RISPERIDONE VERSUS HALOPERIDOL IN ACUTE AND TRANSIENT PSYCHOTIC DISORDER

BIJOY PRATIM CHAUDHURI, DIPESH BHAGABATI & DIPANJALI MEDHI

ABSTRACT

The mechanism of action of a relatively new antipsychotic drug-Risperidone differs from conventional antipsychotics like Haloperidol. We compared low dosages of Risperidone with near equivalent dosages of Haloperidol in first episode drug naive Acute and Transient Psychotic disorder. A single blind randomised four-week study protocol was employed. Highly significant and comparable efficacy as assessed by Brief Psychiatric Rating Scale and Global Assessment of Functioning Scale was seen at the end of the Study protocol in both the groups. Risperidone had significantly, an early onset of action on some of the positive as well as negative symptoms with less incidence of Extrapyramidal Symptoms in comparison to Haloperidol. We conclude that Risperidone may represent a potential useful first line agent in the treatment of Acute and Transient Psychotic Disorder.

Key words: Risperidone in first episode psychosis, risperidone, haloperidol, acute and transient psychotic disorder.

Leysen et al (1988) and Janssen et al., (1988) reported that Risperidone strongly antagonize central serotonin 5-HT2 receptors and Dopamine D2 receptors, whereas conventional antipsychotics such as Haloperidol more strongly antagonize D2 and only weakly block 5HT receptors.

Adityanjee et al. (1995) found encouraging preliminary results in the use of Risperidone in first episode Schizophrenia & provided some support for the early use of Risperidone.

According to Kopala (1997), recent clinical experience in Canada has shown that Risperidone is effective in the treatment of patients with first episode Psychosis and with the further accumulation of data, the mean daily dose of Risperidone required by first episode patients was shown to be close to 4mg. According to Lieberman et al.(1993) and McEvoy et al.(1991) first episode patients have better therapeutic responses to antipsychotic drug treatment, and are more sensitive to develop EPS and require lower doses of medications.

Johnson (1995) reported that although the third consensus conference on methodology of clinical trials of antipsychotics had concluded that the optimal duration of short term trials is between 4 - 8 weeks, it can only indicate a very preliminary & tentative outcome unless it is in individuals who had been previously drug free.

According to Kane (1994), the data from multicentre trials suggest a bimodal response pattern, wherein the 6 mg and 16 mg dose of Risperidone are most effective. Buckley (1997) reported that the modal dose of Risperidone in clinical practice in the united states is 4.6 mg daily.

Danik & Goverdhan (1963); Mountain (1963) have reported success with use of high dosages of haloperidol in the acutely Psychotic patients, while Fitzgerald (1969) & Anderson et al. (1976) had all reported high improvement rates with low dosages of Haloperidol in the acutely ill Psychotic patients.

Khanna et al. (1997) in an Indian trial with low & high dosages of haloperidol on a sample of Acute & transient Psychotic disorders (ICD-10) did not report any significant difference in the improvement rate between the two groups.
According to Kammen and Marder (1995), 0.6 mg of Risperidone is equivalent to 100 mg of Chlorpromazine & 2 mg of haloperidol is equivalent to 100 mg of Chlorpromazine.

The aim of the present study is to compare 4 mg of Risperidone (RIS) with near equivalent doses of Haloperidol (HAL) for outcome of clinical symptomatology at short term in first episode drug naive acute & transient Psychotic disorder (F23, ICD-10).

MATERIAL AND METHOD

The study group consisted of indoor patients in the department of Psychiatry at Gauhati Medical College and Hospital, Guwahati. Subjects were diagnosed as per International Classification of Disease - 10 criteria for acute and transient psychotic disorder (F23). The diagnosis of the cases were reviewed by the senior consultant after the initial workup of the patients by the Post-Graduate residents in the department of Psychiatry.

The sample for the study consisted of subjects who fulfilled the following:

Selection criteria : (1) Age between 16 and 55 years, (2) Patients in the first episode of the disorder, (3) Patients who were free from antipsychotic drug treatment prior to the period of initial assessment, (4) No past history of any Psychiatric morbidity.

The exclusion criteria are the following: (1) Severe medical illness i.e., presence of any physical disorders requiring active medication, or pregnancy & lactation, (2) Patients having neuropsychiatric illness such as epilepsy, mental retardation, drug-induced psychosis, substance abuse disorder, etc. (3) Other psychiatric illness such as bipolar disorder, schizophrenia, etc.

The patients fulfilling the selection criteria were randomly assigned to either risperidone 4 mg (equivalent to 666.67 mg of chlorpromazine) or haloperidol 15 mg (equivalent to 750 mg of chlorpromazine) in a single blind four week protocol. They were administered the semi-structured proforma of Brief Psychiatric rating Scale (Overall et al., 1962) at Day 0, Day 7, Day 14 and Day 28. The dimension of psychopathology was interpreted by scoring subjects on the four BPRS factors (Overall & Gorham, 1962) viz. (1) THINKING DISTURBANCE (consist of conceptual disorganization, hallucinatory behaviour, unusual thought content). (2) HOSTILE SUSPICIOUSNESS (consist of items hostility, suspiciousness and unco-operativeness). (3) WITHDRAWAL RETARDATION (consist of emotional withdrawal, motor retardation, blunted affect). (4) ANXIOUS DEPRESSION (consist of anxiety, guilt, depression).

A high inter-rater reliability was achieved in the administration of the BPRS (correlation co-efficient r=1) prior to the onset of the protocol.

Similarly the Global Assessment of Functioning Scale (GAF) was administered at Day 0, Day 7, Day 14 and Day 28.

