Use of Traditional East Asian Medicine to Diagnose and Kampo Medicine Kamishoyosan to Treat Survivors of the Great East Japan Earthquake 2011: A Retrospective Study

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Introduction

The Great East Japan Earthquake of March 11, 2011 was the fourth earthquake of its size in the world since 1900 [1] and there are many reports of post-traumatic stress disorder (PTSD) associated with it [2]. PTSD is more common than previously thought [3]; for example, 4 years after tsunami caused by the Hokkaido Nanseioki Earthquake, 16.7% of survivors reported that their life remained unsettled [4].

A total of 15,887 persons are known to have died in the Great East Japan Earthquake and the number of people still missing was 2,615 as of July 10, 2014 [5]. The number of refugees and evacuated persons living in temporary housing was 251,419 as of June 12, 2014 [6]. Of the 1,006 victims of the disaster living in the stricken areas of Iwate, Miyagi, and Fukushima prefectures, 59% reported that reconstruction had not been taking place, 53% said that the reason for the lack of reconstruction was that the location of their future residence had not yet been decided, and 24% said that they did not want to return to where they lived before the tsunami. The most common reason given for not returning to their previous home was anxiety about the tsunami [7]. Rescue workers, as well as survivors, are at risk for developing mental disorders [8,9].

Our institution and nursing facility—Tohoku University and the Urayasu special elderly nursing home—were located at the center of disaster area; there were varying responses to the tragic disaster [10-12].

One of the observations that became apparent after the earthquake was that commonly used pharmaceuticals were not always effective and often proved unsatisfactory for patients. For example, the drugs commonly used to treat PTSD were known to have side effects and could pose risks for some people [13-15]. There was also insufficient evidence to recommend Complementary and Alternative Medicine (CAM) approaches, including traditional medicine, as first-line treatments for PTSD. Nevertheless, herbal medicines have been in common use for mental care in traditional East Asian medicine.
(TEAM) from ancient times [16]. Kamishoyosan (Jia-wei-xiao-yao-san) is an example of one such Japanese herbal medicine currently in use [17-23]. After the Sichuan earthquake in China in 2008, Xiao-Tan-Jie-Yu-Fang, which was developed from Jia-wei-xiao-yao-san (Kamishoyosan), was used for patients with PTSD [24]. We used TEAM to treat the survivors of the Great East Japan Earthquake in 2011; 72% of patients, for whom Kamishoyosan was indicated by TEAM syndromes, were prescribed Kamishoyosan. The IES-R-J scores obtained before and after treatment were analyzed based on the medical records.

Materials and Methods

Study design and participants

This retrospective study was conducted in Natori City, which is located near the center of the tsunami disaster area associated with the Great East Japan Earthquake in 2011 (Figure 1). The study participants were surviving employees of the Urayasu nursing home facility, which was destroyed by the tsunami.

After the tsunami disaster, the authors visited the survivors and treated them in the facility to which they had been taken. All the patients were suffering from stress-related disorders such as PTSD. They were diagnosed according to the theories of TEAM and prescribed herbal medicines. To evaluate the effects of the herbal medicines on the patients, IES-R-J assessments were performed before and after prescription of the medicines.

Assessments of the damage to the patients caused by the earthquake and tsunami were carried out in three stages: (1) identifying chief complaints reported at the first examination, which took place 1 to 2 months after the disaster, (2) performing diagnosis according to TEAM theories, and (3) assessing medical records with the Japanese-language version of the Impact of Event Scale – Revised (IES-R-J) [25]. All three stages were performed using the patient’s clinical records. Most of the patients completed the IES-R-J twice, as requested—before and after receiving the prescription. The IES-R-J assessments were analyzed only in patients for whom Kamishoyosan was indicated by TEAM syndromes such as “liver qi stagnation” or “depressed liver qi transforming into fire.”

