LETTERS TO THE EDITOR

RISPERIDONE IN INDIAN PATIENTS WITH SCHIZOPHRENIA

Sir,

We read with interest the study by Agarwal et al. (1998) titled 'Risperidone in Indian patients with Schizophrenia'. Limitations of an open-label study notwithstanding, this study has a few shortcomings which we would like to mention.

First, the patients entering the study were rated on Positive and Negative Symptom Scale (PANSS) after a week's wash-out period. A more meaningful approach would have been to rate the patients at first contact while they were still on medication and then a week after wash-out. This enables an investigator to know whether withdrawal from neuroleptics contributed to any improvement in symptomatology. It is known that many patients under routine clinical treatment actually benefit from a reduction in their medication dose rather than an increase (Johnson & Johnson, 1995). This may be particularly true in patients with extrapyramidal...
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symptoms (EPS) in whom reduction in EPS would have caused decrease in secondary negative symptoms.

Second, the study did not distinguish primary from secondary negative symptoms. This assumes significance in view of the authors' conclusion that risperidone is effective in ameliorating negative symptoms whereas currently there is little evidence to substantiate an independent effect of any of the atypical antipsychotics, including clozapine on primary negative symptomatology (King, 1998).

Third, it is not mentioned whether the study was carried out on stable patients or patients having an acute exacerbation. In acute psychotic episodes an improvement in negative symptoms may be secondary to improvement in positive symptoms, thus eluding the investigator from knowing the true effect of the antipsychotic on negative symptoms (McPhillips & Barnes, 1997). A study carried out on patients maintained on stable neuroleptic regimes is more representative of a measure of improvement in negative symptoms on introducing a new antipsychotic drug.

Fourth, 22% of the patients prior to the beginning of the study had EPS and following treatment with risperidone this figure rose to 65%. Risperidone causes least EPS at doses less than 6 mg per day and its adverse effects increase in a dose-dependent fashion (Schooler, 1994). In this trial, patients were treated at two fixed doses - 6 mg per day and 8 mg per day. It is possible that patients with 8 mg per day schedule may have contributed more significantly towards this increase in the overall EPS figure than the other group. Hence, a break-up of incidence of EPS between the two groups would have been more informative. Furthermore, it is not specified whether the patients were on anticholinergics or not before entering the trial or whether the anticholinergics too were stopped during the wash-out phase. Patients maintained on anticholinergics would obviously have more EPS once this medication was stopped which may explain the increase in the incidence of EPS after treatment with risperidone.

Another point pertaining to adverse effects with risperidone is that initial titration with risperidone does cause autonomic instability in 25% cases (Buckley & Meltzer, 1995). This may, in part explain the increase in autonomic adverse effects after initiation of risperidone.

Fifth, the study uses a fixed-dose design which is not practical in a clinical setting. Also worth mentioning here is that the trial uses the commonly practised regime of hiking risperidone by 2 mg per day till 6 mg per day on day 3. This may be too rapid a titration as has been suggested by a study (Luchins et al., 1998). Thus, in future trials a comparison of adverse effects between this regime and a more gradual one would provide clinically relevant information on the tolerability of risperidone.

Lastly, authors conclude that risperidone is effective for both positive and negative symptoms in Indian patients with schizophrenia. While the efficacy of risperidone for positive symptoms is no doubt a proven one, that for negative symptoms appears mostly confined to secondary negative symptoms (King,1998). Accounting for an antipsychotic's efficacy for primary negative symptomatology requires more rigorous double-blind placebo-controlled trials the recommendations for which have been spell out (Moller, 1995).

Nevertheless, a study of such a magnitude deserves applause and is without reservations, a landmark in context of psychopharmacology in India. This trial would foster further research with risperidone especially in chronic patients with primary, enduring negative symptoms maintained on stable neuroleptic regimes.

REFERENCES

Agarwal, A.K., Bashyam, V.S.P., Channabasavanna, S.M., Dhavale, H.S., Khan, M.A.M., Khanna, S., Pradhan, P.V., Katiyar, M., Rajkumar, R, Niazi, F.R, Jalali, R.K., Gowrishankar, R., Mishra, S.K. & Sood, O.P. (1998) Risperidone in Indian patients with schizophrenia. Indian Journal of Psychiatry, 40, 247-253.
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Buckley, P.F. & Meltzer, H.Y. (1995) Treatment of schizophrenia. In: A Textbook of Psychopharmacology. (Eds.) Schatzberg, A. & Nemeroff, C.D., pp 615-639, Washington DC: American Psychiatric Press.

Johnson, A.L. & Johnson, D.A.W. (1995) Peer review of risperidone in the treatment of patients with chronic schizophrenia a multi-national, multi-centre, double-blind, parallel-group study versus haloperidol. British Journal of Psychiatry, 166, 727-733

King, D.J. (1998) Drug treatment of negative schizophrenia. European Neuropsychopharmacology, 8, 33-42.

Luchins, D.J., Klass, D., Hanrahan, P., Malan, R. & Harris, J. (1998) Alteration in the recommended dosing strategy for risperidone. American Journal of Psychiatry, 155, 365-366.

McPhillips, M.A. & Barnes, T.R.E. (1997) Negative symptoms. Current Opinion in Psychiatry, 10, 30-35.

Moller, H.J. (1995) The negative component in schizophrenia. Acta Psychiatrica Scandinavica, 91, (388 suppl), 11-14.

Schooler, N.R. (1994) Negative symptoms in schizophrenia: Assessment of the effect of risperidone. Journal of Clinical Psychiatry, 55, (5 suppl), 22-28.

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