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Antipsychotic Drug-Induced Movement Disorders: A Forgotten Problem?

Tamara Pringsheim, MD[1] and Thomas R. E. Barnes, MD[2]

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Since the discovery of chlorpromazine's antipsychotic effect in 1952, antipsychotic medications have been the mainstay of therapy for schizophrenia and psychotic disorders. The effect of such medication on the field of psychiatry was profound, contributing to the declining rates of institutionalization witnessed worldwide. Parkinsonian side effects were identified within a few years of the introduction of chlorpromazine,[1] while antipsychotic-induced akathisia was described even earlier.[2,3] Thus, extrapyramidal side effects were recognized almost immediately as common complications of antipsychotic treatment and were considered to be linked to its clinical effectiveness.[4,5] This notion lingered until it was demonstrated, in the late 1980s, that clozapine, an antipsychotic medication with minimal liability for extrapyramidal symptoms, had superior antipsychotic efficacy in treatment-resistant schizophrenia.[6] The search for better tolerated and more effective antipsychotic medications began.[7]

The 1990s brought the second wave of antipsychotic drugs, such as risperidone, olanzapine, and quetiapine, which, although heterogeneous in their pharmacological profiles, tended to share a greater affinity for $5HT_2$ receptors than for D_2 receptors. Compared with the first wave of antipsychotic medications, these drugs had similar efficacy and generally had a lower liability for extrapyramidal symptoms but more prominent adverse metabolic effects. Within a few years of their introduction, these medications largely replaced the first-generation antipsychotic agents, although the burden of extrapyramidal side effects for those prescribed the newer medication may not have been relieved to the degree that might have been expected.[8-10] The 21st century has brought a number of new antipsychotics, including ziprasidone, lurasidone, asenapine, aripiprazole, and brexpiprazole, as well as an expansion of clinical indications for which antipsychotics are prescribed. Several antipsychotics, including quetiapine, aripiprazole, and brexpiprazole, are licensed in several countries as adjunctive therapy to antidepressants for the treatment of major depressive disorder. Other approved uses of second- and third-generation antipsychotic medications include psychosis and agitation in Alzheimer disease, irritability in autism, and tics in Tourette syndrome. Not surprisingly, pharmacoepidemiological studies have shown an increase in the use of antipsychotic medication across all age groups, with widespread prescribing by family physicians in addition to psychiatrists. A Canadian study found that between 2005 and 2012, there was a 300% increase in dispensed prescriptions for quetiapine ordered by family physicians, from 1.04 million in 2005 to 4.17 million in 2012. The most common diagnosis for which quetiapine was prescribed was for mood disorders, followed by psychotic disorders, anxiety disorders, and sleep disturbances.[11] Also in Canada, a pharmacoepidemiological study of quetiapine use in the province of Alberta demonstrated the same trend, with the rate of quetiapine users going from 7.2 per 1000 population in 2008 to 13.3 per 1000 population in 2013. Women were more commonly treated with quetiapine than men (15.8 vs. 10.9 per 1000), and the top 4 diagnostic codes associated with quetiapine use were depression, neurotic disorders, bipolar disorder, and sleep disturbances.[12]

In this 'In Review' series, we seek to focus attention back on the issue of antipsychotic-induced movement disorders (extrapyramidal symptoms). We hope to highlight that while the prevalence of such movement disorders appears to be lower with the newer antipsychotic medications than with the first-generation agents, the 95% confidence intervals often overlap between new and older agents, and the risk remains substantial.[13] Now that antipsychotic medication is used and prescribed by a great number of practitioners to a diverse population of patients, the need for vigilant monitoring has intensified. Many practitioners who began their training in the

[1] Department of Clinical Neurosciences, Psychiatry, Pediatrics and Community Health Sciences, University of Calgary, Alberta
[2] Department of Psychiatry, Imperial College London, London, England

Corresponding Author:
Tamara Pringsheim, MD, Mathison Centre for Mental Health Research and Education, 3280 Hospital, Drive NW, Calgary AB, T2N 4Z6, Canada.
Email: tmprings@ucalgary.ca

era of second-generation antipsychotics have not received the same degree of exposure to the recognition and management of antipsychotic-induced movement disorders. This 'In Review' includes a guideline on the assessment and treatment of akathisia.[14] Antipsychotic-induced movement disorders warrant our attention—they can be stigmatizing and cause patients subjective distress, both of which are disincentives to continue to take medication. In addition, they can confound the clinical assessment of negative symptoms of schizophrenia (parkinsonism) and agitation or psychotic excitement (akathisia) and may lead to misdiagnosis and also the false conclusion that an increase in dose of antipsychotic medication is required, further exacerbating the problem. Physicians prescribing antipsychotic medication require knowledge and skills in this area, which we hope this 'In Review' series can support.

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