Literature Review: Herbal Medicine Treatment after Large-Scale Disasters

Shin Takayama,* Soichiro Kaneko,* Takehiro Numata,* Tetsuharu Kamiya,*
Ryutaro Arita,* Natsumi Saito,* Akiko Kikuchi,* Minoru Ohsawa,*
Yoshitaka Kohayagawa[†] and Tadashi Ishii*

**Department of Education and Support for Regional Medicine*

Department of Kampo Medicine, Tohoku University Hospital

1-1, Seiryomachi, Aobaku, Sendai City, Miyagi Prefecture 980-8574, Japan

[†]National Disaster Medical Center, 8-15 Oota-machi

Fukushima Prefecture 960-8068, Japan

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Abstract: Large-scale natural disasters, such as earthquakes, tsunamis, volcanic eruptions, and typhoons, occur worldwide. After the Great East Japan earthquake and tsunami, our medical support operation's experiences suggested that traditional medicine might be useful for treating the various symptoms of the survivors. However, little information is available regarding herbal medicine treatment in such situations. Considering that further disasters will occur, we performed a literature review and summarized the traditional medicine approaches for treatment after large-scale disasters. We searched PubMed and Cochrane Library for articles written in English, and Ichushi for those written in Japanese. Articles published before 31 March 2016 were included. Keywords "disaster" and "herbal medicine" were used in our search. Among studies involving herbal medicine after a disaster, we found two randomized controlled trials investigating post-traumatic stress disorder (PTSD), three retrospective investigations of trauma or common diseases, and seven case series or case reports of dizziness, pain, and psychosomatic symptoms. In conclusion, herbal medicine has been used to treat trauma, PTSD, and other symptoms after disasters. However, few articles have been published, likely due to the difficulty in designing high quality studies in such situations. Further study will be needed to clarify the usefulness of herbal medicine after disasters.

Keywords: Disaster; Herbal Medicine; Kampo Medicine; Traditional Chinese Medicine; Review.

Correspondence to: Dr. Shin Takayama, Department of Education and Support for Regional Medicine, Department of Kampo Medicine, Tohoku University Hospital, 1-1, Seiryomachi, Aobaku, Sendai City, Miyagi Prefecture 980-8574, Japan. Tel: (+81) 22-717-7507, Fax: (+81) 22-717-7508, E-mail: takayama@med.tohoku.ac.jp

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Introduction

Large-scale natural disasters, such as earthquakes, tsunamis, volcanic eruptions, or typhoons, occur worldwide. In these emergencies, governments and the international community must respond with relief and support activities. In Japan, the last 25 years have seen the Great Hanshin Awaji earthquake of 1995, the Niigata Chuetsu earthquake of 2004, the Great East Japan earthquake and tsunami of 2011, and the Kumamoto earthquake of 2016. In the early phases of disasters, self-defense forces, police, and fire personnel rescued victims. Disaster medical assistant teams provided medical relief, including hospital support, patient transfer within the area, wide-area medical transport, and evacuation and transfer of hospitalized patients (Ishii, 2011).

In a large-scale disaster, damage may be severe or affect a greater area. These situations take longer to resolve, and survivors are often evacuated to shelters or evacuation centers. In shelters, long-term evacuees complain of numerous health problems, including infectious disease, pain, insomnia, or chronic disease (Inoue *et al.*, 2014; Tokuda *et al.*, 2014). The Japanese Medical Association Team, the Disaster Relief Project Team of the Japanese Primary Care Association, and other multi-disciplinary medical assistance teams provide medical support. Teams consist of doctors, nurses, pharmacists, and sometimes physical therapists or acupuncturists (Liu *et al.*, 2012).

Since ancient times, traditional Chinese and Japanese (Kampo) medicine has been used to treat infection, trauma, and pain. Japanese doctors use Kampo formulae as basic prescriptions. Kampo formulas are covered by the Japanese government health insurance. In addition to quality, Kampo extract preparations have advantages, including ease of preparation and transport, and conservation of the environment. A recent investigation reported that over 80% of Japanese doctors use Kampo preparations. Based on the experience of our medical support operation after the Great East Japan earthquake and tsunami, Kampo medicine may also be useful in treating the various conditions of disaster survivors (Takayama *et al.*, 2011).

However, little information is available regarding the indications, duration of treatment, effectiveness, and adverse effects of traditional medicine in disaster situations. In this study, we performed a literature review and summarized the use of herbal medicine after disasters.

