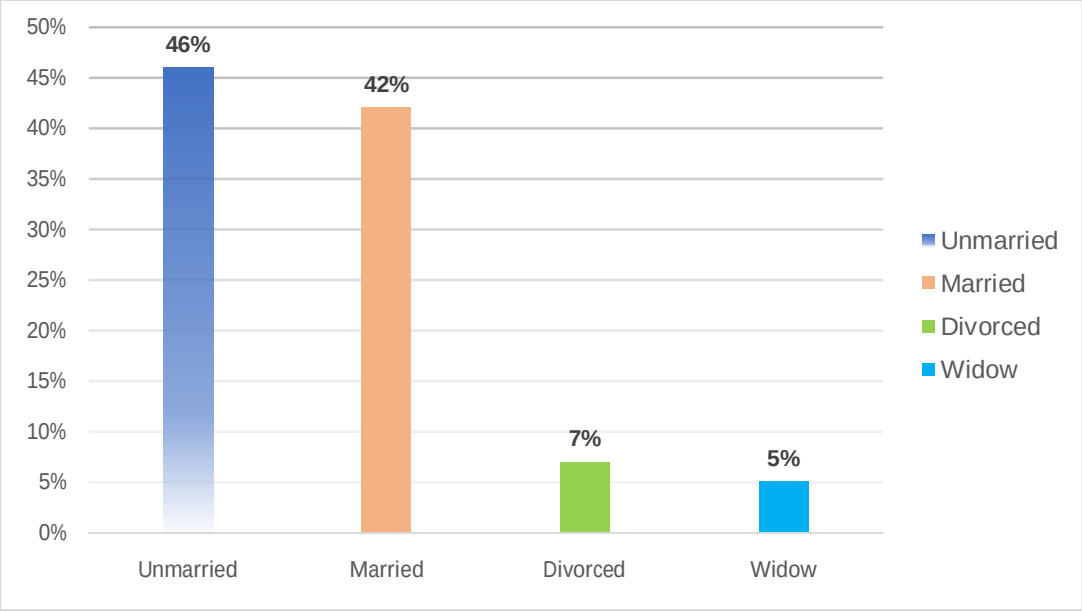

Fig. 1. Marital status of study subjects

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).

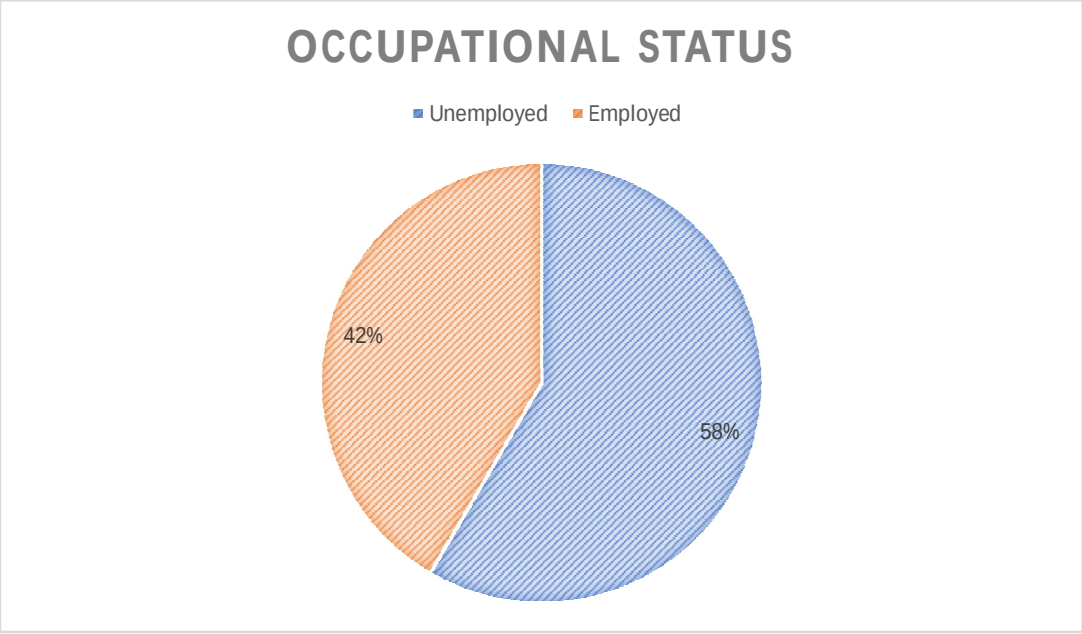

Fig. 2. Occupational status of study subjects

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*). 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*). Further unpaired t test was performed to find the difference between Group A and Group B, the *P* value was observed to be 0.0008** and it is statistically significant (Table 3).

Table 3. Statistical analysis of positive symptoms in Group A and Group B

Positive symptoms [score= 68]		**Group A (n= 30)**	**Group B (n= 30)**	***P* value (unpaired t test)**
Baseline	Mean ± SD	28.86 ± 11.56	27.36 ± 13.46	0.0008**
Endpoint	Mean ± SD	17.50 ± 9.13	10.23 ± 8.42	
Mean difference		-11.36	-17.13	
P-value (Paired t-test)		0.0017*	0.0015*	

n- number of study subjects, *- Paired t-test, **- Unpaired t-test (*P*-value <0.05 – statistically significant), SD- standard deviation.

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*). 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*). Unpaired t test was done to find the difference between Group A and Group B, it was not statistically significant (*P* = 0.2050**) regardless of non-significant *P* value,the observed mean difference implicit the effectiveness of olanzapine over haloperidol (Table 4).

Table 4. Statistical analysis of Negative symptoms in Group A and Group B

Negative symptoms [score= 68]		**Group A (n= 30)**	**Group B (n= 30)**	***P* value (unpaired t test)**
Baseline	Mean ± SD	3.80 ± 2.60	9.60 ± 6.09	0.2050**
Endpoint	Mean ± SD	2.33 ± 2.29	3.30 ± 3.43	
Mean difference		-1.47	-6.3	
P-value (Paired t-test)		0.0019*	0.0011*	

n- number of study subjects, * - Paired t-test, ** - Unpaired t-test (*P*-value <0.05 – statistically significant), SD- standard deviation.

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 5).

Table 5. 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
Endpoint	18.51	10.13	9.76	9.76
P value	0.0019		0.0018	
Mean difference	-14.39		-22.77	

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. This study states that majority of patients (34.98%) belonged to the age group 21-30 years [6].

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 population,unemployed 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].

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 in agreement with the findings of Todd M. Sanger, Jeffery A. Lieberman, Mauricio Tohen, et al. Olanzapine versus Haloperidol treatment in first episodes Psychosis[8].

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) though it was not found to be statistically significant. The study results are in consonant with the findings of Todd M. Sanger, Jeffery A. Lieberman, Mauricio Tohen, et 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 larger 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, individualstreated with olanzapine had a better overall clinical response to treatment than haloperidol. In treating patients with positive symptoms,olanzapine 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.Haloperidol and Olanzapine are the most used oral antipsychotics in our government hospital, these study results will provide insight for clinicians in treating patients with schizophrenia.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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