Predictors of Mortality in Atypical Antipsychotics-Treated Community Dwelling Elderly Patients with Behavioural and Psychological Symptoms of Dementia: A Prospective Population-Based Cohort Study from Italy

L. Sportiello[1], C. Rafaniello[1], F. Lombardo[2], C. Ferrajolo[1], E. Parretta[1], R. Formica[1], S. Potenza[3], A. Irpino[4], R. Raschetti[2], N. Vanacore[2], B. Rinaldi[1], F.Rossi[1], A. Capuano[1]

[1] Regional Centre of Pharmacovigilance and Pharmacoepidemiology, Dept. of Experimental Medicine, Second University of Naples, Naples, Italy.
[2] National Institute of Health, Rome, Italy.
3 Italian Medicines Agency – AIFA, Rome, Italy.
[4] Dept. of Political Science, J. Monnet, Second University of Naples, Caserta, Italy.

Background: Atypical antipsychotics are commonly prescribed off-label for the treatment of behavioural and psychological symptoms of dementia (BPSD) **(1)**. Several studies have determined the mortality risk associated with atypical antipsychotics in patients with dementia, but few studies have evaluated independent mortality predictor factors **(2-4)**. **Objective:** The aim of this study was to evaluate a broad range of covariates implicated in survival in a long-term follow-up cohort of community-dwelling new users of atypical antipsychotics prescribed for BPSD. **Design:** This was a prospective cohort study. **Participants and Setting:** 1,618 subjects aged 65 years or older referring to the Dementia Evaluation Units in the Campania Region (Italy) with a diagnosis of dementia and BPSD and a prescription of oral atypical antipsychotics were recruited from September 2006 to March 2010. **Methods:** The potential predictor role of baseline features for mortality in new users of atypical antipsychotics was assessed with the Cox proportional-hazards model. All variables were explored with univariate models; variables that were significant at a level of 10% were included in the multivariate model. **Results:** The average follow-up was 309 days. 9.3% of 1,618 new users of atypical antipsychotics experienced at least one adverse event: 5.1% deaths, 3.0% drug therapeutic failures, 0.5% extrapyramidal symptoms and 0.2% strokes. At univariate analysis the all-cause mortality rate was 9.0 (6.4-12.7) in patients older than 85 years and 7.5 (5.3-10.6) among male patients. Risperidone was associated with a high all-cause mortality rate (7.3; 95% confidence interval [CI]: 4.8-11.1). In the multivariate analysis, age and gender were associated to all-cause mortality (HR 1.1; 95% CI 1.0-1.1, and HR 1.4; 95% CI 0.9-2.2, respectively). On the contrary, hallucination (0.4; 0.2-0.6) and dosage change (0.4; 0.2-0.78) were significantly associated with a decrease of all-cause mortality. **Conclusions:** The long-term use of atypical antipsychotic medications does not seem to affect significantly survival in patients with BPSD. Hallucination and dose change may be associated with a lower risk of death, whereas age and gender appeared to be predictors of mortality. Since the safety issue of these drugs is still debated, controlled studies of factors that may predict mortality in BPSD patients are urgently needed.

References

1. Trifirò G, Spina E, Gambassi G. Use of antipsychotics in elderly patients with dementia: do atypical and conventional agents have a similar safety profile? Pharmacol Res. 2009; 59(1):1-12.
2. Setoguchi S, Wang PS, Alan Brookhart M, et al. Potential causes of higher mortality in elderly users of conventional and atypical antipsychotic medications. J Am Geriatr Soc. 2008; 56(9):1644-50.
3. Raivio MM, Laurila JV, Strandberg TE, et al. Neither atypical nor conventional antipsychotics increase mortality or hospital admissions among elderly patients with dementia: a two-year prospective study. Am J Geriatr Psychiatry. 2007; 15(5):416-24.
4. Rossom RC, Rector TS, Lederle FA, et al. Are all commonly prescribed antipsychotics associated with greater mortality in elderly male veterans with dementia? J Am Geriatr Soc. 2010; 58(6):1027-34.