

Introduction

Background

In the winter of 2002, severe acute respiratory syndrome (SARS) began to spread throughout the world. More than 5000 cases were reported in the People's Republic of China, including over 1700 cases in China, Hong Kong Special Administrative Region (Hong Kong SAR). The total number of cases reported from Canada and Singapore was more than 200. The total number of SARS worldwide reached 8437 with incidences in 29 countries. Mortality from SARS is estimated at 10–12%.

The World Health Organization (WHO) took effective control measures including international collaboration supported at the highest political level. The global outbreak of SARS was successfully contained in early July 2003.

However, two isolated cases – in Singapore in September 2003 and Taipei in November 2003 – were caused by contamination in a laboratory. Furthermore, in December 2003, two more new SARS cases were confirmed in Guangdong, China where the first ever SARS case had been reported in 2002. Thus far, the source of infection and the mode of transmission for these two cases have not been clarified.

Research on the use of traditional medicine for treatment of SARS patients in China

China has a long history of the use of traditional medicine that has long been integrated into the national health system. When the SARS outbreak occurred in China, the State Administration of Traditional Chinese Medicine of the People's Republic of China immediately initiated clinical research projects on the use of integrated Traditional Chinese medicine (TCM) and Western medicine for treating SARS. A total of 21 research projects were initiated to cover three aspects of SARS, namely, prevention, treatment and rehabilitation. Local governments in Beijing, Guangdong, Shanghai and Tianjin also established similar research projects.

Practitioners of TCM are estimated to have participated in the treatment of SARS in 102 of the 195 SARS-specific hospitals. Ninety-six TCM hospitals sent 2163 professionals to 93 SARS-specific hospitals. Of the 5327 patients with confirmed SARS, 3104 received treatment with TCM, which was 58.3% of the total SARS patients in China. In Hong Kong SAR, research on the use of TCM for the prevention and treatment of SARS, and during convalescence was reported. From the above-mentioned reports, it is clear that TCM and traditional medical physicians made a major contribution to combating SARS in China.

WHO International Expert Meeting

In order to better understand the potential of complementary treatment for patients with SARS and to encourage robust clinical research on SARS and its treatment with traditional medicine, the Chinese Government requested the guidance of WHO and support for 13 clinical trials of integrated treatment with TCM and Western medicine for SARS patients. The Nippon Foundation provided the financial support for WHO to organize an International Expert Meeting on Review of Treatment of SARS by Traditional Chinese Medicine, and the Integration of Traditional Chinese Medicine with Western Medicine, in Beijing, China from 8 to 10 October 2003. Sixty-eight experts from seven countries including Hong Kong SAR, Japan, the Netherlands, the People's Republic of China, Thailand, Viet Nam and the United States of America, attended the meeting (Annex 1: list of participants).

The participants reviewed and evaluated the 13 research reports one by one (10 were from the People's Republic of China, Reports 1-10, and three from Hong Kong SAR, Reports A-C), covering the areas of clinical treatment, convalescence and prevention. After 3 days of discussion, the participants recognized the contribution made by the TCM professionals in providing treatment to SARS patients under very trying conditions. In addition, they had carried out the prospective clinical research in such a way as to produce fruitful results and accumulated a substantial amount of data and valuable experience. Subsequently, the reports were modified to reflect the discussions and comments made during the meeting.

Results of research based on the level of evidence

The research data and findings were reviewed and debated at the meeting and the recommendations of the experts were divided into three levels as described below.

First level

There were sufficient data in the clinical reports to show that integrated treatment with TCM and Western medicine for patients with SARS is safe.

Second level

Of the reported trials, only two clinical trials included patients who were randomly selected for the studies, the others were prospective cohort studies or retrospective studies. The experts considered that the data were insufficient although it was concluded that there could be potential clinical benefits from integrated treatment with TCM and Western medicine for patients with SARS. Such potential benefits include the alleviation of fatigue, shortness of breath and other clinical symptoms; facilitation of lung inflammation absorption; reduction of the risk of oxygen desaturation and the stabilization of abnormal fluctuation of oxygen saturation in the blood; reduction in the dosage of glucocorticoid and antiviral agents (and therefore in their associated side-effects) and reduction of cost (treatment with TCM alone costs less than treatment with Western medicine alone).