Methods

Literature Search

We searched PubMed and Cochrane Library for articles written in English, and Ichushi for those written in Japanese. The articles were published from the inception date of the database to 31 March 2016. We used the following search strategy: (1) Disaster; (2) Earthquake; (3) Tsunami; (4) East Asian Traditional Medicine; (5) Kampo Medicine; (6) Chinese Traditional Medicine; (7) Chinese herbal drugs; (8) Herbal medicine; (9) Medicinal plant; (10) Plant components; (11) Plant extracts; (12) Phytotherapy; (13) Phyto-medicine; (14) Kampo; (15) Oriental medicine; (16) Japanese Traditional Medicine; (17)

#1–16 in Japanese; (18) #1 OR #2 OR #3; (19) #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17; (20) #18 AND #19.

Selection Criteria

We included articles published in English or Japanese that were related to herbal medicine treatment after a disaster. Physical therapy, massage therapy, acupuncture, and acupuncture-related techniques were excluded.

Article Selection

Two reviewers (S.T. and S.K.) independently assessed the relevance of the retrieved articles by title and abstract. Unsuitable studies were excluded and the full texts of all remaining articles were obtained and screened by two independent groups of reviewers (S.T. and S.K., and T.N. and A.K.) for eligibility. When reviewers disagreed, all authors reviewed the full-text. Disagreements were resolved via discussion and consensus.

Data Extraction

Two independent researchers (S.T. and S.K.) categorized eligible articles. Information from the articles was extracted and tabulated, and eligible studies were classified according to study design, type of disaster, subjects, type of intervention and control, endpoints, results, and adverse effects. Articles with elusive data presentation were rated as unclear.

Results

General Aspects

By searching electronic database, 119 potential articles were identified. Sixty-eight articles were excluded, by title or abstract, during the initial screening. The full text of 39 articles was obtained (Fig. 1). One article identified by a manual search was added later. Twelve articles, published between 2008 and 2015, met our inclusion criteria (Table 1). Most were published from Japan (10 of 12; 83.3%) (Takayama *et al.*, 2011; Kimura and Sato, 2012; Kuwahara, 2012; Mitsufuji *et al.*, 2012; Nakae *et al.*, 2012; Raimura, 2012; Watanabe, 2012; Takayama *et al.*, 2013; Numata *et al.*, 2014a; Akazawa, 2015) and China (2 of 12; 16.6%) (Meng *et al.*, 2011; Tianhong *et al.*, 2014). Six articles were published in English (50%) and six in Japanese (50%). Two were randomized controlled trials (RCTs) describing the effects of herbal medicine in patients with post-traumatic stress disorder (PTSD) after a disaster (Meng *et al.*, 2011; Numata *et al.*, 2014a). Four retrospectively investigated the treatment of trauma, primary care conditions, and dizziness (Takayama *et al.*, 2011; Kimura and Sato, 2012; Nakae *et al.*, 2012; Tianhong *et al.*, 2014). Six case reports or case series described the treatment of pain (Kuwahara, 2012; Akazawa, 2015), dizziness (Kuwahara, 2012; Mitsufuji *et al.*, 2012), psychosomatic symptoms

Figure 1. Review process flowchart.

(Watanabe, 2012), and common complaints (Takayama *et al.*, 2013). Representative herbal medicines used to treat symptoms after disasters are shown in Table 2. A map of the areas affected by the large-scale earthquakes described in the articles we reviewed is shown in Fig. 2A.

Herbal Medicine for PTSD

Two articles described the effects of herbal medicine on patients with PTSD after a disaster. Meng *et al.* (2011) reported that the traditional Chinese medicine *Xiao-Tan-Jie-Yu-Fang* (XTJYF), which is related to *Xiao-Yao-San* (*shoyosan* in Japanese), was used to treat the general psychological status of survivors of the Great Sichuan earthquake with PTSD. The efficacy of this treatment was studied in a double-blind RCT involving a placebo group; the results indicated that XTJYF significantly improved the Revised Symptom Checklist-90 index, especially in cases of somatization, obsessive compulsive behavior, depression, anxiety, hostility, and sleep deprivation. Numata *et al.* (2014a) reported that the Kampo medicine *saikokeishikankyoto* (SKK) was used to treat PTSD after the Great East Japan earthquake and tsunami. The efficacy of the treatment was studied in an RCT, and results indicated that SKK significantly improved the Revised Impact of Event Scale score. A subscale analysis showed SKK significantly improved avoidance, hyperarousal, and intrusion, when compared to a control group.

