

Comparative Study of Olanzapine versus Haloperidol in the Treatment of Schizoaffective Disorder.

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ABSTRACT

Background: The growing awareness of the impact of antipsychotic drug on patients quality of life has created the need for deeper insight into the side effects, other best drug for the treatment of schizoaffective disorder. **Objective:-** The study was conducted to find out whether olanzapine is more safe than haloperidol in treating schizoaffective disorder and compare the overall clinical efficacy of Olanzapine Vs haloperidol in Schizoaffective disorder. **Methods:** The sample was taken from sixty patients fulfilling ICD-10 criteria for schizoaffective disorder consenting for study attending the psychiatry OPD and emergency of G.G.S. Medical College and Hospital Faridkot aged between 15-60 years the patients were selected from either sex. After screening the patients who were found positive for schizoaffective disorder, Then these patients were divided into two groups and put on medicine olanzapine (n=30) and tab Haloperidol (n=30) for six weeks. After that all the patients further assessed for clinical status and side effects using BPRS, PANSS, CGI scale, UKU Side Effect Rating Scale and final diagnosis was made according to ICD-10 criteria. **Results:** The current study was a randomized, double blind, parallel design comparative trial between olanzapine and haloperidol for a period of six weeks for the management of schizoaffective disorder. Total 60 patients who met ICD-10 criteria for schizoaffective disorder were randomly allocated: 30 each in olanzapine and haloperidol groups. 55 patients had completed the protocol .27 in haloperidol group and 28 in olanzapine group. In our study, in haloperidol group we had 8 schizoaffective manic type and 9 schizoaffective depressive type patients, while in case of olanzapine group the number of schizoaffective manic type was 7 and depressive type was 21 i.e. comparable in both groups. **Conclusion:** The results of the study revealed that overall superior efficacy and safety advantage of olanzapine over haloperidol suggests that olanzapine represents an important alternate treatment option in schizoaffective disorder. These positive findings are encouraging prospective trails in related disorders such as bipolar depression, depression with psychotic features or other psychotic states with prominent mood symptoms.

Keywords: Haloperidol, Olanzapine, Schizoaffective Disorder.

INTRODUCTION

Schizoaffective disorder is characterized by prominent and persistent symptoms in both the schizophrenic and affective domains. There are three disorders in addition to schizophrenia listed in the fourth edition of Diagnostic and Statistical Manual and Mental Disorder (DSM-IV) in the section "Schizophrenia and other Psychotic Disorders".

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These are Schizoaffective Disorder, Schizophreni form Disorder and Brief Psychotic Disorders". These are Schizoaffective Disorder, Schizophreni form Disorder and Brief Psychotic Disorder. The Schizoaffective Disorder is a complex illness that has changed significantly over time. In its simplest definition it is presently conceived as an illness with coexisting, but independent schizophrenic (Psychotic) and mood components. The 10th revision of international Statistical Classification of Disease and related problems (ICD-10) essentially describes the same disorder. The ICD-10 Schizoaffective Disorder describes single as well as recurrent episodes. Subtypes include manic, depressed and mixed types. Mixed type includes a cyclic schizophrenia and a mixed schizophrenic-mood psychosis. In practice, the diagnostic

