Original Research Paper

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EFFECT OF HALOPERIDOL AND OLANZAPINE ON PHYSICAL PARAMETERS.

Pharmacology

KEYWORDS: Haloperidol and Olanzapine, Physical parameters and Schizophrenia.

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ABSTRACT

The objectives is to compare the effect of haloperidol and olanzapine on physical parameters and also to observe the adverse effects of both the drugs in schizophrenic patients. A prospective observational follow up study was conducted for 18 months by enrolling 121 patients of the age group 18 to 65 from psychiatry clinic. It was found that in both the groups there were more number of male (52.25%) patients and 44.14% patients is from the age group of 18 to 29 yrs. At 12th week Olanzapine treated group shows statistically significant (p=<0.03) gain in body weight and on comparison the groups shows marginal association between weight gain and olanzapine intake at 8th and 12th week. There were no significant difference in systolic and diastolic BP in both the groups at 8th and 12th week.

INTRODUCTION

Psychosis is one of the severe mental disorders and exerts strong negative fitness effects. Its symptom complex is characterized by impairment of behavior, serious inability to think coherently, lack of insight and inability to communicate properly.[1]

Psychiatric disorders may be acute or chronic. Acute psychosis require short term therapy and chronic like schizophrenia require long term therapy.[1] Antipsychotic agents are the cornerstone of acute and chronic psychiatric disorders like schizophrenia, bipolar disorder require lifelong maintenance therapy with typical (conventional) or atypical antipsychotics.[2]

The conventional antipsychotics cause antagonism of D_2 receptor activity in the hyperactive mesolimbic dopamine pathway especially in schizophrenic brain. These agents are effective in reducing positive symptoms like delusions and hallucinations. But they lack selectivity and block almost 90% of the total D_2 receptors involved in other pathways too. So they have substantial risk of extrapyramidal and endocrine effects like increase in prolactin levels ultimately resulting into high rate of relapse.

The atypical antipsychotics act through a large spectrum of receptor types, including serotonergic, cholinergic and adrenergic receptors along with the DA receptors. They have low affinity to the dopaminergic receptors, but a higher affinity for 5-HT_{2A} serotonergic receptors. Thus, they have fewer extrapyramidal side effects as compared to typical antipsychotics.[3]

Some studies reported that use of atypical antipsychotics offers many benefits and may reduce some of the factors related to the morbidity and mortality of psychosis. These drugs appear to be associated with varying degrees of metabolic adverse effects, such as weight gain, impaired glucose metabolism, dyslipidemia and in some cases, more serious morbidity, such as cardiovascular disease.

Presently there are few reported studies, that evaluated the adverse effects of atypical antipsychotic in India. Hence, this study was designed to evaluate the effect of antipsychotics like haloperidol (typical) and olanzapine (atypical) in schizophrenic patients on physical parameters.

Our aims and objectives are to study and compare the effect of haloperidol and olanzapine on physical parameters like blood pressure and weight in schizophrenic patients. To observe the adverse effects of haloperidol and olanzapine in patients of schizophrenia.

METHODOLOGY

The above study was prospective observational follow up study carried out during the period from January 2014 till July 2015, after seeking permission from institutional ethics committee. In this study total 121 patients were enrolled from outdoor patients of psychiatry clinic at tertiary care centre.

In our study we included all newly diagnosed patients in the age group 18 to 65 and also old treated cases of schizophrenia who had not received treatment since last 6 months. We excluded the patients with all other psychotic disorders, mental retardation, Alzheimer, dementia and neurological diseases. Patients diagnosed with conditions like cardiac, respiratory, hepatic, renal diseases, diabetes, tuberculosis, malignancy and pregnancy were also excluded. Total 121 enrolled patients were divided into group A and group B. Group A included 60 patients who received Tab Haloperidol (5 mg) 1 tablet once a day orally after meal in the night. Group B included 61 patients received Tab Olanzapine (5mg) 1 tablet twice a day orally after meal. The patients attending psychiatric OPD were diagnosed by psychiatrist using DSM- IV TR criteria. The selection of study drugs, haloperidol and olanzapine and the enrollment of patients in above two groups was done by psychiatrist. Informed written consent was obtained from each patient. Patients in both the groups before receiving study drugs were examined for baseline recording of body weight and blood pressure and also observe for any adverse effects. Weight was recorded by manual weight machine in kg with an accuracy of one kg. In all the patients both systolic and diastolic blood pressure measured in mm of Hg with the help of sphygmomanometer in the supine position. Medicines for both the groups patients were procured from hospital pharmacy. The comparison was made among each group and statistical test was applied. All the statistical analysis was done using software Graph Pad In Stat V. 3.04. For qualitative data Chi-square test, for the quantitative data unpaired-t- test was applied between the two groups. P value <0.05 was considered significant.

