Pharmacokinetics of paliperidone palmitate injection: evidence from a routine therapeutic drug monitoring service

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The use of long-acting formulations of second-generation antipsychotics has been reported to significantly increase adherence in patients with schizophrenia, reduce their risks of relapse and rehospitalization, and improve their global treatment outcomes. Paliperidone palmitate is a palmitate ester of paliperidone that is given once monthly by injection (deltoid or gluteal) after a recommended initiation regimen on days 1 and 8 This regimen was designed to rapidly attain therapeutic blood levels. There is limited documentation on the pharmacokinetics of paliperidone palmitate in a naturalistic setting. Aim of this study was to investigate the concentrations of paliperidone after intramuscular administration of long-acting injectable paliperidone pamitate in a routine therapeutic drug monitoring setting.

Samples sent to the Unit of Clinical Pharmacology, University Polyclinic Messina, for routine therapeutic drug monitoring (TDM) from schizophrenic patients receiving depot injections of paliperidone palmitate in the period January 2014-April 2015 were included in this study. Samples for which the request forms lacked information about dose and concomitant medications were excluded. The injection intervals were 4 weeks (1 month) in all subjects, and blood samples were collected on the same day of the monthly injection. Serum concentrations of paliperidone were measured by HPLC

To date, samples from 26 patients, 14 females and 12 males, have been included. The age of patients ranged from 32 to 58 years with a median age of 42. The paliperidone palmitate dose was 50 mg/month in 3 patients, 75 mg/month in 8, 100 mg/month in 13 and 150 mg/month in 2 subjects. Serum concentrations of paliperidone ranged from 19 to 78 ng/ml. Concentrations of paliperidone increased with increasing doses. Dose-corrected serum levels of paliperidone did not differ between males and females. There was no correlation between dose-corrected concentrations of paliperidone and age. Three out of the 5 patients with associated adverse effects (extrapyramidal symptoms, hyperprolactinemia and weight gain) had serum concentrations higher than 60 ng/ml.

These preliminary data obtained under the naturalistic conditions of a TDM survey indicate that serum concentrations of paliperidone are closely correlated with the given dose, but are not affected by sex and age. As with the oral formulations, serum concentrations above 60 ng/ml are more frequently associated with adverse effects.