

Original article

Acupuncture and Chinese herbal medicine in the treatment of patients with seasonal allergic rhinitis: a randomized-controlled clinical trial

Background: Patients with allergic rhinitis (AR) increasingly use complementary medicine. The aim of this study was to determine whether traditional Chinese therapy is efficacious in patients suffering from seasonal AR.

Methods: Fifty-two patients between the ages of 20 and 58 who had typical symptoms of seasonal AR were assigned randomly and in a blinded fashion to (i) an active treatment group which received a semi-standardized treatment of acupuncture and Chinese herbal medicine, and (ii) a control group which received acupuncture applied to non-acupuncture points in addition to a non-specific Chinese herbal formula. All patients received acupuncture treatment once per week and the respective Chinese herbal formula as a decoction three times daily for a total of 6 weeks. Assessments were performed before, during, and 1 week after treatment. The change in severity of hay fever symptoms was the primary outcome measured on a visual analogue scale (VAS).

Results: Compared with patients in the control group, patients in the active treatment group showed a significant after-treatment improvement on the VAS ($P = 0.006$) and Rhinitis Quality of Life Questionnaire ($P = 0.015$). Improvement on the Global Assessment of Change Scale was noted in 85% of active treatment group participants vs 40% in the control group ($P = 0.048$). No differences between the two groups could be detected with the Allergic Rhinitis Symptom Questionnaire. Both treatments were well-tolerated.

Conclusions: The results of this study suggest that traditional Chinese therapy may be an efficacious and safe treatment option for patients with seasonal AR.

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Background

In the last two decades, there has been a marked increase in the prevalence of allergic rhinitis (AR) in Western industrialized nations, with studies showing between 10 and 20% of the population to be suffering from this disorder (1). For AR in Europe, direct yearly costs are estimated at 1.0–1.5 billion euros annually, while indirect costs are estimated at 1.0–2.0 billion euros (1). However, despite advances in conventional therapy a remarkable number of patients, including those suffering from atopic diseases, are turning for relief to complementary medical treatments (CAM), such as traditional Chinese medicine (TCM) (2–5). Because of this, CAM has increasingly become the focus of allergy specialists and scientists (6, 7), and well-designed studies

of CAM treatments, such as TCM in patients suffering from AR, are needed.

Acupuncture and Chinese herbal medicine (CHM), the major components of TCM, have been used for centuries to treat symptoms similar to those of AR and are still broadly administered for this purpose in China (8, 9). However, methodologically sound, controlled clinical trials that investigate the efficacy of TCM in the treatment of this disorder *are lacking*. Several studies in China and the Western world have suggested that acupuncture and CHM may be beneficial in the treatment of a variety of other allergic conditions (10–12). For example, a number of randomized-controlled studies have demonstrated the efficacy of CHM in treating atopic dermatitis (13–15). To improve efficacy, acupuncture and CHM are often administered together in TCM (16), although no study

has investigated the efficacy of a combination of these two treatments.

There have been reports of adverse effects from CAM (17). Mechanical injuries such as pneumothorax, cardiac tamponade and infectious complications following acupuncture have been described, and organ toxicity and organ failure have been observed in association with CHM (18–20).

In this randomized, single-blind, controlled study, we investigated whether an individualized TCM therapy consisting of acupuncture and CHM is more efficacious in the treatment of symptomatic AR than a non-specific herbal formula plus acupuncture administered at non-acupoints.

Methods

Setting

The study was planned, supervised, and analysed in the Medical Department I, University of Erlangen-Nuremberg, Germany. Patients were treated from May to September 1999 in an outpatient TCM Department in Munich, Germany, by four physicians who specialise in TCM. Approval was obtained from the local ethics committee at the University of Erlangen-Nuremberg. All patients gave written informed consent before entering the trial and were free to withdraw from the study at any time.

