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ORIGINAL RESEARCH

To compare the efficacy of a typical antipsychotic drug Haloperidol with an atypical antipsychotic drug Aripiprazole in treating schizophrenia

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ABSTRACT

Introduction: Schizophrenia is a chronic mental disorder characterized by a range of cognitive, behavioral, and emotional dysfunctions. This study compares the efficacy and tolerability of Haloperidol and Aripiprazole, two antipsychotics used in its treatment.**Material and method:** the study was Conducted at the Department of Psychiatry, Guru Gobind Singh Medical College and Hospital, Faridkot, the study involved 50 drug-naïve patients aged 18-65, who met the ICD-11 criteria for schizophrenia. Patients were divided into two groups, one receiving Haloperidol (5-15 mg/day) and the other Aripiprazole (5-20 mg/day). The efficacy of the treatments was evaluated using the Positive and Negative Syndrome Scale (PANSS) at baseline and at follow-ups at 2, 6, and 12 weeks. Tolerability was assessed by monitoring adverse drug reactions and extrapyramidal symptoms (EPS) using the Modified Simpson Angus Scale (MSAS).**Results** indicated that both Haloperidol and Aripiprazole significantly improved PANSS scores over time, with no statistically significant differences between the two groups across all time points. However, Aripiprazole showed a trend towards greater improvement in Negative symptoms, though not reaching statistical significance. In terms of tolerability, both medications were comparable, though Aripiprazole's atypical profile may offer advantages in long-term treatment adherence. **Conclusion:**These findings suggest that both Haloperidol and Aripiprazole are effective in treating schizophrenia, with Aripiprazole potentially offering a slightly better outcome in managing Negative symptoms and adherence. The study underscores the importance of individualized treatment approaches in optimizing care for schizophrenia patients.

INTRODUCTION

The World Health Organization (WHO) defines health as “a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.” Mental health is considered optimal when a person can manage everyday stress, work productively, and contribute to their community.[1] In contrast, psychiatric disorders can significantly impact daily life, affecting emotional stability, cognitive processes, interpersonal relationships, and behavior.

Schizophrenia is a complex and enduring mental health condition characterized by a diverse array of symptoms, including hallucinations, delusions, disorganized behavior or speech, and cognitive impairments. The disorder appears to arise from a combination of genetic and environmental factors that disrupt brain development.[2]

The pathogenesis of schizophrenia involves the dysregulation of several neurotransmitter systems, including dopaminergic, glutamatergic, GABAergic, and cholinergic systems.[3] This disruption in neurotransmitter interactions contributes to the development and manifestation of the disorder.[4]

Globally, schizophrenia affects approximately 24 million people, or 1 in 300 (0.32%) individuals, according to WHO estimates. Among adults, the prevalence is slightly higher, affecting 1 in 222 (0.45%) individuals. In Punjab, India, the lifetime

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prevalence of schizophrenia and other psychotic disorders is 0.72%, with a current prevalence of 0.30%, as reported by the National Mental Health Survey of India.[5]

Schizophrenia symptoms differ from patient to patient and from time to time within an individual. Two prominent clusters that are acknowledged are positive and negative symptoms. Positive symptoms include exhilaration, delusions, hallucinations, grandiosity, hostility, conceptual disorganization, and suspicion.[6]

Antipsychotic therapy is associated with a reduced mortality risk and a longer duration of symptom absence in comparison to patients who do not receive treatment. Therefore, they constitute the cornerstone of schizophrenia treatment.[7]

Antipsychotics are classified as "typical" or "atypical" according to their mechanism of action and pattern of clinical effects.

The process of selecting specific antipsychotics for the treatment of schizophrenia involves an individualized assessment of the associated risks and benefits. This evaluation takes into account various factors, including the relative clinical efficacy, safety, and tolerability of the antipsychotic medications currently available[8,9]. The choice of an antipsychotic medication and its dosage have a significant impact on the prognosis, complications, and adherence of individuals diagnosed with schizophrenia.

Antipsychotic agents, both conventional and atypical, are dopamine D2 receptor antagonists. While the efficacy of antipsychotics in treating the positive symptoms of schizophrenia is likely to be contingent upon D2 antagonist activity, the development of a number of the adverse effects associated with antipsychotic use is also associated with D2 receptor occupancy[15]. Researchers have investigated partial D2 agonists as a potential solution to preserve the efficacy of antipsychotics while mitigating or eliminating some of the adverse effects associated with complete D2 receptor antagonism, as a result of the substantial safety and tolerability concerns that result from full D2 receptor blocking. A partial agonist at the D2 receptor functions as a functional agonist when dopaminergic tone is low, while a partial D2 agonist functions as a functional antagonist at the receptor site when dopaminergic tone is high.[16]

