Current Status and Countermeasure of the Research on Rare Diseases in China

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Abstract: Through the description of the epidemic characteristics of rare disease, we have realized the properties of the rare diseases and disease spectrum. In the US and EU, legislation including the Orphan Drug Act (1983) and the Orphan Regulation No 141/2000 has brought many rare disease treatments into clinical practice. Many problems in China on rarity including: less society's attention; difficulties in obtaining timely, accurate diagnoses; lack of experienced healthcare providers; useful, reliable and timely information may be hard to find; research activities are less common; developing new medicines may not be economically feasible; treatments are sometimes very expensive. Emphasis is required to support appropriate research and development leading to better prevention, diagnosis and treatments of rare diseases. Conclusions: In this article , the primary tasks faced by China have been proposed: to call on the government to legislate as soon as possible; to establish information platform of rare diseases and orphan drugs for sharing the global rare diseases resources; to establish Rare Disease Outpatient Service(RDOPS) for improving the level of diagnosis and treatment; to carry out tertiary prevention of the rare diseases; to establish the rare diseases epidemiological surveillance system in our country.
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Definition of Rare Disease

The so-called 'rare diseases' are diseases that affect a small number of people compared to the general population. There are thousands of rare diseases. To date, six to seven thousand rare diseases have been found and approximately five new diseases are described every week in the medical literature. This number also depends upon the accuracy of the definition, accounting for 10 percent of all human diseases. The definitions of rare disease are different in different countries in the world, the World Health Organization (WHO) defines a rare disease as affecting 65/100 000~100/100 000 persons (Heemstra, H.E 2009). A disease is considered as rare when it affects 1 person per 2,000 in Europe, <200 000 people in the United States, <50 000 people (1 person per 2 500) in Japan and 1 person per 10 000 in Taiwan (Harari S, Cottin V 2012 and Iskrov G, Miteva-Katrandzhieva T 2012). In China, the Chinese Society of Genetic Medicine defines rare disease as 'diseases affect less than one over 500 000 and genetic disorders affect with less than one over 50 000 of the incidence in Newborn babies'. The rare disease problem caused by more and more attention.

Epidemiological characteristics of Rare Disease

1 Distribution.

The difference of the morbidity rate exists among different period、races and regions. While most genetic diseases are rare diseases, all rare diseases are not caused by genetic defects. There are very rare infectious diseases for instance, as well as auto-immune diseases and very rare poisonings. To date, the cause remains unknown for most rare diseases. However, this status may vary with time and also depends upon the area considered. For years, AIDS was an extremely rare disease, later it was rare, and now it is a more and more frequent disease in certain populations. In 2011, the highest of sub-saharan Africa's AIDS infection rate is 15% - 15%, China's AIDS infection rate is 1 ‰ (WHO 2011). A genetic or viral disease can be rare in one region, while frequent in another region. Leprosy is a rare disease in France, but common in central Africa. Thalassemia, is rare in Northern Europe, whereas it is frequent in the Mediterranean region. 'Periodic disease' is rare in France, whereas it is common in Armenia. 'Neglected Diseases' are rare in the development countries, whereas they are frequent in the developing countries, such as tuberculosis. There are also many diseases whose variants are rare.

2 Characteristics.

Rare diseases are serious chronic diseases, difficulties in obtaining timely, accurate diagnoses and are often life-threatening. According to report about 80% rare disease is hereditary disease, 90% is severe diseases and 50% affected children (Maiella S, Rath A 2013). For many rare diseases, signs may be observed at birth or in childhood, as in proximal spinal muscular atrophy, neurofibromatosis, osteogenesis imperfecta, chondrodysplasia or Rett

syndrome. However, more than 50% of rare diseases may only appear during adulthood, such as Huntington disease, Crohn disease, Charcot-Marie-Tooth disease, amyotrophic lateral sclerosis, Kaposi's sarcoma or thyroid cancer. Scientific and medical knowledge on rare diseases is lacking and remains to be improved. Neglected for a long time by physicians, scientists and politicians, there were no adequate political and scientific research programmes in the field of rare diseases until a few years ago (Bai JP, Barrett JS 2013). There is no efficient treatment for most rare diseases, but suitable care can improve the quality of life and increase life expectancy. Spectacular progress has been achieved for some diseases indicating that it is not time to give up, but rather to pursue and to intensify research efforts and social solidarity.