RESULTS

In this study, we observe that in both the groups there were more number of male patients compared with the female patients. Both the treatment group had younger age group population between 18 to 29 yrs. Using Chi-square test in relation to gender and age, the p value is 0.59 so, there is no significant difference.

Dropout rate in both group A and group B was 4.13%. 55 patients of group A and 56 patients of group B completed the study. There were 82 (67.76%) patients who were newly diagnosed cases of schizophrenia while 39 (32.23%) patients had not received antipsychotic medications in last 6 months. In this study it was found that Olanzapine treated group (n=56) shows statistically significant (p=<0.0312) gain in body weight at 12th week.

Comparison between patients on haloperidol and olanzapine

Table 1: Table showing comparison of body weight between group A and group B during study period of 8 and 12 weeks.

Body weight	Group A Haloperidol	Group B Olanzapine	P value
At baseline	56.07 ± 4.43	57.18 ± 6.76	0.31
After 8 weeks	55.85 ± 4.54	59.00 ± 7.27	0.06

After 12 weeks	56.38 ± 4.60	59.58 ± 6.86	0.06
Complete visit data of 55 & 56 patients, using Unpaired t test			

On comparison between both the groups at 8th and 12th week shows marginal association between weight gain and olanzapine intake.

Table 2: Table showing comparison of systolic BP between group A and group B during study period of 8 and 12 weeks.

Systolic BP	Group A Haloperidol	Group B Olanzapine	P value
At baseline	122.72 ± 3.29	123.07 ± 3.89	0.61
After 8 weeks	122.25 ± 3.50	123.39 ± 4.01	0.34
After 12 weeks	123.45 ± 3.16	123.96 ± 4.86	0.20
Complete visit data of 55 & 56 patients, using Unpaired t test			

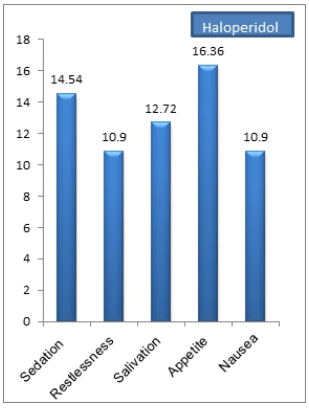
On comparing change in systolic BP in both the groups, at 8th and 12th week, no significant difference was found.

Table 3:Table showing comparison of diastolic BP between group A and group B during study period of 8 and 12 weeks.

Diastolic	Group A Haloperidol	Group B Olanzapine	P value
At baseline	82.98 ± 3.05	81.82 ± 3.01	0.05
After 8 weeks	83.02 ± 3.79	81.03 ±2.19	0.09
After 12 weeks	83.34 ± 3.08	80.71 ± 2.58	0.07
Complete visit data of 55 & 56 patients, using Unpaired t test			

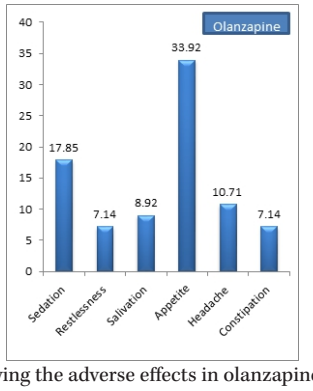
On comparing change in diastolic BP in both the groups, at 8th and 12th week, no significant difference was found.

Graph 23:Graph showing adverse effects of group A during study period.



Graph showing the adverse effects in haloperidol treated group with number of patients 8 (14.54%) with sedation, 6 (10.9%) with restlessness, 7 (12.72%) with increased salivation, 9 (16.36%) with increased appetite and 6 (10.9%) with nausea.

Graph 24: Graph showing adverse effects of group B during study period.



Graph also showing the adverse effects in olanzapine treated group with number of patients 10 (17.85%) with sedation, 4 (7.14%) with restlessness, 5 (8.92%) with increased salivation, 19 (33.92%) with increased appetite and 6 (10.71%) with headache and 4 (7.14%) with constipation.

DISCUSSION

Schizophrenia is a chronic mental disorder, the effective pharmacotherapy is started with advent of antipsychotic drugs. Two groups of antipsychotic medications are commonly used which include Typical (first generation) and Atypical (second generation) antipsychotics. In present study we selected the most commonly prescribed member from each group as a prototype agent as haloperidol and olanzapine.

Typical antipsychotic agents are cost effective, control positive symptoms of schizophrenia effectively but their use is associated with increased risk of extrapyramidal reactions (EPRs), on the other hand atypical antipsychotic agents are costly, controls both positive and negative symptoms with low incidence of EPRs. Today, despite of availability of many antipsychotic agents, adverse effect with their use still remains the problem. Treatment with atypical antipsychotic associated with increased risk of weight gain, hyperglycemia, dyslipidemia and changes in blood pressure.

In this study, it was observed that more males (52.25%) over females patients, this finding is in consistent with the finding of Libermann et al, 2003.[4] He reported 79.39% males and 20.61 females in the olanzapine group and 84.09% males and 15.91 % females in the haloperidol group.