Third level

The experts noted that the data in the reports were inconclusive. An example of this is the clinical observation that the mortality rate is lower for the patients treated with integrated TCM and Western medicine than for those treated with Western medicine alone. As the diagnosis of SARS is very difficult to confirm, and some cases may be misdiagnosed, this could lead to a lower recorded mortality rate. In the prevention studies, the response rate to the questionnaires was only 40% among those subjects who had taken the prevention formula; this was too low to enable an accurate assessment of its effects. In the study on convalescence, the comparison was made between only two groups, one treated with TCM and one with exercise. There was no comparison group that received neither treatment nor exercise programmes.

Utilization of the document

SARS is a newly identified human infection caused by a corona virus unlike any other known human or animal virus in its family. The analysis of epidemiological information obtained from the sites of the outbreak of SARS is still underway, but the overall case fatality ratio is known to approach 11%, although the rate among the elderly is much higher.

Currently, the major challenges for the treatment of SARS are:

- ◆ the source of the SARS virus and mode of transmission are still not well understood;
- ◆ there are problems with diagnostic tools;
- ◆ there is no effective treatment; and
- ◆ there is no vaccine for SARS.

The above-mentioned difficulties and challenges have motivated national authorities, health workers and scientists to explore the potential of complementary treatment.

The results of research on integrated treatment with TCM and Western medicine showed that it is safe and that it also has some potential clinical benefits. Therefore, the experts suggested that records of such experience could serve as reference material for treatment of SARS in the future.

This publication is intended to:

- ◆ share experience in the complementary treatment of SARS patients;
- ◆ share the experience of clinical studies in the field of traditional medicine for treatment of SARS between the physicians and researchers; and
- ◆ to further encourage and promote the quality of research in the field of traditional medicine

It must be emphasized that the purpose of this document is to report on some clinical studies on treatment and prevention selected by the Chinese government, and to record the review of these studies by an international meeting of experts. Only national health authorities have the right to determine what treatment for SARS can be recommended.

Please note that the reports contained in this document were originally written in Chinese, therefore much of the specific terminology and medical descriptions are

direct translations of the original text. It is particularly the case for terms regarding Traditional Chinese medicine though this applies to Western medical terms as well. At the moment there is no standardized international English terminology for Traditional Chinese medicine. WHO is currently working on developing standard terms in English for Traditional Chinese medicine. It is not the scope of this document to propose terminologies or descriptions in the field of Traditional Chinese medicines or SARS. If clarification of anything contained within the reports is necessary, it is recommended that the original reports be referenced.

Report of the International Expert Meeting to review and analyse clinical reports on combination treatment for SARS

Background

Beginning in November 2002, severe acute respiratory syndrome (SARS) spread to 32 countries and areas, reaching a peak between April and May 2003. Up to 7 August 2003 the total number of cases was 8422, of which 5327 occurred in the People's Republic of China, 1755 in China, Hong Kong Special Administrative Region (Hong Kong SAR), 655 in China, Province of Taiwan, 251 in Canada and 238 in Singapore. The average mortality rate was 11%. In China the mortality rate was 7%, in Hong Kong SAR, 17% and in China, Province of Taiwan, 27%. The mortality rates in the other countries were 17% in Canada and 14% in Singapore.

SARS not only had great impact on the global public health system and revealed a general lack of preparedness for handling an outbreak of severe infectious disease, but it also prompted the readjustment and improvement of the existing public health system infrastructure for fighting against epidemics in all countries and areas, including China.

SARS had a direct impact on the economic situation of the world, especially on the tourism industry, its influence surpassing that of any outbreak of typical influenza. Business in the epidemic-affected areas was almost paralysed and tourism in the surrounding areas was also affected. In Asia alone, a total of US\$ 18 billion of tourism revenue was lost. The impact of SARS also spread to other areas of society and the economy.

