Discussion on the Medical Ethics Committee in China from the Perspective of Open Multi-Regional Clinical Trial

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Abstract. This paper introduces the characteristics of multi-regional clinical trial and the benefits of China and expounds the positive significance of China's open international multicenter experiment. It also outlines the great challenge of the system of the medical ethics committee, discusses the problems existing in the committees in China, analyzes the causes of the problem, and adapts to give suggestions to perfect the system of the medical ethics committee, in order to guarantee the successful implementation of multi-regional clinical trial in China.

Introduction

Multi-regional clinical trial (MRCT) is also known as international multicenter clinical trial (IMCT). The medical community's more common understanding of multi-regional clinical trial is the simultaneous clinical trial conducted by multiple researchers at the same time in different countries and regions according to the same drug clinical trial protocol. [1] With multi-regional clinical trial, due to the diversity of ethnic groups in the test population, the breadth of the data is more conducive to the evaluation of the safety and effectiveness of drugs. MRCT directs that development. Its characteristics are:

a) It is possible to collect more subjects in a short period of time. MRCT has broken through the traditional research institution, a regional limitation, and can well meet the cardinal requirements of the large number of cases required by medical clinical trials.

b) MRCT can avoid the limitations of single research institutions and single interpretations with a wider range of representative clinical trial data with wide perspective, high credibility, broad-based conclusions. [2]

c) MRCT can improve the level of clinical trial design, implementation and interpretation of results. First, is the multicenter test to increase the probability of occurrence of test differences, as soon as possible to find and solve the test differences to provide a basis for comparison. Second, multicenter test can enable researchers from different countries or regions to cooperate with each other, brainstorming, and to learn from each other to improve the scientific applicability of the design. Third, multicenter clinical trial can be based on different countries and regions. The national characteristics, cultural level, eating habits and lifestyle differences can be targeted by the design of clinical trial program to reduce the impact of differences on the test to improve the homogeneity of clinical trials. The resulting experimental conclusions are more scientific and reliable. [3]

Compared with the western countries, China has a wealth of test groups, low research costs, a large number of large and medium-sized state-owned hospitals and pharmaceutical research institutions. It also has a huge pharmaceutical consumer market, and has become a global drug research and development (R&D) center for drug clinical trials. As early as 2002 Chinese government passed “Measures for the Administration of Drug Registration” which has proposed the multi-regional clinical trial concept, but the variety and the number of clinical trial has resulted in a plethora of strict restrictions. In order to meet the international trend of drug research, the State Council promulgated
the “Opinions of the State Council on the Examination and Approval System for the Reform of Drugs and Medical Devices” (hereinafter referred to as “Opinions”) on August 18, 2015, which really opened China to multi-regional clinical trial. Article 12 provides for: “Improvement of the clinical trial of drugs to allow the approval of new drugs in the territory after the simultaneous clinical trials, and to encourage domestic clinical trial institutions to participate in multi-regional clinical trial, in line with the requirements of the test data that can be registered in the application and use” [4]

The “Opinions” signifies that China's clinical trial market is fully open to the international community, which will have a positive effect on China's drug research and drug production in line with international standards, and also challenges China's (slightly behind) medical ethics committee system. The ethics committee, as an independent organization of medical professionals, legal experts and non-medical staff, has become the entity ensuring that the safety, health and interests of the patient are met by verifying that the clinical trial program and the attachment are in line with human morals, and has become an important system of protection.

