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. The patient described in this column gave informed consent for the publication of the column.

Long-acting injectable antipsychotics: choosing the right dose

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A man in his 50s with schizophrenia was admitted involuntarily with a severe psychotic exacerbation. He had been stable for years on long-acting injectable antipsychotic medication. The inpatient psychiatrist reviewed the man's recent history and found no drug or alcohol misuse, physical illness or psychosocial stressors. He had received every prescribed dose of his injectable antipsychotic for several years; he took no other medications. Five months before admission, at the patient's request in order to permit a longer dosing interval, his treatment was changed from risperidone long-acting injection (LAI) 50 mg twice every 3 weeks (i.e., every 10 or 11 days) to paliperidone palmitate LAI 100 mg every 4 weeks.

The transition to paliperidone had been discussed with a community pharmacist, and the dose was chosen with the proviso that "if [the patient] finds waning of the product, we can switch to every 3 weeks."

Unfortunately, owing to staffing shortages, the patient did not have access to a psychiatrist for the last 2 months before admission, but he did continue to receive the LAI medication at the pharmacy, which was documented.

The hospitalization lasted 2 months, during which the dose of paliperidone palmitate was increased first to 100 mg every 3 weeks and then to 150 mg every 4 weeks. The patient showed improvement within the first month, and by the end of the second month his condition had stabilized. At discharge, the patient received his first quarterly dose of paliperidone palmitate 525 mg, and over the subsequent 5 months, follow-up with an Assertive Community Treatment team proved to be uneventful. The patient tolerated the paliperidone well with only an intermittent Parkinsonian tremor, for which he declined antiparkinsonian medication. The patient's serum prolactin was elevated at 31.6 (normal 4–19) μg/L, with the sample taken 5 weeks after his second dose of paliperidone palmitate 525 mg.

Long-acting injection antipsychotic preparations have several potential advantages over oral medications, including elimination of the need for daily medication administration, which helps to overcome partial or total nonadherence, makes nonadherence more easy to detect and reduces peak-trough plasma level variations. Long-acting injections are associated with lower relapse rates, improved patient outcomes and better patient and physician satisfaction.[1,2]

Among the disadvantages of LAIs is the time taken to reach steady state levels, which can take up to 8 months for paliperidone LAI administered monthly.[3] Related to this, LAIs take considerable time to wash out, with implications for mean time to relapse and medication adjustments. Supplementary oral medication can be helpful during these transitions. Although LAI antipsychotics are a treatment option at any stage of schizophrenia, paliperidone LAI may be less effective in chronic illness.[4]

In our patient's case, antipsychotic drug levels were not obtained; doing so is not common in clinical practice. Drug level monitoring, however, can be valuable to determine the correct dose and to evaluate potential causes of deterioration. Consensus guidelines have suggested a reference plasma concentration of 20–60 ng/mL for oral paliperidone,[5] and Zipursky and colleagues[6] found that a plasma level near 20 ng/mL was associated with good control of psychosis and minimized adverse effects in patients taking paliperidone LAI. Considerable variation in plasma levels exists among patients; the pharmacokinetics involved are complicated and are affected by particle size.[7] In our patient's case, drug levels might have been lower than desired and, if so, would have provided added guidance on the correct dose.

This case illustrates that changing antipsychotic medications in a stable patient has inherent risks. When starting a new LAI, clinical changes may appear only months after medication changes. Therapeutic drug monitoring can be helpful in monitoring and titrating doses for patients taking paliperidone LAI. Care should be taken when initiating a new LAI medication, and patients should thus be followed carefully for many months to ensure both effective treatment and minimization of adverse effects.

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Details of the case were changed to protect the patient's privacy.

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