

COMPARATIVE STUDY OF RISPERIDONE AND HALOPERIDOL ON CLINICAL AND PSYCHOSOCIAL PARAMETERS IN TREATMENT OF SCHIZOPHRENIA : A RANDOMISED OPEN TRIAL

AMRESH SHRIVASTAVA & SARKHEL GOPA

ABSTRACT

The study compares the efficacy of risperidone and haloperidol in patients of schizophrenia on various clinical and psychosocial parameters.

In the present open, comparative study, in patients suffering from schizophrenia (DSM-IV), 50 patients each were randomly treated with risperidone and haloperidol over a period of 1 year. The clinical improvement was judged on PANSS (Positive and Negative Symptom Scale) and CGIS (Clinical Global Impression Scale). The improvement in psychosocial functioning and other areas was judged using a five point scale (0-4). Though the improvement on PANSS was comparable in both the groups except on the general psychopathology subscale, on CGIS a better improvement profile was observed in risperidone group. In the other psychosocial areas such as social functioning, productivity and education a significantly more number of patients showed improvement in risperidone group as compared to haloperidol group. In significantly less number of patients suicidality and rehospitalization was found in risperidone group as compared to haloperidol group.

Key words : Risperidone, haloperidol, social integration, quality of life

In the last decade number of double blind trials have compared risperidone with haloperidol (Claus et al., 1992; Chouinard et al., 1993; Ceskova & Svestka, 1993; Marder & Meibach, 1994; Peuskens, 1995). These studies have established its efficacy in positive as well as negative symptoms of schizophrenia and its safety in terms of low incidence of extrapyramidal reactions as compared to haloperidol. From these studies, it seems that, typical antipsychotics like haloperidol are not very effective against negative symptoms of schizophrenia. While the atypical antipsychotics like risperidone are useful in alleviating negative symptoms of schizophrenia. Therefore, risperidone may be more effective in improving the overall quality of life.

Over the last decade more and more attention is being paid to the concept of 'health

related quality of life' especially in patients suffering from chronic disorders like schizophrenia. This concept attempts to consider the patients holistically (Bech, 1993; Bech & Angst, 1996). Lehman has discussed this issue at length and has also developed an instrument 'quality of life interview' for patients of schizophrenia (Lehman et al., 1983; Lehman, 1996). When interpreting quality of life information in the context of intervention in schizophrenia Lehman has emphasized that one needs to study the various changes in patient's environment like housing, financial independence, productivity etc.

There seems to be a mutual relationship between pharmacotherapy and improvement in quality of life. The pharmacotherapy, by improving signs and symptoms, improves the quality of life and this in turn improves the compliance of the patients.

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Research data indicate that newer antipsychotic drug like risperidone, with significant antagonist activity at the 5HT and D₂ receptors may be more effective than currently available dopamine antagonists at treating positive as well as negative symptoms of schizophrenia (Carmen et al., 1995). The concept of health related quality of life emphasizes that apart from alleviation in signs and symptoms, the concept of improvement should also take into consideration the effect of clinical recovery into the other areas of life. Thus, the present study was undertaken to examine the comparative efficacy of risperidone and haloperidol in improvement in the signs and symptoms as well as improvement in the other areas of life which are important for social integration and overall improvement in quality of life in patients suffering from schizophrenia.

MATERIAL AND METHOD

Patients' selection : 125 consecutive patients suffering from schizophrenia (DSM-IV) and admitted in the hospital for acute exacerbation of schizophrenia were selected for the study, after taking a due informed consent from them and their relatives, over a period of 1 year. During the acute stage all of them were treated with haloperidol in the dose range of 15-30 mg/day (mean (sd)=23.8 (4.6) mg/day) over a period of 2 to 4 weeks. After the satisfactory clinical control of acute symptoms the patients were randomly divided into two groups (satisfactory control was judged clinically based on improvement in acute signs and symptoms, by a senior psychiatrist). Group-1 patients were gradually switched over to risperidone 2 mg/day over a period of 2 weeks while group-2 patients were continued on the maintenance dose of haloperidol which ranged from 5-15 mg/day (mean (sd)=9.2 (3.8) mg/day). Each of these patients were then followed up for a period of 12 months. During the follow up period 12 patients were lost to follow up and 13 patients had to be switched over to other medications. Thus, at the end both the groups had 50 patients each.