Benefits

On January 30, 2015, China Food and Drug Administration (CFDA) issued the “Guidance on Multicenter Clinical Trial (for trial implementation)” (hereinafter referred to as “Guidance”) which began implementation on March 1, 2015. The Guidance aims to set clear requirements for MRCT involving study sites in China. The Guidance pointed out: “Drug research and development has become increasingly globalized, for drug registration of international multicenter drug clinical trials, and has been registered with the technical requirements of the International Advisory Committee (ICH) area to the non-ICH. Global research and development as a shared resource development model, can reduce the unnecessary duplication of clinical trials, shorten the regional or national drug market delay, and can improve the availability of new drugs.”[5]

a) It speeds up the pace of China's introduction of new drugs. Historically China's long-term-use foreign drugs have entered the Chinese market mainly by imports, innovative products, and through the introduction of generic drugs. In accordance with the provisions of China’s current drug laws, imported drugs must be listed before entering the country. To import must be approved to carry out clinical trials, and then review, which takes a long time to wait, as little as 4-5 years, as many as 7-8 years, resulting in a large number of foreign patients with good foreign demand in urgent need of innovative drugs which cannot enter domestic market. [6]To carry out multi-regional clinical trial is to speed up the introduction of foreign drugs. It shortens the time of foreign drugs in domestic testing to better address the medical needs of domestic patients.

b) It speeds up the innovation of Chinese new drugs. International multicenter trial and global developed countries have brought together new ideas and training to improve the technical level and management level of domestic researchers, data managers and ethics committees. Clinical research can also keep up with the international front, in the domestic population to accumulate more pharmacodynamics, efficacy and safety data, the formation of local innovation base. By participating in the design of large, clinical, randomized, controlled trials, learning and mastering the frontier clinical research information can enhance the domestic clinical researchers and their international counterparts in the right to speak. It speeds up China’s development from generics through transformative, to innovative finished drug products.

c) It accelerates China's pharmaceutical industry’s conformance with international standards. Conformance with international standards is the inevitable trend of the development of China's pharmaceutical industry. With China's participation in multicenter clinical trial and international research cooperation, the relevant Chinese scientific systems and norms is a test, and we can find the gap between the legal system in China and advanced countries. Domestic clinical trial institutions applicable to the international advanced management practices is a pressure, but is also an opportunity. China's clinical research institutions need multi-regional clinical trial to discover non-standard behaviors which will inevitably occur. China will not always be just a simple drug sales
market. With the strengthening of domestic pharmaceutical enterprises, research and development, environmental and technical strength, and a clinical trial management system with international standards, China will integrate into the drug research and development, production and sales in the global market.

**Challenges**

The development of multi-regional clinical trial has brought unprecedented opportunities for the development of Chinese medicine. It also expresses the seriousness of the current Chinese system of drug clinical trial management as “Good Clinical Practice” (GCP) and its related supporting systems, especially the medical ethics examination committee system.

**History of China's Medical Ethics Committee**

In 1987, after the visit of Chinese scholars to the United States and Japan, the term “ethical committee” was introduced, and the prelude to the system of ethics was begun. In 1995, the Ministry of Health issued a document on the clinical pharmacological base of the guiding principles for the first time in the form of departmental rules and regulations, the arrangements for the work of the ethics committee. From the beginning of 1990s, learned foreign concepts combined with China's basic national research and development, China formed the basis of the medical ethics committee system. The system set terms of reference, work content, code of conduct, review procedures and regulations for a full range of Chinese ethics committees.

In 1998, the Ministry of Health set up the first Ethical Committee on Biomedical Research in China, which is responsible for the ethical review and training of domestic biomedical research projects and international cooperation involving human research. The Committee was abolished in 2000, the same year as the establishment of the Ministry of Health Medical Ethics Expert Committee, which is given the advisory function of the commission, and is the only national government level of the medical ethics committee organization.

At the same time the domestic medical science research institutions and medical institutions within the research institutions have set up their own medical ethics committees. Their main duties are to conduct ethical examination of the medical research of the scientific research institution; conduct ethical examination of medical clinical trial on the human body; ethical evaluation and examination of auxiliary reproductive medical technology and medical case; and to carry out medical ethics teaching and training.

The medical ethics committee as set by the medical and health care institutions is now one of the most extensive and complex systems in China. It is mainly responsible for clinical medical trials and medical ethics review, new medical equipment, new medical technology, clinical application of medical theory, medical personnel, medical ethics education and training, medical disputes, ethical advisory services and so on.