The subjects were also assigned oral trihexiphenidyl 6 mg for extrapyramidal symptoms (EPS), and lorazepam 2 mg at bedtime, if required for sedation, which were duly recorded in each case.

Statistical analysis : Carried out by using the Paired 't' test and Fisher's 't' test.

RESULTS

Thirty-five patients gave full informed consent and were included in the study (HAL group=18 & RIS group=17). Five patients dropped out of the study prior to completion of 7 days of protocol. Thus thirty patients completed the 4-week study protocol (HAL=15 & RIS = 15).

Table 1 shows the Distribution of socio-demographic variables in the Haloperidol & Risperidone groups Results indicate no major difference in the distribution of diagnostic categories between the two groups and the majority had acute schizophrenia like psychotic disorders (Table 2). Results on comparison of clinical variable between the two groups indicate no difference in the duration of illness prior to initial assessment; no major difference in distribution of precipitating factors in the three months preceding the onset of illness; and no
TABLE 1
DISTRIBUTION OF SOCIODEMOGRAPHIC VARIABLES IN HALOPERIDOL & RISPERIDONE GROUPS

| Socio-demographic variables | Haloperidol (n=15) | Risperidone (n=15) |
|-----------------------------|-------------------|--------------------|
| Age (yrs.)                  |                   |                    |
| 16 - 25                     | 13 (86.6)         | 11 (73.3)          |
| 26 - 35                     | 2 (13.3)          | 3 (20)             |
| 36 - 45                     | 0                 | 0                  |
| 46 - 55                     | 0                 | 1 (6.6)            |
| Sex                         |                   |                    |
| Male                        | 8 (53.3)          | 7 (46.6)           |
| Female                      | 7 (46.6)          | 8 (53.3)           |
| Educational level           |                   |                    |
| Illiterate                  | 4 (26.6)          | 0                  |
| Upto primary level          | 3 (20)            | 4 (26.6)           |
| Upto high school            | 6 (40)            | 10 (66.6)          |
| College level               | 2 (13.3)          | 1 (6.6)            |
| Occupational status         |                   |                    |
| Student                     | 5 (33.3)          | 6 (40)             |
| Unemployed                  | 3 (20)            | 6 (40)             |
| Daily Wage Earner           | 1 (6.6)           | 2 (13.3)           |
| House Wife                  | 2 (13.3)          | 1 (6.6)            |
| Cultivator                  | 2 (13.3)          | Nil                |
| Skilled labourer            | 1 (6.6)           | Nil                |
| Business                    | 1 (6.6)           | Nil                |
| Marital status              |                   |                    |
| Married                     | 4 (26.6)          | Nil                |
| Unmarried                   | 11 (73.3)         | 14 (93.3)          |
| Widowed                     | Nil               | 1 (6.6)            |
| Socio-economic status (Rs. per month) |           |                    |
| < 1500 p.m.                 | 12 (80)           | 9 (60)             |
| 1500 - 3000                 | 3 (20)            | 2 (13.3)           |
| & less                      | Nil               | Nil                |
| 3000 - 4500                 | Nil               | Nil                |
| & less                      | 4500 & above      | 4 (26.6)           |
| Place of locality           |                   |                    |
| Rural                       | 12 (80)           | 12 (80)            |
| Urban                       | 2 (13.3)          | 3 (20)             |
| Semi-Urban                  | 1 (6.6)           | Nil                |

Figure in parenthesis indicate percentage

TABLE 2
DISTRIBUTION OF DIAGNOSTIC CATEGORIES (ICD-10) AND CLINICAL VARIABLES IN RISPERIDONE & HALOPERIDOL GROUPS

| Diagnostic categories | Haloperidol group (n=15) | Risperidone group (n=15) |
|-----------------------|--------------------------|--------------------------|
| n                    | %                        | n                        | %                        |
| F 23.0                |                          |                          |                          |
| Acute polymorphic psychotic disorder without symptoms of schizophrenia | 1 | 6.6 | Nil |
| F 23.2                |                          |                          |                          |
| Acute schizophrenia like psychotic disorder | 9 | 60 | 9 | 60 |
| F 23.8                |                          |                          |                          |
| Other acute & transient psychotic disorders | 5 | 33.3 | 6 | 40 |
| Clinical variables (A) Duration of illness before assessment (in days) |       |       |       |
| Upto 7                | 9 | 60 | 9 | 60 |
| 8 - 15                | 5 | 33.3 | 5 | 33.3 |
| 16 - 30               | 1 | 6.6 | 1 | 6.6 |
| (B) Precipitating factors (in preceding 3 months) |       |       |       |
| Present               | 7 | 48.6 | 5 | 33.3 |
| Absent                | 8 | 53.3 | 10 | 66.3 |
| (C) Family history of psychosis (first and second degree relative) |       |       |       |
| Present               | 8 | 40 | 7 | 46.6 |
| Absent                | 9 | 60 | 8 | 53.3 |

with those in the HAL group (Table 2).

Results on comparison for use of adjunct medications between HAL group & RIS group indicate that all subjects (15 or 100%) in HAL group required trihexiphenidyl, whereas only 6 (40%) in the RIS group required it by the end of the fourth week of protocol. The results also indicate that more subjects in the RIS group required lorazepam (for sedation), propranolol (for akathisia) & parenteral diazepam when compared with those in the HAL group (Table 2).

Results on comparison for use of adjunct medications between HAL group & RIS group indicate that all subjects (15 or 100%) in HAL group required trihexiphenidyl, whereas only 6 (40%) in the RIS group required it by the end of the fourth week of protocol. The results also indicate that more subjects in the RIS group required lorazepam (for sedation), propranolol (for akathisia) & parenteral diazepam when compared with those in the HAL group (Table 2).

