189. Hearing Impairment Associated with Oral Terbinafine Use

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Background: The Netherlands Pharmacovigilance Centre Lareb received six reports of hearing impairment in association with oral terbinafine use. This study describes these cases and provides support for this association from the Lareb database of spontaneous ADR reporting and from Vigibase, the adverse drug reaction database of the WHO Uppsala Monitoring Centre.

Objectives: The objective of the study is to identify whether the observed association between oral terbinafine use and hearing impairment, based on several cases received by Lareb, supports a safety signal.

Methods: Cases of hearing impairment in oral terbinafine users are described. In a case/non-case analysis, the strength of the association in Vigibase and the Lareb database was determined by calculating the reporting odds ratios (ROR), adjusted for possible confounding by age, sex and possibly ototoxic concomitant medication. RORs are calculated for deafness, hypoacusis, and the combination of both, defined as hearing impairment.

Results: In the Lareb database, six reports concerning individuals aged 31–82 years, who developed hearing impairment after starting oral terbinafine, are present. The use of oral terbinafine is disproportionally associated with hypoacusis in both the Lareb database (adjusted ROR = 3.9, 95% CI: 1.7–9.0), and in Vigibase (adjusted ROR = 1.7, 95% CI: 1.0–2.8). Deafness is not disproportionally present in either of the databases. The pharmacological action of terbinafine is based on the inhibition of squalene epoxidase, an enzyme present in both fungal and human cells. This inhibition might result in decreased cholesterol levels in, among others, the outer hair cells of the cochlea, possibly leading to impaired cochlear function and hearing impairment.

Conclusions: To our knowledge, hearing impairment associated with oral terbinafine use has not been described before. A causal relationship between the use of oral terbinafine and hearing impairment is possible, based on statistical analysis of reported cases in different databases and a possible pathophysiological explanation.

190. Safety Profile of Antiinfectives Used in a 13 Years Period, Report of a National Pharmacovigilance Centre

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Background: It is reported that antibiotics induced adverse events are responsible for an estimated 142,000 emergency department visits per year in the United States. Anti-bacterial agents are responsible for approximately 25% of adverse drug reactions in hospitalized patients. The incidence of antibiotics induced adverse events in hospitalized patients is estimated as 5%.

Objectives: To evaluate all registered cases of adverse events induced by antiinvectives in Iranian pharmacovigilance database. To detect preventive measures for reducing resulted complications.

Methods: All recorded adverse events in pharmacovigilance database from 1998 through 2011 were reviewed for those induced by antiinfectives. The extracted data were categorized based on factors related to patients, suspected medicines and adverse events. Assessment of system-organ classes, seriousness and causality of reactions was performed according to World Health Organization scale. Preventability of adverse events was analyzed based on Schumock questionnaire.

Results: Antiinfectives were the most reported drug class in reported adverse events. Among 29,356 registered adverse events, 8,054 (27.4%) were suspected to be induced by antiinfectives. There were 301 cases of death recorded in our database in which 127 cases were related to antiinfectives. The highest number of detected events was reported with ceftriaxone (2,574 cases). Ceftriaxone (82 cases) and Penicillin (20 cases) were the mostly reported medicines in fatal reactions. The route of administration in recorded fatal cases was mostly reported as intravenous and intramuscular. Anaphylactic reactions had the highest frequency of registered serious reactions. Inappropriate use of medicines was the most detected cause of preventability in evaluated data.

Conclusions: Antiinfectives can induce severe and life-threatening adverse events. The high frequency of serious reactions could be influenced by rapid intravenous injection, unlabeled use and previous patient history of allergic reactions to antibiotics.

191. Abstract withdrawn by author.