Clinical Evaluation of Newly Developed Antihypertensive Drugs

Every nation has a characteristic manner of practicing medicine; it is deeply rooted in racial tradition, socioeconomic state, and many other regional factors. Therefore, it is difficult to determine the superiority of the medical system of one country compared to that of another.

What are unique characteristics of medical practice in Japan? Japan has a well-developed system of health-insurance, enabling everyone to visit a doctor at low cost anytime he or she needs it. However, Japan is rather slow to progress in important fields such as emergency medicine, organ transplantation, hospice care, etc. Another characteristic is ethnic homogeneity; enterprises in Japan are quite similar to each other, as are the schools, regional political systems, life styles, and the way of thinking. Medicine is no exception.

People are usually short-tempered. They easily become interested in everything new, pursue it eagerly at first, but not for the long run. The enthusiasm soon fades away.

When a novel drug is introduced, most doctors are curious about it, and want to immediately study it. Thus it is quite easy to organize a study group to test the new drug. One hundred or more doctors can be easily recruited in a few weeks.

In 1989, the Ministry of Health and Welfare revised the guidelines for the clinical evaluation of antihypertensive drugs. According to the guidelines, it is necessary to test each new drug through three set steps, phases I, II, and III.

Phase II, the dose-finding study, requires about 100 patients, and phase III, the double blind study, 200 or more. To meet these requirements, a study team, consisting of 70–80 doctors, is organized. Each doctor is responsible for only 1 or 2 patients in phase II, and 2 or 4 in phase III.

It can be argued that this system is not good, because the size of the study team is too large and the number of patients each doctor treats is too small. This kind of critique is often brought up in the United States and in other developed countries as well as in Japan. They assert that the results obtained by this system are not reliable, since the data are not homogeneous due to the diversity of participating doctors.

These critiques or assertions, however, appear groundless. Actually, the results of such studies obtained to date in Japan have been quite accurate and reproducible. For instance, captopril, an angiotensin I converting enzyme inhibitor developed by Squibb, was found in Japan to be most useful in the dose range of 37.5–75mg/day. In the United States, it was prescribed in doses of 150–300mg/day, and it showed numerous untoward side-effects: skin rashes, renal injuries, leukopenia, etc. These drawbacks were thought at that time to be inherent to ACE inhibitors, ranking them as second or third choice drugs in antihypertensive armaments. With the low dose regimen administered in Japan, it was still efficacious and the side effects were much less, raising the rank of captopril to first choice therapy.

The GCP (Good Clinical Practice, regulations for the clinical evaluation of drugs, issued by the Government of Japan in 1989) intends to reconcile Japanese traditional test system with that of Western countries. To many clinicians, however, these regulations appear to be too westernized, giving rise to some confusion among them.

International uniformity is important on one hand, and ethnic or national individuality is worthy of esteem on the other. The best situation is in the golden mean between the two. This should be borne in mind in carrying out the clinical evaluation of novel drugs according to the new regulations.

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