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Meeting Report

Symposium on Pharmacovigilance of Herbal Medicines, London, March 28, 2006

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On April 2006, the International Symposium 'Pharmacovigilance of Herbal Medicines. Current Status and Future Directions', was held in London, organized by the Royal Pharmaceutical Society of Great Britain (RPSGB) in conjunction with the most important international societies involved in the field. The Chairperson of the Congress was Prof. Joanna Barnes of the School of Pharmacy of the University of Auckland, NZ.

Major topics of the conference were: evaluation of main concerns about correct reports of adverse reactions to herbal extracts and possible future directions in organizing an international and affordable signaling system and to build a definitive international network on the WHO database.

Compelling problems are due to the wide differences that exist all over the world in nomenclature, administration, extraction and use of medicinal herbs. In addition, the clinical purposes for administration of the same medicinal herbs often differ greatly among traditional therapeutic systems according to the diagnosis of the same diseases and in the recognition of energetic-magical properties of some natural substances.

The congress has highlighted the necessity of a common language not only for the botanical name of the plants but also for the type of extraction, the clinical purpose for the administration of a substance and classification of ADR (Adverse Drug Reaction).

Presented at the conference were: the adverse event database of the WHO, the Yellow Card System of the British MHRA, systems established by the BfArM, the EMA, the ESCOP, the Italian Herb Surveillance Programme of National Institute of Health, the German producers of anthroposophic medicines, the Australian Adverse Drug Reactions Unit, the system installed by the Chinese drug regulatory authorities, although actually still in Chinese language, demonstrating that the emerging problem has been the lack of communication among the systems.

In contrast with the wide traditional use of medicinal herb, there is a lack of reliable scientific data and notwithstanding long tradition there is further confusion since some products can be commercialized for uses completely different from the original traditional use and vice versa.

As Dr Phil Routledge, Wales College of Medicine, outlined strategies for risk management of herbal medicines stressing the need to be based on the following main steps: clear-cut identification, reliable assessment, management and clear communication to the public.

The assessment of risk should be primarily based on the following points: hazard identification and complete estimation of risk.

Dr Shufeng Zou of the National University of Singapore focused attention on the problems of predicting and minimizing herb–drug interactions by expanding knowledge not only of substances contained in the extract but also by improving the quality of the commercial product through controls on the manufacturer, packer and distributor.

Dr Ralph Edwards reported the global experience of the WHO Drug Monitoring Programme. On April 2006, a total number of 3.6 million of ADR were reported and of these, 41 439 have been listed as due to an herbal drug and 17 112 of these as due to interaction with another drug. In the last 12 years, the number of suspected herbal

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ADRs has more than tripled. He stressed the lack of an internationally standardized classification that has led to the publication of the Accepted Scientific Names of Therapeutic Plants and their Synonyms by the WHO and proposed the creation of an Herbal Code Number.

Dr Ulrich Hagemann, of the German Federal Institute for Medical Devices, proposed that one of the main concerns is to develop not only an affordable internationally acknowledged system for herb classification but also to classify substances contained in extracts, based on affordable studies of pharmakokinetic and pharmacodynamic parameters of main herbal components, dosage and real exposure as well as possible ADR versus underlying disease.

Dr Ano Dodoo of Ghana National Centre for Pharmacovigilance described work in Africa to diffuse a program about herbal pharmacovigilance, and to identify products and herbal constituents for full assessment of adverse reaction with the same priorities as Western countries.

The Association of British Pharmaceutical Industry reported a study showing that 60% of people using herbal remedies took them along with conventional medicines and only 10% of the patients taking alternative medicines informed their GPs, stressing the importance of education of both the prescriber and the patient.

The most important medicinal herbal ADR reports centered on *Hypericum perforatum*, kava-kava, pyrrolizidine alkaloid and aristolochic acid. Although these have been the most studied and paradigmatic cases, other problems are pending due to the under-reporting of herbal ADR. Dr Linda Anderson of the Medicines and Healthcare Products Regulatory Agency, UK, stressed that remedies are often made by simple processes with no brand name on the merchandized product and neither written recommendation nor warnings.

Many authors have remarked on the importance of contaminants like pesticides, heavy metals and mycotoxins, and Dr Patricia McElhatton, National Teratology Information Service, UK, in her work reported a lack of rigorous scientific studies on the safety of herbs for pregnant or lactating mothers in contrast with the widespread use of herbal medicines in this group of women.

The implementation of the Directive 2004/24/EC on Traditional Herbal Medicinal Products has introduced a registration scheme which requires traditional herbal medicines to meet specific and appropriate standards of safety and quality, and for the product to be accompanied by the necessary information for safe use. In addition, the 2001 Review of Medicines Legislation has provided a number of new regulatory tolls such as electronic reporting of adverse reactions to the central European database: Eudravigilance.

Dr Tony Booker, Register of Chinese Herbal Medicine, UK, presented data of a study from Mazin Al-Kafai (not published) showing that on a total of 1265 patients taking Chinese herbs for different diseases, 107 patients (8.5%) developed raised levels of ALT after initially having normal results. He pointed out the importance of improving the dissemination of reports among practitioners at all levels.

Dr Simon Mills, an ESCOP (European Scientific Cooperative of Phytotherapy) representative, confirmed the involvement of the institution in pharmacovigilance through publication of a monograph that provides the basis for a formal European harmonized 'core data' sheet. The mission of the EU BIOMED research program is to determine European standards for the safe and effective use of phytomedicines.

According to Dr Stephan Kohler, representative of pharmaceutical industries, the scope of pharmaceutical EU legislation should be not only to plan and control pharmacovigilance and to protect public health but also to increase the competitiveness of the industry and facilitate the development of new products and the movement of safe goods in the community.

Participants approved the principle that pre-clinical tests for a medicinal product may not be necessary when its traditional use has not been harmful under specified conditions during a period of at least 30 years, including at least 15 in the community.

Dr Joanne Barnes, the Congress Chairperson, outlined the importance of the pharmacists' role in controlling ADRs, and also in correctly informing patients on the risk and benefits of herbal medicines.

The best poster award was presented by Dr Paola Moro, Milan Poison Control Centre, I, for reporting details of the 1378 calls they had received concerning alternative remedies since January 2001. The presenters remarked on the difficulties in quickly identifying toxic substances and alerting authorities to take urgent action to protect public health.

In conclusion, the main problems concerning herbal ADRs are botanical and chemical identification of the substances taken by patients, correct evaluation of ADRs following the principles of mainstream medicine and education of practitioners, citizens who commonly think herbs are always safe, producers and merchandizers. The next step will be to build an international cooperative affordable network for pointing out and evaluating herbal ADRs.

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