in vivo *29*: 109-116 (2015)

Efficacy and Side-effects of a Semi-individualized Chinese Herb Mixture "Tiáo Gēng Tāng" for Menopausal Syndrome in China

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Abstract. *Background: Chinese herbal medicine is an alternative therapy for menopausal problems and is widely practiced in China and many other Asian countries. However, efficacies and side-effects are rarely assessed according to the standards of evidence-based medicine. Patients and Methods: This is a prospective observatory study following efficacy and side-effects of a semi-individualized Chinese herbal mixture "Tiáo Gēng Tāng (TGT)" in 30 patients for 3 months. Another group of 30 patients receiving hormone therapy with tibolone was included as a positive comparison. Common questionnaire-based measuring instruments were: modified Kupperman index, menopause rating scale, life quality and Chinese medical symptom scale (CMSS). Follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E_2) were determined before and three months after the treatments. Results: Significant improvement was seen in overall scores of all the four measurements in both groups. For some symptoms, including dry mouth, tinnitus, poor appetite and constipation, TGT was more effective than tibolone. For psychosocial and sexual sub-scales of life quality, tibolone has a slightly higher remedy rate than TGT. TGT lowered FSH and LH significantly, as tibolone did, but elevated E2 significantly less than tibolone. Various adverse events, including body weight increase, abdomen discomfort, nausea/vomiting, emotional instability, pressure in breasts and dizziness, were reported by patients treated with tibolone, whereas only diarrhea was observed in two patients treated with TGT. Conclusion: TGT alleviates menopausal symptoms with similar efficacy as tibolone but has fewer side effects.*

Abbreviations: CMSS, Chinese medical symptoms scale; E_2, estradiol; FSH, follicle-stimulating hormone; LH, luteinizing hormone; MKI, modified Kupperman Index; MRS, menopause rating scale; MENQOL, menopause specific quality of life; TCM, traditional Chinese medicine; TGT, Tiáo Gēng Tāng.

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Key Words: Menopausal symptoms, Chinese herbal medicine, clinical trial, efficacy, adverse effect.

Approximately 80% of menopausal women suffer from related symptoms to various degrees; among them, approximately 25% need treatment (1-4). These symptoms usually continue for 4-5 years or even longer (1, 5). Menopausal syndrome directly affects the life quality of women and is in the long run associated with disorders including osteoporosis and cardiovascular disease (6, 7).

A considerable number of medical professionals and a significant proportion of patients are reluctant to the established hormone therapy for various reasons, such as contraindications, personal preference and side-effects (8, 9). Complementary therapies, using natural products, provide an alternative route of treatment and are increasingly catching attention. Chinese herbal medicine is an alternative therapy for menopausal problems widely practiced in China and many other Asian countries. Tiáo Gēng Tāng (TGT), meaning "decoction that regulates body balances during menopause", is one such Chinese herb mixture with practical history of more than 30 years in the Shanghai area. The core components of TGT are 10 herbs that are assembled according to the concept of Chinese medicine for regaining body balance (10). In the sense of evidence-based medicine, some of the TGT components may contain phytoestrogens and other estrogen-like substances, which modulate the

Table I. *Basic formula of the Tiáo Gēng Tāng.*

Chinese term (pingying)	English term	Latin term	Daily dose
Sheng di huang	Chinese foxglove	Radix rehmanniae	15 g
Bai shao	Chinese peony root	Radix paeoniae alba	9 g
Ba ji tian	Morinda	Radix morindae officinalis	9 g
Ying yang huo	Barrenwort	Herba epimedium	15 g
Zhi mu	Anemarrhena rhizome	Rhizoma anemarrhenae	9 g
Huang bai	Cork-tree bark	Cortex phellodendri	9 g
Sheng long gu	Fossilized vertebrae and bones	Os draconis	30 g
Sheng mu li	Ostracean	Concha ostreae	30 g
Ye jiao teng	Tuber fleeceflower Stem	Caulis polygoni multiflori	30 g
Chai hu	Bupleuri root	Radix bupleurum	9 g

estrogen receptor. However, a fundamental difference is that TGT is not a substitution therapy but rather aims to re-balance the body condition in a defined period of, mostly, less than 6 months. Once the body balance is recovered, the therapy will be terminated. A further key feature of TGT is the individual optimization of its exact composition for each patient based on her body condition and symptoms stratified according to the traditional Chinese medicine concept "Zheng", whereas additional herbs may also be added to modulate other symptoms, which are not directly related to menopause.