confusion and substantial overlap of symptoms make it difficult to choose the best treatment. Somatic approaches, often including polypharmacy, do raise unique clinical pharmacokinetic and pharmacodynamic issues (Keck et-al, 1996). As antipsychotic (Haloperidol) medications were approved for use in schizophrenia, they were almost immediately used for patients with Schizoaffective Disorder. After more than 40 years of dopamine receptor antagonists with often unavoidable extra pyramidal side effects, newer novel antipsychotic drugs have become available that have no or minimal adverse effects, and greater efficacy. These are the serotonin-dopamine antagonists (SDAs), named for their alleged mechanism of action e.g. Risperidone, Clozapine and Olanzapine. Risperidone was the first antipsychotic agent to gain FDA approval after Clozapine. Double blind trials indicates that Risperidone treatment is associated with a dose dependent increase in extra pyramidal side effects as D₂ receptor occupancy increases relative to 5HT₂ receptors occupancy at higher Risperidone doses (Kapur S. et al, 1998). Clozapine was the first SDA to be approved and was discovered in 1958 in Bern, Switzerland. It has a low affinity for D₂ receptors and a high affinity for 5HT₂ receptors, with a low propensity for extra pyramidal side effect. There may be several reasons why patients diagnosed with Schizoaffective Disorder respond favorably to Clozapine. First, Clozapine has been shown to be superior in treating positive symptoms of Schizophrenia and therefore for the positive symptoms of Schizoaffective Disorder. Second, a kinetic syndrome that can mimic depressive syndromes are generally reduced with Clozapine use. Third, some evidence indicates that Clozapine may have mood- stabilizing properties. Clozapine however could not be the first line treatment for patients with Schizoaffective Disorder because of increased risk of agranulocytosis. Olanzapine due to its structural and pharmacological profile similar to Clozapine has better credentials as an antipsychotic of the millennium.

The novel antipsychotic like Olanzapine with its dopaminergic receptor blockade confers antipsychotic activity, serotonin receptor blockade such as 5HT₂, may exert antidepressant effects (Meltzer, 1989) Tran P.V et al, 1999 have shown the efficacy of Olanzapine vs Haloperidol in the treatment of Schizoaffective Disorder. In patients experiencing first episode psychosis, olanzapine has a risk benefit profile significantly superior to that of Haloperidol (Sanger T.M. et al., 1999). Hence keeping in mind the superior safety profile of olanzapine over Risperidone and Clozapine, I have hypothesized its efficacy and safety profile superior to haloperidol among patients with Schizoaffective Disorder by double blind

prospective and controlled trial at G.G.S Medical Collage and Hospital, Faridkot.

Aims and Objectives

The primary objective of this trial was:

- # To examine and compare the overall clinical efficacy of Olanzapine vs in Schizoaffective disorder.
- # To know whether Olanzapine was more safe than Haloperidol in treating Schizoaffective disorder.

MATERIALS AND METHODS

Patient population and settings of trial: All the patients attending the psychiatry OPD and emergency of G.G.S. Medical College and Hospital Faridkot was thoroughly worked up. Those fulfilling the diagnostic criteria ICD-10 of schizoaffective disorder was taken up for the study. Total of sixty patients were selected.

Inclusion criteria was:-

- a) Patients of either sex between 15-60 years of age (so as minimize age induced variation).
- b) Non pregnant females or females not planning conception during trial period.
- c) Patient fulfilling ICD-10 criteria for Schizoaffective disorder (Appendix-II).
- d) Patients with a score of eighteen or more than eighteen in Brief Psychiatric Rating Scale (BPRS)

Exclusion criteria was:

- a) Patients with bipolar disorder, Schizophrenia, other psychotic disorders or any other psychiatric illness.
- b) Patients with history of epilepsy, mental retardation, substances abuse disorders or any other organic brain disease.
- c) Patients with any other medical illness contraindicating the use of Haloperidol and Olanzapine.
- d) Pregnant females or females planning conception during trial period.
- e) Refusal to give informed written consent by patient's guardian.

Study Design:- A randomized, double blind controlled trial of 6 weeks duration was carried out. The primary measure of efficacy was the percentage of patients showing clinical improvement defined as 40% reduction of total BPRS score as compared with base line between two groups.

Procedure:-

- a) All the patients with Schizoaffective disorder attending Psychiatry out Patient and Emergency Department of G.G.S

Medical College and Hospital, Faridkot was screened, as thereafter sixty patients was verified for fulfilling the inclusion and ruled out for presence of exclusion criteria.

- b) All patients have were undergone wash out period of two to five days.
- c) The patients were randomly allocated to one of two groups. Group A (n=30) patients were received tablet Haloperidol 5mg/day. The dose was increased or decreased as clinically warranted. In group B (n=30) patients were received tablet Olanzapine 5mg/day. The dose was increased or decreased clinically warranted.
- d) Both the patient and the investigator were blinded to remove the Bias.
- e) In both the groups anti parkinsonian agents (trihexyphenidyl hydrochloride, diphenhydramine) was added if EPS emerged, hematological examination (Hb, TLC, DLC, Platelet counts) and biochemical examination (S. bilirubin, SGOT, Blood Sugar, S Urea and Creatinine).