The Chinese government took the epidemic extremely seriously and adopted decisive measures, making centralized arrangements to fight SARS using appropriate precautions and sound scientific methods. The State Administration of Traditional Chinese Medicine (SATCM) of China established the Working Group on the Treatment of SARS by Traditional Chinese medicine (TCM) to make overall arrangements to coordinate and provide leadership for developing clinical treatment and conducting scientific research on the application of TCM in the treatment of SARS. On 11 April 2003, SATCM, on the basis of its summing up of the experiences gained in Guangdong Province, formulated and issued the *Technical scheme on the prevention and treatment of SARS with TCM* (provisional), which was subsequently revised twice (on 19 April and 11 May 2003). At the beginning of June 2003, the *Recommendation on the treatment of SARS at the convalescence period* was published. The issuance of technical guidance has played an important role in the prevention and treatment of SARS by TCM. In early May 2003, at the invitation of the Hospital Authority of Hong Kong SAR, TCM experts were sent from Guangdong to Hong Kong SAR to participate in clinical research on SARS treatment using integrated TCM and Western medicine.

It is estimated that TCM practitioners participated in the treatment of SARS in 102 of the 195 SARS-specific hospitals in the People's Republic of China. Ninety-

six TCM hospitals sent 2163 professionals to 93 SARS-specific hospitals. Among the 5327 confirmed SARS cases, 3104 (58.3% of the total SARS patients in China) received TCM intervention.

SATCM immediately initiated basic and clinical research projects on integrated TCM and Western medicine for the treatment of SARS. A total of 21 research projects were established. Local governments in Beijing, Guangdong, Shanghai and Tianjin also established similar research projects.

The prevention and treatment of SARS poses great challenges. Firstly, SARS is a completely new infectious disease, so there is a lack of scientific knowledge. The research results acquired thus far have not produced methods for making an early diagnosis of SARS in order to reduce its spread. Secondly, there is still no specific treatment for SARS. The use of high dosages of antiviral drugs and glucocorticoids is controversial because serious side-effects have been noted during the treatment process. Summarizing the experiences and potential benefits of TCM in treating SARS may be a productive way to find effective approaches for the prevention and treatment of SARS.

The WHO International Expert Meeting to Review and Analyse Clinical Reports on Integrated Treatment for SARS hosted by WHO and SATCM was held from 8 to 10 October 2003 in Beijing, People's Republic of China. Officers from WHO Headquarters, the Western Pacific Region and the China office, as well as 51 official representatives and 17 observers from Hong Kong SAR, Japan, the Netherlands, the People's Republic of China, Thailand, Viet Nam and the United States of America attended the meeting. Officials from the Chinese Ministry of Health, National Commission of Development and Reform, Ministry of Science and Technology, Ministry of Education and SATCM attended the opening ceremony.

Dr Xiaorui Zhang, Coordinator of Traditional Medicine, Department of Essential Drugs and Medicines Policy, WHO, hosted the opening ceremony of the meeting; She Jing, Vice-Minister of Health and Head of SATCM, made a speech; and Dr Henk Bekedam, WHO Representative in China, gave the inaugural speech. Dr Bekedam acknowledged the importance of the efforts and contributions made by TCM in the treatment of SARS. The meeting elected Professor Weng Weiliang of the China Academy of TCM and Dr Vason Pinyowiwat of the Thailand Ministry of Public Health Department of Disease Control to serve as co-chairpersons; Hong Kong SAR representative Dr Andrew Yip and Professor Hong Jing of the China SATCM served as rapporteurs.

Objectives

The objectives of the meeting were to:

- ◆ Review and analyse clinical reports on the integrated treatment of SARS with TCM and Western medicine;
- ◆ Objectively evaluate the efficacy and safety of integrated treatment of SARS with TCM and Western medicine;
- ◆ Discuss the efficacy or underlying efficacy of treatment of SARS with integrated TCM and Western medicine; and
- ◆ Share experiences and knowledge of the treatment of SARS.

Review and analysis

The experts participating in the meeting reviewed and evaluated each of 13 reports (3 of which, Reports A-C, were from Hong Kong SAR), which were relevant to clinical treatment of SARS, convalescence and prevention research.