The IES-R-J is a short, self-reporting questionnaire with 22 questions, 5 of which were added to the original Horowitz (IES) [26] to better capture the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) criteria for PTSD [27]. This tool is an appropriate instrument to measure the subjective response to a specific traumatic event in the senior population, especially in the response sets of intrusion (intrusive thoughts, nightmares, intrusive feelings and imagery, dissociative-like re-experiencing), avoidance (numbering of responsiveness, avoidance of feelings, situations, and ideas), and hyperarousal (anger, irritability, hypervigilance, difficulty concentrating, heightened startle), as well as to produce a total subjective stress IES-R-J score.

Preparation of herbal medicine Kamishoyosan (Jia-wei-xiao-yao-san) and dispensing of the medicine

Kamishoyosan extract is an over-the-counter (OTC) drug that was supplied for prescription to the patients by Kotaro Pharmaceutical Co., Ltd (Osaka, Japan). Kamishoyosan extract is produced by Kotaro Pharmaceutical Co., Ltd. It contains 10 herbs in the following quantities: Bupleuri Radix (1.5g), Angelicae Radix (1.5g), Poria (1.5g), Atractylodis Rhizoma (1.5g), Paeoniae Radix (1.5g), Menthae Herba (0.5g), Glycyrrhizae Radix (1.0g), Zingiberis Rhizoma (0.5g), Moutan Cortex (1.0g), and Gardeniae Fructus (1.0g). These herbs are registered in the Pharmacopoeia of Japan, 15th version. Patients who participated in the study and were approved to receive the Kamishoyosan prescription as the result of having one or more TEAM syndromes received 3 tablets of Kamishoyosan (0.75 g extract) 3 times a day. The processes involved in the production and distribution of Kamishoyosan, in compliance with Good Manufacturing Practices for Kampo products, have also been approved by the Ministry of Health, Labor, and Welfare of Japan.

Statistical Analysis

Scores for the IES-R-J obtained before and after the prescription of Kamishoyosan were compared using paired t-test. The statistical analysis software used was JMP Pro version 11.0 (SAS Institute Inc., Cary, NC, USA). Significance levels were defined as p < 0.05.

Results

Participants

A total of 32 employees (7 men and 25 women; age, 40 ± 13 years) at the Urayasu nursing home facility were enrolled as patients in the research project.

The damage situation for the study patients

The Urayasu nursing facility was completely destroyed by the tsunami. Forty-three of the 163 elderly residents died, along with 4 of the 62 employees. Of the 32 employees enrolled as patients in the study, 31 witnessed the death of one or more residents, or experienced a crisis in their own life. The families of 2 patients died in the disaster and the families of 2 other patients disappeared; 4 patients had their houses completely destroyed, and the houses of 2 other patients were partially destroyed. The cars of 14 patients were carried away by the tsunami.

Chief complaints of patients at the first examination

Figure 2a shows the physical symptoms and Figure 2b shows the mental symptoms at the first examination. Among physical symptoms, insomnia, fatigue, palpitations, and shoulder discomfort were most
prevalent, while anxiety, sense of guilt, dreams, fear, anger, and irritation were the most common mental symptoms. The reasons given by the patients for their anxiety were vague, relating to aftershocks, the tsunami, uncertainty about their future, and lack of employment.

**Figure 2A**: Symptoms at first medical examination.

**Figure 2B**: Mental symptoms at first medical examination.

**Diagnosis according to the TEAM theories (TEAM syndromes)**

The most common TEAM syndromes were “liver qi stagnation” (43%) and “depressed liver qi transforming into fire” (28%) (Figure 3).

**Treatment with herbal medicines at the first examination**

Prescriptions for herbal medicine at the first medical examination were as follows: Kamishoyosan (Jia-wei-xiao-yao-san), 23 patients; Rikkunshito (Liu-jun-zi-shang), 5 patients; Keishibukuryogan (Gui-zhi-fu-ling-wan), 4 patients; Shoseiryuto (Xiao-qing-shang), 2 patients; Shin’iseihaito (Xin-yi-qing-fei-shang), 1 patient; Keigairengyoto (Jing-gai-lian-qiao-shang), 1 patient; and Rokumigan (Liu-wei-wan), 1 patient. Multiple herbal medicines were prescribed to patients, as needed.

