During the 1990s there have been some dramatic advances in the treatment of schizophrenia, and this publication of the Schizophrenia Patient Outcomes Research Team (PORT) study is an opportunity to point out where we believe the "state of the science" is heading. Just as the serotonin re-uptake inhibitor (SRI) class of antidepressants has largely replaced the older and more problematic tricyclic antidepressants (based in large part on safety and side-effect considerations), a shift in the treatment of schizophrenia is now taking place. Some quite recent studies (since the PORT data were collected) indicate that newly available treatments for schizophrenia may offer substantial clinical advantages over the older standard antipsychotic (or "neuroleptic") medications.

The first of the new (post-clozapine) atypical antipsychotic medications, risperidone, was approved for use in the United States in 1994. Its efficacy was superior to placebo and at least equal to haloperidol, but risperidone had a more favorable side-effect profile. In September 1996 the Food and Drug Administration (FDA) approved another new atypical antipsychotic, olanzapine, for use in schizophrenia, and quetiapine was approved in September 1997. Several additional atypicals are currently in large-scale clinical trials and/or pending FDA approval, including sertindole and ziprasidone. The pharmacologic profiles of these newer antipsychotic medications in some ways resemble that of clozapine, but they are not associated with the more severe side effects of clozapine. Thus, the new atypical medications may be effective for the symptoms of schizophrenia, but with fewer troublesome and possibly severe extrapyramidal symptoms (EPS) and other side effects.

Because these medications have been available for only a short time, there is relatively little scientific literature on the subject, but the previous issue of Schizophrenia Bulletin (Vol 23, No. 4, 1997) contains several relevant articles. Sheitman et al. (1997) note that

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In our opinion, the novel antipsychotics currently available (risperidone and olanzapine) and others soon to be marketed (sertindole, quetiapine, and ziprasidone) should be seriously considered as a first-line therapy for a first-episode of psychosis. Enhanced efficacy in the treatment of negative symptoms and a more favorable side-effect profile, particularly less EPS, have been demonstrated in chronic patient samples ... and might be expected to improve medication compliance, allowing longer periods of maintenance treatment in patients at the beginning of their illness ... [p. 659]
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In addition to people newly diagnosed with schizophrenia, we believe that chronically ill patients who have relapsed while on standard antipsychotic medications should be candidates for the new atypical medications. As Conley and Buchanan (1997) state, "Novel antipsychotics should be the first consideration after the failure of conventional drug therapy. With the exception of clozapine (because of its serious side effects), these drugs are also indicated as first-line therapy" (p. 667). And according to Daniel Casey (1997), "Overall, the adverse effects profiles of the newest antipsychotics represent a major improvement over those of the older neuroleptics. Olanzapine, sertindole, and quetiapine produce minimal or no EPS across the effective dose range and probably will have low rates of TD . . ." (p. 61). We believe that people with recent onset schizophrenia, and those with a history of prior treatment failure on standard antipsychotic drugs, should be offered a trial on the new atypical medications.

With the release of several more atypical antipsychotic medications, there will be an additional impetus to update treatment recommendations for 1998 and beyond. The PORT articles and commentaries make strong cases for the need to document the effectiveness of treatments, and to educate practitioners about use of the most safe and efficacious therapies. We also believe it is important to ensure that all patients in clinical care have access to the best available treatments.

References


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