Activities of the Special Committee for EBM of Japan Society for Oriental Medicine (JSOM)

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Introduction

"Evidence" is viewed from three different stages, i.e., "tsutaeru"(つくる, 創): to generate evidence through clinical research; "tsutaeru" (つたえる, 伝) : to review and communicate evidence; and "tsukau" (つかう, 使) : to use of evidence by clinicians, regulators, patients and others. The current accepted definition of the term "evidence-based medicine" (EBM) worldwide is "the integration of best research evidence with clinical expertise and patient values" (2000). This definition was derived from the viewpoint of the user of evidence.

Along with the global movement of EBM, which started in early 1990s in the West and introduced in Japan in the late 1990s, the Japan Society for Oriental Medicine (JSOM) established a Special Committee for EBM in June 2001. The chair of the Committee was Tetsuo AKIBA MD, Ph.D. Soon after establishing the Committee, Dr. Akiba set up a team consisting 61 members.

"EBM in Kampo 2002, Interim Report" (Nihon Toyo Igaku Zasshi [Japanese Journal of Oriental Medicine] 2002: 53 (5), supplementary issue) was published in 2002. This was a pioneering work. It was followed by "Evidence Reports of Kampo Treatment" (Nihon Toyo Igaku Zasshi [Japanese Journal of Oriental Medicine] 2005: 56, EBM supplementary issue) published in 2005. These two publications were intended to present evidence from "good" studies, including randomized controlled trials (RCTs), of Kampo products published between 1986 and 2002. However, those studies showed several weaknesses, such as lack of clear inclusion/exclusion criteria. Thus, some readers raised questions, such as why some particular studies had been or had not been included.

I assumed chairmanship of the second phase of the Committee from 2005 to 2008, and continue to hold this position during its third phase starting 2009. In 2005, three task forces were established. These task forces were aimed for "tsutaeru" of evidence of Kampo medicines. These task forces are described below:

Evidence Report project

The Task Force for Evidence Report (ER-TF) succeeded in implementing activities during the first phase of the Committee. Approach on systematic review methods was adopted and the following improvements were made:

(1) Although all RCTs for the period 1986-2008 were reviewed, only some of these trials were included.
(2) The "systematic review" approach was adopted in literature search, and evidence appraisal was adopted to enhance comprehensiveness, accuracy, and transparency of the review.
(3) The structure of the abstracts included eight standard items, i.e., "objectives," "design," "setting," "participants," "intervention," "main outcome measures," "main results," and "conclusions", and four additional items, i.e., "from Kampo medicine perspective," "safety assessment in the article," "author's comments," and "author's name and date of publication."
(4) Excluded literatures, along with the reasons for their exclusion, were listed.
(5) Because the main mission of the task force was to develop structured abstracts, recommendations were not made. Recommendations will be dealt with during the development of clinical practice guidelines (CPG) in the future.
(6) A system to enable feedback from readers through the internet and other media on the current reports was established.
(7) In order to have transparency and accountability, conflicts of interests (COI) of the members of the Task Force were disclosed.

The Phase 2 Evidence Report includes only RCTs of Kampo products (extract granules, tablets, and capsules, or pills, approved for sale as ethical Kampo prescriptions in Japan). The report excludes studies of in-house formulations such as decoctions, since no quality control criteria have been established. Actually, there were four studies that fall under this category.

The sources of data searches were: (1) the Cochrane Library (CENTRAL), (2) Igaku Chuo Zasshi (Japana Centra Revuo Medicana [JCRM], 医学中央雑誌, Ichushi 医中誌) web, and (3) the database offered by the Japan Kampo Medicines Manufacturers Association (JKMA). Structured abstracts were arranged in the order used in the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD10).

In June 2009, "Evidence Reports of Kampo Treatment 2009: 320 Randomized Controlled Trials" (EKAT 2009) was published in Japanese (http://www.jsom.or.jp/medical/ ebm/index.html). This report contains structured abstracts of 320 RCTs and one meta-analysis from 385 literatures published between 1986 and 2008. It was in 1986 when the current quality control standard for Kampo formulations was established in accordance with the request from the Ministry of Health, Labor and Welfare (MHLW).

An English version of the report was also developed and posted on the same JSOM website. So far the report covers 143 structured abstracts of 180 references published during the period 1999-2008. The English translation of 177 structured abstracts based on references published during the period 1986-1998 is now under construction.

