



Editorial

# H1N1 influenza: Is traditional Chinese medicine effective and safe?



Influenza is a viral respiratory infection that causes an acute febrile illness with myalgia, headache, and cough, and can result in substantially elevated morbidity and mortality rates during an epidemic.<sup>1</sup> A novel influenza H1N1 infection began in March 2009, which rapidly spread and caused the World Health Organization to declare the first influenza pandemic outbreak.<sup>2</sup> The antiviral medication oseltamivir has been approved for use against influenza H1N1 infections; however, careful use of anti-influenza drugs has been recommended due to the emergence of drug resistance and the side effects of these drugs.<sup>3</sup> Chinese herbal medicine, the most important component of traditional Chinese medicine (TCM), has been recommended for preventing and treating influenza due to the limitations of healthcare resources in China. *Shang-Han Lun* (Treatise of Exogenous Febrile Diseases or Discourse on Cold-Damage Disorders) and *Wen-Bing-Tiao-Bian* (Detailed Analysis of Epidemic Warm Diseases) were regarded as the seminal guidelines for treatment of influenza in TCM.<sup>4</sup> In the study of TCM, influenza is differentiated into two types: (1) wind-cold syndrome and (2) wind-heat syndrome. Severe cold, slight fever, absence of sweat, headache, aching pain of the extremities, stuffy nose with nasal discharge, and cough with thin sputum are the primary symptoms of the wind-cold type. Alternatively, a high fever, slight aversion to cold, headache, sore throat with congestion, and expectoration of yellowish sputum are the main symptoms of the wind-heat type.<sup>5</sup> Many studies have shown that Chinese herbal medicine applied to counter the effects of wind-cold or wind-heat types can inhibit influenza virus, with some studies even showing potential modulation of the cellular immune system in animals. For example, *Scutellaria baicalensis* inhibits influenza H1N1 by exerting cytotoxic activity against infected cells.<sup>6</sup> *Hypericum perforatum* L. could reduce the influenza H1N1 viral titer of infected mice by modulation of inflammatory cytokines.<sup>7</sup> However, evidence-based data regarding the therapeutic effects and safety of TCM for treatment of influenza H1N1 in humans remain unclear.

In 2013, Jiang et al<sup>8</sup> assessed the therapeutic effects and safety of Chinese herbal medicine as an alternative or adjunctive therapy to other commonly used drugs for influenza in 18 trials involving 2521 participants. They found in one Chinese herbal trial that TCM is more effective than antiviral

drugs in preventing or treating influenza, and the remaining 17 Chinese herbal trials indicated a similar effect as antiviral drugs in preventing or treating influenza. However, the evidence presented in these studies does not consequently support or reject the use of any particular Chinese herbal preparations for influenza because the included studies were of poor quality. However, no obvious adverse events were reported in the included studies. Furthermore, this meta-analysis did not focus on the therapeutic effects and safety of Chinese herbal medicine against the influenza H1N1 strain.

In this issue, Li<sup>9</sup> analyzed the efficacy and safety of TCM for treatment of influenza H1N1 in 30 trials including 3444 participants. In this study, the Jadad scale was used to evaluate the quality of the clinical trials, and the results showed that only three of those 30 clinical trials proved to be of high quality. Participants who were treated by Chinese herbal medicine had a shorter mean time of defervescence than the control group. However, evidence did not support the proposition that Chinese herbal medicine had a superior effective rate and shortened duration of influenza H1N1 viral shedding than the control group. Nonetheless, this result suggests that Chinese herbal medicine might have comparatively better potential effects on fever resolution than viral shedding in influenza H1N1 infection. However, for participants who were treated with integrated Chinese and Western medicines, the duration of viral shedding was significantly reduced compared with the control group. These data imply that integrated Chinese and Western medicines (i.e., Chinese herbal medicine plus oseltamivir) has beneficial anti-influenza H1N1 viral effects. However, 18 studies in this meta-analysis described the adverse effects of TCM, including nausea, vomiting, diarrhea, abdominal pain, skin rashes, arrhythmia, and neurological symptoms.

Although reports of two meta-analysis suggested that Chinese herbal medicine appears to have a promising future in the treatment of influenza H1N1, the low quality of Chinese herbal trials is a major concern. Therefore, additional studies are required that have demonstrated enhanced methodological quality, substantially more participants, and good reporting to provide stronger and more reliable evidence. Information about Chinese herbal trials carried out for the treatment of influenza H1N1 should be reported in detail according to the

guidelines established by CONSORT.<sup>10</sup> The disease duration upon inclusion should be restricted, and laboratory tests (routine blood tests, serum tests, or pathogenic examinations) and chest X-rays should be conducted to define inclusion and exclusion criteria, if available resources permit. The definition of outcome measures and the incidence of adverse reactions should be given due attention as well. Intervention in the control group should be well-designed as a placebo, with no prior treatment or the commonly used antiviral and anti-pyretic–analgesic drugs. Nonetheless, evidence remains unpersuasive due to methodological limitations of many existing Chinese herbal trials for the treatment of influenza H1N1. Ultimately, more high-quality randomized clinical trials with larger numbers of participants and clear reporting are required to generate reliable results.

### Conflicts of interest

The author declares that he has no conflicts of interest related to the subject matter or materials discussed in this article.

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