RESULTS

The current study was a randomized, double blind, parallel design comparative trial between olanzapine and haloperidol for a period of six weeks for the management of Schizoaffective disorder. Total 60 patients who met ICD-10 criteria for Schizoaffective disorder were randomly allocated: 30 each in olanzapine and haloperidol

groups. 55 patients had completed the protocol. 27 in haloperidol group and 28 in olanzapine group. In our study, in haloperidol group we had 8 schizoaffective manic type and 9 schizoaffective depressive type patients, while in case of olanzapine group the number of schizoaffective manic type was 7 and depressive type was 21 i.e. comparable in both groups. No case of schizoaffective mixed type was found in both the groups.

Assessments were done on the basis of the following parameters:

A). Socio-demographic Profile.

Regarding socio demographic variables, both groups were almost equally represented. No significant difference was found. In our study out of 60 total patients, in haloperidol group 27 patients completed the protocol, two patients were lost to follow up and one patient was dropped from the study as he develops severe side effects. While in olanzapine group 28 patients completed the trails as per protocol and two patients was lost to follow up. Thus 55 patients completed the protocol, 27 in haloperidol and 28 in olanzapine group.

B).Efficacy parameters:

All patients were assessed for clinical status and side effects using the following instruments at base line after the washout period and after six weeks:

- 1). Total BPRS
- 2). Total PANSS
- 3). CGI-S Scale

1) BPRS (Overall and Gorham 1963) Brief Psychiatric Rating Scale.

Table 1: Showing change from baseline to endpoint in total bprs scores in all schizoaffective patients being treated with olanzapine and haloperidol

Drug group	N*	Baseline		End point		Change	
		Mean	S.D**	Mean	S.D**	Mean	S.D**
Olanzapine	28	33.28	5.59	18.00	4.84	15.28	3.45
Haloperidol	27	33.33	4.01	21.15	3.50	12.18	3.92

N*-Number of patients

S.D**-Standard Deviation

Above table shows that olanzapine reduced the mean score from baseline 33.28 to endpoint 18.00 with the change of 15.28 with 't' value 5.1 which is statistically significant at 5% level of significance. While in case of haloperidol the effect was that it reduced mean score from baseline 33.33 endpoint 21.15 with a change of 12.18 with 't' value 5.09 which is also statistical significant at 5% level of significance. It is clear from the above table that

changes were significant for each group statistically. However, change observed in case of olanzapine as more than haloperidol, statistically this difference was not found to be significant when 't' test was applied, the value obtained was 0.805 at 5% level of significance.(P> 0.05 -not significant).

b). Efficacy on PANSS Total PANSS Score in all schizoaffective patients.

Table 2: Showing change from baseline to end point in Total PANSS scores of all schizoaffective patients being treated with Olanzapine and Haloperidol

Drug group	N*	Base line		End Point		Change	
		Mean	S.D.**	Mean	S.D.**	Mean	S.D.**
Olanzapine	28	96.89	6.90	67.75	6.87	29.64	7.87
Haloperidol	27	87.18	7.56	63.48	8.39	23.70	7.30

*=Number of Patients.

S.D.**=Standard Deviation

The above table shows that olanzapine reduced the mean total PANSS score from 96.89 (± 6.90), baseline to 67.25(± 6.87) end point with a change 29.64 (± 7.87) with 't' value 5.90 which is statistical significant at % level of significance ($P < 0.05$ -Significant). While in case of haloperidol the effect was that it reduced the mean total PANSS score from 87.18 (± 7.56) baseline 63.48 (± 8.39) end point with a change of 23.70 (± 7.30) with 't' value

4.96 which also statistical significant at 5% level of significance ($P < 0.05$ -Significant). It is clear from the above table that changes were significant for each group statistically though change observed in olanzapine was more than haloperidol but this difference was not statistically true when 't' test was applied. Value obtained was 0.809 at 5% level of significance. ($P < 0.05$ - not significant).