Patients

Patients were recruited by local newspaper advertisements in the Munich area. Individuals were included if they were (i) between 18 and 65 years of age, and (ii) had a clinical diagnosis of seasonal AR, a positive skin prick test, and mild-to-moderate symptoms. Main exclusion criteria for this trial were (i) treatment with oral or intravenous immunosuppressive agents/corticosteroids, (ii) treatment with acupuncture and/or CHM in the previous 3 months, (iii) ongoing immunotherapy, or (iv) severe physical or mental illness. In order to ensure uniform allergen exposure between the treatment groups, patients planning to leave Munich for a period of 8 weeks or more were not allowed to participate in the study. During the study, patients were asked to continue any medication they might be taking for concomitant diseases and were also allowed to continue any pre-existing treatment of their rhinitis symptoms (with the exception of those mentioned above).

Outcome measures

The main outcome measure was a global patient rating of 'severity of hay fever during the last 7 days', which was assessed using a 10-point visual analogue scale (VAS) with anchors defined as 'no symptoms at all' and 'maximum severity'. In addition to the total score, a remitter criterion was defined by the values 0 (no symptoms) and 1 (very mild symptoms) as a clinically relevant outcome measure at the end of treatment. We used the Allergic Rhinitis Symptom Questionnaire (ARSQ) as a secondary efficacy outcome measure (21). The ARSQ was recorded by the patients in diary format. Patients were asked to rate the severity of 14 symptoms of allergic rhinoconjunctivitis in lungs, nose, eyes, and mouth on a daily basis and for a total of 8 weeks using a 4-point scale (0 = no symptoms to 3 = severe symptoms). The diary entries were sum-

marized both per item (item score) and across all items (total score) for 7-day periods (range of total score per week: 0–294). Intake of anti-allergy medication was scored (1-point for each tablet, eye-drops, or spray). Finally, a Global Assessment of Change Scale (GACS) was administered to the patients in order to make global assessments of any changes in rhinitis severity (7-point scale ranging from -3 = significantly worse to +3 = significantly better) in comparison with previous allergy seasons. Additionally, for this scale a responder criterion was defined as any improvement (i.e. slightly better, much better, very much better). Quality of life was assessed using the disease-specific Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) (22, 23) and the health-related SF-36 Quality of Life Questionnaire (24). The RQLQ evaluates impairment of everyday life (activity, sleep, everyday life problems, condition of health) caused by symptoms of the eyes and nose (range: 0–360). For the SF-36, which has been broadly validated in therapeutic studies (25), two standardized component scales (mental, physical) can be calculated in addition to 10 subscale scores. In order to test blinding to treatment and assess the credibility of the respective treatment methods, patients filled out a credibility questionnaire containing 4-items (ranking from 0 to 6, with score 6 indicating highest credibility), both at their first and last visit (26).

Any use of medication during the study had to be documented every day. For each application of a medicament/eye drop/nose spray for allergic rhinitis one point was assigned. For each study week, all points for medical use was scored.

Study schedule and safety parameters

During the first visit, inclusion and exclusion criteria were checked and patients informed about the concept of the study. RQLQ, SF-36, and VAS were completed during the first visit and after a 1-week run-in period (baseline), in which either no treatment, or only local symptom-relieving treatment, was administered. Patients were asked to complete the ARSQ on a daily basis during the entire run-in period. A blood sample was taken in order to determine laboratory safety parameters (liver enzymes, creatinine, red and white blood cell and thrombocyte count). All patients were diagnosed based on their individual symptoms (9, 16) and according to TCM – diagnostic methods (cf. TCM-D, Table 1). Stratified randomization to active or control treatment was performed centrally after visit 1 by an external institute (IMEREM) with a semi-deterministic procedure software and using the following stratification variables (27): gender, age (18–35 and > 35 years), duration of disease (≤ 10 and > 10 years), and therapist ($n = 4$). We assessed VAS, ARSQ, RQLQ, and SF-36 at the end of the 1-week run-in period (baseline), after 3 weeks of study intervention, and 1 week after treatment completion. The GACS was completed by all patients at the end of the study. All patients' self-ratings were organized by an external study coordinator, who was independent from the study health providers or acupuncturists. The physicians' ratings were performed by the treating acupuncturists. Patients were monitored for any adverse events or worsening of symptoms at each visit, and blood samples for safety evaluation were drawn at baseline and end-point to assess for adverse changes in transaminases and serum creatinine levels.