There is speculation that the activity of 5-HT2A receptor antagonists is associated with improving negative symptoms of schizophrenia[21,22], as well as potentially enhancing cognitive function and alleviating depressive symptoms.[15] Functioning as a dopamine–serotonin system stabilizer, aripiprazole's distinctive pharmacodynamic profile is most consistent with functional stabilization of the dopamine and serotonin systems[23]. Given its potential efficacy in treating a wide spectrum of schizophrenic symptoms, aripiprazole may also offer a potentially superior profile of tolerability and safety when compared to alternative antipsychotic agents that are currently available. The goal of therapy with antipsychotics is to achieve and maintain remission in symptoms and make patient realize highest level of function.[24] Drug tolerability refers to the degree to which drug's overt adverse effects can be tolerated. Focused evaluation of drug tolerability (i.e. the patient's perspective of adverse drug reaction) being important should become routine.[25] Due to intolerable side effects, poor adherence to medication is seen which greatly contributes to loss of symptom control and diminished long-term outcomes.[26]

We hereby attempt to compare the efficacy of a typical antipsychotic drug Haloperidol with an atypical antipsychotic drug Aripiprazole in treating schizophrenia in terms of improvement in symptoms with PANSS scale and tolerability by Adverse Drug Reactions reported with Extra Pyramidal Symptoms assessed on Modified Simpson Angus Scale for EPS, lipid profile level at completion of study vs baseline.

MATERIAL AND METHODS

The study took place at the Department of Psychiatry, Guru Gobind Singh Medical College and Hospital, Faridkot, over an 18-month period. It was a comparative follow-up study involving 50 drug-naïve patients aged 18-65, who met ICD-11 criteria for schizophrenia. Inclusion criteria included being non-pregnant and having informed consent. Exclusion criteria included other psychiatric disorders, a history of epilepsy, substance abuse, contraindications to Haloperidol or Aripiprazole, pregnancy, or severe medical conditions.

Patients were selected via non-random convenience sampling and divided into two groups: one receiving Haloperidol (5-15 mg/day) and the other Aripiprazole (5-20 mg/day). Data collection involved psychiatric assessments using tools such as the PANSS scale for symptoms, the WHO-UMC Causality Assessment Scale for adverse drug reactions, and the MSAS for extrapyramidal symptoms. Follow-ups were conducted at 2, 6, and 12 weeks to monitor symptom improvement and any adverse effects.

RESULTS AND OBSERVATIONS

Table 1: Sociodemographic factors comparing both groups

Factor	Category	Aripiprazole (n=25)	Haloperidol (n=25)	p-value
Gender	Female	9 (36.00%)	12 (48.00%)	0.39
	Male	16 (64.00%)	13 (52.00%)	
Age at Presentation	Mean (SD)	31.24 (10.26)	30.56 (5.95)	0.77
Weight	Mean (SD)	56.16 (6.64)	58.24 (6.33)	0.262
Family Income	Mean (SD)	28,520.00 (16,163.54)	26,560.00 (10,866.92)	0.617

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Residence	Rural	18 (72.00%)	18 (72.00%)	1
	Urban	7 (28.00%)	7 (28.00%)	
Religion	Hindu	5 (20.00%)	10 (40.00%)	0.123
	Sikh	20 (80.00%)	15 (60.00%)	
Marital Status	Married	15 (60.00%)	11 (44.00%)	0.258
	Unmarried	10 (40.00%)	14 (56.00%)	
Occupation	Farmer	2 (8.00%)	4 (16.00%)	0.31
	Labourer	5 (20.00%)	1 (4.00%)	
	Private Job	0 (0.00%)	1 (4.00%)	
	Student	2 (8.00%)	1 (4.00%)	
	Unemployed	16 (64.00%)	18 (72.00%)	
Family History	No	21 (84.00%)	22 (88.00%)	0.31
	Yes	4 (16.00%)	3 (12.00%)	
Socioeconomic Status	Lower Middle	6 (24.00%)	10 (40.00%)	0.396
	Upper Lower	12 (48.00%)	11 (44.00%)	
	Upper Middle	7 (28.00%)	4 (16.00%)	

Table 2: Comparison of PANSS Positive, Negative, General psychopathology and Total PANSS scores between two groups at baseline.

Baseline	Aripirazole group		Haloperidol group		Z	p-value
	Mean	SD	Mean	SD		
Positive score	25.00	5.35	24.20	6.52	-0.370	0.712
Negative score	17.04	5.63	19.32	6.64	-1.324	0.186
General psychopathology score	45.28	7.49	45.68	6.21	-0.185	0.853
Total PANSS score	87.32	13.11	89.20	13.02	-0.971	0.331

Data shows comparison of PANSS Positive, Negative, General psychopathology and Total PANSS scores between the two groups at baseline. Positive scores are comparable to each other with p value .0712, Negative scores show p value of 0.186, General psychopathology score show p value of 0.853 and total PANSS score shows p value of 0.331. All the score are comparable to each other with no statistically significant difference among various groups seen.