Results on comparison for use of adjunct medications between HAL group & RIS group indicate that all subjects (15 or 100%) in HAL group required trihexiphenidyl, whereas only 6 (40%) in the RIS group required it by the end of the fourth week of protocol. The results also indicate that more subjects in the RIS group required lorazepam (for sedation), propranolol (for akathisia) & parenteral diazepam when compared with those in the HAL group (Table 2).
### TABLE 3

**COMPARISON IN USE OF ADJUNCT MEDICATIONS BETWEEN HALOPERIDOL & RISPERIDONE GROUPS**

| Medication                  | Haloperidol Group | Risperidone Group |
|-----------------------------|-------------------|-------------------|
|                             | 1st wk | 2nd wk | 3rd wk | 4th wk | 1st wk | 2nd wk | 3rd wk | 4th wk |
| Trihexyphenidyl (fixed dose - 6 mg for EPS) | 4 (26.67) | (46.6) | (93.3) | (100) | Nil | (40) | (40) | |
| Tab Lorazepam 2mg HS (for sedation) | 7 (7) | 7 (7) | 7 (7) | 10 | 9 | 9 | 9 | |
| Propranolol 40 mg (fixed dose for Akathisia) | Nil | Nil | Nil | Nil | Nil | Nil | 2 (13.3) | (26.6) |
| Inj. Diazepam 20mg (SOS) | (66.6) | (33.3) | (13.3) | (6.6) | (60) | (60) | (60) | |

% in parenthesis.

### TABLE 4

**COMPARISON OF CHANGES IN (a) B.P.R.S. (b) G.A.F. SCORES BETWEEN RESPECTIVE DAYS OF ASSESSMENT IN HALOPERIDOL & RISPERIDONE GROUPS**

| Day 0 | Day 7 | t | Day 0 | Day 7 | t | Day 0 | Day 7 | t |
|-------|-------|---|-------|-------|---|-------|-------|---|
| Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) |
| (a) 80.7±32.46 | 56.53±26.16 | 4.8892 (p<0.001) | 81.46±26.41 | 46.00±17.15 | 5.7165 (p<0.001) |
| (b) 25.66±4.5 | 38.4±10.09 | 4.8375 (p<0.001) | 23.86±4.5 | 38.4±12.06 | 5.1582 (p<0.001) |

Day 0 | Day 14 | t | Day 0 | Day 14 | t | Day 0 | Day 28 | t | Day 0 | Day 28 | t | Day 0 | Day 14 | t | Day 0 | Day 14 | t | Day 0 | Day 28 | t | Day 0 | Day 28 | t | Day 0 | Day 14 | t | Day 0 | Day 14 | t |
|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|
| Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) |
| (a) 80.7±32.46 | 45.26±27.55 | 5.7488 (p<0.001) | 81.46±26.41 | 30.73±7 | 7.831 (p<0.001) |
| (b) 25.66±4.5 | 53.2±17.1 | 6.4104 (p<0.001) | 23.86±4.5 | 55.6±16 | 8.9436 (p<0.001) |

Day 7 | Day 14 | t | Day 0 | Day 14 | t | Day 0 | Day 28 | t | Day 0 | Day 28 | t | Day 0 | Day 14 | t | Day 0 | Day 14 | t | Day 0 | Day 28 | t | Day 0 | Day 28 | t | Day 0 | Day 14 | t | Day 0 | Day 14 | t |
|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|
| Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) |
| (a) 56.53±26.16 | 45.26±27.55 | 5.0768 (p<0.001) | 46.00±17.15 | 30.73±7 | 5.2035 (p<0.001) |
| (b) 38.4±10.09 | 53.2±17.1 | 7.2422 (p<0.001) | 38.4±12.06 | 55.6±16 | 6.9359 (p<0.001) |

Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t | Day 14 | Day 28 | t |
|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|-------|-------|---|
| Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) | Mean SD | Mean SD | (p value) |
| (a) 45.26±27.55 | 30±10.15 | 4.1822 (p<0.001) | 46.00±17.15 | 27.2±10.6 | 4.7587 (p<0.001) |
| (b) 53.2±17.1 | 59.2±19.6 | 4.1936 (p<0.001) | 55.6±16 | 70.8±21.8 | 5.9369 (p<0.001) |
TABLE 5

COMPARISON OF SCORE BETWEEN HALOPERIDOL GROUP AND RISPERIDONE GROUP AT RESPECTIVE DAYS OF ASSESSMENT (a) BPRS & (b) GAF

Fishers 't' test

| Day of assessment | Haloperidol (n=15) Mean SD | Risperidone (n=15) Mean SD | t (p value) |
|-------------------|---------------------------|---------------------------|------------|
|                   | (a) 80.7±32.45 81.48±26.41 | 81.46±26.41 25.66±4.5   | 0.0706     |
|                   | 23.86±4.53        | 23.86±4.53                | 1.125      |
|                   | 56.53±26.16 46±17.15 | 46.91±17.15               | 1.3113     |
|                   | 38.4±10.09        | 38.4±10.09                | 0          |
|                   | 45.26±27.5        | 30.73±27                  | 1.9094     |
|                   | 53.2±17.1         | 55.6±16                   | 0.398      |
|                   | 30.±10.15         | 27.2±10.6                 | 0.7368     |
|                   | 59.2±19.6         | 70.8±21.8                 | 1.5466     |
|                   | 90.7±32.45        | 81.48±26.41               | 0.0706     |
|                   | 23.86±4.53        | 23.86±4.53                | 1.125      |
|                   | 56.53±26.16       | 46.91±17.15               | 1.3113     |
|                   | 38.4±10.09        | 38.4±10.09                | 0          |
|                   | 45.26±27.5        | 30.73±27                  | 1.9094     |
|                   | 53.2±17.1         | 55.6±16                   | 0.398      |
|                   | 30.±10.15         | 27.2±10.6                 | 0.7368     |
|                   | 59.2±19.6         | 70.8±21.8                 | 1.5466     |