Dr. Sun and Dr. Xu, co-authors of this work, have been treating their patients with TGT for more than 30 years. According to their experience, TGT is especially effective for several major menopause-related symptoms, including hot flashes, sleep disturbance and emotional instability (11). However, the effects of TGT have not been systematically and comprehensively assessed according to the standards of evidence-based medicine. On the other hand, a standardized clinical trial requires randomization, placebo-control and blinding and is, therefore, extremely difficult, especially from the ethical point of view. Therefore, we designed the present observational study as an alternative and carried out this pilot study in which we followed 30 patients on TGT treatment for 3 months using 4 common measuring instruments: modified Kupperman Index (MKI), menopause rating scale (MRS), menopause-specific quality of life (MENQOL) and Chinese medical symptoms scale (CMSS). We compared the results with those of 30 patients on hormone treatment.

Patients and Methods

Study design and study patients. The present study is a prospective observational study including a study group of patients receiving the Chinese herbal prescriptions TGT and a comparison group of patients receiving hormone replacement therapy with tibolone. The observational period of three months is sufficient since the effects of both hormone therapy and Chinese herbal therapy can be followed and registered readily after 2 weeks. In addition, Chinese herbal therapies are usually conceived for short periods of up to 6 months.

The study was conducted with the approval of the Institutional review board of Longhua Hospital and the ethics committee of Longhua Hospital, Shanghai University of traditional Chinese medicine. Patients were recruited at the Outpatient Department of Shanghai Longhua Hospital of Shanghai University of Traditional Chinese Medicine (TCM) from November 2012 to February 2014. Written consent to the study was obtained from all participants.

Choice of treatment was based on clinical indication and personal wish of the patient. A total of 34 patients receiving Chinese medicine and 34 receiving tibolone formed the study and the comparison groups for observation, respectively. All patients fulfilled the following inclusion criteria.

Inclusion and exclusion criteria. Inclusion criteria were (i) aged 40-60 years, (ii) spontaneous menopause, (iii) suffering hot flashes and sweating, emotional instability, dizziness, tinnitus, palpitations, insomnia, disturbed sleep, back pain and other symptoms related to menopause, (iv) total modified Kupperman Index score ≥15, (v) "Yin deficiency Zheng" stratified as kidney yin deficiency Zheng, kidney and liver yin deficiency Zheng, yin deficiency and excessive liver yang Zheng, heart-kidney non-interaction Zheng, kidney yin-yang deficiency Zheng, (vi) endometrium ≤5mm by ultrasound and (vii) written consent for the study.

Exclusion criteria were (i) major diseases, such as hypertension, ischemic heart disease, stroke, dementia, diabetes, thyrotoxicosis and malignancy and (ii) "Yang deficiency Zheng" with kidney yang deficiency, spleen-kidney yang deficiency and patients with thick greasy tongue.

TGT formula and Chinese medicine Zheng stratification. The TGT formula has a basic part (Table I) and an individualized additional formula. Chemical components are not yet completely profiled. However, preliminary studies using high-performance liquid chromatography coupled with photodiode array detection method have detected three major constituents of tiaogentang, including Paeoniflorin, 2,3,5,4'-tetrahyoxystilbene-2-O-β-D-glucoside and Icariin.

Individualized additional formula is prescribed based on Chinese medicine Zheng stratification. Patients with "Yin deficiency Zheng" (see inclusion criteria) were further stratified into 5 groups based on

the traditional Chinese medical concept Zheng differentiation (14, 15) and additives were assembled accordingly:

(i) Zheng group "kidney yin deficiency"
- Major symptoms: hot flashes, sweating.
- Minor symptoms: dizziness and tinnitus, waist and knee pain, vexing heat in the five hearts, dry and itching skin, heel pain, red tongue, thin or less coating, thin and fast pulse
- Additives: no

(ii) Zheng group "kidney and liver yin deficiency"
- Major symptoms: same as group (i).
- Minor symptoms: dizziness and tinnitus, chest tightness and (or) hypochondriac pain, vulva itching, headache and (or) dizziness, emotional instability, dry eyes, red tongue, less coating, thin, string, fast pulse.
- Additives: nv zhen zi (Fructus Ligustri Lucidi) 12g, gou qi zi (Fructus Lycii) 12g, huang jin (Rhizoma Polygonati) 9g.