Herbal Medicine for Common Diseases

Kampo medicine was used in evacuation centers after the Great East Japan earthquake and tsunami disaster. Takayama *et al.* (2011) reported that infectious diseases, common colds,

Table 1. Review of the Eligible Articles

Authors	Disaster	Subjects	Intervention (n)	Control	Endpoints	Results	Adverse Effects
Numata <i>et al.</i> (2014a)	GEJED	PTSD	Saikokeishikankyoto (SKK) 7.5 g/day (n = 21)	Waiting (n = 22)	IES-R	Total IES-R score and subscale scores (avoidance, hyperarousal, and intrusion) improved significantly in the SKK group compared with control group.	Light coughing in a case; the symptom spontaneously improved
Meng <i>et al.</i> (2011)	GSE	PTSD	Xiao-Tan-Jie-Yu-Fang (XTJYF) 12 g/day (n = 123)	Placebo (n = 122)	Symptom Checklist (SCL)-90-Revised	SCL global indices significantly improved in XTJYF group.	Six cases had side effects
Tianhong <i>et al.</i> (2014)	GSE	Multiple fractured ribs and pulmonary contusions	Conventional treatment with Panax notoginseng (PN intravenously) (n = 18)	Conventional treatment (n = 17)	Visual analog scale (VAS) pain scores and arterial oxygen saturation	VAS scores in the PN group were lower than in the control group. The duration of mechanical ventilation, systemic analgesics administration, and hospital stay in the PN group remarkably decreased as compared to the control group.	Unclear
Takayama <i>et al.</i> (2011)	GEJED	Evacuee in the evacuation centers	Kampo preparations individually prescribed (n = 220)	None	Symptom	Common diseases including infectious diseases, common cold, hypothermia, allergies, and mental distress were treated with Kampo preparations according to Kampo diagnosis.	Unclear
Nakae (2012)	GEJED	Evacuee in the evacuation centers	Kampo preparations individually prescribed for common diseases (n = 12)	None	Symptom	Coldness, joint pain, muscle pain, allergy symptoms, and depression were treated with Kampo preparations.	Unclear

Table 1. (Continued)

Authors	Disaster	Subjects	Intervention (n)	Control	Endpoints	Results	Adverse Effects
Kimura and Sato (2012)	GEJED	Dizziness or vertigo	Hangekobokuto, Hangebyakujutsutennmato, or Ryokeijutsukanto (n = 15)	None	Symptom	Floating sensation were successfully treated with Kampo preparations according to the abdominal examination.	Unclear
Akazawa (2015)	GEJED	Chest pain	Daisaikoto and Shigyakusan (n = 1)	None	Symptom	Chest pain, related to psychological stress, after the earthquake improved with daisaikoto and shigyakusan.	Unclear
Mitsufuji <i>et al.</i> (2012)	GEJED	Orthostatic headache	Goreisan and/or Hochuekkito (n = 4)	None	Symptom	Orthostatic headache that presented after the earthquake was successfully treated with Kampo preparations.	Unclear
Kuwahara (2012)	GEJED	Tongue pain	Yokukansan (n = 2)	None	Symptom	Tongue pain improved after yokukansan administration.	Unclear
Watanabe (2012)	GEJED	Anxiety with palpitation or low grade fever	Saikokaryukotsuboreito (n = 2)	None	Symptom	Physical and mental/emotional symptoms that occurred after the earthquake improved on administration of saikokaryukotsuboreito.	Unclear
Raimura (2012)	GEJED	Dizziness, anxiety, and palpitation	Kamishoyosan or Orendokuto (n = 2)	None	Symptom	Symptoms relieved after additional therapy with orendokuto.	Unclear
Takayama <i>et al.</i> (2011)	GEJED	Common cold, hypothermia, rhinitis, or mental distress	Kampo preparations individually prescribed (n = 4)	None	Symptom	Symptoms relieved after Kampo treatment according to Kampo diagnosis.	Unclear

Notes: GEJED: Great East Japan earthquake disaster; GSE: Great Sichuan earthquake; PTSD: Post-traumatic stress disorder.

Table 2. Representative Herbal Medicines Used to Treat Various Symptoms After Disasters

