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REVIEW

Current Situation and Progress in Integrative Medicine in China

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ABSTRACT In the past 50 years, integration of traditional Chinese medicine and Western medicine, known as the Chinese version of integrative medicine (IM), has achieved significant developments. In this article, the present situation and progress in IM development in China are summarized from the aspects of IM application, policy making, scientific research, education, academic exchanges, and its future development. With continuous support from the Chinese government and successful scientific achievements in the past 50 years, the authors believe that IM will be moving forwards to a full globalization.

KEY WORDS current situation and progress, integrative medicine, China

Integrative medicine (IM) is a new term that emphasizes the combination of both conventional and alternative approaches to address the biological, psychological, social and spiritual aspects of health and illness. It emphasizes respect for the human capacity to heal, the importance of the relationship between the practitioner and the patient, the collaborative approach to patient care among practitioners, and the practice of conventional, complementary, and alternative health care that is evidence-based. In the 1950s, some doctors of Western medicine (WM) in China were systematically trained in traditional Chinese medicine (TCM), while some TCM scientists were systematically trained in WM. At that time, a new discipline called integrated TCM and WM was primarily formed in China. This primary discipline would be the Chinese version of IM. In 1981, the Chinese Association of Integrated TCM and WM (now renamed as Chinese Association of Integrative Medicine, CAIM) was established. In 1983, the first issue of the Chinese Journal of Integrated Traditional and Western Medicine was published. The journal has been published monthly since then. At present, IM has become a mature and independent academic discipline, and there are about 300 IM hospitals, 30 IM departments in medical universities, and more than 100 IM-specific institutes across the nation. Many IM projects have been funded by the government, and great progress in IM research has been made[1].

IM in China

Public recognition of IM and the number of patients and/or doctors who accept IM are important for the development of IM. A national survey in China was conducted through questionnaires in 2004 by CAIM with the support of the State Administration of Traditional Chinese Medicine of the People's Republic of China (SATCM)[2]. Various divisions of CAIM in each province participated in this arduous task, including 56 IM hospitals and 12 IM research institutes. All together, 19 824 medical professionals were investigated. The results showed that 91.21% and 93.52% respondents favored IM as the best diagnostic method and therapeutic method, respectively. Of all the patients who had once gone through TCM, WM and IM therapies, 68.85%, 65.45% and 71.20% respondents most appreciated IM, IM hospitals and IM therapeutic treatments, respectively. Most of the 6 595 respondents held that the optimal scientific research strategy in TCM should be done by integrating modern medical research methods (2 380 cases) or modern scientific methods (2 920 cases). These results indicate that IM reflects patients' social needs and doctors' aspirations in China.

Clinical practice in TCM hospitals usually includes IM approaches. Regarding disease diagnosis in TCM hospitals, patients obtain both WM diagnosis and TCM syndrome differentiation. For treatment, patients mainly obtain herbal medicine. However, they may also receive some WM treatment depending on their condition. In general, TCM practice could be considered as IM practice.

Clinical practice in the WM hospital usually follows a biomedical model. There is a department of TCM in most WM hospitals in China, and TCM doctors are asked to participate in the treatment for some patients (as requested by patients or by WM doctors). In China, IM approaches are included in clinical practice in many WM hospitals.

Clinicians in IM hospitals definitely focus on IM

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approaches in clinical practice. More importantly, a number of ongoing IM clinical studies are aimed to set up guidelines for IM clinical practice and to show the advantages of IM approaches.

IM Policies in China

For a long time, Chinese governmental authorities have been doing their best to create a positive environment for the development of IM. "The Regulations of the People's Republic of China on Traditional Chinese Medicine" (Abbr. as Regulations) was adopted at the Third Session of the State Council on April 2, 2003 and carried out on October 1, 2003. "Regulations" indicates clearly that the nation must protect and support TCM development, pay equal attention to TCM and WM, and encourage TCM and WM doctors to learn from each other and complement each other for IM development. Following the "Regulations", SATCM issued a document called "Suggestions on Strengthening the Work on Integrated Traditional and Western Medicine" on December 5, 2003 to address the policies more clearly for IM development in China. Premier WEN Jia-bao proposed to develop TCM actively in the Government Work Report at the Second Session of the 10th National People's Congress at 2004. He also wrote down "Performing IM and Developing TCM" for the 50th anniversary of the Journal of Traditional Chinese Medicine. In 2006, a total of 16 ministries in China together issued a guideline for TCM modernization, in which the creation of new medicine (the combination of TCM and WM) was listed as the key aim for TCM modernization. Dr. CHEN Zhu, the Minister of the Ministry of Health, emphasized at the Senior Pacific Forum for Health in 2007 that scientists should break the obstruction between TCM and WM gradually. He predicted that the basic theory of TCM would have far-reaching effects in medicine. On April 20, 2008, Dr. CHEN Zhu at the 6th National General Congress of CAIM presented a good example describing the advantage of IM. He said that everyone must know that one plus one should be equal to two. Thus, TCM plus WM (or IM) should contribute more to public health. Recently, SATCM has been planning to construct a crop of research hospitals, and more IM hospitals will be included. "The Eleventh Five-Year (from 2006 to 2010 year) Development Program of TCM" focuses on inheriting and innovating with TCM, and advocates the integration of TCM and WM. All of these policies provide strong support for IM development in China.

