are known to be liver toxic were used but these reports led to concerns about the safety of some frequently used herbs such as *Dictamnus dasycarpus* or *Paeonia* species.
Objective: To evaluate feasibility of using a case control study to assess potential toxicity of individual Chinese herbs, and obtain preliminary data on frequency of use of herbs in CHM.
Method: Herbal formulas used in 37 reports of liver toxicity possibly associated with use of CHM were identified. For each of these 'Patient' prescriptions, 3 'Control' prescriptions were obtained from patients matched on gender and reason for use who did not develop any abnormal liver function during TCM treatment. Odds ratios (OR) were calculated for the most frequently used herbs.
Results: The medicinal herbs that were used most frequently were *Glycyrrhiza* spp, *Rehmannia glutinosa* and *Paeonia* spp. The top twenty herbs in both Patient and Control groups were similar. Of 137 herbs used by the Patient group only 14 were used in more than 20% of formulas. Similarly of 166 herbs in the control group, only 11 were used in more than 20% of formulas. The only herb with a statistically significant increase in OR is used to treat hepatitis. There was no association (OR > 1) with herbs such as *Glycyrrhiza spp*, *Rehmannia glutinosa* or *Dictamnus dasycarpus*.
Discussion: Case control studies can be used for herbal investigations but there are specific difficulties and limitations of such studies when applied to CHM. As in Chinese medicine up to 20 herbs may be used in a formula, but only single or combinations of 2 herbs could be tested in this type of study. However it was possible to counteract the claim that some frequently used herbs cause liver toxicity as no association was found in this study. As hepatotoxicity may be the result of interactions between 2 or more herbs a larger more detailed study is needed.

61. The Contribution of Periodic Safety Reports (PSURs) To Safety Related Regulatory Actions of Biopharmaceuticals

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Introduction: A periodic safety update report (PSUR), composed by marketing authorization holders and submitted to regulatory authorities on predetermined time points, provides an update of the worldwide safety experience of a pharmaceutical. Information is lacking on how PSURs contribute to safety related regulatory actions.
Aim: The objective of the study is to analyze the contribution of PSUR evaluations to the initiation of safety related regulatory actions of biopharmaceuticals.
Methods: We performed a retrospective analysis of all safety related type II variations of biological products centrally approved in the European Union (since 1995) for which ≥1 safety-related Direct Healthcare Professional Communication (DHPC) was issued until December 2009. An evaluation of the role of PSUR assessments in the initiation of safety associated regulatory actions was performed through an analysis of European Public Assessment Reports and updates of the Summary of Product Characteristics (SPC). We compared "urgent" variations, defined as variations accompanied by the distribution of a DHPC, with "less urgent" variations, i.e. safety related SPC variations for which no DHPC was distributed. For each variation we determined if any reference was made to the contribution of PSUR evaluations. We determined the data source and nature of the safety issues included in the variations. Each variation could include ≥1 safety issue and ≥1 data source could contribute in a single variation.
Results: We identified 133 safety related type II variations for 15 biological products. Reference to PSUR evaluations was made in 2/24 (8.4%) of all urgent type II variations and 48/109 (44.0%) of the less urgent variations (x^2, $p < 0.01$). Data sources that contributed to the urgent variations were: 14 (58%) spontaneous reports, 9 (28%) clinical trials and 2 (8%) an analysis of pooled data. For the non-urgent variations, these were 53 (49%), 40 (37%) and 18 (17%) respectively. Overall, most of the variations concerned events from the System Organ Classes (SOCs) Infections and Infestations (32%), General Disorders and Administration Site Conditions (26%), Neoplasms (14%), Blood and Lymphatic System Disorders (14%) and Nervous System Disorders (14%). No differences in SOCs were observed between safety-related regulatory actions that did or did not result from PSUR assessments.
Conclusions: The contribution of PSUR evaluations was lower in urgent safety related regulatory actions when compared with less urgent safety issues. Despite the modest role of PSURs, spontaneous reports contributed to the majority of the urgent safety related regulatory actions.

62. Bile Salt Export Pump Inhibition Properties of Drugs not Associated with Disproportionate Reporting of Drug-Induced Jaundice in WHO-UMC VigiBase

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Background: One of the proposed mechanisms of drug-induced cholestasis involves inhibition of the bile salt export pump (BSEP). It has been suggested that molecular properties of drugs are related to BSEP inhibitory potential, and may be a useful predictor of drug-induced cholestasis to be applied in preclinical research. In this study, we identified drugs that have been associated with drug-induced jaundice in individual case safety reports (ICSR) from the WHO Global ICSR database, VigiBase, and related these to their BSEP inhibitory potential.
Methods: Using the online VigiMine tool, we selected all drugs with at least 100 reports of drug-induced jaundice from the WHO-UMC VigiBase, which contained 5 057 235 ADR reports at May 1, 2010. From this list of 53 drugs, we excluded 4 combination preparations and 1 vaccine. For the remaining 48 drugs we noted the information components (IC) for jaundice produced by VigiMine. Subsequently, we looked up the chemical structure and calculated the predicted inhibition of ABCB11-mediated taurocholate transport, a measure for BSEP inhibition, using the method proposed by Hirano et al.[1] We plotted the predicted BSEP inhibition against IC-values and fitted a linear regression line.
Results: The 3 drugs most strongly associated with jaundice were prajmalium (IC 6.07), halothane (IC 5.25) and fusidic acid (IC 4.81).