Diseases and Symptoms		Herbal Medicine (in Chinese)	References
PTSD		(Xiao-Tan-Jie-Yu-Fang)	Meng <i>et al.</i> (2011)
		Saikokeishikankyoto (Chai-Hu-Gui-Zhi-Gan-Jiang-Tang)	Numata <i>et al.</i> (2014a)
Trauma	Multiple fracture in ribs and pulmonary contusions	Panax notoginseng	Tianhong <i>et al.</i> (2014)
Common diseases	Common cold	Kakkonto (Ge-Gen-Tang)	Takayama <i>et al.</i> (2011)
		Maobushisaishinto (Ma-Huang-Fu-Zi-Xi-Xin-Tang)	Takayama <i>et al.</i> (2011)
	Tonsillitis	Kikyoto (Jie-Geng-Tang)	Takayama <i>et al.</i> (2011)
	Hypothermia	Tokishigyakukagoshuyushokyoto (Dang-Qui-Si-Ni-Jia-Wu-Zhu-Yu-Sheng-Jiang-Tang)	Takayama <i>et al.</i> (2011)
	Enterocolitis	Rikkunshito (Liu-Jun-Zi-Tang)	Takayama <i>et al.</i> (2011)
		Goreisan (Wu-Ling-San)	Miura <i>et al.</i> (2011); Takayama <i>et al.</i> (2011)
	Rhinitis	Shoseiryuto (Xiao-Qing-Long-Tang)	Baba <i>et al.</i> (1995); Takayama <i>et al.</i> (2011); Nakae (2012)
	Itchy eyes	Eppikajutsuto (Yue-Bi-Jia-Zhu-Tang)	Takayama <i>et al.</i> (2011)
	Dry cough	Bakumondoto (Mai-Men-Dong-Tang)	Fujimori <i>et al.</i> (2001); Mukaida <i>et al.</i> (2011); Takayama <i>et al.</i> (2011)
	Constipation	Mashiningan (Ma-Zi-Ren-Wan)	Cheng <i>et al.</i> (2011); Takayama <i>et al.</i> (2011)
	Insomnia	Sansoninto (Suan-Zao-Ren-Tang)	Takayama <i>et al.</i> (2011)
	Irritation	Yokukansan (Yi-Gan-San)	Iwasaki <i>et al.</i> (2005); Matsuda <i>et al.</i> (2013); Takayama <i>et al.</i> (2011); Hyde <i>et al.</i> (2017)
	Anxiety	Kamikihito (Jia-Wei-Qui-Pi-Tang)	Takayama <i>et al.</i> (2011)
	Fatigue	Hochuekkito (Bu-Zhong-Yi-Qi-Tang)	Tatsumi <i>et al.</i> (2009); Takayama <i>et al.</i> (2011); Nakae (2012)
	Abdominal pain	Daikenchuto (Da-Jian-Zhong-Tang)	Takayama <i>et al.</i> (2011); Nakae (2012); Numata <i>et al.</i> (2014a)
	Leg edema or numbness of lower extremities	Goshajinkigan (Niu-Che-Shen-Qi-Wan)	Nakae (2012)
	Cramping in the calves	Shakuyakukanzoto (Shao-Yao-Gan-Cao-Tang)	Kumuta <i>et al.</i> (1999); Nakae (2012)

Table 2. (Continued)

Diseases and Symptoms		Herbal Medicine (in Chinese)	References
Dizziness or vertigo		Hangekobokuto (Ban-Xia-Hou-Po-Tang)	Kimura and Sato (2012)
		Hangebyakujutsutemmato (Ban-Xia-Bai-Zhu-Tian-Ma-Tang)	Kimura and Sato (2012)
		Ryokeijutsukanto (Ling-Qui-Zhu-Gan-Tang)	Kimura and Sato (2012)
		Orengedokuto (Huang-Lian-Jie-Du-Tang)	Raimura (2012)
Pain	Chest pain	Daisaikoto (Da-Chai-Hu-Tang)	Akazawa (2015)
	Tongue pain	Yokukansan (Yi-Gan-San)	Kuwahara (2012)
Psychosomatic symptoms	Anxiety, low grade fever, fatigue, coldness, sweating, dry mouth, shoulder stiffness and dizziness	Saikokaryukotsuboreito (Chai-Hu-Jia-Long-Gu-Mu-Li-Tang)	Watanabe (2012)

(A)

(B)

Figure 2. A map of the affected areas in the Great Sichuan earthquake and the Great East Japan earthquake and tsunami (A), intervention and investigation period of herbal medicine treatment after the Great Sichuan earthquake (B), and after the Great East Japan earthquake and tsunami (C).

(C)

Figure 2. (Continued)

and hypothermia were frequent during the first two weeks after the disaster; allergy symptoms increased two weeks later, and mental distress was commonly observed six weeks later. A total of 220 cases were treated with Kampo medicine. The same authors reported four patients treated with Kampo medicine for the common cold, hypothermia, allergic symptoms, and psychosomatic symptoms (Takayama *et al.*, 2013). Nakae *et al.* (2012) reported 13 cases treated with Kampo medicine for symptoms of coldness, joint pain, muscle pain, allergy, and depression.

Herbal Medicine for Dizziness or Vertigo

Dizziness or vertigo increased after the Great East Japan Earthquake due to multiple aftershocks. Kimura and Sato (2012) reported treating patients with dizziness or vertigo after the earthquake with *hangekobokuto* (12 cases), *hangebyakujutsutemmato* (two cases), and *ryokeijutsukanto* (one case).

