Safety profile of H1-antihistamines in children: an analysis based on data from VigiBase

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H1-antihistamines are commonly used in infants and children for the relief of histamine-mediated symptoms in a variety of conditions including allergic rhinitis, allergic conjunctivitis and urticaria. They are also used against coughs, colds and insomnia, even if the evidence for effect is lacking or there are more appropriate products available (Fitzsimons 2014).
Despite being marketed for many years, little is known about the safety profile of H1-antistamines in young children. Furthermore, literature suggest a widespread use starting from the first weeks of life although several products lack full pediatric approval or are licensed only from at least 2 years of age (DRUGDEX® 2014).
We aimed to conduct a comparative analysis of the safety profiles of H1-antihistamines using data from the WHO database (VigiBase™).
We selected reports on H1-antihistamines in children (0-14 y) up to June 2014 from VigiBase using Medical Dictionary for Regulatory Activities (MedDRA) terminology for ADRs. The analysis was performed for drug-reaction pairs calculating Reporting Odds Ratio (ROR) with 95% confidence interval.

The final analysis was performed on 6022 reports corresponding to 12576 drug reaction pairs and to 65 different drugs. Fifty-four percent of reports involved males, 41% females while information on gender was missing in 5%. Regarding to age group, 4% were newborns (0-27 days), 14% infants (28 days-23 months), 66% child (2-11 y) and 17% adolescent (12-16 y). Twenty-one point five percent of the cases were serious and 16.6% were not serious; in the 61.8% this information was missing. Two hundred twenty-three cases had a fatal outcome: 37.7% involved newborns, 12.1% infants, 33.2% child and 17.0% adolescent. Most of the serious ADRs are not listed in the Summary of Product Characteristics (SPCs) (i.e. ventricular septal defect, heart disease congenital, coma, coarctation of the aorta) or not systematically listed (i.e. apnoea, hepatic failure, angioedema, cardiac arrest) (Micromedex 2014).
We found a significant disproportionality for several drug-reaction pairs. For example, significant RORs was obtained for 'delirium' and promethazine (ROR=4.66; CI 95% 1.94 - 11.17), 'hypoxia' and 'opisthotonus' and diphenhydramine (4.71; 1.49 - 14.86 and 3.3; 1.13 - 9.66), 'convulsion' and loratadine (ROR=1.41; CI 95% 1.01 - 1.97), 'ventricular septal defect' and ketotifen (5.84; 1.92 - 17.79), ', desloratadine and 'heart disease congenital' (6.3; 1.83 - 21.71), 'opisthotonus' and diphenhydramine (3.3; 1.13 - 9.66), 'electrocardiogram QT prolonged' and fexofenadine (4.32; 1.3 - 14.34).
Considering the widespread use of H1-antihistamines, our findings suggests a limited risk for serious ADRs. Nevertheless, data from VigiBase™ highlights possible associations with serious or unexpected ADRs often occurring in age groups where use of the products are unlicensed.
SPCs should be updated on indication and risk of ADRs enabling clinicians and parents to make proper choices on treatment and for the early detection of ADRs in order to maximizes the benefits and reduce the risk of negative effects.

Fitzsimons et al. (2014). *Arch Dis Child Educ* Pract *Ed.* 2014 Aug 21. pii: edpract-2013-304446. doi: 10.1136/archdischild-2013-304446.
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