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RESEARCH LETTER

Rapid remission of severe tardive dyskinesia and tardive dystonia with quetiapine

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Severe tardive dyskinesia (TDk) and tardive dystonia (TDt) are serious movement disorders that are potentially disabling side effects of conventional antipsychotic treatment (Barnes and McPhillips, 1998). Atypical antipsychotics represent an important step in both prevention and treatment of these symptoms (Barnes and McPhillips, 1998). We report on an elderly woman who developed TDk and TDt while receiving conventional antipsychotic treatment and demonstrated rapid remission of these symptoms following a switch to quetiapine.

CASE REPORT

A 62-year-old woman presented with severe symptoms of TDk and TDt, particularly rocking, twisting, grimacing and movements of the forehead. She had a 30-year history of schizoaffective disorder and had been treated with conventional antipsychotics since first admission to hospital in 1973. The patient had been taking zuclopenthixol (10 mg/day) for more than 10 years and had developed TDk and TDt during this time, though her symptoms had worsened considerably during the last 6 months, with a score of 9 on the Abnormal Involuntary Movement Scale (AIMS). Anticholinergic medication (biperiden 2 mg, bid) was initiated during the early 1990s to control the patient's extrapyramidal symptoms and discontinued in 2000 to avoid anticholinergic side effects as the patient had developed a urinary infection with delirium. Other medication history included tricyclic antidepressants (clomipramine 75 mg up to three times daily; mianserin 30 mg/day) for depressive episodes and, during the 1990s, occasional treatment with the selective serotonin re-uptake inhibitor paroxetine (up to 30 mg/day). Concomitant medication at the time of presentation with severe TDk and TDt was divalproex sodium (500 mg three times daily), clotiapine (20 mg/evening), mianserin (30 mg/evening) and atenolol (100 mg/day). We decided to switch the patient from zuclopenthixol to quetiapine, but gradual withdrawal of zuclopenthixol before quetiapine initiation (dose reduction to 6 mg/day in 1 week) resulted in severe worsening of TDk and TDt, with an increase in AIMS score to 34. The dose of zuclopenthixol was therefore returned to 10 mg/day, and this led to an improvement in TDk and TDt over the next 7 weeks, with a reduction in AIMS score to 17. A cross-tapering method of switching was subsequently introduced; quetiapine was started at 25 mg/day, increasing to 200 mg/day over 2 weeks, while the dose of zuclopenthixol was slowly reduced until it was discontinued 4 weeks later. When the switch was complete, there was a marked improvement in TDk and TDt with an AIMS score of 3, and this improvement has been maintained with a dose of 200 mg/day quetiapine for the past 2 years. Furthermore, the patient remains stable with respect to her psychotic symptoms; she will soon be discharged from hospital into nursing home care.

DISCUSSION

This case supports emerging literature reporting the use of quetiapine in the treatment of existing

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drug-induced movement disorders (Alptekin and Kivircik, 2002; Emsley *et al.*, 2004) though little is known about the mechanism(s) for this effect. One plausible hypothesis arises from quetiapine's relatively low affinity for dopamine D_1 receptors, since preclinical studies in monkeys have shown that D_1-receptor agonism results in orofacial dyskinesia (Lublin and Gerlach, 1988). Other hypotheses centre on quetiapine's similar receptor-binding profile to clozapine [also reported to reduce TDk (Barnes and McPhillips, 1998)]. Conventional antipsychotics block dopaminergic neurons in the basal ganglia, leading to a decreased efflux of dopamine and resulting in postsynaptic D_2-receptor upregulation with hypersensitivity. Clozapine, and possibly quetiapine, can downregulate the D_2-receptor density in the striatum, by stimulating dopamine efflux (Dean *et al.*, 2001). Furthermore, both quetiapine and clozapine have a greater affinity for 5-HT_2- and H_1-receptors than for D_1- or D_2-receptors, and may therefore suppress TDk by blocking these receptors rather than dopamine receptors. Finally, the gamma-aminobutyric acid (GABA)-insufficiency hypothesis suggests that clozapine increases GABA turnover in the substantia nigra and, since low levels of GABA are associated with TDk, this could be a mechanism for clozapine's low propensity for TDk (Casey, 2000). However, it is unclear whether this is also the case for quetiapine, and further research to elucidate the mechanism for its beneficial effect on TDk and TDt is warranted.

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