Medication . As mentioned earlier all the patients in group-1 were switched to risperidone at the dose of 2 mg/day while all the patients in group-2 were continued on haloperidol. The dose schedule in both the groups was flexible and it was titrated according to the clinical discretion of the study team. Concomitant antiparkinsonian agent were administered as and when required. Evaluation : In order to have an uniform clinical assessment of improvement or exacerbation, patients were rated on Clinical Global Improvement Scale (CGIS) at the baseline and at the end of the study.

They were also assessed on Positive and Negative Symptoms Scale (PANSS) (Kay et al., 1987, 1988) at the beginning of the study and at the end of the study.

The improvement in psychosocial aspect was assessed on a five point scale (0-4) using operational criteria in the following areas : i) social functioning; ii) productivity; iii) economic independence; iv) education; v) suicidality; vi) rehospitalization and vii) exacerbation of symptoms.

This scale was designed for the present study by the authors themselves.

RESULTS

In Group-1, there were 29 males and 21 females. The mean (sd) age was 36.2 (3.5) and mean (sd) duration of illness was 5.6 (3.8) years. While in Group-2, there were 30 males and 20 female. The mean (sd) age was 31.8 (4.8) and mean (sd) duration of illness was 5.1 (3.2) years. Both the groups were comparable on duration of illness and male to female ratio. Though there was a significant difference in the mean age of the two groups ($t=2.74$, d.f.=48, $p<0.05$), this difference was more statistical rather than clinical.

As evident from table-1, there was a significant reduction in total mean score and all the subscales scores of PANSS at the end of the study period. There was no significant difference between the two groups as far as the improvement assessed by PANSS was concerned in all but one subscale. A significantly

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TABLE 1
CHANGE IN PANSS SCORES

PANSS SCORE - MEAN (SD)						
Sub-Scales	RISPERIDONE GROUP			HALOPERIDOL GROUP		
	Baseline	At the end of 1 year	Reduction mean (sd) (% reduction)	Baseline	At the end of 1 year	Reduction mean (sd) (% reduction)
Positive	20.2 (4.2)	@ 09.0 (3.3)	11.2 (4.2) (55.5%)	21.0 (3.2)	@ 11.0 (3.1)	10.0 (3.0) (47.6%)
Negative	31.1 (4.2)	@ 12.8 (3.6)	18.3 (4.0) (58.8%)	29.3 (3.4)	@ 14.3 (3.3)	15.0 (3.5) (51.2%)
Gen-Psy	40.4 (5.6)	@ 20.0 (3.6)*	20.4 (4.9) (50.5%)	39.5 (4.4)	@ 12.5 (2.2)*	27.0 (3.7) (68.4%)
Total	91.9 (5.9)	@ 41.5 (3.6)	50.4 (5.7) (54.8%)	89.1 (4.8)	@ 37.1 (3.4)	52.0 (4.1) (58.4%)

@ Baseline scores and scores at the end of 1 year were compared in both the groups using unpaired t-test.

@ A significant difference was noticed on all the subscale scores and total scores in baseline scores and scores at the end of 1 year in both the groups.

* The baseline scores between the groups and scores at the end of 1 year between the groups were compared using unpaired t-test.

* Significant difference was noticed between the two groups in the scores at the end of 1 year in general psychopathology sub-scale ($t=2.15$, $df=48$, $p<0.05$).

* No other differences were found to be significant between the groups.

more reduction (68.4%) was observed in general psychopathology subscale in haloperidol group as compared to risperidone group (50.5%).

in Group-1 had suicidal ideation or attempts and rehospitalization. No significant difference was observed between the two groups on the parameters of economic independence and exacerbation.

TABLE 2
CLINICAL IMPROVEMENT AT THE
END OF 1 YEAR (CGIS)

	Risperidone group	Haloperidol group
Very much	18	05
Much	22	36
Minimal	10	09

$\chi^2=10.77$ $p<0.1$

On CGIS, a significantly more number of patients showed very much improvement in risperidone group as compared to haloperidol group.

Table-3 shows the improvement in different psychosocial factors. As there were only 50 patients in each group, in 5 by 2 table, observed and expected values in many cells were less than 5. Therefore the tables were dichotomized for the purpose of analysis. Patients having scores of 0 and 1 were considered together in one group and patients having scores 2, 3, and 4, were considered together.