Table 3: Showing change from baseline to end point in CGI-S SCALE in Schizoaffective patients being treated with Olanzapine and Haloperidol

Drug group	N*	Base line		End Point		Change	
		Mean	S.D.**	Mean	S.D.**	Mean	S.D.**
Olanzapine	28	5.11	0.99	2.46	0.55	2.65	0.86
Haloperidol	27	5.03	0.93	2.96	0.71	2.07	0.99

*= number of patients

S.D**=Standard Deviation

It is clear from above table that mean of total severity score at baseline in olanzapine group was 5.11(+0.99), whereas in haloperidol group it was 5.03(+0.93). At the end point; it was 2.65(+0.86) in olanzapine group and 2.07(+0.99) in haloperidol group. After application of 't' test the 't' value for olanzapine was 5.09 at 5% level of significance. ($P < 0.05$ -significant). Similarly, in case of haloperidol, t value was 4.70 at 5% level of significance ($P < 0.05$ -significant). It is clear from the above table that changes were significant for each group statistically. Though change observed in case of haloperidol but after application of 't' test it was observed that significant difference doesn't exist between both the groups. Value obtained was 0.62 at 5% level of significance ($P > 0.05$ -not significant).

C. Safety (on the basis of U.K.U. rating scale)

In patients who were treated with olanzapine, common side effects observed were sleepiness (3/28), weight gain(10/28), constipation(8/28) and decreased salivation(6/28) while in patients who received haloperidol, common side effects were tremors (16/27), akathisia (9/27), rigidity(8/27), hypokinesia(8/27) and increased salivation(6/27). It is clear from the mentioned above that patients in haloperidol group had higher incidence and severity of extrapyramidal side effects than olanzapine group.

Concomitant Medication: The requirement of Antiparkinsonian Medication (trihexiphenidyl) varied in both groups i.e more patients in haloperidol group required trihexiphenidyl (13/27) than olanzapine (6/28). Statistically 'Chi Square test', was applied, the value was 4.33 at 5% level of significance ($P < 0.05$ -significant).

The primary measure of olanzapine and haloperidol efficacy will be percentage of patients showing clinical improvement of at least 40% of total BPRS score from baseline to end point.

The secondary Efficacy will be the mean change in Positive and Negative Syndrome (PANSS) score, extrapyramidal symptoms and overall drug safety. Statistical analysis will be carried out by using standard statistical tools.

DISCUSSION

Schizophrenic disorder is characterized by prominent and persistent symptoms in both schizophrenic and affective domains. As noted by Keck et al (1996), it is difficult to find pharmacological literature references to the treatment of schizoaffective disorder in which trial have been well controlled (Tran PV. Et al, 1999). Further, even fewer published results are available from controlled clinical studies of schizoaffective disorders, depressed type. Conventional neuroleptics, while widely prescribed as treatment for psychotic disorders, present three primary weaknesses. First the therapeutic benefits of conventional anti psychotics are primarily limited to positive symptoms and effect sizes are variable. Second, conventional neuroleptics are of limited benefit for depressive signs and symptoms, cyclic antidepressants are often added as therapeutic adjuncts. Moreover, conventional D2 antagonists may cause a neuroleptic induced dysphoria. Third, extrapyramidal symptoms are among the leading causes of poor compliance with antipsychotic treatment. Casey (1995) has suggested that neuroleptic induced extrapyramidal symptoms are among the most troublesome side effects.

After the neurotransmitter serotonin (5HT) has been implicated in pathogenesis of schizophrenia and other psychotic disorders, newer anti psychotics like clozapine, risperidone and olanzapine have come more into use. the atypical antipsychotic clozapine has been reported to be useful treating in the schizoaffective disorder, but its routine use remains restricted by the risk of blood dyscrasias (Keck et al ,1996) . Olanzapine

with pharmacological profile similar to that of clozapine, has been shown to be effective in treatment of schizoaffective disorder (Tran PV, et al, 1999)

The current study was undertaken with the aim of comparing efficacy and adverse effect profile of olanzapine and haloperidol in schizoaffective disorder. This study was a double blind, randomized, prospective, comparative trial with parallel treatment design for duration of 6 weeks. In our study, a total of 60 patients were included.