As a government-supported academic organization, CAIM has more than 60 000 members, 45 specialized committees, and 31 local associations. As an important advisory academic organization, CAIM has contributed much to IM policy making.

As part of scientific policy, the awarding system is important for academic development in China. The national academic awarding system places a great amount of emphasis upon IM research. Approximately 6-8 TCM projects receive the National Science and Technology Development Prize each year, and about 40 TCM projects have received the China Association of Chinese Medicine (CACM) Prize, with majority of the projects being on IM research. Moreover, CAIM established the "Science and Technology Prize on Integrative Medicine" in 2005, and 37 projects were awarded in 2007. These measurements ensure the progress of IM in China.

IM Scientific Research in China

The Chinese government has offered a large amount of scientific research funding for IM research. The Major State Basic Research Development Program of China (the 973 Program), offering the highest level of basic research grants, has funded several projects in the TCM field, and IM approaches constitute the most important methods in all of these projects. Recently, the National Natural Science Foundation of China (NSFC) has been accepting about 2 000 grant proposals in the TCM field every year, and among them IM research is the most important. Furthermore, IM approaches are included in almost all proposals. The Ministry of Sciences and Technology and SATCM have special funds for TCM research, including IM or IM approaches.

With support from the government, there are many well-known achievements in IM research in China and abroad, such as acupuncture complementary to anaesthesia, and the treatment of leukemia, Japanese B encephalitis, cardio-/cerebrovascular diseases, acute abdomen, burns and fracture with IM approaches[1]. Some new concepts and theories related to IM have been created, such as the theories of activating blood circulation to resolve blood stasis, etc.

IM Clinical Practice Mode

In the past few decades, the "combination of disease identification and syndrome differentiation" mode in clinical practice has been gradually formed and widely used for the treatment of various diseases. The mode refers to applying disease identification in biomedicine and syndrome differentiation in TCM, and treatment with biomedicine drugs and TCM herbal formulas. Combination of disease identification and syndrome differentiation in TCM can not only improve the standardization of TCM diagnosis and herbal therapeutic effects, but also supply more information for biomedicine.

The disease diagnosis mainly depends on having information on etiology, pathology and illness location.

Many clinical manifestations, including subjective symptoms, tongue figure and pulse picture, are excluded. However, these clinical manifestations are important for TCM syndrome differentiation. It has been proved that both TCM and WM are effective in clinical practice, and thus the combination of diagnostic information both in TCM and WM would be reasonable and useful. The research on TCM syndrome differentiation is one of the cut-in points in IM research, and this type of research may improve the clinical application of IM approaches[3]. Take for example the clinical manifestations in rheumatoid arthritis (RA) in the view of TCM syndrome differentiation, the diagnosis in biomedicine is focused on the joint pain and other immunological evaluations. TCM syndrome differentiation is focused on the other symptoms, such as thirst, dizziness, and other signs, including the tongue figure and pulse picture. Clinical observations show that there are some positive relationships between the TCM symptoms and the biomedical immune response. Results suggest that TCM symptoms may contribute to the disease development analysis and therapy selection[4]. In 2003, based on the disease diagnosis in Western medicine and syndrome differentiation in TCM, great success was achieved in acute respiratory syndrome (SARS) prevention and treatment in China[5]. In fact, most good effects in clinical practice are obtained through this mode of practice, as exemplified by good efficacy obtained in the treatment of coronary heart disease[6, 7], cerebrovascular diseases[8] and other diseases with the clinical practice of IM.

An Increasing Number of Randomized IM Clinical Trials

One of the reasons why most people accept IM is that IM shows positive clinical effects. Many clinical studies have demonstrated that IM is effective for the treatment of cardiovascular diseases[9], cerebrovascular diseases[10, 11], acute abdomen[12], bone fracture[13], acupuncture anesthesia[14] and other diseases.