Treatment protocol

Each patient received a total of six acupuncture sessions. Sessions were scheduled once a week, and each session lasted 20 min. CHM was to be taken three times per day over a period of 6 weeks, and parallel to acupuncture treatment. TCM and control therapy were

Table 1. Acupuncture points and herbal formulation according to traditional Chinese medicine (TCM) diagnosis in the active treatment group (daily dosages of raw herb in g) and the Sham acupuncture points used in the control group

TCM-diagnosis	Used acupoints	CHM-formulae
Every patient	L.I. 4, L.I. 20, GB 20, Lu 7, Liver 3	Herba Schizonepetae (jingjie) 5, Flos Chrysanthemi (juhua) 10, Semen Cassiae torrae (juemingzi) 10, Semen Plantaginis (cheqianzi) 12, Fructus Tribuli (baijili) 10
D1: wind-heat in lung	+ L.I. 11	+ Herba menthae (bohe) 4, Folia Mori (sangye) 10, Herba Lemnae seu Spirodela (fuping) 5, Radix Paeonia lact. (baishao) 10
D2: liver heat and fire	L.I. 11, GB 37, GB 42, T.B. 5	Fructus Forsythiae (lianqiao) 3, Fructus Gardeniae (zhizi) 6, Radix Paeoniae rubra (chishao) 6, Radix Rehmaniae viride (shengdihuang) 10
D3: lung Yin depletion	Lu 5	Radix Ophiopogonis (maimendong) 10, Radix Glehniae seu Adenophorae (shashen) 10
D4: cold in lung	U.B. 12, U.B. 13	Herba cum Radix Asari (xixin) 3, Radix Angelicae dahurica (baizhi) 6
D5: spleen qi depletion	S 36, T.B. 6, Lu 9 extra point <i>yintang</i>	Radix Astragali (huangqi) 12, Poria alba (fuling) 10, Radix Codonopsis (dangshen) 18, Rhizoma Atractylodis macro. (baizhu) 6, Radix Glycyrrhizae (gancao) 3
Sham acupuncture points		
Point forearm	Ulnar side, half between epicondylus ulnaris and ulnar side of the wrist	
Point foot	On the inner and outer side of the calcaneus	
Point lower leg 1	Half distance between medial edge of patella and calcaneus internus at the medial edge of the tibia	
Point lower leg 2	Four fingers above the tip of the calcaneus internus, close to the Achilles tendon	
Point forearm 1	Half between the inner side of the elbow and the axillae	

performed on a single-blinded basis by four physicians. In order to participate in the study, physicians had to (i) be a medical specialist with a degree in internal medicine and general medicine, (ii) have a certified degree in TCM by a German society for medical acupuncture, and (iii) have at least 5 years of practical experience in TCM (according to the German Acupuncture Societies' Working Group standard).

Acupuncture. In the TCM group, all patients received a standardized acupuncture treatment. Depending on each patient's individual symptoms, additional acupoints were selected (Table 1). All patients were treated in a supine position. After insertion into the skin, the needles were manipulated in order to obtain a needle sensation (described in TCM as 'De-Qi'). Ten minutes after the start of treatment, all acupuncture needles were manipulated once again by the acupuncturist. In the TCM group, Hwato® 0.32 × 40 mm needles were used. Moxibustion was avoided.