Herbal Medicine for Trauma

Tianhong *et al.* (2014) reported the effect of *Panax notoginseng Radix* in survivors of the Great Sichuan earthquake with multiple rib fractures and pulmonary contusions. In a retrospective study, the combination of *Panax notoginseng Radix* and conventional treatment was compared with conventional treatment alone. Visual analogue scales of pain were lower in the combination group at one and two weeks. In the combination group, the duration of mechanical ventilation, systemic analgesia administration, and hospital stay was significantly lower than in the conventional treatment group.

Herbal Medicine for Pain Management

Seven cases of pain were treated with Kampo medicine; chest pain was treated using *daisaikoto* in one case (Akazawa, 2015), tongue pain using *yokukansan* in two cases (Kuwahara, 2012), and orthostatic headache using *hochuekkito* and *goreisan* in four cases (Mitsufuji *et al.*, 2012).

Table 3. Characteristics of the Great Sichuan Earthquake and the Great East Japan Earthquake and Tsunami Disasters

	Great Sichuan Earthquake	Great East Japan Earthquake and Tsunami
Type of earthquake	Inland crustal earthquake	Megathrust earthquake
Date	5/12/2008	3/11/2011
Scale	Moment magnitude 7.9	Moment magnitude 9.0
Death or missing	87,476	18,455
Main cause of death	Crushed to death	Drowning by tsunami
Collapsed or damaged houses	4,366,000	400,326
Evacuees	15,147,400	470,000

Herbal Medicine for Psychosomatic Symptoms

Multiple psychosomatic symptoms, including anxiety, low-grade fever, fatigue, coldness, sweating, dry mouth, shoulder stiffness, and dizziness were treated with *saikokar-yukotsuboreito* in two cases (Watanabe, 2012).

Intervention Period

Figures 2B and 2C show the intervention or investigation periods of herbal medicine treatment after the Great Sichuan earthquake (B) and the Great East Japan earthquakes and tsunami (C). Herbal medicine was used for the first two months to treat trauma, and for primary care in hospitals and evacuation centers. However, treatment for PTSD began 6–8 months after the disaster. The characteristics of the two major disasters are described in Table 3.

Adverse Effects of Herbal Medicine

Two RCTs reported side effects; the others were unclear in this regard. Nausea, diarrhea, and malaise were observed with the use of XTJYF, but the symptoms were not considered serious, and there were no significant differences between the XTJYF and placebo groups (Meng *et al.*, 2011). Light coughing occurred in one case; however, this symptom spontaneously resolved after the SKK was discontinued (Numata *et al.*, 2014a).

Discussion

Interpretation of Results

Herbal medicine has been used to treat PTSD, trauma, common complaints, dizziness and vertigo, pain, and psychosomatic symptoms. Two articles were RCTs, while the others were investigative studies. The evidence was insufficient to assess the effectiveness of herbal medicine for the treatment of various symptoms or diseases after large-scale disasters.

*Prior Studies Regarding the Evidence and Effectiveness of Herbal Medicine
Post-Traumatic Stress Disorder*

Two articles described the effects of herbal medicine on patients with PTSD. [Meng et al. \(2011\)](#) reported the efficacy of XTJYF to treat the general psychological state, and [Numata et al. \(2014a\)](#) described the efficacy of SKK to treat PTSD. In a rat model of chronic stress, XTJYF upregulated the expression of serotonin (5-hydroxytryptamine; 5-HT) 1A receptor in the hippocampus, potentially suppressing depression in PTSD ([Xiu et al., 2007](#)). The formula is a modification of *Xiao-Yao-San* (*Free and Easy Wanderer*) (*shoyosan* in Japanese), which consists of eight herbs: *Bupleuri Radix*, *Angelicae sinensis Radix*, *Poria*, *Atractylodis macrocephalae Rhizoma*, *Paeonia alba Radix*, *Menthae Herba*, *Glycyrrhizae Radix Praeparata*, and *Zingiberis rhizoma*. A modified form of *Xiao-Yao-San*, XTJYF is made by adding additional herbs including *Ostreae Concha*, *Os Draconis*, *Rhei Radix et Rhizoma Praeparata*, *Acori graminei Rhizoma*, *Coptidis Rhizoma*, *Pinelliae Rhizoma Praeparata*, and *Citri reticulatae Pericarpium*. There are more pharmacological studies on *Xiao-Yao-San* than on XTJYF. *Xiao-Yao-San* is reported to be involved in the upregulation of the expression of serotonin receptors ([Bao et al., 2008](#)) and the α -amino-3-hydroxy-5-methyl-4-isoxazole-propionate (AMPA) receptor subunit GluR2/3. The expression of the protein interacting with protein kinase C alpha is downregulated by *Xiao-Yao-San* ([Yue et al., 2007](#)). [Xu et al. \(2011\)](#) reported that *Xiao-Yao-San* maintained the stability of hippocampal neurons and inhibited the hypothalamic-pituitary-adrenocortical axis negative feedback regulation ([Xu et al., 2009](#)). Another formula made by modifying *Xiao-Yao-San* is called *Free and Easy Wanderer Plus*. *Free and Easy Wanderer* consisted of the eight herbs of *Xiao-Yao-San*, and three additional herbs, *Scutellariae Radix*, *Moutan Cortex*, and *Gardeniae Fructus* ([Zhang et al., 2007](#)). *Free and Easy Wanderer* improves PTSD-like behavior in stressed rats ([Qiu et al., 2015](#); [Wang et al., 2009](#)) by stimulating allopregnanolone biosynthesis ([Wang et al., 2009](#)).