Recently, more and more randomized clinical trials (RCTs) in IM have been conducted to demonstrate and confirm the clinical efficacy of IM in clinical practice. Li, et al[15] took a survey on TCM-related clinical trial reports based on Consort (Consolidated Standards for Reporting Trials, 2001) items. Four Chinese universities of TCM (Beijing, Shanghai, Guangzhou, Chengdu) had published a total of 960 clinical trial reports from the year 2000 to 2005, of which 365 (38.02%) were RCT reports. The Chinese Journal of Integrated Traditional and Western Medicine published a total of 1 874 clinical reports from 1999 to 2004, of which 1 288 (68.73%) were RCT reports. Thirteen TCM Chinese journals surveyed had published a total of 26 263 clinical reports from 1999 to 2004, of which 7 422 (28.26%) were RCT reports. The proportions of RCTs for each year were 18.59%, 23.94%, 27.49%, 28.75%, 33.04% and 35.90%, respectively, showing a year-on-year increasing trend. The results described above indicate that the number of RCT reports on TCM has been continually increasing, with improved quality, during the past few years.

More and more IM researchers have realized that the quality of TCM clinical trials will affect the objective evaluation of the clinical effectiveness of TCM, and it has become one of the most significant obstacles of TCM internationalization. Hence, in IM clinical research, the RCT method is the main study means. Recently, some RCTs on TCM with IM approaches have gained significant achievement, such as the studies on restenosis after percutaneous coronary intervention[7], the treatment of SARS with IM[16], the treatment of acute pancreatitis[17] and acute promyelocytic leukemia with IM[18], TCM treatment on cancers[19, 20], IgG nephropathy[21], hypertension[22] and etc. Good effects obtained from IM clinical studies have resulted in a wider application of IM.

Methodology for IM Clinical Research

The clinical efficacy of a drug or therapy is not only based on the effective rate in a randomized controlled trial, but also based on more specific indicative findings on the drug or therapy with multiple clinical trials. Multiple consecutive clinical trials aim to refine the indications, which is one of the more important methods in IM clinical research[23-25]. When a clinical trial is conducted, we have a specific indication (usually a disease) designed in the case report form, and then we get the effective rate of the drug or therapy. Moreover, it is possible to find something more from the results of the trial to guide the next clinical practice. For example, if a drug or therapy has obtained an effectivity rate of 40% for a specific disease treatment in a well-designed clinical trial, it means that 40% of patients could be treated effectively with the drug or therapy, and 60% of patients could not be treated effectively. In the next clinical practice, if we select cases with similar characteristics to the 40% of patients in whom the therapy was effective, a higher effective rate would definitely be obtained.

One thing important in the first clinical trial is to compare the differences between the effective cases and ineffective cases, and to try to determine which are positively or negatively related to efficacy. Theoretically, a correlation can be found if enough information is obtained. In a clinical trial, the case report form mainly contains diagnostic or other efficacy-related information, which are needed for diagnosis and efficacy evaluation. However, more information can be obtained from the patients. Many diagnosis-irrelevant symptoms (such as thirst in rheumatoid arthritis, and heavy limbs in diabetes), diagnosis-irrelevant pathological, immunological

and biochemical changes, and pharmacometabolic, pharmacogenomic and pharmacoproteomic information, all of which aim to realize individual therapy, should be obtained to compare the effective and ineffective cases since they share the same diagnosis. All information may be useful when further analysis using mathematical and statistical evaluations to find efficacy-correlated information are done.

A more specific indication can be found by adding the efficacy-correlated information in the inclusion and exclusion criteria in the next clinical trial. The efficacy in this clinical trial can be enhanced by comparing it to the first trial, since the indication is more specific to the drug or therapy even if both clinical trials share the same diagnosis and efficacy evaluation criteria. Similarly, another clinical trial can be conducted based on the results, and more clinical trials may be needed to repeat the process.

Overall, it is more important to find a more specific indication of a drug or a therapy (even if its effective rate is not high) than to find a new drug or therapy since it is impossible to find a new drug or therapy with an effectivity rate of 100%. The most important task for medical research professionals is to find the right patient for the right drug or therapy.