In the control group, patients were treated using standardized non-acupuncture points (Table 1). The non-acupuncture points used in this study were chosen because they were distant from any 'meridians'. Needling in this group was superficial and exclusively intracutaneous, and needle sensation ('De-Qi') was avoided. For the control group, only small needles (Hwato®, 0.13 × 20 mm) were selected and physicians were instructed to avoid any form of manipulation. Therapeutic setting, procedure, and frequency of sessions were similar in both groups. The acupoints selected in the initial acupuncture session were not changed in subsequent sessions.

CHM-treatment. All herbs used in the present study were imported from China by a single German TCM herbal medicine import company (Sinores, Lueneburg, Germany). The herbal formulations

were examined and confirmed to be free of biocides (major organic toxic compounds), heavy metals, and other contaminants by an independent qualified laboratory (Handelschemisches Laboratorium Hofmann, Bremen, Germany). All herbs were prepared in dried, minced pieces, and then sealed in generic paper sachets by a pharmacist in order to render the herbal formulation nonidentifiable for patients. Herbs containing essential oils in fluid form (e.g. Herba menthae, Herba schizonepetae) were dispensed in sealed plastic sachets. The herbal formulations for the TCM group were designed by a herbalist (Carl-Hermann Hempen) and prepared by a pharmacist who both specialise in Chinese herbal medicine (S. Dietz, Franz-Joseph-Pharmacy, Munich, Germany). In addition to the basic formula, every patient received a second additional formula tailored to his or her individual TCM diagnosis (Table 1). The most important herbs used in this trial were *Chrysanthemi flores* (juhua), *Mentha herba* (bohe), *Mori foliae* (sangye), *Cassiae torrae semen* (juemingzi).

The patients in the control group received a non-specific formulation consisting of Chinese and Western herbs. The formulation contained *Semen coicis* (yiren) 15, *Radix glycyrrhizae* (gancao) three, *Poria alba* (fuling) 10, *Humulus lupulus* one, *Fructus oryzae* germ. (guya) 10, *Fructus hordei* germ. (maiya) 10, *Fructus crataegi* (shanzha) six, *Massa medicata fermentata* (shenqu) 10 (daily dosages of raw herb in g).

Patients in both groups were instructed to prepare the herbal formulation as a decoction according to the following directions: (i) Soak herbs in 250 ml water for 1 h. (ii) Add 1000 ml cold water and boil for 20 min at 60–80°C. (iii) Add herbs containing essential oils in fluid form 3 min before boiling phase is complete. (iv) Store formulation in a cool place (4–8°C). (v) Three times

daily add 150 ml of decoction to a cup of boiling water and drink.

Statistical methods

Number of patients. The available literature did not allow for a reliable prediction of the expected effect size for differences between the TCM vs the control group. Therefore, sample size estimation was determined for this trial to detect at least a ‘strong’ effect according to Cohen’s classification (28) with an expected effect size of $ES = \delta/\sigma = 0.8$ for the differences in the VAS severity rating between both treatment groups using error probabilities of $\alpha = 0.05$ (1-sided) and $1-\beta = 80\%$. Based on these assumptions, at least $n = 26$ patients were required per treatment group.

Statistical analysis. All data in this paper are presented as mean \pm SD, or as frequencies. No statistically relevant baseline differences were observed. Therefore, statistical comparisons are based on end-points. Confirmatory testing of superior efficacy of TCM vs placebo with the VAS assessment at end-point (main outcome measure) was based on the intention-to-treat (ITT) population, including all treated patients with at least one postbaseline measure using the last observation carried forward (LOCF) method. Also the main outcome measure and all other statistical comparisons were interpreted in an exploratory manner for results from the per protocol (PP) set (see below). The end-point data from the VAS, ARSQ, RQLQ, SF-36, and GACS, as well as serum parameters from the two treatment groups were compared using the two-sample *U*-test. Frequency analysis of remitters or responders made use of the exact Fisher’s chi-square test. Nominal *P*-values of <0.05 were regarded as statistically significant.

