The Emerging Role of Atypical Antipsychotics in the Treatment of Tardive Dyskinesia Induced by Other Atypical Antipsychotics

To the Editor: We read with great interest the article by Chan et al[1] comparing the efficacy of risperidone and olanzapine in schizophrenic patients with tardive dyskinesia on treatment with first-generation antipsychotics. The authors of the study concluded that both medications led to significant improvement in dyskinesia scores; however, a statistically significantly greater change was seen in the risperidone group compared with the olanzapine group ($P = .0001$).

We believe this study raises important questions concerning the role of atypical antipsychotics in the generation and treatment of tardive dyskinesia. In a previous double-blind, placebo-controlled study, Bai et al[2] reported significant improvement with risperidone in tardive dyskinesia induced by first-generation antipsychotics. Importantly, previous atypical antipsychotic use was an exclusion criterion in this study. Notably, there is an increasing number of case reports supporting a therapeutic effect of atypical antipsychotics on tardive dyskinesia caused by other atypical antipsychotics.[3]

Plausible pathophysiologic mechanisms involved in the development of the drug-induced movement disorder include dopamine receptor supersensitivity, degeneration of cholinergic striatal interneurons, γ-aminobutyric acid depletion, and free radicals. Interestingly, Bressan et al[4] suggested that lower antipsychotic striatal D_2 receptor occupancy is associated with a lower chance of developing tardive dyskinesia. Thus, an atypical antipsychotic with faster dissociation from dopamine receptors compared to another could have a therapeutic effect on tardive dyskinesia caused by the first. This hypothesis is in accordance with the "fast-off" theory of atypicality, as proposed by Kapur and Seeman.[5]

Undeniably, the etiopathogenesis of tardive dyskinesia remains elusive. At present, there is no specific treatment for tardive dyskinesia. Atypical antipsychotics could be a promising therapeutic alternative for this disabling movement disorder. More research with double-blind studies and head-to-head comparisons is needed to determine any differences with respect to the efficacy of atypical antipsychotics in treating tardive dyskinesia induced by typical or atypical antipsychotics. Future studies of the antidyskinetic effects of atypical antipsychotics should not exclude patients with previous exposure to these agents, but rather focus on such cases. Another interesting patient group for future studies could be young psychotic patients treated exclusively with atypical antipsychotics who present with tardive dyskinesia. Switching to another atypical agent with antidyskinetic potential could be a useful option; still, the relative differences of atypical antipsychotics in this aspect require study.

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