Score Type	Time Point	Aripiprazole Group (n=25)	Haloperidol Group (n=25)	Z	p-value
Positive Score	**Baseline**	25.00 (5.35)	24.20 (6.52)	-0.37	0.712
	First Follow-up	22.84 (4.59)	22.20 (5.52)	-0.282	0.778
	Second Follow-up	19.72 (4.04)	19.24 (4.63)	-0.068	0.946
	Third Follow-up	17.00 (4.05)	16.72 (4.22)	-0.127	0.899
Negative Score	**Baseline**	17.04 (5.63)	19.32 (6.64)	-1.324	0.186
	First Follow-up	15.96 (4.56)	18.28 (6.30)	-1.406	0.16
	Second Follow-up	15.24 (4.08)	17.60 (6.42)	-1.171	0.242
	Third Follow-up	12.72 (4.08)	15.64 (5.98)	-1.765	0.078
General Psychopathology Score	**Baseline**	45.28 (7.49)	45.68 (6.21)	-0.185	0.853
	First Follow-up	41.44 (6.26)	41.64 (5.31)	0	1
	Second Follow-up	36.64 (5.74)	36.56 (5.27)	-0.535	0.593
	Third Follow-up	32.60 (7.23)	33.04 (6.87)	-0.185	0.853
Total PANSS Score	**Baseline**	87.32 (13.11)	89.20 (13.02)	-0.971	0.331
	First Follow-up	80.24 (9.06)	82.12 (10.48)	-1.088	0.277
	Second Follow-up	71.60 (8.31)	73.40 (9.59)	-0.952	0.341
	Third Follow-up	62.32 (9.74)	65.40 (11.43)	-1.021	0.307

The table shows that the PANSS Positive, Negative, General Psychopathology, and Total scores for both the Aripiprazole and Haloperidol groups are similar at baseline and during follow-ups. No statistically significant differences were observed between the groups across all time points.

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Table: Comparison of the difference in PANSS Positive score, Negative score, General psychopathology score, and Total PANSS among both the groups at a different timeline

		Aripiprazole group		Haloperidol group		Z	p-value
		Mean	SD	Mean	SD		
Positive score	Baseline to First Follow-up	2.16	1.82	2.00	1.47	-0.246	0.805
	Baseline to Second follow-up	5.28	2.65	4.96	2.47	-0.440	0.660
	Baseline to Third follow-up	8.00	3.29	7.48	3.61	-0.657	0.511
Negative score	Baseline to First Follow-up	1.08	1.73	1.04	1.84	-0.544	0.587
	Baseline to Second follow-up	1.80	2.83	1.72	2.42	-0.262	0.793
	Baseline to Third follow-up	4.32	2.84	3.68	3.20	-1.123	0.262
General score	Baseline to First Follow-up	3.84	2.69	4.04	3.25	-0.179	0.858
	Baseline to Second follow-up	8.64	4.56	9.12	5.55	-0.176	0.861
	Baseline to Third follow-up	12.68	5.60	12.64	5.89	-0.078	0.938
Total PANSS	Baseline to First follow-up	7.08	5.78	7.08	5.91	-0.098	0.922
	Baseline to Second follow-up	15.72	9.04	15.80	9.62	-0.058	0.953
	Baseline to Third follow-up	25.00	10.54	23.80	11.44	-0.807	0.420

Across all time intervals, there were no significant differences in the changes in Total Positive Score, Negative Score, General Psychopathology Score, and Total PANSS Score between the Aripiprazole and Haloperidol groups. This indicates that both treatments resulted in similar improvements in these scores over time.

DISCUSSION

The study was conducted in the Department of Psychiatry, Guru Gobind Singh Medical College and Hospital, Faridkot to evaluate the efficacy and tolerability of Haloperidol and Aripiprazole in patients of Schizophrenia. Also, the efficacy and tolerability of Haloperidol and Aripiprazole were compared in Schizophrenia cases. The results of the present study are discussed below:

The overall mean age of the study population was 30.46±28.50 years. The mean age in the Aripiprazole group is 31.24 years ± 10.26, while in the Haloperidol group, the mean age is 29.68±8.13 yearsindicating no statistically significant difference in age between the two groups. The results of the present study were in accordance with the study conducted by Kasper et al[30] in 2003 to compare the efficacy of Aripiprazole and Haloperidol. They found no significant difference between the age groups between the groups. The mean age in Aripiprazole was 37.3±0.4 years while for the Haloperidol group, it was 36.8±0.5. the overall mean age was 37.1±0.3 years. McCue et al[33] in 2018 compared antipsychotics and observed that the mean age of the patients was 40.5 years in the Aripiprazole group and 35.7 years in the Haloperidol group. No significant difference was seen in the groups. This was similar to the present study.