3 Disease Spectrum.

On the one hand, disease spectrum means a disease process composed of a fixed spectrum. Although the incidence of a certain rare disease is low, but the total population affected is huge. The research on single-disease process is more and more important, each spectrum is closely linked not separated. Diseases are generally developing from the former to the next. Disease occurring can be influenced by environment and other factors, especially in the early stage, such as 80% rare diseases are genetic diseases. Research of basic medicine is significance for understanding the pathogenesis, control of heredity and prevention and cure of rare diseases. On the other hand, disease spectrum means that many rare diseases are in order along with their risk stratification for people in an area. Rare disease spectrum varied in different countries and regions. The arrangement of rare disease spectrum can reflect the status of rare diseases distribution in a country or region, also can guide the relevant departments to determine the research priorities and to control the deployment.

4 Orphan Drugs.

Orphan drugs are those intended to diagnose, prevent or treat rare diseases or pathologies that are serious or life threatening, and whose development costs are superior to the expected return on investment. Orphan drugs definition is based on the epidemiological data for target disease and economics data for drug market in US, Japan, Australia, EU (Kanavos P, Nicod E 2012). In addition to this, rare rare disease also stressed the seriousness and treatment of irreplaceability in Japan and the EU regulations. After registered for orphan drugs, developers are can enjoy a series of preferential policies, such as the fund, tax breaks, expenses for assessment breaks, counsel help and market monopoly, etc.

With the development of science and technology, our ability to improve various disease has been greatly enhanced, of course including the rare diseases. Under the stimulus of orphan drugs policy, drugs which involve rare hereditary disease, malignant disease, children rare disease and other rare disease categories were developed to fill in the blanks, which potential beneficiaries are about 13 million in the United States. During 2001-2007.6, the FDA had been registed 1749 orphan drugs, but only 315 kinds had been approved on the market. The EU registered 450 orphan drugs in 2001-2007.6, but 37 kinds had been approved (Hughes-Wilson W, Palma A 2012).

Current Status of Rare Disease in China

1 Lack of social attention.

All orders of society have insufficiency social concern about significance for rare diseases prevention and control including government, media, clinicians, medical scientist and so on. The government do not attache great importance to the rare disease and its huge burden of family. At present, our country has not yet been introduced enough related legal protection on rare diseases and orphan drug. Health care and treatment for rare diseases is a human rights issue. According to the WHO definition of rare diseases incidence, we could estimate tens of millions patients involved in rare diseases in our country, due to the population base is very different, Henan province, as the most populous province, rare diseases prevalence was probably at around 100000. Focus on the question of rare disease, it is the embodiment of the state livelihood issues to make them enjoy the equal subsistence and health rights.

2 Difficulties in obtaining timely and accurate diagnoses.

Timely and correct diagnosis for rare diseases is extremely difficulty. The current domestic research on rare diseases is still in the initial stage, the practical value information can not be timely used in diagnostic, so that most of the rare disease has been the misdiagnosed or missed diagnosed. In China, more than 30% of the rare disease depends on 5-10 doctors; 44% patients were misdiagnosed as other diseases; 1 in 4 initial symptoms appeared is delayed by between 5 and 30 years; 75% of the patients' treatment is not correct and specifications.

3 lack of research funding.

About rare diseases, research activities are less common, owing to less relevant legislation, inadequate funding, few of rare diseases institutions, experts, specialized laboratory and talents. Scientific research achievements are mainly concentrated in looking for new mutations which has reported by foreign literature, while most of the rare disease research are still blank, so far, no independent research of rare diseases drugs registed in our country.

It can be said that rare disease resource has not been effective utilization in China.

4 Low satisfaction of the medication accessibility.

Due to the low marketing and low profit and high cost, there is almost no drug company would like to invest on the R&D, production and supply. During 1983-2007.12, there are 254 orphan drugs for 315 rare diseases, among which, 130 were available in China, accounting for 51.18%. There is no research on management strategies of improving access to orphan drugs in China.

Countermeasures for improving the status

These five points are provided as countermeasures to improve the health status of rare disease patients,

1 Responsibility of the government on rare diseases.

Risen awareness. Government should recognize that rare diseases create disparities and vulnerabilities in health status for affected populations.

Equality policies. Government should recognize the human rights issues inherent in rare disease health care and treatment across the lifespan. Specific programs and health insurance policies may be needed to guide those rights.

Support and funding for research. The society emphasise a need for a rare disease research policy that is both comprehensive (from basic to clinical research) and integrated (national level) and demonstrate recognition of the importance of investing in our country.