(iii) Zheng group "yin deficiency and excessive liver yang"
- Major symptoms: same as group (i).
- Minor symptoms: bitter mouth and/or acid regurgitation, dizziness and/or headache, rib-side distening pain, irritability, red complexion, red and dry tongue, thin and string pulse or strings and powerful pulse.
- Additives: qing hao (Herba Artemisiae Annuae) 30g, gou teng (Ramulus Uncariae Cum Uncis) 15g, tian ma (Rhizoma Gastrodiae) 9g.

(iv) Zheng group "heart-kidney non-interaction"
- Major symptoms: same as group (i).
- Minor symptoms: paltipation, emotional instability, restlessness, insomnia and/or dreaminess, forgetfulness, easily frightened, red tongue, thin coating, fast pulse.
- Additives: huang lian (Rhizoma Coptidis) 6g, rou gui (Cortex Cinnamomi) 3g, ling chi shi (Magnetitum) 30g.

(v) Zheng group "kidney yin-yang deficiency"
- Major symptoms: same as group (i).
- Minor symptoms: shift hot and cold, dizziness and (or) tinnitus, backache and (or) fatigue, vexing heat in the five hearts and/or cold limbs, lower extremity edema, pale tongue, thin, weak pulse.
- Additives: dang shen (Radix Codonopsis) 15g, huang qi (Radix Astragali) 15g, zao xin tu (Terra Frava Usta) 30g.

Treatment. TGT therapy was carried out by following the established protocol in routine clinical care. The TGT decoction was prepared by soaking 7-day portions of the semi-individually assembled herb mixture in 1.5 liters of water for 60 min and subsequently boiling for 45 min. The extraction was repeated once and the two decoctions were pooled together and stored in 14 portions in a refrigerator. Two portions were taken daily 30 min after breakfast and after dinner, respectively.

Hormone therapy with Livial containing tibolone (Nanjing Organon Pharmaceutical Co., Ltd., City, China) was carried out following the established standard protocol in routine clinical care.

Outcome measures. Four measure instruments were applied including (i) MKI, (ii) MRS, (iii) MENQOL, (iv) CMSS (16-18). All parameters were assessed using questionnaires at 4 time points: before the treatments, 1, 2 and 3 months after beginning of the treatments. Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E2) were determined before the treatments and 3 months after beginning of the treatments.

CMSS consisted of 18 symptoms. A scale ranging from 0 to 3 points was used to describe the severity of the perceived menopausal symptoms as none, mild, moderate and severe, respectively.

Statistic evaluation. Improvements within a subject before and on treatment at various time points were assessed using the paired *t*-test. The between groups differences in improvement at various time points were evaluated using a general lineal model for repeated measurements. Significant and highly significant differences were defined as $p<0.05$ and $p<0.005$, respectively. All tests were two-sided.

Results

Patients and drop-outs. Initially, a total of 68 participants were included for observation; 34 in each group. The drop-out rate was 12% (8/68), whereas most drop-outs from the follow-up were due to contact loss (4 cases in both groups) and interruption of the therapy for unrelated health problems (2 cases in the TGT group). Two other patients in the tibolone group stopped the therapy due to symptoms, which may be possibly related to the therapy. The remaining 60 participants, 30 in each group, were followed over three months and included in the evaluation. Age (52.93±3.26 *vs*. 53.17±3.12 years), height (161.47±4.81 *vs*. 162.03±5.26 cm), body weight (61.73±8.12 *vs*. 62.23±5.21 kg) and base-line parameters were all compatible between the two groups (Table II).

Outcome. Readily one month on treatment, highly significant improvement was obtained in both groups for total scores of the measurements (Figure 1). The improvement observed was not temporary but kept increasing continuously for the whole follow-up period of 3 months (Figure 1). No significant difference was observed between the TGT and tibolone groups regarding total scores of all 4 measurement instruments (Table II).