However, according to socio-demographic profile we found that maximum number of patients in both groups belong to age group of 15-45 years. This study also reveals that schizoaffective disorder is more common in females and patients from rural background, Sikh farmers, housewives. The reason for this could be that in our part i.e. west of Punjab, agriculture being non-remunerative and females are more vulnerable to psychotic problems. 60-70% of patients had family history of psychiatric illness and majority of patients in both groups had duration of illness less than 12 months, however, educational status in both groups were not significant. It was also observed that above parameters had no influence on treatment response.

Efficacy:

Both the BPRS and the positive and negative symptoms scale is widely accepted psychometric instrument for assessment of antipsychotic efficacy.

BPRS Total Score:

No difference in baseline scores for severity of illness was observed, While in case of haloperidol the effect was that it reduced mean score from baseline 33.33 endpoint 21.15 with a change of 12.18 with 't' value 5.09 which is also statistically significant at 5% level of significance. So that baseline values were not used as covariates. Rather, the change from baseline to endpoint was used as the outcome variable.

PANSS Total Scores:

The comparative changes in positive and negative syndrome scale total score were that olanzapine group reduced the mean change from baseline 96.89 \pm 6.90 to end point 67.25 \pm 6.87 with a change 29.64 \pm 7.87 't' 5.90, $p < 0.05$. While in the case of haloperidol the effect was that it reduced the mean score from baseline 87.18 \pm 7.56 to end point 63.48 \pm 8.39 with a change 23.70 \pm 7.30, 't' 4.96 $P < 0.05$. Changes for each group were significant statistically. But statistically this difference was not found to be significant when 't' test was applied to both the groups ('t' 0.0809, > 0.05 not significant). Point failed to reach statistical significance on any of the efficacy measures, although the difference was numerically greater for the olanzapine treated patients.

CGI- Severity Scale:

In our study the mean change score in CGI-S scale in olanzapine group from baseline (5.11 \pm 0.99) to

end point (2.46 \pm 0.55) was 2.65 \pm 0.86 't' 5.09 $p > 0.05$ significant while in case of haloperidol group mean change was 2.07 \pm 0.99, 't' 5.70, $p < 0.05$ significant.

Response Rate:

An alternative treatment of two respective treatment effects was clinical response which was defined as 40% or more improvement in BPRS score from baseline and at least 3 study weeks completed. Olanzapine treated patients had significantly higher response rate than haloperidol treated patients for the overall patient population 67.85 versus 44.45% and two subtypes i.e. manic 71.42% versus 62.50 and depressive subtype 66.66 vs. 36.84%

Our results are consistent with following studies:

Tran PV et al, (1999) compared the efficacy of olanzapine with haloperidol in 300 DSM-111-R schizoaffective patients from a double blind, prospective, International study who were allocated to 6 weeks of earlier olanzapine (5-20 mg/day) or haloperidol (5-20 mg/day) treatment; responders were followed for one year of double blind, long term maintenance therapy. Olanzapine treated patients showed significant improvement than haloperidol treated patients on the BPRS Total, PANSS total, PANSS positive, PANSS negative and MADRS total. No statistically significant differences were found between the two treatment groups with regard to gender, age or origin. A statistically significantly greater percentage of olanzapine treated (55.1%) than haloperidol treated (33.7%) schizoaffective patients completed this phase. However, no difference in the baseline score for severity of illness was observed, rather the change from baseline to endpoint was used as the outcome variable. The efficacy parameters for between two drug groups i.e. olanzapine versus haloperidol were the BPRS total from baseline 33.17 \pm 10.40 with a change -10.52 \pm 13.38 versus from baseline 34.08 \pm 12.24 with a change -5.50 \pm 10.32), PANSS total from baseline 87.95 \pm 18.56 with a change -17.05 \pm 22.24 versus from baseline 90.67 \pm 22.30 with a change -9.06 \pm 17.38, PANSS positive (from baseline 20.45 \pm 5.56 with a change -4.11 \pm 6.82 versus from baseline 20.63 \pm 6.25 with a change -7.49 \pm 5.77), PANSS negative from baseline 21.95 \pm 6.45 with a change -4.16 \pm 6.07 versus from baseline 23.29 \pm 7.48 with a change -2.07 \pm 5.70 and MADRS total, from baseline 20.96 \pm 9.99 with a change -7.39 \pm 10.32 versus from baseline 20.07 \pm 9.65 with a change -0.79 \pm 9.99.