d.f.=28, p>0.05, not significant

Comparison of scores (Table 6) between HAL group & RIS group at respective days of assessment indicate that at day 14, the score on THINKING DISTURBANCE in RIS group is significantly lower than that of HAL group (p<0.05); At day 14, the score on HOSTILE SUSPICIOUSNESS in RIS group is significantly lower than that of HAL group (p<0.05); At day 7, WITHDRAWAL RETARDATION in the RIS group is significantly lower than that of HAL group (p<0.05), whereas at day 0, 7, 14 & 28, the analysis of ANXIOUS-DEPRESSION showed no significant difference between the two groups (p>0.05).

Results from (Table 6) show change in score between respective days of assessment in HAL group and RIS group which indicate that for THINKING DISTURBANCE, in HAL group, the rate of improvement between day 0 & 7, day 0 & 14, day 0 & 28 is highly significant (p<0.001). The rate of improvement in the first two weeks being more significant (p<0.001) than the last two weeks of protocol (p<0.05). In RIS group, rate of improvement between day 0 & 7, day 0 & 14, day 0 & 28 is highly significant (p<0.001). The rate of improvement in first two weeks is highly significant (p<0.001), but there is no further significant improvement during the last two weeks of protocol (p>0.05). Analysis of HOSTILE SUSPICIOUSNESS indicates that both HAL group & RIS group have similar results. Improvement is highly significant between day 0 & 7, day 0 & 14, day 0 & 28 (p<0.001). Rate of improvement between day 0 & 7 is more significant (p<0.001) than between day 7 & 14 (p<0.05) & rate of improvement between day 0 & 14 is more significant (p<0.001) than between Day 14 & 28 (p<0.05). Analysis of WITHDRAWAL RETARDATION indicates that in HAL group there is significant worsening between day 0 & 7 (p<0.001) and also between day 0 & 14 (p<0.05) but there is significant improvement between day 0 & 28 (p<0.05). The rate of improvement in first two weeks is less significant (p<0.05) than that during the last two weeks of protocol (p<0.01), in the RIS group the rate of improvement is significant between day 0 & 7, day 0 & 14, day 0 & 28 (p<0.01). The rate of improvement between day 0 & 7, day 0 & 14, day 0 & 14 & day 14 & 28 are all similarly significant (p<0.01). Analysis of ANXIOUS DEPRESSION indicates that in HAL group the rate of improvement is significant between day 0 & 7, (p<0.01), day 0 & 14 (p<0.05), day 0 & 28 (p<0.05) day 7 & 14 (p<0.05) & day 14 & 28 (p<0.05), whereas in RIS group the rate of improvement is highly significant (p<0.001) between day 0 & 7, day 0 & 14, day 14 & 28 & day 0 & 28. Significant improvement is also seen between day 7 & 14 (p<0.01).