**Status of China's Medical Ethics Committee and Current Issues**

China's ethics committee system is currently concerned with national policy requirements, not protecting the rights and interests of patients. With its focus on training and education, its intent to protect patients is diluted. In many institutions and hospitals within the purview of the ethics committee, its legal positioning is not clear, the nature of the organization is difficult to define, neither the administrative body nor the institution; neither social groups nor academic institutions.

Because of the serious lag in the medical ethics committee system, and the lack of legal effect, the government, the public and even the medical personnel, are unfamiliar with it. There is much chaos in medical experimentation, especially in the drug clinical trials, an event that damages the rights and interests of the patient. Patients in clinical trials, unaware or deceived to accept test drugs, are a serious violation of the international community medical ethics system and the recognized “informed consent” principle, having been deprived of their right to self-determination, resulting in the patient’s injury or even death. It can be seen that the current medical ethics committee of our country, whether
from its institutional system, or review of the monitoring mechanism, the ethics committee to review the professional level and experience, or the number and quality of employees, are not enough to deal with the fast-growing multi-regional clinical trial reality.

a) China's current ethics committee system, the lack of legal top-level design, its establishment, operation, responsibilities, lack of effectiveness of legal guarantee, lack of mandatory ethics committee review procedures, and standards are not uniform norms. Because of the failure of the ethical review and supervision system, the effectiveness of the examination results cannot get social validity.

b) Ethical review of the ethics committee lacks a clear access mechanism. Its members and researchers lack effective training, so the professional level and structure are uneven. The ethical review of the program lacks the necessary checks and balances on the ongoing review of the study, so there is a great deal of randomness and the quality of the review lacks effective assessment and regulation.

c) At present, most of the domestic ethics committee and clinical trial institutions belong to individual hospital management. According to the survey of 199 hospital ethics committees in 2007, 59% of the members of the ethics committee were served by the president or secretary of the institute, and 29% were appointed by the department.[7] Since the leader of the ethics committee is both referee and player, the ethics of its independence is questionable. However, the “Helsinki Declaration” states that “the ethics committee must be independent of the researchers, donors and should not be affected by other undue influence.”

d) Because of the lack of publicity and education of the ethics committee system in our country, the public and even some scientific and technical personnel lack knowledge of the ethics committee review system. Many ethical reviews that appear in the information provided by researchers are incomplete, and lack authenticity.

Analysis of the Causes of the Problem

China's ethics committee system has been in existence more than 20 years. Compared with developed countries, there is no significant difference between establishment documents, some of which are even replicas of those of developed countries, but the implementation can be very different. There are many violations of principles of medical ethics, such as:

a) The concept of medical ethics has its roots in Western philosophy. Rational, legal, normative concept, and the concept of Western ethics, required the establishment of a modern medical ethics system in the Western countries. Because the Chinese people for thousands of years were guided by “Confucianism”, “Taoist” and “Buddhist” thoughts, the formation of a unique Oriental world view still exists. The development and implementation of the medical ethics committee system will inevitably produce differences, and the domestic medical ethics committee system has a significantly different “soul”.

b) For institutional reasons, the research of medical science in China has long been scientifically dominated by the development of ideas, the implementation of government administration and restraint, and the lack of awareness of medical ethics supervision. Chinese people are accustomed to supervision and government oversight, so that the ethics committee supervision is only a symbol. This understanding is pervasive among ordinary civilians, some medical experts and government officials. Many times, the domestic ethical committees attached to research institutions, is just a business card credit for some hospitals and research institutions. Medical science in the long-term administrative management model is also used to validate the administration of the Chief executive, especially in the interest of disputes to the implementation of the medical ethics committee system in an embarrassing situation. If the clinical trial is correct but does not coincide with the medical ethics review, the guiding ideology of development priorities prevails.

c) There is a national lack of medical science and medical ethics knowledge of publicity and education. When a post appeared on a number of websites suggesting that a large number of “Chinese people have been turned into lab rats for foreign medical experiments”. [8] Chinese people began to
fear and conflicts arose with medical clinical trials including China’s open multi-regional clinical trial. Although there is a large enough base to choose clinical trials from, people have generally resisted and refused. Although a large number of clinical trials projects came to China, they cannot normally get qualified subjects, leading to the abuse of the informed consent principle. There is a lot of concealment, deceit, and this violation once disclosed, causes even more resentment and conflict, resulting in a vicious circle.