After 3 days of discussion, the participants recognized the contribution made by the TCM professionals working in the clinical and research fields in providing treatment to many SARS patients in an extremely dangerous and urgent situation, while at the same time carrying out prospective clinical research that produced fruitful results and accumulating a considerable amount of data and experience.

The experts recognized the difficulties and challenges in conducting research on the treatments of SARS while the epidemic of this new disease was spreading. Due to the relative scarcity of medical resources and the heavy clinical workload, clinical research on SARS faced difficulties never previously encountered. The researchers nevertheless made every effort to improve the research design to assure quality and reduce bias.

The experts recognized that integrated treatment by TCM and Western medicine for SARS is generally safe. The following potential benefits were also recognized:

- ◆ alleviation of clinical symptoms such as fatigue, shortness of breath and tachypnoea among others;
- ◆ facilitation of absorption of lung inflammation;
- ◆ reduction of the risk of oxygen desaturation and the stabilization of abnormal fluctuation of oxygen saturation in the blood;
- ◆ promotion of normalization of levels of peripheral blood lymphocyte and increase in levels of T cell subgroups;
- ◆ decrease in the dosage of glucocorticoid and antiviral agents and consequently in their associated side-effects;
- ◆ decrease in the incidence of abnormal levels of alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and blood urea nitrogen (BUN), suggesting that integrated treatment with TCM and Western medicine is safe;
- ◆ the cost of treatment by TCM only is lower than that of treatment with Western medicine.

The following clinical observations were also noted:

- ◆ A group of patients at the early stage of SARS treated only with TCM all recovered without the need for glucocorticoid, antiviral agents, antibiotics or immunomodulators and were discharged from hospital.
- ◆ For those cases with comparable age, disease severity and underlying disease, analysis showed that the mortality rate was lower for the patients treated with integrated TCM and Western medicine than for those treated with Western medicine only.
- ◆ No SARS cases occurred among health care workers exposed to SARS patients and who had taken TCM for prophylaxis.
- ◆ During the convalescence period, treatment with TCM improved physical strength, alleviated clinical symptoms and decreased lung inflammation.

These last two situations are unique in that no specific treatments with Western medicine were evaluated for these cases so no comparison can be made.

Recommendations

The following recommendations were made by the experts who attended the meeting:

- ◆ According to the 13 clinical reports, treating SARS with integrated TCM and Western medicine is safe, provided that treatment is applied according to TCM principles; the potential benefits may be greater if treatment is started at an early stage.
- ◆ Continued follow-up of SARS patients is needed and the long-term effects of various treatments should be observed and compared.
- ◆ Design of clinical research projects would be further improved by paying attention to the clinical features of SARS and the individualized diagnosis and treatment principles of TCM, while strengthening the quality control of clinical research in order to minimize bias.
- ◆ Improve epidemiological research on SARS and its treatment schemes and increase the efficacy of treatment with integrated TCM and Western medicine. Research and develop effective TCM treatments and perfect quality control standards.
- ◆ Strengthen research on health economics, especially the evaluation of the effectiveness of prevention.
- ◆ Fully utilize TCM resources by bringing TCM into the clinical treatment system for public health emergencies, establish research networks, prepare plans for responding promptly to SARS outbreaks and for conducting research, and strengthen staff training.
- ◆ The experiences of treating SARS with integrated TCM and Western medicine described in the 13 clinical reports can serve as a reference for other countries in developing strategies for preventing and treating acute epidemics.

The experts who attended the meeting reached consensus that while the government and health workers of different countries are implementing clinical

treatment of SARS, they should first reinforce preventive and protective measures to reduce all nosocomial transmission.

Recommendations to WHO

Experts made the following recommendations to WHO:

- ◆ Continue to support research to improve trial design and implementation for traditional medicine in treating SARS and other diseases.
- ◆ Provide and support training courses, facilitate the sharing of experience and information on treatment of SARS with integrated TCM and Western medicine.
- ◆ Publish research relating to treatment of SARS with integrated TCM and Western medicine.