ADVERSE DRUG REACTIONS ASSOCIATED WITH NEWER LONG-ACTING INJECTABLES ANTIPSYCHOTICS: AN ANALYSIS OF THE ITALIAN SPONTANEOUS REPORTING SYSTEM DATABASE

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Long-acting injectable (LAI) antipsychotics have been developed to reduce the risk of relapse and rehospitalization due to nonadherence in patients with schizophrenia. In addition to first-generation LAI antipsychotics, in recent years LAI formulations of some second-generation antipsychotics have also become available including risperidone LAI (marketed in 2006), olanzapine pamoate (2010), paliperidone palmitate (2012) and aripiprazole LAI (2014). Aim of the present study was to describe adverse drug reactions (ADR) associated with newer LAI antipsychotics based on the Italian pharmacovigilance database.

We performed an analysis of the Italian Spontaneous Reporting System (SRS) database, selecting all the adverse drug reaction (ADR) reports attributed to second-generation LAI antipsychotic drugs from their launching to December 2016. Literature cases were excluded from the analysis. We described the frequency of compound-specific ADRs by MedDRA System Organ Class (SOC) and Preferred Terms (PTs).

We identified 304 reports of ADRs related to second-generation LAI antipsychotics over a 10 year period (2006-2016). The mean age of patients was about 45 years; 57.6% males (n=175), and 42.4% females (n=129). Serious ADRs accounted for 38.2% (n=116) of total second-generation LAIs-related reports. Paliperidone palmitate was the compound associated with the higher number of ADR reports (n=97; 31.9%), followed by olanzapine pamoate (n=86; 28.3%), risperidone LAI (n=63; 20.7%) and aripiprazole LAI (n=58; 19.1%). The most represented ADRs were those involving nervous system, such as sedation (n=61), extrapyramidal symptoms (n=38) and neuroleptic malignant syndrome (n=6), followed by hyperprolactinemia (n=31), weight increase (n=19) and injection-site reactions (n=17). The rate of extrapyramidal effects on total ADRs reports for each drug was 23.7% with paliperidone palmitate, 20.6% with risperidone LAI, 17.2% with aripiprazole LAI and 8.1% with olanzapine pamoate. Hyperprolactinemia was mainly represented in the ADRs related to risperidone LAI (20,6%) and paliperidone palmitate (16,5%), while weight increase was most reported in ADRs referred to aripiprazole LAI (10,3%). Regarding olanzapine pamoate, we identified 15 ADR reports describing a symptomatology characterized by excessive sedation, confusion, disorientation, resulting in some instances into coma, occurring within few hours after injection. These symptoms are consistent with the potentially serious ADR known as post-injection delirium/sedation syndrome.

The results of this analysis indicate that the tolerability and safety profile of second-generation LAI antipsychotics differ among the available agents and is substantially similar to that of the corresponding oral formulations. However, several cases of post-injection delirium/sedation

syndrome were associated with olanzapine pamoate, confirming the need for a 3-hours post-injection observation period.