COMMENTARY

The Importance of Clinical Epidemiology for Development of Appropriate Treatment Modalities for Asian Populations

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Abstract

The Asian countries with their own particular cultural background and risk factors differ from the Western world regarding their disease burden, including the incidences of different cancers. The lack of awareness and effective screening programs in many parts of Asia means that the stage at presentation with a neoplasm is often more advanced than is typical elsewhere, with all the inherent associated problems in cancer control. In addition, the presence of racial variation in genetic polymorphisms may mean that different populations in Asia may not respond to chemotherapy or other treatment modalities in the same way as their counterparts in Europe or the United States. Therefore it is essential that research be conducted into the clinical epidemiology of efficacy of drug protocols in Asian groups, with an appropriate focus on influencing factors.

Key words: Asian countries - clinical epidemiology - treatment efficacy - influencing factors

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Introduction

Many cancers, like adenocarcinomas of the breast, colon, prostate and lung, are on the increase in Asia, while squamous cell carcinomas of the cervix and head and neck continue to be of major importance. In order to improve survival to levels achieved in the Western world it is essential that tumours are diagnosed early and the patients receive the optimum treatment available. Therefore a two pronged approach is necessary: firstly, awareness and screening need to be emphasized; secondly clinical data need to be obtained regarding therapeutic efficacy and influencing factors. Unfortunately, there is only limited basic cancer information for many Asian nations, and immediate action is called for to correct this. In particular, the clinical epidemiology scientific database is weak and its fragmentary nature means it is difficult to draw helpful conclusions.

Ethnic Variation

New drugs which have potential in cancer therapy are emerging every day and there is an increasing demand for clinical trials. Asia is the most populated continent and naturally has a large market for drug sales, but the clinical epidemiology of disease may differ from that in the developed world. Within Asia one might also expect major variation. The different Asian populations may have specific genomic factors that might affect response to drug treatment. In addition, there are cultural issues to be considered (Leung, 2007).

To give a concrete example, increased responsiveness to gefitinib among Asian patients has been reported (Park and Goto, 2006) and it has been emphasized that geographic and ethnic differences in toxicity and efficacy need to be considered in the design and comparison of clinical trials (Edelman et al., 2006). African-Americans appeared to experience less treatment-related toxicity with adjuvant chemotherapy than Caucasians (McCollum et al., 2002). Comparison of Chinese and Caucasian patients, revealed higher myelotoxicity in the former, possibly related to a lower body mass index with a higher percentage of body fat composition, and the popular practice of concurrent alternative medicine during chemotherapy (Ma et al., 2002). The observed higher incidence of hepatoxicity might possibly be associated with endemic chronic hepatitis B infection in China (Ma et al., 2002). Regarding the genetic impact, Asian populations are well known to demonstrate differences in penetration of polymorphisms (Hamajima et al., 2003). For example, significant ethnic variation in a thymidylate synthase gene regulatory element might have significant impact on pyrimidine homeostasis and drug therapy (Marsh et al., 1999). The ethnic distribution of NAD(P)H quinone oxidoreductase polymorphisms also has clear implications for anti-tumour drug development and use (Kelsey et al., 1997).

Late stage presentation is also a major influence on treatment efficacy and requires a specific focus on dealing with the associated problems and especially palliation. Naturally, all efforts should be made to guarantee that patients go to their physicians as soon as they find any symptoms but we also need to concentrate attention on the specific treatment modalities which are most effective for advanced cases and also how best to organize palliative measures.

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Drug Development

For the pharmaceutical industry, planning decisions are not only aimed at applications for regulatory approval, but also rely on an accurate clinical picture, and clinical epidemiology data are indispensable as a stimulus to clinical research relevant to cancer. Research information needs to be relevant to industry if we are to expect appropriate development of medical supplies, with all of the financial implications of developing a new drug. Unlike medicines for high blood pressure or diabetes, where there is a huge long-term market due to the chronic nature of the diseases, so that planning and insurance coverage are relatively easy to achieve, an antineoplastic drug for a specific cancer has a small market, and treatment is generally of short duration. Furthermore, as the world advances into the post-genome era, drug design is evolving rapidly, and development of a new antineoplastic agents is complicated by the need for coordinated use of different treatments, including molecular targeting. Individual tailoring of therapy demands that a comprehensive understanding of any particular patients biology is available.

As one response to the need for data taking racial differences into account, Hideyuki Akaza and other urologists from across Asia have formed a consortium to coordinate activities for effective treatment of prostate cancer (Akaza et al., 2007). It has been proposed that similar groups are set up to focus in the same way on other cancers, like adenocarcinoma of the breast, for example (Moore and Tajima, 2006). Evaluation criteria and safety standards will inevitably change, with attention to respiratory symptoms, the condition of the skin, blood toxicity and digestive organ conditions as aspects of Quality of Life. Therefore the present huge centering on Western medicine manufacture of antineoplastic drugs may not be appropriate from a global viewpoint. Using European and American data for dosage is of particular concern.

Considering patients in Japan, the drug lag time required for approval for sale of medical supplies is a significant problem. Although the private importation of non-recognized medicines is also increasing by the spread of the Internet, the individual choices involved clearly raise important questions. Who really takes responsibility for safety? It is national duty to check the validity and safety of a medicine suited to the constitution of the average Japanese. In the Japanese Ministry of Health, Labour and Welfare research-and-development division, there is pressure to keep up with technical innovation and state-of-the-art drug design technology to progress quickly in simultaneous development with the West. Genome-based drug discovery and application of nanotechnology with global standards incorporating the latest regulatory know-how is the way of the future. It is also simultaneously clear that there is criticism from international society about enjoying only benefits without contributing to risk. At the same time the high cost of performing clinical trials in Japan must be borne in mind (Kakizoe, 2003).

The Japanese National Cancer Center former President, Tadao Kakizoe, introduced "infrastructure improvement of an international common clinical trial must be needed focusing on cancer peculiar to Asia for the patient's medical treatment" as a subject for discussion by heads of various Asia National Cancer Centers at a conference held in Tokyo in March of this year. From discussions with leading representatives of industry, it appears that epidemiological information is particularly required for intrinsic factors responsible for individual differences in treatment effects, such as metabolic enzymes, and extrinsic factors inherent in the clinical situation in different countries. One example might be use of Western and Chinese medicines in combination. Illness can be acquired in different environments, and optimal integration of scattered information among the many countries of Asia where diagnostic technology and medical treatment levels also differ greatly will require effective coordination. A question therefore naturally arises. Who will be responsible for such an international endeavour here in Asia?

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