Specific counterbalancing policies. Government and health systems should offer incentives to encourage development of rare disease treatments and recognize problems with the research and development costs of such treatments. Government should establish the stimulating mechanism for the R& D, production, supply and use of orphan drugs. Regulatory requirements for clinical trials are important protections for patient safety, and it should be considered to approach these requirements differently for rare and very serious diseases.

2 Information Networks of Rare Diseases and Orphan Drugs.

Medical professionals are increasingly turning to the internet to help with diagnosis. The preferred tools are Google and PubMed, but while they are useful for finding published information on common conditions, they are harder to use to find good sources on rare diseases. Rare Diseases is usually defined as one that occurs in fewer than 1 in 2,000 people. A team in Denmark has developed a powerful new search engine dedicated to finding well-sourced online information about rare diseases. In an evaluation study FindZebra outperformed Google, making the case for specialized search engines for specialized tasks (Dragusin R 2013). The practical and perfect information networks should be established which adopt resources towards all aspects of rare diseases, including information resources, basic research, clinical care, treatment development and clinical research.

3 Rare Disease Outpatient Service (RDOPS).

The rare disease patients general face many difficulties such as nowhere to diagnosis. Clinician and patients themselves all lack the specialty and screening equipments in order to misdiagnosis and missed diagnosis. Although a few of tertiary hospital have focused on rare disease in the clinical research and treatment. At present, the department of health should set up specialized Rare Disease Outpatient Service (RDOPS), while organize related professional training to improve the knowledge of rare diseases. At the same time, the clinical medical personnel should enhance the awareness to aontact with RDOPS when find the suspected case.

4 Rare Disease Control and Prevention.

Primary Prevention (Health Education). Different heath education program should be established, according to special target. Health education may strengthen the public awareness in order to reduce cost. For medical personnel will be carried out nationwide special continue education program on diagnosis and treatment of rare diseases, improving the diagnosis and treatment level, so the life quality of patients will be better.

Secondary Prevention (Early detection, Early diagnosis and Early treatment). About 80% of rare diseases are caused by genetic defects, so prevention of the rare hereditary disease is very important, which the best strategy is to build three lines of defence including ‘genetic testing’, ‘prenatal screening and prenatal diagnosis’ and ‘the newborn screening’. Doctors should suggest genetics inspections and genetic counseling for male and female planning to be to give birth to a child. The pregnant women can be reduced the risk of birth by prenatal screening and prenatal diagnosis. Some rare diseases may be detected through the current genetic techniques (Gorzelany JA 2013). In addition, the clinical doctor may formulate individualized treatment for the child timely when found the diseases.

Third Prevention (improving the quality of life). Government should ensure three capacity of the medical and health institutions especially community outpatirnt clinic as following: the ability of first diagnosis on rare diseases; the ability of giving health education for patients and their families; the ability of providing effective drugs for rare patients. According to different properties of rare diseases, grassroots and

community medical service center can adopt different treatment strategies, provide continuing medical and health services in order to improve the rare patients quality of life.

5 Surveillance of Rare Disease

Definition of epidemiology standard. According to the epidemiological characteristics, definition of rare disease and orphan drugs should be made as soon as possible in our country.

Establishment of Surveillance. In recent years, some of the agencies have begun to detect some rare disease, for example, Creutzfeldt Jakob diseases (CJD) surveillance had been established in 2002 in China (Shi, Q 2007). The existing statistical data of rare disease is limited relative to the large group of rare disease in our country.

Epidemiologic methods in study of rare disease. Small clinical trials are necessary when there are difficulties in recruiting enough patients for conventional frequentist statistical analyses to provide an appropriate answer (Cornu C 2013). These trials are often necessary for the study of rare diseases as well as specific study populations e.g. children. More literatures have reported that epidemiologic investigation and statistics method are applied in rare diseases at home and abroad (Griggs, R.C. 1976, Guo, Z.M 2009 and Korn EL 2013).

CONCLUSIONS

Common themes can be identified. There is a need for China, as well as individual state, to recognize the need and importance of rare disease, which frequently leads to more understanding of common diseases and to invest in it. The diagnosis, prevention and treatment needs of patients with most rare diseases and conditions remain largely unmet despite the significant efforts of many stakeholders. All countries are encouraged to implement specific research and development activities within their individual capabilities. Only when this has occurred will all patients around the world have equal access to necessary interventions to maximize the potential of every individual.

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