Table 7, indicate comparison of scores between both groups, for individual items at respective days of assessment. The results indicate that for hallucinatory behaviour, subjects
| Dimensions of psychopathology | A - At respective days of assessment (Fisher's 't' test d.f. = 28) | B - Between respective days of assessment (Paired 't' test d.f. = 14) |
|-------------------------------|---------------------------------------------------------------|----------------------------------------------------------------|
|                               | Haloperidol group (n=15) Mean SD | Risperidone group (n=15) Mean SD | 't' (p value) | Haloperidol Mean SD | Risperidone Mean SD | 't' (p value) |
| (a) Thinking disturbances      | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 |
| 0                             | 5.42±2.09 | 5.46±2.06 | 0.0526 (p>0.05) | 4.68 | 5.31 | 0.001 | 0.001 | 7.34 | 0.001 | 0.001 | 7.34 | 0.001 | 0.001 |
| 7                             | 3.63±2.5  | 3.15±1.1  | 0.6 (p>0.05) | 5.72 | 5.72 | 0.001 | 0.001 | 7.32 | 0.001 | 0.001 | 7.32 | 0.001 | 0.001 |
| 14                            | 2.56±2.03 | 1.32±0.5  | 2.2962 (p<0.05) | 5.92 | 5.92 | 0.001 | 0.001 | 7.32 | 0.001 | 0.001 | 7.32 | 0.001 | 0.001 |
| 28                            | 1.88±1.2  | 1.26±0.5  | 1.77 (p<0.05) | 4.23 | 4.51 | 0.001 | 0.001 | 4.51 | 0.001 | 0.001 | 4.51 | 0.001 | 0.001 |
| 0                             | 4.49±1.9  | 4.04±2.1  | 0.803 (p<0.05) | 2.36 | 1.83 | 0.05 | 0.05 | 1.83 | 0.05 | 0.05 | 1.83 | 0.05 | 0.05 |
| (b) Hostile suspiciousness     | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 |
| 7                             | 3.05±2.3  | 2.14±1.1  | 1.34 (p<0.05) | 4.24 | 5.09 | 0.001 | 0.001 | 5.09 | 0.001 | 0.001 | 5.09 | 0.001 | 0.001 |
| 14                            | 2.6±2.1   | 1.43±0.86 | 2.0526 (p<0.05) | 5.91 | 6.91 | 0.001 | 0.001 | 6.91 | 0.001 | 0.001 | 6.91 | 0.001 | 0.001 |
| 28                            | 1.25±0.5  | 1.37±0.1  | 0.3636 (p<0.05) | 2.93 | 3.40 | 0.05 | 0.05 | 3.40 | 0.05 | 0.05 | 3.40 | 0.05 | 0.05 |
| 0                             | 1.85±1.54 | 1.87±1.07 | 0.04 (p<0.05) | 2.92 | 2.85 | 0.05 | 0.05 | 2.85 | 0.05 | 0.05 | 2.85 | 0.05 | 0.05 |
| (c) Withdrawal retardation     | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 |
| 7                             | 2.45±1.2  | 1.68±0.7  | 2.1388 (p<0.05) | 2.87 | 3.53 | 0.05 | 0.05 | 3.53 | 0.05 | 0.05 | 3.53 | 0.05 | 0.05 |
| 14                            | 1.99±1.15 | 1.53±0.6  | 1.03 (p<0.05) | 2.88 | 2.93 | 0.05 | 0.05 | 2.93 | 0.05 | 0.05 | 2.93 | 0.05 | 0.05 |
| 28                            | 1.35±0.4  | 1.29±0.3  | 0.43 (p<0.05) | 4.547 | 3.76 | 0.05 | 0.05 | 3.76 | 0.05 | 0.05 | 3.76 | 0.05 | 0.05 |
| 0                             | 3.86±2.6  | 4.09±1.9  | 0.27 (p<0.05) | 3.07 | 3.11 | 0.01 | 0.01 | 3.11 | 0.01 | 0.01 | 3.11 | 0.01 | 0.01 |
| (d) Anxious depression         | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 | Day 0 & 7 | Day 0 & 14 | Day 0 & 28 | Day 7 & 14 | Day 14 & 28 |
| 7                             | 3.44±2.4  | 2.33±1.2  | 1.59 (p<0.05) | 2.70 | 5.62 | 0.05 | 0.05 | 5.62 | 0.05 | 0.05 | 5.62 | 0.05 | 0.05 |
| 14                            | 2.45±1.9  | 1.62±0.5  | 1.6 (p<0.05) | 3.27 | 5.26 | 0.05 | 0.05 | 5.26 | 0.05 | 0.05 | 5.26 | 0.05 | 0.05 |
| 28                            | 1.61±0.7  | 1.49±0.8  | 0.43 (p<0.05) | 3.11 | 3.33 | 0.05 | 0.05 | 3.33 | 0.05 | 0.05 | 3.33 | 0.05 | 0.05 |
| 0                             | 4.09±2.6  | 4.09±1.9  | 0.27 (p<0.05) | 2.69 | 4.93 | 0.05 | 0.05 | 4.93 | 0.05 | 0.05 | 4.93 | 0.05 | 0.05 |

In RIS group at day 14 are more significantly improved (p<0.05) than those in HAL group; for hostility subjects in RIS group at day 7 are significantly more improved (p<0.01) than those in HAL group; For SUSPICIOUSNESS subjects in RIS group at day 14 are significantly (p<0.05) more improved than those in HAL group. For EMOTIONAL WITHDRAWAL subjects in RIS group at day 7 are significantly better off (p<0.05) than those in HAL group. For MOTOR RETARDATION the scores in RIS group at day 7, are significantly (p<0.05) lower than those...
### TABLE 7
COMPARISON IN SCORES OF INDIVIDUAL ITEMS (A) AT RESPECTIVE DAYS & (B) BETWEEN RESPECTIVE DAYS OF ASSESSMENT

