Policy Forum

DOI: 10.5582/irdr.2012.v1.1.10

Rare diseases research in China: Opportunities, challenges, and solutions

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Summary **Rare diseases research in China can be traced back to the 1980s. Currently, control of rare diseases has become a national concern. This paper describes developments concerning rare diseases in China with regard to epidemiology, case registration, basic research, establishment of medical networks, and orphan drugs. A national program for rare disease research is being implemented in China to promote international cooperation in the future.**

Keywords: Rare disease, China, development, epidemiology

1. Introduction

Rare diseases are also known as orphan diseases. Based on WHO criteria, China has rare diseases population of at least 10 million. The diagnosis and treatment of rare diseases has been a long-standing medical problem, yet it also provides a unique perspective to understand the body's physiological and pathological mechanisms. Many breakthroughs in the study of rare diseases have promptly led to new approaches to researching common diseases.

In China, public concern about rare diseases can be traced back to the 1980s, when some radiologists often met to discuss baffling cases. The plight of patients with rare diseases also attracted their attention, and the Chinese version of the concept of rare diseases was proposed by Professor Gui Lin of Fudan University and Professor Chenglin Wang of Peking University Shenzhen Hospital (*1*). The concept was soon confirmed by several well-known Chinese medical experts such as Professor Jieping Wu. With their supports, Professor Wang and his colleagues organized a series of national academic conferences on rare diseases. In 1994, the "Chinese Journal of Rare and Uncommon Diseases," China's first journal of rare diseases, was founded. However, the issue of control of rare diseases had not become a national concern until five years ago. Several academic societies that deal with rare diseases prevention and treatment have been established and many patients' advocacy groups, such as osteogenesis imperfecta organizations, have been created in regions like Shandong Province and the city of Shanghai. Legislation on rare diseases is also encouraged. That said, research on and control of rare diseases in China still faces enormous challenges.

2. Epidemiology

Several epidemiological studies of some rare diseases have been conducted in China. The National Surveillance System for Creutzfeldt-Jakob Disease was established in 2002. Thanks to this system, several organizations, which included the Chinese Center for Disease Control (CDC), obtained epidemiological data on Creutzfeldt-Jakob disease in 2008 (*2*). Continued improvements in China's national system of newborn screening have provided epidemiological data on rare diseases, which include congenital hypothyroidism and phenylketonuria. That said, the lack of important epidemiological data on the overall distribution, definitions and criteria, and types of rare diseases have severely hampered the introduction of national laws dealing with rare diseases.

To determine the distribution of rare diseases, Wang *et al*. (*1*) conducted a statistical study of 117 journals

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in clinical medicine published from 1978 to 1988. Their work covered 19,727 publications and 23,215 reported cases. They found that 10,147 cases (81.8%) were distributed among 12 regions, including Beijing, Shanghai, Hubei, and Zhejiang. Analysis based on the resident population at the time indicated that the rate of rare diseases detection per 100,000 population was 6.77 in Beijing, 4.65 in Shanghai, 1.86 in Hubei, 1.67 in Zhejiang, 1.56 in Jiangsu, 1.41 in Shandong, 1.28 in Hebei, 1.20 in Guangdong, 1.17 in Anhui, 1.10 in Hunan, 1.07 in Henan, and 1.01 in Sichuan.

3. Registration of cases of rare diseases

Forrest *et al*. (*3*) recently proposed the establishment of a global system for patient registration in order to promote epidemiological and basic research and improvement of clinical treatment of rare diseases. In China, a patient organization known as the China-Dolls Care and Support Association started voluntary registration in May 2010. So far it has registered 30 rare diseases and 3,000 cases, about 1,000 of which are osteogenesis imperfecta (*4*).

The current authors and their colleagues from Shandong Academy of Medical Science are proposing a system for registration of rare diseases. An online database for registration of cases of rare diseases has been created (*http://www.chinards.com*) (*1*). Case information is to be collected through a national network of 100 hospitals. Medical specialists will be registering clinical data on around 50 types of rare diseases. The system should be formally implemented in 2012.

4. Genetic identification of rare diseases

Due to the country's large population, there is a large population of patients with rare diseases in China, and the spectrum of diseases reflects regional characteristics. For example, ossification of the ligamentum flavum (OLF) is considered a rare disease in the West, but X-ray screening of a random sample of 1,736 residents of southern China revealed that OLF is not a rare disease in China (*5*). Therefore, China can draw on a large population of patients with rare diseases. Recently, the Beijing Genomics Institute (BGI) launched the "1000 Mendelian Disorders Project". Using exome sequencing, Zhang *et al.* (*6*) confirmed the pathogenic role of *NCSTN* mutations in acne inversa (hidradenitis suppurativa); Wang *et al*. (*7*) identified *TGM6* as a novel gene causing spinocerebellar ataxias; and Yang *et al*. (*8*) identified *ZNF644* gene mutations in high myopia.

These influential developments have greatly stimulated Chinese researchers' interest in genetic studies of the pathogens responsible for rare diseases. So far, the 1,000 Mendelian Disorders Project has initiated genetic studies of the pathogens responsible for over 150 diseases, and more than 50 projects are in the later stages of validation.

China's genetic studies of the pathogens responsible for rare diseases are not confined to new-generation sequencing. Zhang *et al*. (*9,10*) of the Shandong Academy of Medical Sciences conducted a genome-wide association study (GWAS) of leprosy given abundant samples. His team established the world's largest repository of leprosy samples, and they have identified 9 pathogenic genes associated with leprosy thanks to that repository.

5. Establishing networks for treatment of rare diseases

Creating a national network for rare diseases is a medical policy that should significantly reduce misdiagnosis and improve the level of treatment. A number of centers offering counseling on rare diseases have been established in major Chinese cities like Beijing and Shanghai, but a national network has yet to be created. Unlike in countries and regions such as Europe, North America, and Japan, there is a huge gap in terms of medical services in different areas of China. Only several large hospitals can ultimately diagnose rare diseases, so the needs of most Chinese patients are not met. Therefore, the pressing task is to improve China's level of care for rare diseases by creating a national network of diagnosis and treatment and to foster the ability of primary hospitals to recognize rare diseases.

6. Orphan drugs

In 1999, new drugs for rare diseases were included in China's "Regulations for Drug Registration", but orphan drugs have not been clearly defined and no policies for incentives have been adopted. Therefore, there is almost no development of drugs to treat rare diseases in China. Expensive imported drugs are a heavy financial burden on Chinese patients. In recent years, the development of drugs to treat rare diseases has attracted the government's attention. The development of orphan drugs was included for the first time in a national program for innovative new drugs in 2010.

7. Conclusion

In China, the level of care for common diseases such as tumors and cardiovascular disease has significantly improved. Now, the prevention and treatment of rare diseases is also attracting attention. More and more pathogenic genes are being successfully identified, so Chinese researchers have gained greater interest in rare diseases. More importantly, a growing number of clinicians, researchers, and health officials are aware of

the importance of resource allocation, epidemiological study, and clinical study of rare diseases in China. At the moment, a program for collaboration on rare diseases research is being implemented at the national level. This program is committed to promoting the study of rare diseases in China and will encourage international cooperation in this regard.

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(Received January 4, 2012; Revised January 31, 2012; Accepted February 1, 2012)