For most symptoms, including hot flushes, sleeping disturbance and emotional instability, significant improvement was obtained in both groups; both in measuring scales and in rate of remedy (Table III). For example, for vasomotor and physical (two subscales of menopause-specific life quality), the remedy rate was similar in the TGT and the tibolone groups: 69% *vs*. 63% and 42% *vs*. 36%, respectively. For psychosocial and sexual sub-scales of the life quality, tibolone reached a significantly higher remedy rate than TGT: 29% *vs*. 15% and 29% *vs*. 12% (Table III, Figure 1).

When measured with the CMSS, TGT was more effective than tibolone. For example, for several symptoms, including dry mouth, tinnitus, poor appetite and constipation, significant improvement was only achieved in the TGT group (Table IV).

Female hormone change. FSH and LH were significantly decreased after 3 months of treatment in both groups. The between-group difference, regarding change of these two

Table II. *Improvement of total scores in four different rating methods and change in serum hormones after 3 months of treatment.*

Measurement	Baseline	TGT	Baseline	Tibolone	Differences	
	% Improvement				Within subjects	Between groups
Modified Kupperman Index	28±7	16±6	29±8	16±7		
	45±19	43±18				
Menopause Rating Scale	19±6	10±4	19±5	12±4		
	45±14	39±14				
Menopause Specific Quality of Life	62±14	38±11	63±16	37±12		
	38±14	41±12				
Chinese Medical Symptoms Scale	24±6	12±5	23±5	15±4	Significant	Not significant
	50±20	36±13				
	% Change in serum concentration					
FSH	88±36	66±38	86±33	67±36		
	26±29	22±29				
LH	38±14	29±15	33±11	28±12		
	23±33	15±27				
E2	30±21	43±32	32±20	67±40		p=0.03
	71±147	153±173				

Values are all mean±standard deviation. TGT, Tiáo Gēng Tāng; E2, estradiol; FSH, follicle-stimulating hormone; LH, luteinizing hormone.

hormones, was not significant. In contrast, although TGT also elevated E_2, this elevation was significantly lower (p=0.03) than that of tibolone (Table II).

Side-effects. Various adverse events have been reported by patients taking tibolone, including body weight increase in two cases, abdomen discomfort, nausea/vomit, emotional instability, pressure in breasts and dizziness (Table V). The last two adverse events let to termination of the hormone replacement therapy.

In contrast, the only adverse event reported by patients taking TGT, possibly related to therapy administered, was diarrhea in two cases (Table V). This symptom disappeared in one case and improved in the other one after adjusting the formulation of TGT.

Discussion

Alleviating effects of TGT for menopausal symptoms were demonstrated by significant improvement in the scores of 4 common outcome measuring instruments. For major related symptoms, the effects of TGT were nearly equivalent to those of hormone replacement therapy with tibolone. Only for psychosocial and sexual scales TGT was less effective than tibolone. However, TGT showed effects on a number of symptoms, such as constipation and tinnitus for which tibolone did not have a significant outcome.

We are aware of certain limitations of the present study, which was of an observational nature and, therefore, lacked randomization, placebo-control and blinding. In addition, the outcome measurements were carried out by means of questionnaires, which reflect a subjective perception of the patients. Therefore, we cannot exclude partial placebo effects in the reported improvement. However, this limitation can be compensated to some extent by three considerations: (i) the outcome parameters were repeatedly measured 3 times after the onset of therapy and showed continuously increasing effects of TGT, thus attenuating the possibility of placebo effect, (ii) the changes in hormone levels were objectively determined and are, therefore, less likely the results of placebo effect and (iii) as long as the effects of TGT is statistically significant, its benefit for women suffering from menopausal syndrome is real, even if some of the effects are psychological.

Despite the equivalent effects in a number of parameters, the TGT and tibolone therapy do differ from each other. The most apparent difference can be seen in the adverse events. While TGT had merely two hardly noteworthy transient diarrhea cases, much more severe adverse events were reported by patients receiving tibolone, which are all within the spectrum of well-known side-effects of hormone replacement therapy. Another substantial difference between TGT and tibolone is the E_2 level that was elevated significantly less by the former. Furthermore, for several symptoms, such as tinnitus and constipation, only TGT showed an effect, while tibolone did not. All these findings suggest that TGT has similar effects as hormone replacement therapy, yet the function mechanisms of the two therapies are likely different.