**Adverse events**

There were no reports of adverse events associated with the use of the medicines.

**Discussion**

This study showed the potential effectiveness of the herbal medicine Kamishoyosan in improving the IES-R-J scores of tsunami survivors with stress-related disorders like PTSD at 1 to 2 months after the Great East Japan Earthquake.

**TEAM treatment for PTSD and syndromes in earthquake survivors**

Meng et al. used the herbal medicine Xiao-Tan-Jie-Yu-Fang to treat patients with PTSD after the 2008 earthquake in China. Xiao-Tan-Jie-Yu-Fang was modified from a classic formula, Shoyosan (Xiao-Yao-San), the basic component of Kamishoyosan that we used on the earthquake survivors in Japan. Numata et al. used...
Saikokeishikanyakoto, which, like Kamishoyosan, is applied when there is “liver qi stagnation.” TEAM syndromes in patients with PTSD, who were recruited by posting flyers or ads in the local media, were “liver qi stagnation,” “heart shen disturbance” and “kidney deficiency” in another study [28].

### Table 1: Scores of IES-R-J before and after prescription of Kamishoyosan.

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Item</th>
<th>Before Mean ± SD</th>
<th>After Mean ± SD</th>
<th>P value</th>
<th>Subscale</th>
<th>Item</th>
<th>Before Mean ± SD</th>
<th>After Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Int</td>
<td>Any reminder brought back feelings about it</td>
<td>2.5 ± 1.1</td>
<td>1.4 ± 0.7</td>
<td>&lt;.0001</td>
<td>Avo</td>
<td>I was aware that I still had a lot of feelings about it, but I dint deal with them</td>
<td>1.4 ± 1.1</td>
<td>0.7 ± 0.6</td>
<td>0.0008</td>
</tr>
<tr>
<td>Int</td>
<td>I had trouble staying asleep</td>
<td>1.8 ± 1.3</td>
<td>0.9 ± 0.9</td>
<td>0.0028</td>
<td>Avo</td>
<td>My feelings about it were numb</td>
<td>1.2 ± 1.2</td>
<td>0.9 ± 1.1</td>
<td>0.1631</td>
</tr>
<tr>
<td>Int</td>
<td>Other things kept making me think about it</td>
<td>1.6 ± 1.4</td>
<td>0.7 ± 0.7</td>
<td>0.0009</td>
<td>Int</td>
<td>I found myself acting about it were kind of numb</td>
<td>0.9 ± 1.2</td>
<td>0.6 ± 0.8</td>
<td>0.0827</td>
</tr>
<tr>
<td>Hyp</td>
<td>I felt irritable and angry</td>
<td>1.3 ± 1.0</td>
<td>0.9 ± 0.8</td>
<td>0.007</td>
<td>Hyp</td>
<td>I had trouble falling asleep</td>
<td>1.4 ± 1.2</td>
<td>0.7 ± 0.8</td>
<td>0.0043</td>
</tr>
<tr>
<td>Avo</td>
<td>I avoided letting myself get upset when I thought about it or was reminded of it</td>
<td>1.7 ± 1.0</td>
<td>0.9 ± 0.6</td>
<td>0.0007</td>
<td>Int</td>
<td>I had waves of strong feeling about it</td>
<td>2.1 ± 1.0</td>
<td>1.2 ± 0.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Int</td>
<td>I thought about it when I dint mean to</td>
<td>2.1 ± 1.1</td>
<td>1.3 ± 0.7</td>
<td>0.0134</td>
<td>Avo</td>
<td>I tried to remove it from my memory</td>
<td>0.8 ± 0.9</td>
<td>0.4 ± 0.6</td>
<td>0.069</td>
</tr>
<tr>
<td>Avo</td>
<td>I felt as if it hadn’t happened or wasn’t real</td>
<td>1.6 ± 1.2</td>
<td>0.9 ± 0.9</td>
<td>0.0229</td>
<td>Hyp</td>
<td>I had trouble concentrating</td>
<td>1.4 ± 1.5</td>
<td>0.8 ± 1.2</td>
<td>0.0079</td>
</tr>
<tr>
<td>Avo</td>
<td>I stayed away from reminders of it</td>
<td>1.6 ± 1.1</td>
<td>1.0 ± 1.0</td>
<td>0.0445</td>
<td>Hyp</td>
<td>Reminds of it caused me to have physical reactions, such as sweating, trouble breathing, nausea, or a pounding heart</td>
<td>1.4 ± 1.2</td>
<td>0.9 ± 1.0</td>
<td>0.0081</td>
</tr>
<tr>
<td>Int</td>
<td>Pictures about it popped into my mind</td>
<td>1.5 ± 1.0</td>
<td>0.8 ± 0.8</td>
<td>0.0018</td>
<td>Int</td>
<td>I had dreams about it</td>
<td>0.9 ± 1.1</td>
<td>0.4 ± 0.6</td>
<td>0.046</td>
</tr>
<tr>
<td>Hyp</td>
<td>I was jumpy and easily started</td>
<td>1.8 ± 1.3</td>
<td>0.9 ± 0.9</td>
<td>0.009</td>
<td>Hyp</td>
<td>I felt watch full and on-guard</td>
<td>1.9 ± 1.1</td>
<td>1.2 ± 0.9</td>
<td>0.0018</td>
</tr>
<tr>
<td>Avo</td>
<td>I tried not to think about it</td>
<td>1.3 ± 1.1</td>
<td>0.6 ± 0.5</td>
<td>0.0346</td>
<td>Avo</td>
<td>I tried not to think about it</td>
<td>0.8 ± 0.8</td>
<td>0.5 ± 0.6</td>
<td>0.0827</td>
</tr>
</tbody>
</table>