IM Clinical Practice Guidelines

Since more IM clinical studies have been conducted, and more scientists have participated in IM research, it is natural to call for clinical practice guidelines (CPG). CAIM has contributed very much to formation of the CPG stipulating on the use of IM. At present, the CPG of IM on SARS, peptic ulcer, gastritis, liver fibrosis, small cell lung cancer, ischemic cerebrovascular disease and coronary heart disease have been issued by CAIM, CACM and SATCM.

Progresses in Basic Research on IM

IM basic research focuses on the exploration of the relationship between disease identification in WM and syndrome differentiation in TCM, the TCM diagnostic information (such as tongue figure and pulse picture), and efficacy and TCM syndrome information.

The research on blood stasis syndrome and the promotion of blood circulation to remove blood stasis, which won the first prize of the National Sci-Tech Progress Awards, mainly explored the scientific connotation, basic treatment regularity and action mechanism of blood stasis. Promoting blood circulation to remove stasis was proposed as the key principle to treat coronary heart disease all over China and showed positive effects in the prevention and treatment of restenosis (RS) after percutaneous coronary intervention (PCI) and the recurrent angina[6, 26].

The research on Shen (肾) in TCM demonstrated that patients of Shen-yang deficiency would have been diagnosed with hypoadrenocorticism in the early 1950s. It has been proved that the pathological chain of TCM Shen-yang deficiency syndrome includes the hypothalamus[27]. Furthermore, the neuro-endocrine-immune network is believed to be involved in the function of TCM Shen, and herbal preparations for tonifying Shen can regulate many molecular networks related to the hypothalamus[28, 29].

The scientific mechanism of TCM syndrome differentiation is one of the cut-in points in IM research[30]. Applying modern bioinformatics and biostatistics methods may reveal the correlation between TCM syndrome differentiation and WM diagnosis identification. Literature and data mining, factor and cluster analysis, as well as other correlation analysis may demonstrate the relationships between syndromes and diseases. Previous studies have shown that factor analysis could be used to find the correlation between TCM symptoms and WM efficacy responses in RA patients[31] so as to analyze the role of the clinical characteristics in TCM and WM in RA classification[32], and to clarify the value of TCM diagnosis information in patients with Helicobacter pylori infection[33]. All of these studies further explained that TCM syndrome differentiation from the viewpoint of modern scientific and technical backgrounds could contribute more to the development of IM from the point of view of basic research.

In addition, there are some new techniques applied for TCM four-diagnosis modernization research, such as computer and imaging techniques for tongue figure determination and pulse picture determination. Tongue figure and analysis instruments have been developed to acquire digital color tongue images[34]. Some pulse picture instruments have been produced and applied in clinical practice although it is not common[35, 36].

Application Research of IM Is Mainly Focused on Herbal Formulas

Herbal prescription is one of the characteristics of TCM in therapeutics, and is based on TCM syndrome differentiation. Determining the herbal formula is a key part of IM application research, since the research not only helps further clinical application, but also initiates the discovery and development of new herbal medicine products. For example, the application of an Arteannuin complex prescription can shorten the course of malaria and the fourth generation Arteannuin complex prescription (Artequick) has been developed[37].

Chin J Integr Med 2008 Sep;14(3):234-240

Studies on Shengmai Powder (生脉散), which has the activity of tonifying qi in TCM, have shown that the formula principle is pharmacologically based, and the composition ratio has been optimized with scientific data[38]. Studies on Qingkailing Injection (清开灵注射液) have clarified its active components, and different combinations of the active components can result in different pharmacological activities. A comparison between a single active component and combined components (such as baicalin and jasminoidin) showed that the activities on focal cerebral ischemia-reperfusion injury were different and that the combination was more effective than each one alone[39]. Recently, a study on promyelocytic leukemia treated with the Chinese medicinal formula Realgar-Indigo naturalis has made a breakthrough. The pharmacological pathways have been explored at the molecular, cellular, and organic levels[40]. Since many herbal products have been used in clinical practice, it is essential to have a high level of quality control for TCM herbal products. Taking the Shengmai Injection (生脉注射液) as a target herbal product, the fingerprint platform has been developed for Shengmai Injection, and furthermore, this technique has been proposed to be used as quality control for all botanical drugs[41].

For the pharmacological evaluation of herbal products, some technical platforms have been developed. For example, the enteric mucosal immune response platform has been used for the immune regulation of herbal products, especially for herbal polysaccharides[42, 43]. At the same time, many studies are applying biological and chemical techniques to explore the pharmacological activities and to clarify the chemical components of single herbs, such as the metabolism regulation of *Radix Astragali*[44], and new chemical constituents of *Radix Polygoni Multiflori* after processing[45].