Azzam H et al, 2009 reported the gender distribution of the patients in both the groups which was 77.8% men and 22.2% women in the haloperidol group, 75% men and 25% women in risperidone, clozapine, olanzapine and aripiprazole group.[5]

The study shows the maximum i.e 44.14% patients were from age group of 18 to 29 yrs. Schizophrenia in young people between the ages of 18 to 28 years, exhibits a hereditary tendency and generally is a recurring illness.[6] All the cases included in the study were from poor socioeconomic status.

In this study it was found that the dropout were 8.26% the reason of dropout were, (1) relocation to other place, (2) lack of money to reach treatment centre, (3) after receiving initial treatment patient felt better and discontinue it, (4) voluntary withdrawals from the study for miscellaneous reasons.

Rosenheck et al in 2006, reported a high dropout rate in their randomized control trial.[7] Similarly, Barnwal A et al in 2012, found the high dropout rate (26.7%) which is expected in patients with psychiatric illnesses.[1]

Present study shows that the baseline body weight in haloperidol treated group was 56.07 kg, at the end of 8th week of treatment there was apparent loss in body weight to 55.85 kg although the change was statistically not significant while in olanzapine treated group there was apparent gain in weight i.e from 57.18 kg to 59 kg at the end of 8th week the result were statistically not significant.

At the end of 12 week olanzapine treated group shows statistically significant weight gain from 57.18 kg to 59.58 kg while during the same study period, that in haloperidol treated group there was no change in weight record from its baseline and 8th week value. The result shows that there was significant increase in body weight after 8 week in olanzapine treated group as most of the patients complains of increase in appetite however there was no statistical significant difference found between two treatment groups. At 12 week of treatment with olanzapine shows statistically significant weight gain (p=0.03) compared with baseline value.

Neredumilli PK et al, reported that there was no significant increase

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in body weight seen in patients receiving olanzapine, risperidone and haloperidol.[8] However in this study it was found that statistically significant results were observed at end of 12 week of treatment with the olanzapine.

A review of absolute weight gain in various trials found that the relative incidence and magnitude of weight gain was not equal among antipsychotic medications. John et al, 2006 reported that short term treatment with various antipsychotic agents were produced increase in body weight ranging from less than 1 kg to more than 4 kg.[9]

Study parameters like blood pressure shows that there were no significant change in systolic and diastolic blood pressure with baseline values throughout the study period. Kinon B.J et al, in there study found that, a diastolic blood pressure in olanzapine-treated patients shows a relationship with weight change that was statistically significant (≤ 0.001).[10]

Young Sup Woo et al, reported that there was a significant increase in systolic and diastolic blood pressures in the clozapine group, but no change in olanzapine group.[11] This may be due to short duration of this research. Any future research of longer duration and larger sample size may be able to find changes in blood pressure.

It was observed that in haloperidol treatment group 9 patients (16.36%) complain of increased appetite, 8 patients (14.54%) having sedation, 7 patients (12.72%) having increased salivation and 6 patients (10.9%) complain of restlessness & nausea. In olanzapine treatment group, 19 patients (33.92%) complains of increased appetite, 10 patients (17.85%) having sedation, 6 patients (10.71%) having headache, 5 patients (8.92%) having increased salivation and 4 patients (7.14%) complains of restlessness & constipation. The adverse effect reported by Lingeswaran A et al, 2010 with olanzapine treatment were 18.3% cases of weight gain, 7% cases of tremors and increased appetite each, 4.2% cases of hyperglycemia.[12] In another study by Tollefson GD et al, 1997 reported increased appetite in 12.4%, salivation in 19.5%, nausea in 13.7% and tremor in 26.3 % in patients on haloperidol group while salivation in 8.7%, tremors in 16.5%, increased appetite in 24% and dry mouth in 22.2% patients reported with olanzapine group.[13]

Various studies have reported that atypical antipsychotic group of drugs are responsible for the occurrence of metabolic effects.

Charles De Battista 2015, stated that the atypical antipsychotics are also associated with metabolic syndrome that may increase the risk of coronary artery disease, stroke and hypertension.[14]

The limitations in this study were (a) study carried out in small population, (b) study duration was short, (c) it was an open label study (d) study parameters utilized were limited i.e body weight and blood pressure, (e) unable to utilize parameters (due to limited resources) like fasting blood glucose estimation, lipid profile, BMI, HbA1c estimation, plasma prolactin and insulin levels etc.

Thus, more studies are needed to evaluate the metabolic status of schizophrenic patients put on atypical antipsychotic drugs treatment.

CONCLUSIONS

Olanzapine tends to cause significant changes in the body weight. However it could not reciprocate the similar increase in blood pressure within short span of 12 weeks. Haloperidol did not show significant change in study parameters.

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