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Antipsychotic drug interactions and mortality among nursing home residents with cognitive impairment: results from the SHELTER study

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BACKGROUND

- Behavioral and Psychiatric Symptoms of Dementia (BPSD) are common in Nursing Homes residents with dementia.
- Antipsychotics are commonly used drugs for treatment of BPSD but they are associated with an increased risk of adverse effects.
- Multiple medications, used to treat comorbidities associated with dementia, can interact with antipsychotics.

STUDY PURPOSE

The aims of this study are:

1. to estimate the **prevalence** of potential drug interactions involving antipsychotic medications
2. to assess their **effect** on increasing the risk of death in a population of elderly individuals treated with antipsychotics and residing in nursing homes.

SHELTER STUDY

The SHELTER study (Services and Health for Elderly in Long TERm care) involved 4156 residents in 57 nursing home of 7 EU countries + Israel

METHODS (1)

- Study design: retrospective cohort study
- Assessment instrument: interRAI LTCF
- Follow up: 12 months
- Inclusion criteria: mild to moderate cognitive impairment, antipsychotic treatment
- Exclusion criteria: age less than 65 years and unwillingness to participate to the study.

METHODS (2)

Interactions were classified into:

Pharmacodynamic interactions causing QT prolongation, increased risk of neutropenia, sedation, anticholinergic side-effects, seizures, decreased blood pressure /falls, increased weight gain/metabolic changes;

Pharmacokinetic interactions involving the induction or inhibition of cytochrome P450 1A2, 2D6 and 3A4.

Participants with at least one interaction were defined as exposed to antipsychotic drug interactions