In addition, animal models for the TCM syndrome have been explored in recent decades. There are about 40 animal models developed for both IM basic research and pharmacological evaluation. The combination of the disease-syndrome animal model has been explored, such as the animal model of RA with Shen-deficiency syndrome[46]. This type of animal model may contribute more to basic research in IM if it is fully justified in solid scientific exploration.

IM Education in China

The Academic Degrees Committee of the State Council assigned IM as one of the disciplines in biomedicine in 1980. The Hunan College of TCM compiled the first edition of IM textbooks (clinical serials) for the 7-year IM educational system in 2003. The first edition of programmed teaching materials on IM (including 16 books) was officially published in 2005. Marked by the official publication of textbooks on IM, the educational and training system for IM is now basically formed.

Until 2007 there had been 7 universities of TCM with the 7-year IM educational system, 9 medical universities and colleges with the 5-year IM educational system, 5 medical universities and colleges with the junior IM educational system, and 3 academies with the secondary technical IM educational system in China.

More than one thousand IM medical students have graduated in the past few decades. The Capital Medical University in Beijing set up the Department of IM in April, 2008. Some comprehensive universities (such as Peking University, Tsinghua University, Tongji University, Sun Yat-sen University, Shanghai Jiaotong University, Fudan University, Hongkong University, Hongkong Baptist University, The Chinese University of Hongkong, and the Macao University of Science and Technology) are actively developing IM education.

IM hospitals are main clinical practice training organizations. The first IM hospital in China was established in the early 1980s. There were only 21 IM hospitals in 1988. The number had since increased to 63 in 2000 and 207 in 2002. Twenty-one IM hospitals were approved as national key hospitals by SACM up to 2007. In addition, more than 40 training programs each year are organized by CAIM, SATCM, CACM, and other associations. Besides, Training Classes on Learning Traditional Chinese Medicine for doctors of WM are organized regularly all over China.

Wide Academic Exchanges of IM

Academic exchanges on IM have become more active and academic conferences on IM have become a hot topic. For example, CAIM organizes nearly 40 domestic academic conferences each year. CACM also organizes about 50 conferences each year and many of them are involved in IM. The First World Integrative Medicine Congress was held in Beijing in 1997, with participants from 24 countries and regions. The Second World Integrative Medicine Congress was held in 2002, with more than 1 000 participants from 27 countries and regions. In 2007, the Third World Integrative Medicine Congress was held in Guangzhou. More than 1 100 medical doctors and scientists on IM attended the congress, and among them, about 300 were from abroad. At the same time, more and more Chinese IM scholars went abroad for academic exchanges.

The quality of journals on IM in China has been improving greatly. The Chinese Journal of Integrated

Traditional and Western Medicine now publishes two language editions, including Chinese and English. The English edition (Chinese Journal of Integrative Medicine) was included in the "Science Citation Index-Expanded" (SCI-E) in early 2008. Moreover, more than twenty-five journals on IM have been issued in China. The Chinese Journal of Integrated Traditional and Western Medicine, the Chinese Journal of Integrative Medicine and the Journal of Chinese Integrated Medicine are indexed in Medline.

Recently, many books about improving the clinical effect of IM have been published. These books include "Practical diagnostics and therapeutics of integrated traditional Chinese and Western medicine", "Practical orthopaedics and transmotology of integrated traditional Chinese and Western medicine", "Practical obstetrics-gynecology of integrated traditional Chinese and Western medicine", "Practical neurology of integrated traditional Chinese and Western medicine", "Practical oncology of integrated traditional Chinese and Western medicine", "Nursing of integrated traditional Chinese and Western medicine", and etc.

Future IM in China

The development of IM in China represents a trend in medical science development. With the strong and continuous support from the Chinese government, successful scientific achievements and the professionalization of the IM team, IM must be moving forward to globalization. However, as a new discipline, IM will still face more challenges in the future.

Firstly, more effective IM approaches should be developed for resolving clinical problems; more RCTs should be conducted, and cost-effectiveness analyses should be performed. Also, CPG on IM approaches should be formed for further IM application worldwide.

Secondly, more basic exploration on TCM syndrome differentiation with biomedical approaches should be carried out. More papers on IM basic research with high quality should be published internationally.

Thirdly, more international collaborations on IM research should be established. More IM projects in China should be open to international scientists, and IM scientists in China should be encouraged to join international projects.

IM has been used in China for more than 50 years, and it has become a hot topic in the medical sciences. Based on previous studies and clinical applications, it is reasonable to believe that IM will have a bright future.

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