Results

Study population

Of 59 randomized patients, 52 (26 in each treatment group) completed the trial according to protocol (Fig. 1). In the TCM group, a total of four patients left the study prematurely (reasons: sports injury, move to another city, professional and private reasons). In the control group,

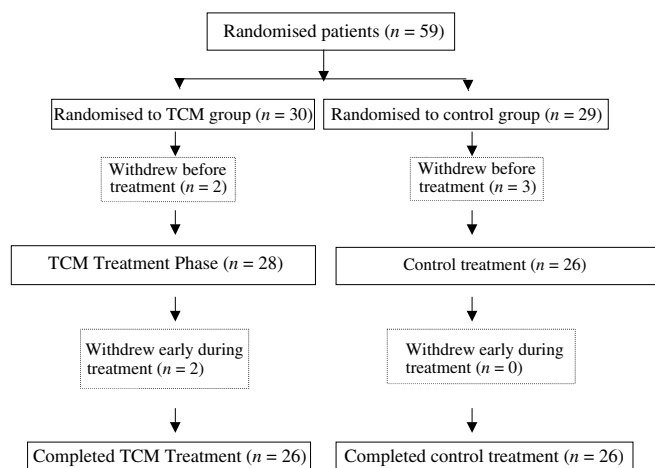


Figure 1. Trial profile.

Table 2. Demographic and disease-related data (intention-to-treat population). If not otherwise mentioned number of patients are reported

	TCM group	Control group
Number of patients	28	26
Gender (male/female)	10/16	14/12
Age in years (mean \pm SD/range)	34 \pm 9.5/20–58	33 \pm 9.0/22–56
Duration of disease in years (mean \pm SD/range)	17 \pm 10/3–32	18 \pm 10/3–38
TCM diagnosis (n)	28 (100%)	26 (100%)
D1: wind-heat in lung	23	14
D2: heat and fire in liver	3	4
D3: depletion of Yin in lung	1	1
D4: cold in lung	0	2
D5: depletion of Qi in spleen	1	5

three patients left prior to study completion (reasons: car accident, injury, move to another city). Five patients (TCM: two; controls: three patients) dropped out during the run-in phase, the other two patients after 1 week of treatment. None of these patients dropped out of the study due to adverse events. As end-point measures, only VAS rating and adverse event documentation were available for the two patients who had been treated for 1 week. As a result, we based both the primary end-point and safety analyses on the ITT population. All ITT patients could be evaluated. All secondary efficacy criteria are analysed for the PP population.

Demographic data and disease-related information on the 54 randomized patients of the ITT population did not differ between the groups (Table 2).

Efficacy

The average scores at baseline and at end-point are summarized for all efficacy data (Table 3). Hay fever severity, as assessed by a VAS, was moderate in both groups at baseline. At study completion, however, hay fever severity was significantly less pronounced in the TCM group than among the controls. This finding could be observed in both populations analysed with ITT and per protocol. Remission (scale categories: 0 = no symptoms at all and 1 = very mild symptoms) occurred in the TCM group twice as often as in the control group. As shown in Fig. 2, the final status of the patients was quite independent of their initial severity score. Similarly, 84.6% of TCM patients experienced any improvement on the GACS. This percentage was significantly higher than in the control group, in which only 40% of patients showed an improvement by the end of the treatment period. In contrast to these findings in global scales, the total scores on the disease-specific severity scale ASRQ for rhinitis and conjunctivitis symptoms did not differ significantly between groups. Although the ASRQ severity score at study completion was 54.1% of the initial mean value in the TCM group, it was also improved in 37.1% of control patients. When the large SDs are taken