Pharmacological studies revealed the mechanisms of SKK. Administration of SKK for 14 days significantly increased serotonin in the hippocampus and the corpus striatum, and norepinephrine in the hippocampus ([Itoh et al., 1996](#)). SKK also regulates the levels of plasma interleukin-6 and the concentration of soluble interleukin-6 receptors, and improves the depressed mood of climacteric women with insomnia ([Ushiroyama et al., 2005](#)). PTSD is associated with increased levels of inflammatory markers, including interleukin-6 and tumor necrosis factor alpha ([Passos et al., 2015](#)), suggesting that PTSD may be related to chronic low-grade inflammation. SKK may decrease symptoms of PTSD by altering levels of neurotransmitters and decreasing inflammation.

Trauma, Pain, and Cramping

In Japan, *jidabokuippo* (*Zhi-Da-Po-Yi-Fang*) has been used to alleviate pain and swelling after trauma. In an RCT, [Nakae et al. \(2012\)](#) reported that treatment of rib fracture with *jidabokuippo* resulted in shorter duration of treatment and decreased healthcare expenditure, when compared to treatment with nonsteroidal anti-inflammatory drugs.

Takeda (2010) reported that *jidabokuippo* was more effective for alleviating pain and swelling after injury of the lateral ankle ligaments than Loxoprofen Sodium Hydrate. *Shakuyakukanzoto* has been used for the treatment of cramping. In a double blind RCT, Kumada *et al.* (1999) reported the efficacy of *shakuyakukanzoto* for cramping in patients with cirrhosis. The cramping score significantly improved in the *shakuyakukanzoto* group, when compared to the placebo group. Two components included in *shakuyakukanzoto* are believed to improve muscle cramping: *Glycyrrhizae Radix* promotes opening of extra-cellular potassium channels, and *Peoniae* decreases inflow of intracellular calcium (Kimura, 1992).

Common Cold

Ephedrae Herba and/or *Cinnamoni Cortex* are used during the early phases of the common cold. In addition, Okabayashi *et al.* (2014) reported on the effects of *kakkonto* on the common cold. An RCT comparing *kakkonto* with multiple Western-style cold medicines demonstrated no difference in the ability to alleviate common cold symptoms, including coldness, nasal, throat, or bronchial symptoms. Furthermore, Chang *et al.* (2012) reported that in cell lines from human upper and lower respiratory tracts, *kakkonto* inhibited respiratory syncytial virus-induced plaque formation in a dose-dependent fashion. *Kakkonto* enhanced phagocytic activity of macrophages, an *in vivo* defense mechanism, suggesting that *kakkonto* suppresses replication of the common cold and influenza viruses. In addition, *kakkonto* exhibited antiviral and anti-inflammatory effects, followed by a reduction in cold symptoms, while multiple Western-style cold medicines suppressed cold symptoms. Nabeshima *et al.* (2012) and Kubo *et al.* (2007) reported that *maoto* (Ma-Huang-Tang), which includes the components of *kakkonto*, shortened the duration of fever during an influenza infection. The effect is similar to that of neuraminidase inhibitors reported in RCTs.

Enterocolitis

In an RCT, Miura *et al.* (2011) reported the effectiveness of *goreisan* to treat norovirus-induced enterocolitis. When compared to conservative care, *goreisan* significantly shortened the duration of vomiting, diarrhea, and abdominal pain (vomiting in the *goreisan* group: 79 min, conservative group: 1702 min; diarrhea: 110 min vs. 1728 min; abdominal pain: 122 min vs. 1813 min).

Rhinitis

A double-blind trial using *shoseiryuto* and placebo for treatment of perennial allergic rhinitis included 220 patients. Administration of *shoseiryuto* for two weeks alleviated symptoms including spasmodic sneezing, mucus production, and rhinostenosis ($p < 0.001$) (Baba *et al.*, 1995). *Shoseiryuto* decreased the number of T-helper 2 (Th2) cells and the level of interleukin-4. Th1 cells were not altered (Ko *et al.*, 2004).