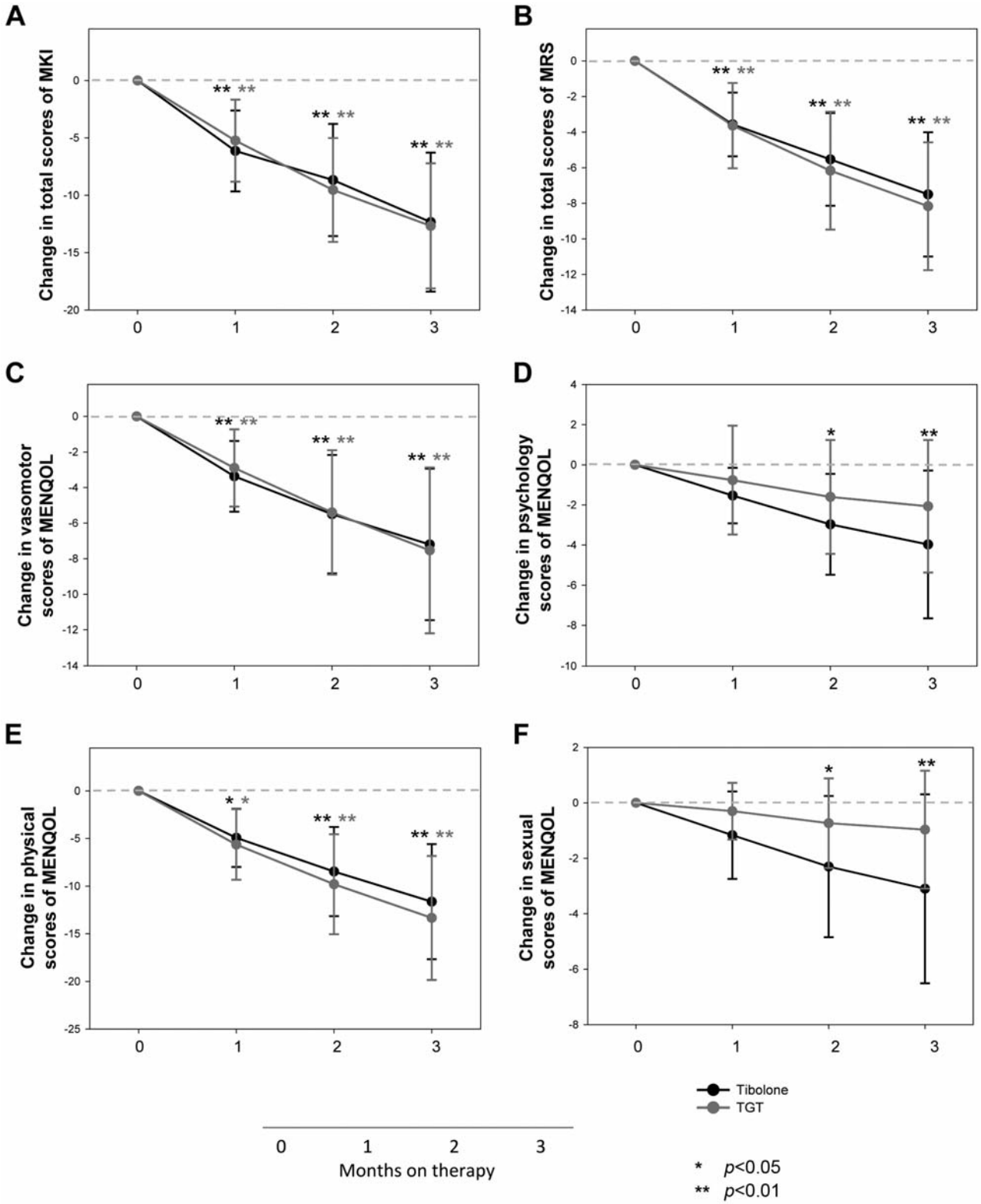

Figure 1. *Changes of total scores of MKI (A), MRS (B) and four sub-scales of MENQOL (C-F) 1, 2 and 3 months after beginning of the treatment. Changes (scores of 0, 1, 2, 3 months of the treatment minus the baseline) at each time point were compared to those before the treatment. Significant (p<0.05) and highly significant (p<0.001) improvements were marked with * and **, respectively, black for tibolone and red for TGT. MKI, Modified Kupperman index; MRS, menopause rating scale; MENQOL, menopause-specific quality of life; TGT, Tiáo Gēng Tāng.*

Table III. *Improvement of sub-scales of Menopause Specific Quality of Life*.