| Individual items in the dimensions of psychopathology (from BPRS) | (a) At respective days of assessment (Fisher's 't' test d.f = 28) | (b) Between respective days of assessment (Paired 't' test d.f = 14) |
|---|---|---|
| | Days of assessment | Haloperidol group (n=15) | Risperidone group (n=15) | 't' (p value) | Days of assessment | Haloperidol group (0-28) | Risperidone group (0-28) | 't' (p value) |
| Hallucinatory behaviour | | | | | | | | |
| 0 | 5.8±2.5 | 6.2±2.3 | 0.39 (p>0.05) | Day 0 & 7 | 4.33 (p<0.001) | 5.47 (p<0.001) |
| 7 | 3.8±2.7 | 3.3±1.7 | 0.60 (p>0.05) | Day 0 & 28 | 4.86 (p<0.001) | 7.17 (p<0.001) |
| 14 | 2.9±2.5 | 1.27±0.5 | 2.41 (p<0.05)* | Day 7 & 14 | 5.46 (p<0.001) | 4.89 (p<0.001) |
| 28 | 2.2±1.8 | 1.29±1 | 1.65 (p>0.05) | Day 7 & 28 | 4.57 (p<0.001) | 4.52 (p<0.001) |
| Hostility | | | | | | | | |
| 0 | 4.3±3.1 | 3.8±2.9 | 0.44 (p>0.05) | Day 0 & 7 | 3.03 (p<0.01) | 3.35 (p>0.01) |
| 7 | 3.06±3.1 | 1.6±1.05 | 3.90 (p<0.05)* | Day 0 & 28 | 3.89 (p>0.01) | 4.32 (p<0.001) |
| 14 | 2.2±2.7 | 1.13±0.3 | 1.46 (p>0.05) | Day 7 & 14 | 1.93 (p<0.05) | 1.195 (p>0.05) |
| 28 | 1.1±0.5 | 1.4±1.05 | 0.90 (p>0.05) | Day 7 & 28 | 2.37 (p<0.05) | 2.97 (p<0.01) |
| Suspiciousness | | | | | | | | |
| 0 | 5.33±2.3 | 6.6±2.8 | 0.28 (p>0.05) | Day 0 & 7 | 5.18 (p<0.001) | 4.67 (p<0.001) |
| 7 | 4.2±2.7 | 3.2±1.8 | 2.01 (p>0.05) | Day 0 & 28 | 9.36 (p<0.001) | 9.18 (p<0.001) |
| 14 | 3.6±2.3 | 2.2±1.5 | 2.13 (p<0.05)* | Day 7 & 14 | 6.21 (p<0.001) | 5.52 (p<0.01) |
| 28 | 1.6±1.02 | 1.73±1.5 | 0.14 (p>0.05) | Day 7 & 28 | 2.45 (p<0.001) | 4.4 (p<0.001) |
| Emotional withdrawal | | | | | | | | |
| 0 | 2.0±1.1 | 2.4±1.8 | 0.49 (p>0.05) | Day 0 & 7 | 3.87 (p<0.01) | 2.67 (p<0.05) |
| 7 | 2.4±1.1 | 1.5±0.7 | 2.35 (p<0.05)* | Day 0 & 28 | 2.16 (p<0.05) | 2.92 (p<0.05) |
| 14 | 1.6±0.9 | 1.3±0.2 | 0.96 (p>0.05) | Day 7 & 14 | 2.64 (p<0.01) | 3.4 (p<0.01) |
| 28 | 1±0 | 1.07±0.2 | 1.4 (p>0.05) | Day 7 & 28 | 4.59 (p<0.001) | 2.19 (p<0.05) |
| Motor retardation | | | | | | | | |
| 0 | 1.6±1.6 | 1.27±0.5 | 0.87 (p>0.05) | Day 0 & 7 | 3.76 (p<0.01) | 3.89 (p<0.01) |
| 7 | 2.4±1.5 | 1.6±0.7 | 2.12 (p<0.05)* | Day 0 & 28 | 2.96 (p<0.01) | 1.89 (p<0.05) |
| 14 | 2.2±1.2 | 1.73±0.7 | 1.5 (p>0.05) | Day 7 & 14 | 2.84 (p<0.05) | 4.55 (p<0.001) |
| 28 | 1.6±0.9 | 1.47±0.6 | 0.46 (p>0.05) | Day 7 & 28 | 3.10 (p<0.01) | 3.20 (p<0.01) |
| Anxiety | | | | | | | | |
| 0 | 5.2±2.1 | 3.7±2.1 | 2.13 (p<0.05)* | Day 0 & 7 | 6.48 (p<0.001) | 2.91 (p<0.01) |
| 7 | 3.7±2.6 | 3.3±1.3 | 0.63 (p>0.05) | Day 0 & 28 | 6.65 (p<0.001) | 6.45 (p<0.001) |
| 14 | 2.6±1.3 | 2.4±1.1 | 0.44 (p>0.05) | Day 7 & 14 | 5.26 (p<0.001) | 5.85 (p<0.001) |
| 28 | 1.6±1.3 | 1.8±1.3 | 0.14 (p>0.05) | Day 7 & 28 | 4.99 (p<0.001) | 4.42 (p<0.001) |
| Guilt | | | | | | | | |
| 0 | 3.6±3.5 | 5.8±3.7 | 4.93 (p<0.05)* | Day 0 & 7 | 2.10 (p<0.05) | 4.78 (p<0.001) |
| 7 | 2.6±3.5 | 2.07±2.3 | 1.4 (p>0.05) | Day 0 & 28 | 2.91 (p<0.05) | 4.68 (p<0.001) |
| 14 | 2.47±2.7 | 1.13±0.5 | 1.84 (p>0.05) | Day 7 & 14 | 2.10 (p>0.05) | 1.7 (p>0.05) |
| 28 | 1.27±0.4 | 1.27±1.03 | 0 (p>0.05) | Day 7 & 28 | 2.93 (p<0.01) | 1.52 (p<0.05) |
| Conceptual disorganization | | | | | | | | |
| 0 | 5.2±2.5 | 4.4±1.6 | 1.33 (p>0.05) | N.B. : No further analysis for these items carried out as no significant difference (p>0.05) is seen between both the groups at respective days of assessment. | | |

Day 0 & 7 & 28
Day 0 & 14
Day 0 & 28
Day 7 & 14
Day 7 & 28
Day 14 & 28
Day 0 & 7 & 14
Day 0 & 28
Day 7 & 28
Day 14 & 28
Day 0 & 7 & 14
Day 0 & 28
Day 7 & 14
Day 7 & 28
Day 14 & 28

286
from the HAL group; Subjects in HAL group at baseline assessment (day 0) have significantly (p<0.05) less ANXIETY than those in RIS group. Subsequently there is no significant difference at day 7, 14 & 28. For all the other items comprising the dimensions of Psychopathology in the BPRS, no significant difference in scores (p>0.05) between the two groups are found at the respective days of assessment.