Suggestions

In order to improve our medical ethics committee system, here are some suggestions to face the challenge:

a) Accelerate the top down review of the design of the Chinese ethics committee system.

Establish the legal status of the medical ethics committee. The vast majority of the current committee is in a spontaneous state. There is no independent legal representation so the ethical committee’s legal status is established from the superficial rather than the substantive review. It is recommended that the medical ethics committee be changed to the registration system, it should establish the standards and conditions for the establishment of the ethics examination committee, and should insist on the examination of the qualifications of the selected personnel.

There should be legal review of the behavior of the medical ethics committee and remind its members of the consequences of the law. Change the opinion that the ethical committee's recommendations are only suggestion, and require the ethical committee to make recommendations based on the legal issues and consequences. Channels should be implemented to ensure fairness and impartiality to all parties involved in clinical trials.

Scientifically define the content and scope of the review of the medical ethics committee. The medical ethics committee should review ethical content and leave the review of medical science issues to scientists. Content design should focus on the ethical requirements of the test, the social evaluation of the test benefits, the implementation of the principle of informed consent, the protection measures and the implementation of the relevant content. The development of ethical review of the operating norms, should have particular emphasis on the clinical trial process set. It should also pay attention to the process of review and the rectification of the establishment of procedure, in order to ensure the smooth conduct of medical experiments and to ensure implementation of ethical principles throughout the test.

b) Regulate the institution of the medical ethics committee.

Currently there is a fundamental conflict of interest in the makeup of the medical ethics committee that belong to hospital management. We should change existing domestic ethics committees and clinical trial institutions to adhere to international principles of independence. It is recommended to set up an independent third party to review the findings of the ethics committee. China's national situation may require the design of a national medical ethics expert committee, central ethical review committee and regional ethics review committee. The three of them are intended for guidance, and should set up a possible error correction mechanism among the three.

There should be established education and training standards of medical ethics committee members to strengthen and enhance the science of ethical review, and the necessary medical science knowledge among committee members.

Establish an effective medical ethics committee to assess and supervise the mechanism. Establish the registration authority for the ethics committee of the regulatory body to develop a project quality assessment. There should be annual assessment of the ethics committee quality evaluation mechanism to review the progress of the committee. The medical ethics committee should establish principles of fair practice, and establish parameters for punishment of violations of set standards.

c) Increase the education and publication of the medical science and medical ethics committee findings.
It is not just the responsibility of the government to educate and publicize scientific results of medical clinical trials, it is also incumbent upon the medical ethics committee to increase medical science knowledge and specifically of medical clinical trials to the nation at large. The Nation needs to teach scientific knowledge, increase the ability of scientific identification, and consciously integrate into the global tide of science and technology. We need to correctly understand the medical science behind medical experimental trials, to eliminate people's fear.

Conclusion

China's comprehensive multi-regional clinical trial has great positive significance for the development of China's pharmaceutical industry and the world. We can accelerate the development of China's pharmaceutical industry and ensure that it is in line with the standards of the international pharmaceutical industry. But China's medical ethics committee system has brought great challenges from the MRCT, such as the institutional system, the monitoring mechanism, the professional and experience level, the number and quality of employees, all of whom are not enough to deal with the rapid growth of the MRCT reality. Therefore to supplement the establishment of the legal system, perfect committee institutional arrangements, and enhance the scientific preparation of the whole people, we are creating a more perfect system of the medical ethics committee to guarantee the successful implementation of the multi-regional clinical trial.

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