

## Safety profile of antipsychotic drugs: an Analysis of Sicilian Region Spontaneous Reporting System

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**Introduction:** Antipsychotic drugs are used to treat schizophrenia and bipolar disorder. Though the tolerability and safety profile of traditional agents is relatively well defined, the side effect profile of newer antipsychotics is still incomplete. Spontaneous reporting systems (SRSs) are critical for signal detection. Moreover, data from SRSs suggest an under-reporting in psychiatry in terms of adverse effects, drug interactions and lack of therapeutic efficacy. The aim of this study was to describe ADR reports associated with antipsychotics based on Sicilian region SRS.

**Methods:** We analyzed the spontaneous reports of suspected adverse reactions attributed to antipsychotics (ATC class N05), sent to the Sicilian Regional Pharmacovigilance Centre during the period from 01/01/2010 to 30/04/2017. We excluded literature cases. Adverse drug reactions (ADRs) were classified by the Medical Dictionary for Regulatory Activities (MedDRA). Analyses of ADRs were conducted using MedDRA Preferred Terms (PTs) and System Organ Classes (SOCs).

**Results:** During the observation period, a total of 14207 ADR reports have been collected into Sicilian SRS database, 575 (4%) of which contained at least one antipsychotic as suspected drug. Of these, 137 reports were sent in 2010-2013, while 438 were collected in 2014-2017 with a peak in 2014 (n=259). The vast majority of ADR reports referred to A.S.P. Catania (n=119; 20.7%) followed by A.S.P. Trapani (n=92; 16%) and A.S.P. Messina (n=80; 13.9%). The spontaneous reports were equally divided by gender (291 males, 278 females). The mean age of antipsychotic users was 50±22 years. Among of all ADRs, 27 cases concerned the pediatric age, 381 reports related to adulthood and 163 regarded to elderly patients. Serious ADRs accounted for 31.4% (n=180) of total antipsychotics-related reports. Quetiapine (n=161; 28%), olanzapine (n=131; 22.8%), clozapine (n=73; 12.7%), risperidone (n=72; 12.5%), aripiprazole (n=44; 7.6%) and haloperidol (n=22; 3.8%) were frequently reported into Sicilian SRS database. Only 37 (6.4%) ADR reports regarded the use of long-acting injectable (LAI) antipsychotic drugs with risperidone LAI (n=13), haloperidol LAI (n=12), aripiprazole LAI (n=5), paliperidone LAI (n=4), olanzapine LAI (n=3). Analyzing ADRs by SOCs, the most reported were psychiatric disorders including insomnia (n=31), aggression (n=25), restlessness (n=23), intentional self-injury (n=22), drowsiness (n=21) and agitation (n=21), nervous system disorders consisting of psychomotor hyperactivity (n=28) and somnolence (n=23), skin disorders, involving in pruritus (n=26), gastrointestinal disorders, in particular vomiting (n=22), cardiac disorders like tachycardia (n=21), respectively. The most frequent signaled ADR was lack of efficacy (n=157; 27.3%) that was mainly quoted for quetiapine (n=60; 38.2%), olanzapine (n=37; 23.6%), clozapine (n=35; 22.3%) and risperidone (n=20; 12.7%).

**Conclusions:** Analysis of regional spontaneous reporting data did not show any new safety signal in relation to antipsychotic drugs. Interestingly, our data showed an under-reporting about ADR reports related to long-acting injectable antipsychotic drugs and pointed out a relatively high

frequency of reports of therapy non-responder mainly when antipsychotics were given as generic formulations.