According to this study, response rate for two treatment groups i.e. olanzapine and haloperidol for the overall patient population and sub types were 50.3% versus 27.0%, 51.1% versus 29.6% and 49.2% versus 23.3% respectively. Tollefson, Beasley, Tran et al, 1997

In a large international, multi centre double blind, olanzapine (N=1336) was compared to haloperidol (N=660) over six weeks in the treatment of schizophrenia, schizoaffective and schizophreniform disorders. Starting doses were 5mg./day for both drugs which could be increased to a maximum of 20 mg./day. Olanzapine demonstrated clinical results superior to those of haloperidol on overall improvement according to the BPRS score -10.9±12.9 versus haloperidol -7.9 ±12.2, the principal efficacy measure defined in the study protocol. The comparative changes in positive and negative syndrome scale (PANNS) total scores -17.7 ±21.8 versus Haloperidol -13.4±20.6 confirmed this advantage, which included both positive -4.7±6.8 vs. -3.8±6.3 and negative symptom scores -4.5±6.3 versus haloperidol -3.2±6.1. Furthermore, the treatment effect on associated depressive symptom revealed that olanzapine treated patients had a twofold greater improvement in a MADRS total scores -6.0±8.7 versus haloperidol -3.1±8.8. No significant treatment by gender interaction was noted on these five efficacy measures. Statistical significant advantages of olanzapine treatment were related to 1). Changes in negative symptoms; 2). Extrapyramidal symptom profile; 3). Effect on prolactin levels; 4). Response rate. Response rate in their study olanzapine treated patients had a significantly higher response rate (52%) than haloperidol treated patients (34%) $\chi^2=42.4$, df1 $P<0.001$.

In addition, significantly more patients in the olanzapine treatment group than in the haloperidol treatment group were retained in the study. This superiority in retention in treatment is consistent with the pattern of results of previous studies of atypical and conventional antipsychotic drugs in first-episode patients (. Lieberman JA, Phillips M, Gu H, Stroup S, Zhang P, Kong L, Ji Z, Koch G, Hamer RM: Atypical and conventional antipsychotic drugs in treatment-naive first-episode schizophrenia: a 52-week randomized trial of clozapine vs chlorpromazine. *Neuropsychopharmacology* 2003; 28:995–1003 31.). This pattern of results suggests that atypical drugs are more likely to be associated with better long-term adherence and a potentially lower risk of symptomatic recurrence, as has been demonstrated with patients with chronic disorders (. Wahlbeck K, Tuunainen A, Ahokas A, Leucht S: Dropout rates in randomised antipsychotic drug trials. *Psychopharmacology (Berl)* 2001; 155:230–233 32.)