Primary outcome: 1-year mortality

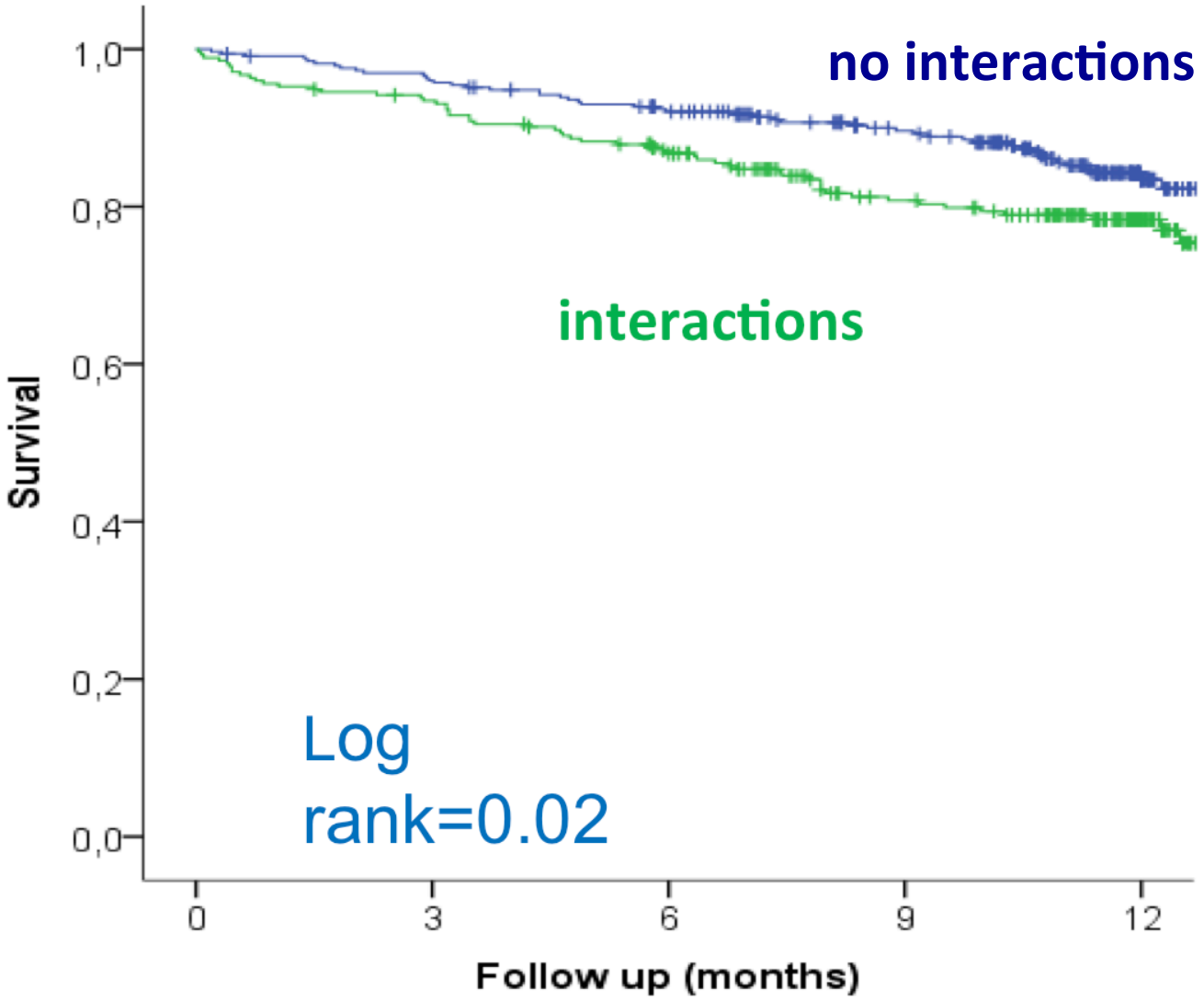
MOST COMMON INTERACTIONS

Possible adverse effect	N (%)	Interaction
Lower BP and falls	210 (34.8%)	Risperidone + Diuretics Risperidone + Betablockers Tiapride + Diuretics
QT prolongation	44 (7.3%)	Tiapride + Citalopram/ Escitalopram Haloperidol + Citalopram/Escitalopram
Sedation effect	43 (7.1%)	Quetiapine + Benzodiazepines Quetiapine + Oppioids
Interactions with inhibitors of cytochrome p450	9 (1.5%)	Olanzapine + Paroxetine Olanzapine + Sertraline Promazine + Sertraline Haloperidol + Sertraline
Anticholinergic effects	2 (0.3%)	Melperone + Anticholinergic drugs Olanzapine + TCA Olanzapine + Anticholinergic drugs
Any	**278 (46.0%)**	

CHARACTERSTICS OF PARTICIPANTS

Sample characteristics	No interactions	Interactions	P value
Age, years (mean ±SD)	82.9 ± 9.2	82.9 ± 8.3	0.964
Women, n (%)	226 (68.5%)	207 (75.5%)	0.055
N of drugs, (mean ±SD)	6.9 ± 3.4	8.4 ± 3.0	< 0.01
Ischemic heart disease, n (%)	89 (27.3%)	100 (36.0%)	0.022
Heart failure, n (%)	39 (12.0%)	51 (18.3%)	0.028
N diseases (mean ±SD)	2.4 ± 1.3	2.7 ± 1.5	0.002
ADL disability* Assistance required Dependent	 215 (66.0%) 97 (29.8%)	 181 (65.1%) 86 (30.9%)	0.939
Depression rating scale (mean±SD)	2.8 ± 3.1	2.6 ± 2.9	0.511

Kaplan-Meier Survival Curves according to presence of interactions involving antipsychotic drugs



ANTIPSYCHOTIC DRUG INTERACTIONS AND MORTALITY

	Mortality rate	incident rate per p-y	RR (95% CI)
No interactions	49 (15.0%)	0.17	**1**
Interactions	59 (21.2%)	0.26	**1.68 (1.13-2.49)**
No interactions	49 (15.0%)	0.17	**1**
1 interaction	51 (20.6%)	0.25	**1.66 (1.10-2.49)**
≥ 2 interactions	8 (26.7%)	0.35	**1.84 (0.85-3.97)**

LIMITATIONS

- No information on the time of initiation of antipsychotic treatment
- No information on the specific cause of death
- Possible residual confounding, although numerous variables have been taken into account
- Generalizability

CONCLUSIONS

- Interactions involving antipsychotics are common
- Antipsychotic –drug interactions are associated with a nearly 70% increased risk of death.
- Part of the excess risk of death observed in patients with dementia treated with antipsychotics may be due to antipsychotic-drug interactions
- The possibility of antipsychotic-drug interaction should be carefully evaluated.