Breakthrough symptoms after switching long-acting injectable paliperidone palmitate from the gluteal to the deltoid site of administration

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A 34-year-old white man in whom schizophrenia was diagnosed at the age of 24 years was trialed over the course of illness on risperidone, olanzapine and aripiprazole. Although he responded well to these medications, he experienced relapses secondary to nonadherence. After discussing options to improve compliance and prevent relapse, he agreed to try long-acting injectable paliperidone palmitate. The initiation regimen consisted of 150 and 100 mg administered into the deltoid muscle on days 1 and 8, respectively, followed by 150 mg every 28 days into the gluteal muscle. On this regimen, the patient was free of positive symptoms. After 14 months, his maintenance dose was changed to the deltoid muscle (150 mg every 28 d). Four months later, the week before his next scheduled injection, he had breakthrough auditory hallucinations. As a consequence, the maintenance regimen was changed to 150 mg administered into the deltoid muscle every 3 weeks. The patient has been on this regimen for 9 months without any breakthrough symptoms.

The breakthrough symptoms may have been due to differences in the rate and extent of drug absorption between the sites of injection. The rate of absorption from a depot into the vasculature is influenced by many factors. For example, formulations using different vehicles and salts of the active drug are used to control the rate of drug absorption. Injection technique also impacts bioavailability of drugs administered intramuscularly. Although intended to penetrate the striated muscle fibres, poor technique can result in the drug being deposited into the subcutaneous adipose tissue, resulting in a slower and more erratic rate of absorption. Physiologic factors also impact absorption and bioavailability of drugs administered intramuscularly. Compared with the gluteal muscle, the deltoid muscle has greater blood flow, allowing for a faster rate of drug absorption. Exercise that increases blood flow will also result in a faster rate of drug absorption. Finally, obesity to the point of being deposited into the subcutaneous adipose tissue, resulting in a slower absorption of paliperidone. Since the rate of absorption via deltoid administration is faster, it is possible that a therapeutic plasma concentration may not be maintained for the duration of the manufacturer’s recommended dosage interval of 4 weeks. In such cases, reducing the dosage interval to every 21 days may be appropriate; not every patient receiving paliperidone palmitate via the deltoid muscle needs to be on a 3-week regimen. The rate of absorption from the deltoid muscle is patient-specific and thus the dosing interval will reflect this.

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References