Antihistamines are recommended as a standard therapy for allergic rhinitis (Bousquet *et al.*, 2012). Although side effects, such as sleepiness, have decreased with the development of newer drugs, side effects still exist. Since *shoseiryuto* does not affect histamine H1 receptors, there are fewer effects such as sedation and drowsiness (Sakaguchi *et al.*, 1996).

Cough

Bakumondoto is a traditional herbal medicine used for the treatment of bronchitis, bronchial asthma, and cough. In an RCT, Fujimori *et al.* (2001) reported that compared to dextromethorphan hydrobromide, *bakumondoto* was more effective in treating post-infectious cough. Mukaida *et al.* (2011) showed that *bakumondoto* was effective in suppressing cough in elderly patients diagnosed with chronic obstructive pulmonary disease. *Glycyrrhizae Radix*, one of herbs contained in *bakumondoto*, may have a persistent anti-tussive effect, and the metabolites liquiritin apioside and liquiritigenin, may be involved in these effects. *Ophiopogonis Radix*, another herb in *bakumondoto*, has anti-inflammatory activity, and ruscogenin and ophiopogonin D are two of its active components.

Irritation

Iwasaki *et al.* (2005) reported that *yokukansan* improved the behavioral and psychological symptoms of dementia, such as hallucinations, delusions, agitation, and aggression. Two meta-analyses examined the effect of *yokukansan* on behavioral and psychological symptoms of dementia (Matsuda *et al.*, 2013; Hyde *et al.*, 2017). *Yokukansan* did not increase extrapyramidal symptoms. *Yokukansan* controls the concentration of serotonin in the synaptic cleft via partial agonist of 5-HT1A receptors (Terawaki *et al.*, 2016), and 5-HT2A receptor expressions are downregulated by *yokukansan* (Egashira *et al.*, 2008). *Yokukansan* inhibits the release of glutamate resulting in a decreased concentration of glutamate at synaptic clefts in the brain, and promotes glutamate uptake by astrocytes (Takeda *et al.*, 2008a, 2008b; Kawakami *et al.*, 2010).

Fatigue

Tatsumi *et al.* (2009) reported in elderly patients with chronic obstructive pulmonary disease, that *hochuekkito* may be superior to conventional therapy in improving fatigue and malaise, and the objective indexes of systemic inflammation and nutritional status. *Hochuekkito* increases titers of influenza virus-specific IgA antibody and total IgA antibody in the nasal cavity (Kiyohara *et al.*, 2006). Furthermore, *hochuekkito* inhibits rhinovirus infection in human tracheal epithelial cells, by decreasing intercellular adhesion molecule-1 levels, and blocks viral RNA from entering the cytoplasm via the airway epithelial cell endosomes (Yamaya *et al.*, 2007). Glycyrrhizin may be partly responsible for the inhibition of rhinovirus infection by *hochuekkito*, since it stimulates the upper respiratory tract mucosal immune system, and modulates airway inflammation by reducing cytokine production. *Hochuekkito*, since it stimulates the immune system, is considered a tonifying drug.

Panax ginseng Radix and *Astragali Radix*, ingredients of *hochuekkito*, are believed to confer these effects, which correspond to “vital energy” or “signaling” in Western medicine. Tonifying drugs enhance energy uptake through digestion and absorption (in the case of *Panax ginseng Radix*) or through respiration (in the case of *Astragali Radix*). Similarly, *Angelicae Radix*, *Paeoniae Radix*, and other herbs are thought to support blood production, while *Rehmanniae Radix*, *Ophiopogonis Radix*, and others reinforce liquid formation.

