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DRUG INTERACTIONS WITH ANTIDEMENTIA DRUGS: CLINICAL CONSEQUENCES

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Alzheimer´s disease (AD) is a major public health problem, and it is at the origin of a significant burden: 15% of direct costs in dementia are attributed to pharmacological treatment. Persons with dementia often have comorbidities and receive multiple medications. Both factors increase the risk of drug-drug interactions (DDIs) which can result in adverse drug reactions (ADRs). In a study, a total of 1058 spontaneous reports were identified that involved cholinesterase inhibitors (ChEIs) in the French Pharmacovigilance Database; 35.5% contained at least one DDI; 118 of them (31.4%) were the cause of ADRs. Pharmacodynamic interactions play a far greater role than pharmacokinetic interactions in the significance of DDIs. Some known interactions with ChEIs are:

1. atropinic drugs aggravate cognitive disorders;
2. combinations of ChEIs and antipsychotics are associated with an increased risk of extrapyramidal adverse effects;
3. combining ChEIs with drugs that reduce the heart rate, depress cardiac conduction, or induce torsades de pointes increases the risk of arrhythmias and cardiac conduction disorders.

Recent studies suggest that the therapeutic response in Alzheimer´s disease is genotype specific, depending on genes associated with AD pathogenesis and/or genes responsible for drug metabolism. APOEe4/e4 genotype carriers are the poorest responders to treatments. Some ChEIs are metabolized via CYP-related enzymes and can interact with other drugs that are substrates, inhibitors or inducers of the CYP system. Health professionals should be aware of the potential adverse effects of ChEIs, including the possible DDIs and antagonist effects with other drugs.

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