In the present study the total number of patients in each group is 25, with 42% (21 patients) being female and 58% (29 patients) being male. No significant difference was seen between the two groups. In the study by McCue et al also in both groups, more males were affected than females. In a study by Kasper et al 59% of patients were males in the Aripiprazole group while in the Haloperidol 57% were males and overall 59% were males. This was in accordance with the present study where also male predominance was seen.

The mean weight for the Aripiprazole group is 56.16±6.64 kg compared to 58.24±6.33 kg in the Haloperidol group. No significant difference was observed between the two groups (at baseline). A study by Kasper et al[30]. also found no significant difference between the mean weight of patients with schizophrenia in both groups, which is in accordance with the present study.

In the present study, no significant difference in between the two groups with respect to education, residence, occupation, marital status and family history.

At baseline, there were no significant differences between the Aripiprazole and Haloperidol groups in PANSS Positive, Negative, General Psychopathology, and Total PANSS scores. Similarly, at the first follow-up, no significant differences were found between the two groups in any of the scores. At the second follow-up, the scores remained comparable with no significant differences observed. By the third follow-up, the PANSS Positive, Negative, General Psychopathology, and Total PANSS scores showed no significant differences between the groups. Across all time intervals, there were no significant differences in the changes in PANSS Positive, Negative, General Psychopathology, and Total PANSS scores between the Aripiprazole and Haloperidol groups. This indicates that both treatments resulted in similar improvements in these scores over time. However, the improvement in Negative scores over subsequent follow-ups was more pronounced in the Aripiprazole group than in the Haloperidol group, with a greater mean change for Aripiprazole at each follow-up. Although these differences were not statistically significant, they still suggest a more favorable outcome for Aripiprazole over time.

Patients who were given Aripiprazole had significantly better improvements in positive symptoms compared to those who were given a placebo, according to a study by Kane et al., with a p-value of less than 0.001 on the PANSS Positive Subscale scores. These results were comparable to

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those observed in patients given Haloperidol.[28] Regarding negative symptoms, which significantly affect patient functioning and health-related well-being, Aripiprazole-treated patients showed statistically significantly greater improvements compared to placebo ($p = 0.001$), similar to those seen with Haloperidol. Overall, the effect sizes for individual negative symptoms were lower than for positive symptoms, suggesting that more time may be needed to achieve improvements in negative symptom domains.[28]

In their study, Banerjee and Sinha demonstrated that there was no significant difference in PANSS total scores between the Haloperidol group (mean 105.93±19.80) and the Aripiprazole group (mean 103.00±14.91) at baseline ($p= 0.65$). The three subscale scores for Positive syndrome, Negative syndrome, and General Psychopathology also did not differ significantly. Both the Haloperidol and Aripiprazole groups showed statistically significant improvements in PANSS total scores between the beginning and end points of the four-week treatment period.[41]

The safety and effectiveness of Aripiprazole (30 mg/day) compared to Haloperidol (10 mg/day) over the long term were studied in two 52-week randomized, double-blind, multicenter trials by Kasper et al. The studies were selected for pooled analysis based on their similar methods; they included 1294 patients with chronic schizophrenia experiencing acute relapse who had responded to antipsychotic therapy in the past. When compared to Haloperidol, Aripiprazole showed similar long-term efficacy across all symptom measures, with Aripiprazole showing considerably higher improvements in PANSS Negative subscale scores.[30]

CONCLUSION

Both medications demonstrated significant improvements in Positive, Negative, General Psychopathology, and Total PANSS scores over time, with no statistically significant differences between the two groups at any follow-up point. Although Aripiprazole showed slightly greater improvements in Negative symptoms, these differences were not statistically significant. The findings suggest that both Haloperidol and Aripiprazole are effective in managing schizophrenia symptoms, with comparable efficacy across various symptom domains.

Tolerability was also a crucial focus of the study, as it directly impacts medication adherence and long-term treatment outcomes. The study underscored that intolerable side effects, which are often associated with antipsychotic therapy, can lead to poor adherence and, consequently, a loss of symptom control. Despite the lack of statistically significant differences in efficacy, Aripiprazole's slightly better profile in improving Negative symptoms, combined with its atypical antipsychotic properties, may offer an advantage in terms of patient adherence and long-term outcomes. This highlights the importance of individualized treatment approaches in schizophrenia, considering both efficacy and tolerability to optimize patient care.