Subscales	Months	Scores/success rate		Between group differences
		TGT	Tibolone	
Vasomotor	0	11±5	11±5	not significant
	1	8±4	8±3	
	2	6±4	6±3	
	3	3±3	4±3	
	Remedy rate (%)	69±28	63±20	
Psychosocial	0	11±5	12±6	significant
	1	10±4	10±5	p=0.04
	2	10±4	9±5	
	3	9±4	8±4	
	Remedy rate (%)	15±17	29±21	
Physical	0	32±10	32±10	not significant
	1	26±10	27±8	
	2	22±8	24±7	
	3	18±8	20±8	
	Remedy rate (%)	42±15	36±15	
Sexual	0	8±6	8±5	significant
	1	8±6	7±4	p=0.005
	2	7±6	6±4	
	3	7±6	5±3	
	Remedy rate (%)	12±22	29±34	

Values are all mean±standard deviation. TGT, Tiáo Gēng Tāng.

Table IV. *Remedy rate for symptoms listed in the Chinese medicine scale system*.

Symptoms	Remedy rate in %-Nr. of remedy cases/Nr. of symptom cases		Improvement of score within subject
	TGT	Tibolone	
Hot flushes	87%-26/30	83%-24/29	Significant in both groups
Sleep disturbance	74%-17/23	75%-21/28	
Emotional instability	63%-15/24	59%-16/27	
Heart discomfort	74%-17/23	64%-14/22	
Exhaustion	71%-20/28	81%-22/27	
Muscle fatigue	62%-16/26	41%-11/27	
Headache	63%-12/19	81%-17/21	
Hot palm	76%-18/21	36%-8/22	
Dizziness	74%-14/19	38%-6/16	
Dry eyes	60%-15/25	29%-7/24	
Itchy skin	59%-10/17	52%-11/21	
Joint cold pain	35%-6/17	53%-10/19	
Dry mouth	84%-21/25	39%-11/28	Significant only in TGT group
Tinnitus	50%-10/20	15%-3/20	
Poor appetite	68%-17/25	26%-6/23	
Constipation	78%-14/18	25%-4/16	
Leg swelling	20%-2/10	36%-4/11	Not significant
Thin stools	42%-5/12	8%-1/13	

TGT, Tiáo Gēng Tāng.

Table V. *Adverse events possibly related to therapy*.

Group	Event	Months on treatment	Measure	Follow-up
TGT	Diarrhea	2	Recipe adjustment	Cured
	Diarrhea	1	Recipe adjustment	Improved
Tibolone	Body weight increase	3	/	/
	Body weight increase	3	/	/
	Abdomen discomfort	2	No	Cured
	Nausea, vomit	1	No	Cured
	Emotional instability	1	No	Cured
	Pressure in breast	2	Terminating therapy	Dropped out
	Dizziness	1	Terminating therapy	Dropped out

TGT, Tiáo Gēng Tāng.

The present study is an observational study assessing clinical effects of TGT. We did not focus on the working mechanism of TGT, which is an essential issue for future studies. One of the most important aspects is the component profile and the effective ingredients of TGT. Studies are in progress for this key issue. Furthermore, more objective measurements should be conducted, which may provide reliable evidence for the effects of the therapy and valuable data for understanding its mechanism of action. For example, functional neuroimaging may elucidate possible effects on cognition objectively and urinary levels of phytoestrogens may clarify the extent of their uptake by the patients. Another important issue is the long-term side-effects that have to be assessed in well-designed comprehensive studies. Also, clarification is needed as to whether or not and how long the observed improvement can be sustained after termination of the TGT therapy. At the present stage, available data suggest that TGT is beneficial in alleviating menopausal symptoms and has no major observable side-effects. These promising results also provide evidence for justifying a randomized, blinded and placebo-controlled clinical trial, which is now in preparation.