A significantly more number of patients from Group-1 showed improvement in the areas of social functioning, productivity, education. Similarly, significantly less number of patients

DISCUSSION

As mentioned earlier, number of studies have compared the efficacy of risperidone with haloperidol in patients of schizophrenia (Claus et al., 1992; Chouinard et al., 1993; Ceskova & Svestka, 1993; Marder & Meibach, 1994; Peuskens, 1995). These studies have established the efficacy of risperidone on positive as well as negative symptoms of schizophrenia and its safety in term of low incidence of extrapyramidal reactions.

In the present study, there was no significant difference noticed between the risperidone and haloperidol group on PANSS except on general psychopathology subscale. A significantly more reduction was observed in haloperidol group on general psychopathology subscale. In contrast, a significantly more number of patients were rated as 'very much improved' on CGIS in risperidone group as compare to

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TABLE 3
CLINICAL IMPROVEMENT IN PSYCHOSOCIAL
AREAS AT THE END OF 1 YEAR (CGIS)

	Risperidone group	Haloperidol group
a) <i>Social functioning</i>		
0 Withdrawn & limited interaction	} 16	28
1 Express desire of interaction		
2 Definite evidence of improved functioning	} 34	22
3 Improvement functioning and relationship		
4 Functioning with satisfaction $X^2 = 4.91, p < 0.02$		
b) <i>Productivity</i>		
0 Unproductive	} 15	32
1 Expression of productivity	} 35	18
2 Occasional productive		
3 Productive with support		
4 Productive without support $X^2 = 10.28, p < 0.001$		
c) <i>Economic independence</i>		
0 Complete dependence	} 19	21
1 Desire to earn	} 31	29
2 Attempt with failure		
3 Attempt with success		
4 Satisfactorily independent $X^2 = 0.04, N.S.$		
d) <i>Education</i>		
0 Unable to resume	} 10	15
1 Feels confidence but unable to start	} 40	25
2 Attempt but not sustained		
3 Sustained without satisfaction		
4 Sustained with satisfaction $X^2 = 8.61, p < 0.003$		
e) <i>Suicidality</i>		
0 No intent	} 45	33
1 Occasional death wish	} 05	17
2 Contemplating suicide		
3 Experiencing suicidal crisis		
4 Attempted suicide $X^2 = 7.05, p < 0.009$		
f) <i>Rehospitalization</i>		
0 Not required	} 44	35
1 Required unrelated to the current illness	} 06	15
2 Required due to side effects		
3 Required due to additional stress		
4 Required due to relapse $X^2 = 3.84, p < 0.05$		
g) <i>Exacerbation</i>		
0 No exacerbation	} 43	44
1 Mild behavioural exacerbation		
2 Moderate exacerbation	} 07	06
3 Severe exacerbation without admission		
4 Severe exacerbation with admission $X^2 = 0.068, N.S.$		

haloperidol group. At first sight it may appear as a bias of a clinician in favour of risperidone, especially in this kind of open trial, but it is likely that due to overall improvement in other psychosocial areas, more number of patients received the rating of 'very much improved' on CGIS in risperidone group than in haloperidol group. This is evident from table-3, as significantly more number of patients could sustain education with satisfaction and were productive with or without support in the risperidone group than in haloperidol group. In addition, significantly more number of patients showed 'no suicidal intent' in risperidone group than in haloperidol group.

The findings of the present study needs to be taken with caution in view of it being an open trial as well as descrepency in the results on PANSS and Clinical Global Assessment. It is also difficult to rule out the possibility of better improvement on Clinical Global Assessment in risperidone group due to the possibility of lower rates of extrapyramidal reactions in risperidone group.

In conclusion, from the findings of the present study it appears that though risperidone and haloperidol may be comparable as far as the improvement in signs and symptoms of schizophrenia is concerned, risperidone may have an edge over haloperidol as far as improvement in some of the psychosocial areas and overall clinical improvement is concerned.

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AMRESH SHRIVASTAVA*, MD (Psy), DPM, Consultant Psychiatrist & SARKHEL GOPA, MA (Clinical Psychologist), Consultant Clinical Psychologist, Silver Mind Hospital, 209, Shivkrupa Complex, Gokhale Road, Thane, Mumbai-400 602.

* Correspondence