Table 3. Outcome measures at baseline and end-point

Efficacy measure	TCM		Control		P-value*
	Baseline	End-point	Baseline	End-point	
VAS intention-to-treat†	4.2 ± 3.1	1.2 ± 1.8	4.2 ± 2.7	2.7 ± 2.5	0.006
VAS per protocol	4.1 ± 2.5	1.0 ± 1.8	4.2 ± 2.7	2.7 ± 2.5	<0.001
VAS remitter (n %):‡	–	80.8	–	34.6	<0.001
GACS	–	1.7 ± 1.2	–	0.7 ± 1.9	0.018
GACS responder (n %)	–	84.6	–	40.0	0.048
RQLQ	16.1 ± 6.6	4.8 ± 5.4	16.6 ± 6.5	7.8 ± 5.9	0.015
ASRQ	56.7 ± 43.4	30.7 ± 35.5	58.3 ± 33.1	36.7 ± 40.5	0.497
Drug score§	7.7 ± 15.3	3.4 ± 8.8	7.7 ± 9.7	6.0 ± 19.3	0.527
SF-36 physical	48.7 ± 8.1	52.0 ± 8.0	50.8 ± 4.7	52.0 ± 7.8	0.497
SF-36 mental	46.5 ± 9.7	51.7 ± 6.2	46.4 ± 9.5	47.6 ± 10.4	0.049

Outcome measures at baseline and end-point [visual analogue scale (VAS)], global assessment of change scale (GACS), rhinitis quality of life questionnaire (RQLQ), allergic rhinitis symptom questionnaire (ASRQ), quality of life questionnaire SF-36 (subscales). If not otherwise specified, mean ± SD are reported.

* P-value associated with comparison of end-points between both treatments (Wilcoxon *U*-test, Fisher's exact test in case of remitters and responders, one-sided). † Intention-to-treat population was used for comparison of primary efficacy criterion; all other measures were analysed in the per protocol set.

‡ Remitter rate for intention-to-treat was 75.0% in the traditional Chinese medicine (TCM) group (identical in the control group).

§ Frequency of concomitant anti-allergy drugs for 1 week, 1 dose = 1 point.

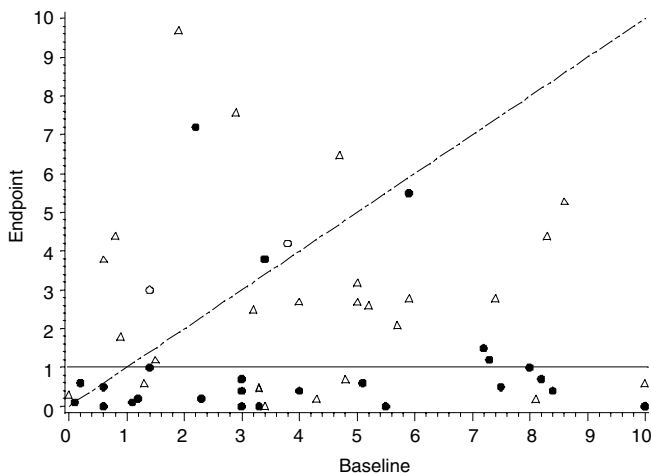


Figure 2. Individual changes between baseline (abscissa) and end-point (ordinate) on the visual analogue scale (VAS). This scale ranges from 0 = no symptoms at all to 10 = maximal severity of symptoms. Black circles: patients with traditional Chinese medicine (TCM) therapy (per protocol); open circles: Patients who dropped out during TCM therapy; triangles: patients from the intention-to treat (ITT) and per protocol populations of the control treatment. Patients above the diagonal experienced worsening, those below the diagonal improvement of VAS score between baseline and end-point. Patients below the parallel to the abscissa at end-point score = 1 are analysed as remitters.

into account, the average differences in the ASRQ between both groups appear to be low. In the disease-specific quality of life instrument RQLQ, the total score

was in favour of the TCM group ($P = 0.015$). Analysing subscales of RQLQ (data not shown), we found that the benefit of TCM therapy was primarily due to an improvement in symptoms in eyes ($P = 0.048$) and nose ($P = 0.006$), a higher level of physical activity ($P = 0.030$), and an improved psychological condition ($P = 0.030$). Importantly, we were able to observe a difference between groups with regard to the concomitant application of local treatments for rhinitis and conjunctivitis symptoms.