Table 7b shows the comparison of scores for individual items between respective days of assessment in HAL & RIS group and indicate that, for HALLUCINATORY BEHAVIOUR the improvement is highly significant (p<0.001) in both HAL & RIS group between the days - day 0 & 7, day 0 & 14 & day 0 & 28. In both the groups the improvement between day 0 & 14 is more significant (p<0.001) than between day 14 & 28 (p>0.05, not significant). Analysis of HOSTILITY indicate that in both the groups there is significant improvement (p<0.01) between day 0 & 7, day 0 & 14 & day 0 & 14. In HAL group the improvement between day 0 & 28 is significant (p<0.01) while in RIS group it is highly significant (p<0.001) between day 0 & 28. There is significant improvement (p<0.01) in both the groups between day 0 & 14 while between day 14 & 28 there is no significant change in scores (p>0.05) in both the groups. Analysis of SUSPICIOUSNESS indicate that in both the groups the rate of improvement is highly significant (p<0.001) between day 0 & 7, day 0 & 14 & day 0 & 28. In HAL group the rate of improvement between day 7 & 14 is highly significant (p<0.001) whereas in RIS group it is less significant (p<0.01). The rate of improvement in HAL group between day 14 & 28 is more significant (p<0.001) than what it was in RIS group (p<0.01). Analysis of EMOTIONAL WITHDRAWAL indicate that in HAL group there is significant worsening of symptoms (p<0.01) between day 0 & 7 followed by significant improvement (p<0.01) between day 7 & 14. The improvement between day 0 & 14 & day 14 & 28 is similarly significant (p<0.05). While in RIS group, there is significant improvement between day 0 & 7 (p<0.05), day 0 & 14 (p<0.01) & day 0 & 28 (p<0.01), the improvement between day 7 & 14 is more significant (p<0.01) than between day 0 & 7 (p<0.05). The improvement in the last two weeks of protocol i.e. between day 14 & 28 is similarly significant (p<0.01) as that present in the first two weeks of protocol (p<0.01). Analysis of MOTOR RETARDATION indicate that in HAL group, there is significant worsening (p<0.01) between day 0 & 7. Thereafter, there is significant improvement (p<0.01) between day 0 & 14 & day 0 & 28 & also between day 7 & 14 (p<0.05). The rate of improvement in the first two weeks & last two weeks of protocol are both similarly significant (p<0.01). In RIS group there is significant worsening of motor retardation between day 0 & 7 (p<0.01), day 0 & 14 (p<0.01). But between day 0 & 28 the worsening is not significant (p>0.05). Results also indicate highly

RISPERIDONE VS. HALOPERIDOL IN ACUTE PSYCHOTIC DISORDERS

| TABLE 7 (CONTD..) |
|-------------------|
| **Unusual thought content** |
| **7** | **4.07±2.8** | **3.5±3** | **0.50 (p>0.05)** |
| **14** | **2.4±2.1** | **1.27±0.7** | **1.98 (p>0.05)** |
| **28** | **1.5±1.4** | **1.26±0.2** | **0.65 (p>0.05)** |
| **0** | **2.93±2** | **2.9±1.8** | **0.04 (p>0.05)** |

| **Blunted affect** |
| **7** | **1.36±1.7** | **1±0** | **0.06 (p>0.05)** |
| **14** | **1±0** | **1±0** | **0 (p>0.05)** |
| **28** | **1.87±1.5** | **2±1.4** | **0.25 (p>0.05)** |

| **Depression** |
| **7** | **2.53±1.6** | **1.93±0.9** | **1.25 (p>0.05)** |
| **14** | **2.2±1.5** | **1.93±0.8** | **0.59 (p>0.05)** |
| **28** | **1.47±0.6** | **1.4±0.5** | **0.35 (p>0.05)** |
| **0** | **3.47±3.5** | **2.93±3.2** | **0.44 (p>0.05)** |

p>0.05, not significant, *p<0.05 & *p<0.01 is significant & *p<0.001 is highly significant.
significant worsening between day 7 & 14 (p<0.001) while significant improvement is seen between day 14 & 28 (p<0.05). Analysis of ANXIETY indicate that in the HAL group the rate of improvement is highly significant (p<0.001) when comparisons are made, while in RIS group, the rate of improvement is less significant between day 0 & 7 (p<0.01) than the highly significant improvement (p<0.001) seen between day 0 & 14, day 7 & 14, day 14 & 28 & day 0 & 28. Analysis of GUILT in the HAL group indicate no significant change in score between day 0 & 7 (p>0.05), while between day 0 & 14 & day 0 & 28, significant improvement is seen (p<0.05). The improvement is also significant between day 7 & 14 (p<0.05), while no significant improvement has taken place between day 14 & 28 (p>0.05). In RIS group, highly significant improvement (p<0.001) is seen between day 0 & 7, day 0 & 14 & day 0 & 28, while no significant improvement (p>0.05) has taken place between day 7 & 14 & day 14 & 28.

DISCUSSION

Our findings suggest that Risperidone is of comparable efficacy to Haloperidol in the overall improvement of clinical symptomatology in Acute Psychosis, which is corroborated by Grant & Filton (1994), Min et al. (1993) and Umbricht & Kane (1995).

The findings of significant improvement of ‘Thinking Disturbance’ and ‘Hallucinatory Behaviour’ by Day 14 in the Risperidone group, suggests the superiority of Risperidone over Haloperidol in positive symptoms in Acute Psychosis during the early phase of treatment. This efficacy has also been advocated by Cardonix et al. (1995) and McEvoy (1994).

The rate of improvement of ‘Anxiety’ in the ‘Anxious Depression’ subscale in the HAL group, can be attributed to the anxiolytic effect of Haloperidol. However to be fair, Kaplan and Sadock (1994) suggest use of trihexyphenidyl for Extrapyramidal symptoms in 40% of subjects in RIS group by Day 28, is similar to the findings of Emsley et al. (1995) who concluded that the risk of EPS in the first episode Schizophrenic patients treated with Risperidone is considerably higher (close to 60%) than earlier studies, but is still significantly less than in a control group treated with Haloperidol. We used trihexyphenidyl in 100% of subjects in the HAL group by Day 28. Owens (1994) and Min et al. (1993) too concluded that the severity of EPS in the RIS group is significantly less than in the HAL group. We can suggest that early worsening of ‘Motor Retardation’ a component in the subscale of ‘Withdrawal Retardation’ in HAL group as well as in the RIS group is because of the development of EPS, and subsequent recovery at the end of the protocol can also be attributed to the use of trihexyphenidyl.

