Use of antihistamines and risk of ventricular arrhythmia: a nested case-control multi-database study in 5 European Countries

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Background

There is appreciable utilisation of systemic antihistamines (AHs) among a number of European countries, principally for the treatment of allergies. They are either prescribed by physicians or directly purchased by patients as self-medications. Arrhythmia caused the withdrawal/restriction of use of some AHs in '90s. No well-defined differences have been identified among single agents so far.

Objective

To estimate the exposure over a 15-year period (1996-2010) in 5 European Countries and evaluate the risk of ventricular arrhythmia associated with AHs.

Methods

Data were retrieved from 7 different healthcare databases; AARHUS [Denmark], GEPARD [Germany], HSD and ERD [Italy], PHARMO and IPCI [Netherlands], and THIN [UK], covering a total population of 27 million individuals. Cases of VA were selected through harmonized DB-specific coding-algorithms including validated diagnostic codes or free-text search. Up to 100 controls were matched to each case by index-date, sex, age and database. Current exposure to AHs was defined when prescription of drugs was within 30 days before the VA event. Only those agents with at least 5 exposed cases were included in the analysis. The odds ratio (OR) of current use for individual AHs relative to no-use was estimated using conditional logistic regression, adjusting for confounders.

Results

Overall, 5,228 cases and 521,596 matched controls were identified. Out of all cases, 759 were currently exposed to antihistamines. Dimetindene ($OR_{Adj.}$=3.08 [1.31-7.27]), promethazine ($OR_{Adj.}$=1.46 [1.16-1.83]) and cyclizine, ($OR_{Adj.}$=5.28 [4.12-6.77]) were associated with a statistically significantly increased risk of VA ($p<0.05$) in the pooled analysis. No statistically significant associations in AARHUS, ERD, HSD and IPCI were observed, when DB-specific analyses were conducted, except for dimetindene and ebastine in GEPARD, dexchlorpheniramine and promethazine in PHARMO and cyclizine in THIN.

Conclusion

Current use of dimentidene, promethazine, cyclizine ebastine and dexchlorpheniramine was associated with an increase in the risk of VA. Because of the frequent use of AHs as self-medication, the risk assessment using electronic health care records is very difficult and only an integration of different sources of data (general practice and claim databases) allowed us to do assess the risk of this rare adverse event in the ARITMO project.