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The rational use of medications in acute psychotic presentations — the case for less is more

A 22-year-old man was brought to the emergency department of a general hospital by his mother, because his behaviour had become progressively inappropriate. He was loud, verbally aggressive and stayed awake all night writing copious musical notes. There was no recent history of drug abuse, nor any previous psychiatric history. The patient was admitted on a Form 1, because he refused voluntary admission to hospital. The provisional diagnosis was "acute psychotic episode — likely manic."

In the emergency department, he received 1 injection of zuclopenthixol acetate at a dose of 100 mg. He was also prescribed regular olanzapine at a gradually increasing dose up to 30 mg. The patient continued to be uncooperative, aggressive and at times violent. At that point, valproic acid was started at a dose of 200 mg, and the dose was increased over the next 24 hours to 500 mg. However, the patient continued to be uncooperative and his behaviour uncontrollable, demanding discharge. The psychiatrist on call ordered a small dose of chlorpromazine, 100 mg, for the purpose of sedation. The patient's behaviour became more appropriate, less combative and more cooperative over the next 24 hours, during which chlorpromazine was continued at 100 mg, 3 times a day. However, over the following 24 hours, he became once more very irritable, anxious, aggressive and significantly dysphoric, even though he seemed to be adequately sedated.

A difference of opinion about management arose within the clinical team, with a few nurses pressing for the use of more chlorpromazine. The patient was put in restraints for his own safety as his aggressive behaviour escalated, and a psychiatric consultation was requested. The consultant's recommendations included the immediate discontinuation of chlorpromazine and increasing the valproic acid dose to 750 mg and eventually to 1000 mg, as well as a gradual reduction of the olanzapine dose to 20 mg over the next few days. Over the next 48 hours, the patient's behaviour gradually improved, becoming more cooperative and lucid. The patient was discharged a week later with the confirmed diagnosis of bipolar mood disorder — manic.

This clinical situation is not uncommon, whereby patients present to the emergency department with uncontrolled aggressive psychotic behaviour. Frequently, they are given multiple dosages of antipsychotic medications within a relatively short period of time. The usual response in such situations is either to rapidly escalate the dose or add another sedating antipsychotic such as chlorpromazine, as in this case. As the psychotic behaviour deteriorates after a brief period of improvement, frequently the staff is inclined to continue the high dose of the antipsychotic or even increase the dose on the assumption of getting better control. What is frequently missed or unrecognized is that some patients respond to such high dosage by becoming significantly dysphoric, with noticeable deterioration in their behaviour. Although neuroleptic-induced dysphoria has been clinically recognized for over 50 years, it is only recently that its neurobiological basis has been clearly elucidated (Voruganti et al, *Neuropsychopharmacology* 2001;25:642-50). A recent dopamine-depletion single-photon-emission computed tomography study in medication-free patients with schizophrenia demonstrated that the incidence of dysphoric reaction is inversely related to the dopamine-binding ratio in the nucleus accumbens and in the nigrostriatal complex. In other words, those patients who have low dopamine function are particularly vulnerable to developing dysphoria when given potent dopamine D_2 blockers such as chlorpromazine. From our studies, it also became clear that the term neuroleptic dysphoria, which was coined over 30 years ago, does not adequately describe such a phenomenon. We have demonstrated that neuroleptic-induced dysphoria is more complex than dysphoria alone, because it also includes, in addition to the dysphoric response, a high level of anxiety, tension and irritability, as well as motor and cognitive changes.

This clinical case clearly demonstrates that in using antipsychotic medications, less is frequently more, particularly when using first-generation antipsychotics. Neuroleptic dysphoria needs to be considered in clinical situations in which unexpected behavioural deterioration occurs in the face of what looks like adequate or high doses of medications. It also has to be recognized that neuroleptic-induced dysphoria has significant clinical consequences, most notably lack of adherence to medications and subsequent symptomatic deterioration and relapse (Awad and Voruganti, *Acta Psychiatr Scand Suppl* 2005;427:6-13; Voruganti and Awad, *Psychopharmacology [Berl]* 2004;171:121-32).

A. George Awad, MB, BCh, PhD
Professor Emeritus
Department of Psychiatry
and the Institute of Medical Science
University of Toronto
Chief of Psychiatry
Humber River Regional Hospital
Toronto, Ont.

Competing interests: Dr. Awad has been a research consultant for Janssen, Pfizer, AstraZeneca and Eli Lilly.

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.