Functional Abdominal Pain or Constipation

In Japan, *daikenchuto* is widely used to prevent ileus after abdominal surgery. *Daikenchuto* can be used to treat patients with pain or cold sensations in the abdomen, and those who cannot eat due to nausea. Numata *et al.* (2014b) reported that *daikenchuto* alleviated functional constipation in post-stroke patients. A subscale analysis showed that *daikenchuto* significantly improved constipation scores. After therapy with *daikenchuto*, abdominal gas volume assessed by radiographic examination was significantly reduced. *Daikenchuto* treats abdominal symptoms by enhancing the secretions of motilin (Nagano *et al.*, 1999), substance P (Kono *et al.*, 2008), calcitonin gene-related peptide, and adrenomedullin (Kono *et al.*, 2010, 2011), and activating the transient receptor potential vanilloid (Kikuchi *et al.*, 2013). *Keishikashakuyakuto* is also used to treat functional abdominal pain, and the effects on irritable bowel syndrome have been investigated in a double blind RCT (Sasaki *et al.*, 1998). Abdominal pain in irritable bowel syndrome with diarrhea significantly decreased after *keishikashakuyakuto* (Gui-Zhi-Jia-Shao-Yao-Tang) administration, and the effect was superior to that of a placebo. Adverse effects of *keishikashakuyakuto* were not significantly different from placebo, suggesting that *keishikashakuyakuto* is safe. Effects of *mashiningan* have also been evaluated in a double blind RCT (Cheng *et al.*, 2011). Increased complete spontaneous bowel movements, relief of constipation and straining, and reduction in the use of rescue therapy was noted in individuals in the *mashiningan* group. The results were superior to those of a placebo group, and no serious adverse effects were reported. *Aurantii Fructus Immaturus*, which is an ingredient of *mashiningan*, increases digestion and regulates bowel function, and hemp seed oil acts as a stool softener.

Dizziness or Vertigo

Nakamura *et al.* (2000) conducted an RCT study of *goreisan* for orthostatic hypotension in patients with diabetes mellitus. They reported that *goreisan* significantly diminished the drop in blood pressure after standing. *Goreisan* also improved subjective symptom of orthostatic dizziness. There are so many case reports and small size studies regarding Kampo treatments for dizziness or vertigo, since treatments for them differ depending on its causes and accompanying symptoms. Formulae for orthostatic dizziness are *ryokeijutsu-kanto* or *hochuekkito*. *Hangebyakujutsutemmato* and *takushato* (Ze-Xie-Tang) have been used for treating paroxysmal vertigo. If patients have dizziness with cold feelings and fluid

retention, *shinbuto* (Zhen-Wu-Tang) may be used. In case of dizziness caused by mental stress, *hangekobokuto* and *saikokaryukotsuboreito* can be administered.

Duration of Treatment

Immediately after a large-scale disaster, the disaster medical assistance teams provide emergency care. These teams primarily treat trauma and crush injuries. During this period, emergency care should be a priority. Survivors are later evacuated to shelters or evacuation centers. Evacuees may experience health problems and medical support activities, including hygiene maintenance, primary care, and psychological support. Figures 2B and 2C show that herbal medicine treatment after a disaster tends to occur in two periods. Herbal medicine was used in the evacuation center early after the disaster, and for as long as six months after the disaster for treatment for PTSD. There may have been more medical support involving herbal treatments during other treatment periods. However, they did not fall within the scope of this review.

Points to Remember

Few articles mentioned adverse effects. SKK was associated with the onset of cough in one of 27 patients; however, coughing spontaneously resolved after the treatment was discontinued (Numata *et al.*, 2014a). SKK contains *Scutellariae Radix*, which has been reported to cause interstitial pneumonia in rare cases. In general, adverse effects associated with the herbal medicines are well tolerated. The Japan Geriatrics Society guidelines describe five herbs with known adverse effects: *Processi Aconiti Radix*, *Glycyrrhizae Radix*, *Ephedrae Herba*, *Scutellariae Radix*, and *Gardeniae Fructus*. These herbs are listed in the pharmacopeia, and adverse reactions have been reported and published by the Pharmaceutical and Medical Devices Agency. *Glycyrrhizae Radix*, which can cause hypokalemia, is a component of approximately 70% of herbal preparations in Japan. Prolonged and heavy use of *Glycyrrhizae Radix* should be avoided. If adverse effects are thought to be associated with herbal medicines, treatment should be stopped, and a proper examination should be performed.

Limitations

It is difficult to confirm the effectiveness of herbal treatments in disasters. Immediately after the disaster, rescue and relief operations are the top priority and for this reason, few studies have been carried out during this period. The studies carried out immediately after a disaster had biases in their design. Therefore, evidence for the effectiveness of herbal treatments in disaster situations is insufficient. Investigations on the effectiveness of herbal treatments should be performed in less extreme situations. One common problem for both Western and traditional medicine is the insufficient transport of medicines. Furthermore, in disaster situations, clean drinking water, which is required to take some medicines, is often scarce.

Future Perspectives

Herbal medicine may be useful to treat various symptoms and diseases after large-scale disasters. However, there have been few reports, and further studies will be needed to confirm the effectiveness of herbal treatment these situations. Nonetheless, future studies will be performed considering the feelings of the disaster victims.

In conclusion, herbal medicine has been used to treat trauma, PTSD, and other symptoms in primary care. Two of the articles reviewed were RCTs and the others were investigative studies. In disaster situations, it is difficult to design high quality studies to confirm the effectiveness of herbal medicine. Further studies will clarify the usefulness of herbal medicine in treating patients after large-scale disasters.

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