STANDPOINT FROM HOSPITAL PHARMACY - LABELING

H. Sato and T. Iga

Department of Pharmacy, University of Tokyo Hospital, Faculty of Medicine,
University of Tokyo, Bunkyo-ku, Tokyo 113-8655, Japan

Pharmacists collect drug information from a number of resources, including drug labeling as a minimum but legal basis of drug information. We will review the present status and perspectives of drug labeling with respect to drug interactions from the standpoint of hospital pharmacy, where pharmacists are striving to establish proper usage of medicine.

1) Importance of drug labeling and the key role of pharmacists in the avoidance of dangerous drug interactions:

In Japan, the importance of drug labeling had not been well recognized by physicians, and perhaps even by some of the pharmacists, until they experienced the so-called "Sorivudine Case" in 1993, in which fifteen patients died from the incidental combination of an antivirus agent sorivudine and a fluorouracil anticancer agent. From this undesirable event, the Japanese regulatory agency came to require in 1997 that all drug labelings be revised until the end of 1999 to comply with the guidelines (1996) of the "Working Group on Drug Labeling Revision". The guidelines require that drug labeling be legible and concise using a tabular form and described quantitatively and statistically based on reliable evidence as much as possible. Since then, drug labelings have been frequently revised by pharmaceutical companies aiming to fulfill the above guidelines, but at the same time to be exempted from responsibility associated with the drug-associated misadventure based on the PL (product liability) Law enforced in Japan in 1995. Hence, while the older drug labelings tended to lack necessary information, the newer drug labelings tend to overload information especially on drug interactions and adverse side effects, so that really dangerous drug combinations might not be easily identified to be avoided. Generally, if there is too much information which must be processed by physicians, things tend to just slip by. In this regard, pharmacists are expected to play a key role to evaluate complicated information of drug interactions and rearrange them in a clinically meaningful context. For this purpose, we have to keep updating a list of clinical significance of various drug interactions and reduce noise from many distractions, by which pharmacists can reasonably recommend physicians to reduce, replace, or cancel either of the interacting drugs. As a good example of doing so, a simple but practical drug interaction-detecting system implemented in our hospital is to be presented.
2) Limitations of drug labeling for avoiding dangerous drug interactions:

Since drug labeling at its first distribution is prepared just after clinical trials, there is a dilemma that the drug must be used widely in clinical settings (not as well controlled as in clinical trials) before we encounter less common but serious adverse drug events including those caused by hazardous drug combinations. Moreover, as far as drug labeling goes with packages already on the market, it does not function as a real-time information resource in the case of emergency. Ideally, drug labeling should be distributed via the internet with related useful information linked as hypertext structure. Therefore, the electronic drug information system (http://www.pharmasys.gr.jp/) developed by the regulatory agency in April, 1999, to provide constantly updated drug labeling and case reports of adverse drug events via the internet is a very important and useful tool for reimbursing the disadvantages of the conventional printed form of drug labeling.

3) Perspectives of drug labeling with regard to drug interactions:

As pharmacists facing patients routinely in clinical settings, we think it very urged to have drug labeling provided with information-rich descriptions of clinical events and symptoms, severity (necessary level of avoidance), mechanism(s), risk factors, and quantitative changes in blood concentration in plasma (for PK interactions) or in pharmacological activity (for PD interactions), as well as both generic and brand names of the hazardously interacting drugs. Description of drug interactions in any drug labeling should conform to the same tabular format listing the above contents, preferably with references for their evidence. Above all, drug labeling should not be merely as a collection of various information as insurance forms, but an information resource which can provide systems-oriented solutions to make drug therapy run more smoothly, safely, and efficiently for the benefit of patients. Moreover, considering the present situation where a unified management system of patients' medication records at community pharmacies has not been implemented yet, we have proposed that patients themselves could convey necessary drug information between different hospitals or clinics, using "Drug History Handbook" which we have developed. The patient education system implemented in our hospital to protect them from severe drug interactions is to be also presented here.

1983 B.S. degree from Faculty of Pharm. Sci., Univ. of Tokyo
1985 M.S. degree from Faculty of Pharm. Sci., Univ. of Tokyo
1986 Assistant Prof. in Faculty of Pharm. Sci., Kanazawa Univ.
1991 Ph.D. degree from Faculty of Pharm. Sci., Univ. of Tokyo
1991 Assistant Prof. in Toyama Med. Pharm. Univ. Hospital
1991-1992 Research Fellow in NCI, NIH, Bethesda, USA
1992-1993 Invited Scientist in Basel Research Institute (Sandoz)
1997 Associate Prof. in University of Tokyo Hospital