Quality of RCTs contained in the Report have been reviewed using the CONSORT statement (2001)

Clinical Practice Guidelines project

The Task Force on Clinical Practice Guidelines (CPG-TF) was originally established in response to the project on CPGs for traditional medicine initiated by the World Health Organization's (WHO) Regional Office for the Western Pacific (WPRO) which started in May 2004. It would be worthwhile to mention some background of this WHO project here.

A major weakness of this WHO/WPRO project was that the intended users of CPGs were poorly specified. The definition of target users is one of the key components of the Appraisal of Guidelines Research and Evaluation (AGREE) statement of 2003. Eliminating this ambiguity is necessary because WPRO member countries vary widely in healthcare, medical licensing, and drug regulation practices. Unlike China and Republic of Korea, Japan does not have separate licensing system for Kampo practitioners.

A working group on CPGs was established in the Japan Liaison of Oriental Medicine (JLOM) in May of 2005. The JLOM comprises four major academic societies for Oriental medicine in Japan. These include the Japanese Society for Oriental Medicine (JSOM), the Medical and Pharmaceutical Society for WAKAN-YAKU (WAKAN), the Japanese Society of Acupuncture and Moxibustion (JSAM), and the Japanese Society of Pharmacognosy (JSP).

Between May of 2004 and February of 2006, there were four WHO/WPRO conferences for the development of CPGs governing traditional medical practices (held in Beijing or Daegu). The first two meetings concerned policy development, the selection of target diseases, and methodology. Discussion was not focused on the problem of defining CPG users, and a consensus was not reached on this topic.

The JLOM working group on CPGs as well as the JSOM CPG Task Force indicated that the WHO/WPRO project suffered from organizational and methodological shortcomings. As mentioned above, the main problems were ambiguities concerning target users. The JLOM therefore withdrew from the WHO/WPRO project. The most recent two meetings of the WHO/WPRO project targeted lung cancer and eye diseases, respectively. The JLOM did not formally participate in the meeting on lung cancer in November 2005, but instead sent an unofficial liaison to monitor progress. The JLOM boycotted the meeting on eye disease in February 2006.

Following the discussions during the 2006 World Congress of Chinese Medicine in Hong Kong in November 2006, The Hong Kong Baptist University held a meeting on the development of CPGs for traditional medicine in December 2007, in collaboration with WHO/WPRO. The participants agreed to

abandon policies for developing a global CPG for traditional medicine. Instead, the participants produced "A guide to develop CPGs for traditional medicine". It has not been yet published despite repeated follow up by the participants of the meeting.

During the international discussions on the WHO/WPRO project, the Japanese participants, i.e. members of JSOM task force identified the need for current information on Japanese CPGs for traditional medicine. Therefore, the TF started to review domestic CPGs in 2006. CPGs are primarily used to govern the practice of Western medicine in Japan.

A quasi-comprehensive list of Japanese CPGs available from the Toho University Medical Media Center (TUMMC) was searched. By the end of December 2008, 44 (9.6%) of the 455 CPGs listed by TUMMC contained descriptions of Kampo products.

Of these 44 CPGs, 7 were Type A (described as having both the strength of evidence and strength of recommendations); 16 were Type B (described as having references only), and 21 were Type C (which contains the term Kampo without references).

Thus, citation rate of Kampo medicines in CPGs was approximately 10%; some pivotal RCTs for Kampo medicines were not quoted in CPG. Kampo medicines in CPGs should be assessed more comprehensively and scientifically

Best Case project

Kampo medicine, which is a Japanese variation of Chinese medicine has roughly 1,000 years of history. It have not necessarily "tsukurareru" generated by RCTs which evolved in 1930-40s in the West. Other study designs should not be forgotten.

Using NAFKAM in Norway and Best Case Series (BCS) project at National Cancer Institute of National Institutes of Health (NCI/NIH) of the United States, the Best Case Task Force (BC-TF) was established in 2005.

This Task Force aims to collect cases showing "dramatic" course of effect after using Kampo medicines and post them on the website. It is an exploratory study on the efficacy as well as safety of Kampo medicines. Its impact on clinical decision making will also be reviewed. Kakkonto (葛根湯) was selected as a model formula inasmuch as an estimated 1.2 million people in Japan uses this formula, which make it the most widely used among 148 formulas marketed as ethical Kampo products in Japan. The protocol of this project was approved by the Ethics Committee of JSOM in March 2007.

The UMIN system, which has strict system for the protection of privacy information, was used in the data collection. But it was found that this system is not user friendly for ordinary physicians, and there are not many cases registered so far. Revised research policy is being developed to have meaningful outcome from the project