**Instruction Factor (Subtotal)**: 14.6 ± 7.1, 8.1 ± 3.6, <.0001

**Hyperarousal Factor (Subtotal)**: 11.3 ± 6.0, 6.4 ± 3.9, 0.0002

**Avoidance Factor (Subtotal)**: 7.1 ± 4.0, 4.2 ± 3.0, 0.0008

**Total**: 32.9 ± 14.5, 18.8 ± 7.9, <.0001

Int = Instruction Factor; Hyp = Hyperarousal Factor; Avo = Avoidance Factor

In the present study, patients were diagnosed with TEAM and, where indicated, herbal medicines were prescribed. However, it was observed that all of the TEAM syndromes other than “liver qi stagnation” that were found in patients could have come from “liver qi stagnation,” and the majority of patients (72%) were diagnosed as having “liver qi stagnation,” for which the herbal medicine Kamishoyosan was indicated. It is known that the main cause of “liver qi stagnation” is mental stress. Thus, according to TEAM theories, it is reasonable to suggest that these patients were suffering from mental stress. The TEAM syndromes “depressed liver qi transforming into fire,” “effulgent heart-liver fire” and “liver qi invading the stomach,”
which some patients were suffering, can show as irritable conditions [29].

**Indication and mechanisms of action of Kamishoyosan**

Traditionally, Kamishoyosan has been used to treat a wide variety of mental and physical problems, including limb problems, heaviness of the head, dizziness, insomnia, irritability, burning sensation, menstrual abnormalities, and hot flashes [30], and has effects on mild-to-moderate somatization disorders [31], women’s general malaise and agitation [32], affective disorders [33,34], psychological stress insomnia [17], and depression [22,35].

In the IES-R-J scores of the study patients, it was found that three avoidance factor items—“My feelings about it were kind of numb,” “I tried to remove it from my memory,” and “I tried not to talk about it”—plus one intrusion factor item—“I found myself acting or feeling like I was back at that time”—did not change significantly after prescription of Kamishoyosan (Table 1). This may show the limitations of Kamishoyosan in treating PTSD-like stress.

Some of the major ingredients in Kamishoyosan are known to produce a sedative effect; they include the following: Angelicae Radix has a sedative effect in rabbits [36]; Paoniae Radix has sedative and analgesic effects in mice [37]; Bupleuri Radix affects the central nervous system, causing sleep prolongation, sedation, and analgesia [38]; and Liquiritin, a flavone compound derived from Glycyrrhizae Radix, has shown an antidepressant effect in animal studies [39].