Conflicts of Interest

The Authors declare that they have no competing interests.

Acknowledgements

Funded by the National Natural Science Foundation of China (81273793).

References

1 Nelson HD: Menopause. Lancet *371*: 760-770, 2008.
2 Xiao XM, Zhou YP, Rong H, Min HZ and Yang HJ: Investigation of health status and demands of perimenopausal women. Maternal and child health care of China *25*: 5437-5438, 2010. [Article in Chinese]
3 North American Menopause Society: Estrogen and progestogen use in peri- and postmenopausal women: March 2007 position statement of The North American Menopause Society. Menopause *14*: 168-182, 2007.
4 Kronenberg F: Hot flashes: epidemiology and physiology. Ann NY Acad Sci *592*: 52-86; discussion 123-133, 1990.
5 Rödström K, Bengtsson C, Lissner L, Milsom I, Sundh V and Björkelund C: A longitudinal study of the treatment of hot flushes: the population study of women in Gothenburg during a quarter of a century. Menopause *9*: 156-161, 2002.
6 Avis NE, Colvin A, Bromberger JT, Hess R, Matthews KA, Ory M and Schocken M: Change in health-related quality of life over the menopausal transition in a multiethnic cohort of middle-aged women: Study of Women's Health Across the Nation. Menopause *16*: 860-869, 2009.
7 Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD and Skurnick J: Factors associated with age at natural menopause in a multiethnic sample of midlife women. Am J Epidemiol *153*: 865-874, 2001.
8 No authors listed: Herbal medicines for menopausal symptoms. Drug Ther Bull *47*: 2-6, 2009.
9 Singh B, Liu XD, Der-Martirosian C, Hardy M, Singh V, Shepard N, Gandhi S and Khorsan R: A national probability survey of American Medical Association gynecologists and primary care physicians concerning menopause. Am J Obstet Gynecol *193*: 693-700, 2005.
10 Xu LW, Kluwe L, Zhang TT, Li SN, Mou YY, Sang Z, Ma J, Lu X and Sun ZJ: Chinese herb mix Tiao-Geng-Tang possesses antiaging and antioxidative effects and upregulates expression of estrogen receptors alpha and beta in ovariectomized rats. BMC Complement Altern Med *11*: 137, 2011.
11 Xu LW and Sun ZJ: Treating 45 patients with menopausal syndrome by liver and kidney theory. Shanghai Journal of Traditional Chinese Medicine *37*: 25-26, 2003. [Article in Chinese]
12 Zhang J and Jin Y: Evaluating efficacy of Livial on menopausal syndrome via 350 cases observation. Maternal and Child Health Care of China *22*: 5137-5138, 2007. [Article in Chinese]
13 Sang Z and Xu LW: The clinical observation of 89 cases for Tiao Geng Tang balancing yin and yang on menopausal syndrome. Jiang-su TCM Journal *27*: 79-80, 2006. [Article in Chinese]
14 Ministry of Health of People's Republic of China: Traditional Chinese Medicine Clinical Research Guidelines. Beijing, Chinese Medical Science and Technology Press, pp. 3-4, 1997. [Book in Chinese]
15 Zhang YZ, ed: Gynecology of Chinese Medicine. Beijing, China Press of Traditional Chinese Medicine, pp. 168-172, 2002. [Book in Chinese]
16 Cao ZY: Chinese Obstetrics and Gynecology. Beijing, People's Medical Publishing House, pp. 2281, 2005. [Book in Chinese]
17 Hauser GA, Huber IC, Keller PJ, Lauritzen C and Schneider HP: Evaluation of climacteric symptoms (Menopause Rating Scale). Zentralbl Gynakol *116*: 16-23, 1994.
18 Hilditch JR, Lewis J, Peter A, van Maris B, Ross A, Franssen E, Guyatt GH, Norton PG and Dunn E: A menopause-specific quality of life questionnaire: development and psychometric properties. Maturitas *24*: 161-175, 1996.

Received September 2, 2014
Revised October 2, 2014
Accepted October 7, 2014