'doubtful', ', S2 'plausible' or S3 'likely' in type 1-ADR sample files is 58.4%, 34% and 6%, respectively (1.6% not determined); conversely the distribution of type 3-OD sample files is 23%, 44.2% and 28.2%, respectively (4.6% not determined). The distributions according to 'chronological criteria' (C0 'unlikely', C1 'doubtful', C2 'plausible' or C3 'likely') were similar in type 1-ADR (e.g., C3: 14.34%) and type 3-OD (e.g., C3: 15.19%).

Conclusions: These study tends to indicate that the distinction of two types of criteria in the French imputation method could be of particular interest in the case of the medicines overdoses (semiological score S3 'likely' $= 28, 2\%$ for medicines ODs versus 6% for ADRs). No difference surprisingly was observed in the case of misuses (mainly represented as 'others'), but the total number considered was very low. This observation should cause a renewal of interest for the use and development of imputation methods, as particularly the French one, for the causal assessment of medicines overdoses. The context is favourable because all the countries, of which those of the European Union, encourage to be concerned with overdoses in the double preoccupation of public health and medicines dangerosity management, as WHO ever did it.

References:

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455. Medicinal Herbs: Safety Versus Toxicity

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Morocco has the largest number of plant species in North Africa (more than 4 000 species). Among these many are largely used in traditional medicine to treat a wide range of ailments. The use of these plants is not always safe and many cases of severe poisonings and deaths occur and are of different origins. The pharmacovigilance should also apply to the use of these herbs.

Among the plants commonly used, an attempt is made to rank them according to their toxicity level. Three classes of medicinal plants according to their toxicity may be defined using an analogy to modern drugs. (1) Medicinal plants with low toxicity and mild side effects, (2) Medicinal plants with moderate toxicity and side effects, (3) Medicinal plants that are highly toxic.

460. Risk Management of Tiotropium: Pharmacologically Expected Safety Profile Versus Reported Safety Profile of Tiotropium

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Introduction: In COPD cholinergic activity is thought to be one of the most important reversible components of airway obstruction. Therefore anticholinergic drugs play an important role in COPD management. Tiotropium is a quaternary ammonium compound and is structurally related to ipratropium. Tiotropium antagonises muscarinic M1, M2 and M3 receptors. However, unlike ipratropium tiotropium has shown some kinetic selectivity. It dissociates more slowly from M1 and, more importantly, from M3 receptors (which are responsible for bronchoconstriction and bronchial mucous secretion) than from M2 receptors. This kinetic selectivity is responsible for the long duration of action permitting once-daily administration. Furthermore, it has been suggested that blocking of M2-receptors, which may be responsible for the paradoxal bronchoconstriction by functioning as a negative feedback mechanism.

Aim of the study: Determination of the compatibility of the pharmacologically expected safety profile and the reported adverse drug reactions (ADR's) of tiotropium in the Netherlands.

Methods: The theoretically safety-profile of tiotropium has been composed based on pharmacodynamic and pharmacokinetic properties of tiotropium. The reported ADR's of tiotropium have been compared with this theoretical safety-profile.

Results: According to the composed theoretical safety profile gastrointestinal disorders, cardiovasculair disorders and skin and subcutaneous tissue disorders are the most expectable ADR's of tiotropium. Furthermore, eye disorders and urinary disorders could be expected also. Disorders of the central nervous system are not expected, because quaternary ammonium compounds do not penetrate the blood-brain-barrier due to the positive charge at physiological pH.

Until 16 may 2003 the Netherlands Pharmacovigilance Centre received 93 ADR's

In general, the reported ADR's fit to the theoretically safety-profile of tiotropium. Gastrointestinal disorders and disorders of skin and subcutaneous tissue were reported the most, both 16 times (17.2%). Eye disorders, such as blurred vision, vision abnormal, accommodation disorders and dry eyes were reported 7 times (7.5%).

In contrast with the theoretical safety profile, 14 ADR's concerning the central nervous system and 2 ADR's concerning psychiatric disorders were received.

Conclusion: This analysis suggests that at first sight the reported ADR's on tiotropium in general are compatible with the theoretical safety-profile except for ADR's concerning the central nervous system and psychiatric disorders.