The highly significant rate of improvement of ‘Anxiety’ in the ‘Anxious Depression’ subscale in the HAL group, can be attributed to the anxiolytic effect of Haloperidol. However to be fair, Kaplan and Sadock (1994) suggest use of...
RISPERIDONE VS. HALOPERIDOL IN ACUTE PSYCHOTIC DISORDERS

low dosages of Haloperidol in the treatment of anxiety disorder, although this efficacy is to be weighed against the potential risk of Extrapyramidal side effects.

We can conclude that Risperidone at 4mg/day has an overall therapeutic activity comparable to Haloperidol 15 mg/day on outcome of clinical symptomatology at short term in first episode Acute and transient psychotic disorder with Risperidone holding a more efficacious and early onset of action on some of the positive & negative symptoms in comparison to Haloperidol. We feel that it may represent a potentially useful first line antipsychotic agent in the treatment of Acute Psychosis in their first episodes.

ACKNOWLEDGEMENT

Dr. Kangan Pathak, MD, Resident Physician, Department of Psychiatry, Gauhati Medical College & Hospital, Guwahati - 781 032, Assam.

REFERENCES

Abel,K., O'Keane,V., Murray,R.M. & Cleare,A.J. (1977) Serotonergic function & Negative & Depressive symptomatology in Schizophrenia & Major Depression. Psychoneuroendocrinology, 22, 539-48.

Adityan, P. & Pelsonero,A.L. (1995) Prescribing Risperidone. Psychiatric Serv., 46, 291-292.

Anderson,W.H., Kuehrle,J.C. & Catanzano,D.M. (1976) Rapid Treatment of Acute psychosis. American Journal of Psychiatry, 133, 1076-1078.

Buckley,P.F. (1997) New Dimensions in the Pharmacologic treatment of Schizophrenia and Related Psychoses. J. Clin. Pharmacol., 37: 363-378.

Cardonix (1995) Risperidone : Review and Assessment of its role in the treatment of Schizophrenia. Ann Pharmacotherapeutic (June) 29, 65610-65618.

Czobor,P., Volavka,J. & Meilbach,R.C. (1995) Effect of Risperidone on Hostility in Schizophrenia. J. Clin. Psychopharmacol., Aug., 15, 4, 243-249.

Danik,J.J. & Goverdhan,M. (1963) Haloperidol in the treatment of 120 Psychotic patients. American Journal of Psychiatry, 12,39, 391.

Daradkeh,T.K., Reda,F. & Karim,L. (1996) Efficacy & Safety of Risperidone in Psychotic Patients : an open study. J. Int. Med. Res., 24, 3, 291-295.

Emsley,R.A, McCreadie,R. & Livingstone, M. (1995) Risperidone in the treatment of first episode patients with schizophreniform disorder a double blind multicenter study. Presented at the American Psychiatric Association 148th Annual Meeting. Miami.

Fitzgerald,G.H. (1969) A double-blind comparison of Haloperidol with Fluphenazine in acute psychotic episodes. Current Therapeutic Research, 11, 515 - 519.

Grant,S. & Filton,A. (1994) Risperidone: A review of its pharmacology & Therapeutic potential in the treatment of Schizophrenia. Drugs, 48, 2, 253-273.

Janssen,P.A.J., Nlemegers,C.J.E., Awouters,F., Schellakens,K.H.L., Megens, A.A.H.P. & Meert,T.F. (1988) Pharmacology of Risperidone (R 64 765), a new antipsychotic with serotonin S2 and dopamine D2 antagonistic properties. Journal of Pharmacology and Experimental Therapeutics. 244, 685-693.

Johnson,D.A.W. (1995) Peer Review of 'Risperidone in the treatment of patients with chronic Schizophrenia : a multinational, multicenter, Double-blind, parallal - group study versus Haloperidol'. British Journal of Psychiatry, 165, 727-753.

Kammen,D.P.V. & Marder,S.R. (1995) Dopamine Receptor Antagonist. In :
Risperidone in the treatment of Schizophrenia. American Journal of Psychiatry, 151, 6, 825-835.

McEvoy, J.P. & Hogarty, G.E. (1991) Steingars: Optimal dose of Neuroleptic in acute Schizophrenia: A controlled study of the neuroleptic threshold and higher haloperidol dose. Archives of General Psychiatry, 48, 739-745.

McEvoy, J.P. (1994) Efficacy of risperidone on positive features of Schizophrenia. Journal of Clinical Psychiatry, ISSN: 0160 - 6689.

Meltzer, H.Y. (1995) The role of Serotonin in Schizophrenia & the place of serotonin-dopamine antagonist antipsychotics. J. Clin. Psychopharmacol, 15, (suppl. 1), 25-35.

Min, S.K., Rhee, C.S., Kim, C.E. & Kang, D.Y. (1993) Risperidone versus haloperidol in the treatment of chronic schizophrenic patients: a parallel group double-blind comparative trial. Yousei - Med Journal, (June), 34, 2, 179-190.

Mountain, H.E. (1963) Crash tranquilisation in a milieu therapy setting. Journal of Fort Logan Health Centre, 1, 43-44.

Overall, J. & Gorham, D. (1962) Brief Psychiatric Rating Scale. Psychol Rep., 10, 799.

Owens, D.G. (1994) Extrapyramidal side effects & tolerability of Risperidone: A Review. Journal of Clin. Psychiatry, (May), 55, (Suppl), 29-35.

Umbricht, D. & Kane, J.M. (1995) Risperidone: Efficacy and Safety. Schizophr. Bull., 21, 4, 593-606.