Concluding Remarks

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In closing, I would like to review the rationale for developing new atypical agents for antipsychotic pharmacotherapy and to summarize information presented at this symposium about the innovative drug olanzapine.

Numerous reviews of the literature suggest that the typical antipsychotic medications are far from optimal in treating psychosis. For example, Goff and Shader[1] reported that more than half of patients receiving such a drug do not respond optimally. Furthermore, when a response does occur, it is usually limited to positive symptoms; negative symptoms and dysphoria may actually worsen. Moreover, it is well documented that the rate of noncompliance with conventional medications may exceed 50%, and that approximately 75% of those with schizophrenia who discontinue their antipsychotic medication will suffer a relapse during the subsequent 12 months. A key factor in noncompliance, as Dr. Casey pointed out in a recent review,[2] is the occurrence of extrapyramidal symptoms, which have been reported in up to 90% of patients receiving conventional antipsychotic drugs.

Thus, a clear need exists for novel antipsychotic medications that will treat a broader spectrum of symptoms beyond the typical drugs and do so with less potential for troublesome side effects. Specifically, drug development efforts have focused on designing agents that relieve negative as well as positive symptoms of schizophrenia, are effective for patients who have not responded to conventional medications, do not cause disabling extrapyramidal symptoms, cause less chronic elevations in plasma prolactin, and are not associated with other serious adverse effects such as agranulocytosis or cardiac arrhythmias.

I think the information presented at this symposium demonstrates that olanzapine is such an innovative antipsychotic medication with promise as a first-line choice in the treatment of psychosis. The results of several controlled clinical trials have shown that olanzapine has overall superior efficacy compared to 5 to 20 mg/day of haloperidol in the treatment of psychosis, including significantly greater efficacy for negative symptoms.

Because the recommended starting dose of olanzapine, 10 mg/day, is also a therapeutically effective dose, patients may begin to receive antipsychotic drug benefits earlier. From the perspective of tolerability, patients receiving olanzapine within the recommended dosage range were no more likely to discontinue studies due to adverse events than those receiving a placebo. In these studies with olanzapine, no dose-response relationship emerged for incidence of extrapyramidal side effects (EPS) or akathisia as determined with standard rating scales. Furthermore, a 17-center, 1996-patient, phase III study found significantly lower rates of EPS and treatment-emergent tardive dyskinesia with therapeutic dosages of olanzapine than with haloperidol (5–20 mg/day).[3] In summary, the atypical antipsychotic olanzapine appears to be a significant addition to the clinician's armamentarium for treating psychosis.

REFERENCES

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