The psychological effects of Shoyosan, the basic component of Kamishoyosan, have also been reported; they include the following: antidepressant effect on rats in metabolomics study [40], amelioration of brain cortex 5-HT and 5-HIAAA content in a mouse model of depression [41], regulation effect on the expression of AMPA receptors in chronic immobilization stress [42], upregulation of AMPA receptor subunit mRNA expression in the hippocampal region CA1 and amygdala [43], maintenance of the stability of hippocampal neurons [44], inhibition of hypothalamic-pituitary-adrenocortical axis negative feedback regulation [45], and counteraction on an increase in Ca2+ concentration in hippocampal synaptosomes [46].

**Situation of the study participants**

The patients who participated in the study were employees at the nursing facility for the elderly when it was hit by the tsunami. Thus, they were both rescue workers for the elderly at the facility and victims of the disaster. When the tsunami hit, their priority was to save the elderly residents of the nursing facility rather than focusing on their own need to escape and save themselves.

Most of the patients in the study lost their cars in the tsunami, and there was little gas available for those that still had cars. As a result, these patients did not have the opportunity to visit clinics for their own health. Moreover, because of the damage to transportation networks, hospitals, and the factory that produces Kampo medicine (Japanese herbal medicine), the availability of medical supplies in the disaster-stricken area was limited. OTC herbal medicines were supplied free by Kotaro Pharmaceutical Co., Ltd (Osaka, Japan). Authors visited the study facility as medical volunteers every weekend.

The earthquake and tsunami survivors suffered psychological as well as physical damage. The earthquake occurred on March 11, 2011, but from then until April 30, 2011, there were a total of 165 aftershocks with seismic intensity of 4 or more [47]. It was said that many of the survivors were affected psychologically, and 1 to 2 months after the disaster, many had become disillusioned [48]. Eleven of the 32 patients reported anxiety about the tsunami and aftershocks. Some of the patients with insomnia refused to take the soporific, because of the fear of another tsunami coming.

The victims of the Great East Japan Earthquake will need to receive ongoing care for physical and mental health issues for some time in the future. PTSD is associated with high healthcare costs [49]. Because herbal medicines are inexpensive and have few side effects, they are being used to treat many earthquake and tsunami victims in Japan. Furthermore, a matter of urgency is the predicted “Tokai Earthquake,” a giant magnitude 8 earthquake with an epicenter inland of Shizuoka prefecture (near Tokyo), from the Gulf of Suruga [50].

Further investigation is warranted to explain the mechanisms of the use of the herbal medicine Kamishoyosan in the treatment of PTSD. The strategy of using an inexpensive herbal medicine to treat PTSD is worth studying.

**Limitations**

This retrospective study was limited by the fact that it included only a small number of participants (32) who survived the earthquake, and there were no controls. Second, because of the dynamics of the post-earthquake situation, the authors were unable to have the study participants diagnosed by psychiatrists. Third, the herbal medicines that were given to the study participants were OTC products because of the limited medical conditions at the time; therefore, the quantity of herbal medicine prescribed may not have been sufficient to effect the desired results in some patients.

**Conclusion**

Survivors of the Great East Japan Earthquake who had limited access to medical care were diagnosed and treated according to TEAM theories and syndromes. More than 40% of the patients included in the study showed the TEAM syndrome “liver qi stagnation” 1 to 2 months after the disaster. They suffered not only stressful disorders like PTSD but also other TEAM syndromes caused by mental stress. The IES-R-J scores obtained for the patients showed improvement after administration of the herbal medicine Kamishoyosan to those for whom it was indicated by TEAM. However, the mental state of patients who had particularly violent or unpleasant experiences during or after the earthquake was exacerbated. The study suggested that the herbal medicine Kamishoyosan can be helpful in treating some stressful disorders like PTSD that result from disasters such as earthquakes.

**Acknowledgements**

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