SYMPOSIUM PRESENTATION

Safety Regulation for Medicines and Foodstuffs

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Abstract

In Japan, for medicines we have the Pharmaceutical Affairs Law and for food the Food Sanitation Law, these two being applied appropriately for security management. The range of test data needed to be obtained by examination is prescribed by the laws, and each test method is notified in the form of guidelines which are regularly revised in line with progress in science and technology and international harmony. With medicines, a monitoring system is always maintained also after marketing, taking account of the existence of side effects along with efficacy.

Key Words: Safety regulation - medicines - foodstuffs

Asian Pacific J Cancer Prev, **10**, 22-23

Introduction

Human being through eating and drinking are exposed to medicines as well as foodstuffs. The food is necessary for health in maintenance of the body, and the medicine is for treatment/diagnosis/prevention of illness, but the ways of thinking about their safety are different. With medicines, on the premise of efficacy against disease, it is acceptable that there be serious side effects as long as the risk is not greater than the benefit at administered. Naturally close attention is necessary, and there is a system whereby specialists such as doctors or pharmacists provide guidance and management for use.

On the other hands, with food for nourishment, the amount and the kind consumed is dependent on the judgment of individual and therefore there is not the same flexibility with regard to risk of harmful action.

Thus for medicines we have the Pharmaceutical Affairs Law and for food the Food Sanitation Law, these two being applied appropriately for security management.

Security Management of Medicines

The actions to guarantee safety security of medicines are carried out at all stages on the basis of systematic regimes such as a performance of pre-clinical and clinicaltests during the period of development, examination by the regulatory authorities, and side effect surveillance after marketing. Actually, the proportion of products for which development is stopped because of toxicity and clinical safety problems at the development stage is considerably high.

In addition, there were the products withdrawn for reasons of clinical safety issues at the post-marketing stage. The range of test data needed to be obtained by examination is prescribed by the law, and each test method is notified in the form of guidelines which are regularly revised in line with progress in science and technology and international harmony. As for a carcinogenicity test, it is not carried out for reasons of the case that the long-term prolongation of human life cannot expect of the patient with the anticancer drug, but, is carried out in case of medicines which are concerned about carcinogenicity, and planned for long term treatment.

For carcinogenicity evaluation, a long-term carcinogenicity test with rodents and a short/middle term in vivo test with rodents are recommended, and development of a medicine is canceled when a result of unequivocal carcinogenicity is obtained. Post-marketing stage, surveillance of side effects is also performed to ensure that any carcinogenicity is detected. For example, attention awakening is performed in a package insert withan anticancer drug when a second carcinogenicity risk becomes clear by the investigation of long-term survival patients. In addition, since carcinogenicity risk rises with immunosuppression and effects on growth factors, monitoring after the marketing is performed with long usage patients focusing on immunosuppressants and hormones like somatotropin and insulin. For an example which needs restriction, there is the case of hormone replacement therapy (HRT) in post menopausal woman. Large- scale clinical tests and epidemiologic studies have been performed in Europe and US where HRT is common, and it was shown that the risk of breast and ovarian cancer rises with long-term use, so that long term use for HRT is restricted, and reporting to the patient and periodical

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examination are performed.

Security Management of Foodstuffs

On the other hand, in the field of the foodstuffs, products used intentionally during processing and production, like food additives, are used only when their safety has been confirmed by non-clinical testing. In the case of foods themselves, when a food has a clear hazardous property or the probability of hazard, prohibiting sue may be necessary. As for the management of the carcinogenicity risk in the field of food, evidence of genotoxic carcinogenicity should result in banning use or limitation to below the level of detection in final foods in the case of additives and pesticides. In the case of the non-intentional contents such as pollutants, the approach is to set criteria for limiting exposure, with intake guidance and reduction measures.

For a recent topic of interest, we should mention the voluntary recall of products with contamination beyond 10ppb of benzene, which is a criterion limit for tap water. This was performed based on information that benzoic acid and ascorbic acid react in soft drinks, and small amounts of benzene can thereby be generated.

With newly developed foods which human beings do not have long-term experience of eating and drinking or where larger quantities are consumed than usual, especial care is necessary for safety evaluation, and powder/tablets of Amamesiba (*Sauropus androgynus*) were prohibited recently for health damage occurrence (bronchiolitis obliterans).

Summary

With medicines, a monitoring system is always maintained also after marketing, taking account of the existence of side effects along with efficacy. Foods are thought to be usually safe, except in the case of a chemical substance and newly developed products which require prior safety evaluation by non-clinical testing. Safety measures such as prohibition may need to be imposed if health damage occurs. As for the management of the carcinogenicity risk, in the field of medicine, warnings may be necessary with an anticancer drug. Prohibition is generally the option with a drug for long-term convalescence disease, and recommendations against use over a long period are appropriate in cases of non-genotoxic carcinogenicity.

On the other hand, in the field of the foodstuffs, evidence of carcinogenicity should result in banning use or limitation to below the level of detection in final foods in the case of additives and pesticides used intentionally, and in the case of non-intentional contents the approach is to set criteria for limiting exposure, with intake guideline and reduction measures.