Tolerability:

A second objective was to compare the safety profiles of olanzapine and haloperidol among schizoaffective patients. In the study, a significant advantage of olanzapine was evident in the incidence of premature study discontinuations due

to adverse events, fewer olanzapine patients discontinued therapy (6.6%) than did their haloperidol treated counterparts (10%). This difference corresponds to a superior six week response rate for olanzapine treatment (67.85%) versus haloperidol treatment (44.45%). During the six week study period, among treatment emergent adverse events which showed a statistically significant difference between the treatment groups, only two events i.e. weight gain and somnolence were common in olanzapine treated patients, but other events like akathisia, tremors, hypokinesia and rigidity were more common in haloperidol treated patients. Olanzapine treated patients had greater weight gain than haloperidol treated patients [35.71%(10/28) versus 7.40(2/27); $\chi^2=6.46$]. The entire novel antipsychotics recently released appear to share this adverse event. Both clozapine (Hummer M, Kemmler; et al, Lamberti JS. et al, 1992) and risperidone (Owens DG. et al 1994 and Umbrichi D. et al, 1996) demonstrate significantly more weight gain in patients than haloperidol or typical antipsychotics. Other adverse effects documented to more frequent with olanzapine than with haloperidol were sleepiness [46.42% (13/28) versus 18.51% (5/27) $\chi^2=4.58$, df1 $p<0.05$ significant] increased duration of sleep [32.14%(9/28) versus 11.11% (3/27); $\chi^2=3.81$, df1 $p < 0.05$ significant], reduced salivation [21.42% (6/28) versus 14.81% (4/27), $\chi^2=0.38$, df1 $p > 0.05$ not significant] and constipation [28.57% (8/28) versus 18.51% (5/27); $\chi^2=0.75$ df1 $p > 0.05$ not significant]. Olanzapine was associated with significant fewer incidences of tremors, nervousness and salivation. In our study the most dramatic treatment difference was the comparative incidence of treatment associated extrapyramidal symptoms. Haloperidol-treated patients experienced higher rates of treatment emergent akathisia [33.33% (9/27) versus 10.7% (3/28); $\chi^2=4.10$ df1 $p <0.05$ significantly], rigidity [29.62% (8/27) versus 3.57% (1/28); $\chi^2=6.82$ df1 $p < 0.05$ significant], hypokinesia [33.33% (9/27) versus 3.57% (1/28) $\chi^2=8.19$ df1 $p < 0.05$ significant Tran PV. et al (1997), (Tollefson et al (1997) in placebo controlled trials, the only adverse event documented to be more frequent with olanzapine than with placebo were somnolence (12-39%), constipation (6-15%) and weight gain (0-12%). Anticholinergic effects such as constipation and dry mouth, increased in a dose dependent fashion, reflecting the drug affinity for cholinergic receptors.

Compared to haloperidol, olanzapine had been reported to be associated with significantly less incidence of tremor, nervousness and salivation Tran PV. et al, 1996. Beasley et al, 1996, Tollefson et al, 1997 pooled safety results from three large double blind controlled trials in 2606 patients demonstrated that olanzapine had a significantly

lower rate of any extrapyramidal symptom versus haloperidol ($p < 0.001$). This suggests that the use of olanzapine may be associated with better long term compliance due to fewer adverse effects.

Concomitant Medication Use:

The proportion of olanzapine patients taking at least one dose of permitted concomitant drug was significantly smaller than the proportion of their haloperidol treated counterparts for antiparkinsonian medications [6/28 (21.42%) versus 13/27 (48.14%); $\chi^2=4.33$, $P<0.005$ -significant]. A meaningful difference in rates for taking a benzodiazepine was not observed between olanzapine and haloperidol treated patients [17/28 (60.72%) versus 18/27 (66.67%); $\chi^2= 0.18$, $P>0.05$ -not significant).

Vital Signs and Laboratory Analysis:

Assessment of vital signs reveals no clinical significant treatment difference. Neither compound showed evidence haemotoxicity. No case of agranulocytosis and elevation of hepatic enzymes were reported in our study.

The primary limitation of the study was small group size. The primary strength of result was that they come from in double blind, well controlled-clinical trial comparing a novel antipsychotic with a conventional neuroleptic. Very few studies at this rigorous design are available.

CONCLUSION

Compared to haloperidol, olanzapine had been reported to be associated with significantly less incidence of tremor, nervousness and salivation. Some other weight gain and somnolence were common in olanzapine treated patients, but other events like akathisia, tremors, hypokinesia and rigidity were more common in haloperidol treated patients. Olanzapine treated patients had greater weight gain than haloperidol treated patients.

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