The SF-36 score measures health-related quality of life in a global manner. Two dimensions were influenced differently by the treatments. By the end of the treatment period, emotional well-being (data not shown) had improved more in the TCM group than in the control group ($P = 0.028$). A favourable difference for TCM was also seen on the standardized mental component scale ($P = 0.049$).

For the laboratory parameters, nearly identical average values were observed at baseline and at end-point.

Compared with the baseline, the permitted drug intake for allergic rhinitis symptoms decreased substantially from 7.7- to 3.4-points in the TCM group whereas we found only a slight decrease in the control group (7.7–6.0). There was no significant difference between both groups at the end-point.

There were no substantial differences in the credibility ratings of either intervention based on the answers patients provided on the credibility questionnaire. For example, the main question for the credibility score ('Do you believe that the therapy can reduce your complaints?') was 4.9 in the TCM group vs 4.8 in the control group at the first visit and 5.3 vs 5.0 at the last visit (maximum = 6, highest credibility).

Safety

Among the 54 patients treated in our study, 10 patients (four in the TCM group, six in the control group) reported 10 adverse events attributable to study treatment. There were four complaints about severe needle pain (TCM: $n = 2$, control: $n = 1$) or haematoma (control: $n = 1$), all of which resolved within a few days. One patient (control group) felt a paresthesia in the left arm that persisted for 7 days following acupuncture treatment. A total of five patients reported symptoms following intake of their CHM decoctions, including nausea (TCM: $n = 2$, control: $n = 1$) and bitter taste (control: $n = 2$). During the trial, there were no clinically notable changes in any of the laboratory safety measures, and none of the patients experienced severe or serious adverse events, which would have necessitated withdrawal from the study.

Discussion

To our knowledge, this is the first clinical study to investigate the efficacy of a semi-standardized treatment

for AR that combines acupuncture therapy with CHM according to TCM diagnostic methods.

Unlike most previous studies of acupuncture, our study required participating acupuncturists to fulfill a number of rigorous standards with regard to their medical education and practical training in TCM (cf. 'Treatment Protocol' above). A common criticism of acupuncture research has been the lack of such requirements, and the approach taken in the present study can truly be considered state-of-the-art (29).

Patients who received semi-standardized acupuncture and CHM treatment improved significantly compared with controls according to the primary efficacy measure, the VAS for hay fever severity.

In addition, patients in the active treatment group showed improvements according to the GACS. Furthermore, quality of life as assessed by the disease-specific RQLQ and parts of the health-related SF-36 (emotional well-being, positive mental condition) were better in the TCM vs the control group.

It must be noted that the sensitivity of our outcome measures varied. Whereas the global scales (VAS, GACS) and quality of life instruments (RQLQ, SF-36) all showed significant benefits in the TCM group, the disease-specific severity scale (ARSQ) did not reveal a significant benefit. This inconsistency may be due to the fact that the ARSQ is a methodologically inefficient instrument. Its diary approach requires patients to make daily assessments of 14-items and to document the use of concomitant medications for a period of up to 10 weeks. Thus, patients' compliance may have been overtaxed in this regard. In addition, the resulting sum score is comprised of items, which are not at all interrelated. A factorial evaluation of this instrument that would allow for a multidimensional – instead of unifactorial – item structure is not currently available. Using another scale in patients with, e.g. viral infections suggest several dimensions (30), which in case AR includes at least three different dimensions: rhinitis, bronchitis, and pain. From a clinical perspective, the more complex structure of the ARSQ is more appropriate for AR patients who present with heterogeneous symptom patterns (e.g. due to different allergens). However, its multidimensional structure might be unstable over time, as symptoms of AR can change within the same patient, such as when the symptom 'runny nose' changes into 'congestion'.

Interestingly, it was primarily emotional well-being which on the quality of life scales (SF-36, RQLQ) turned out to be different between both treatment groups at study completion. The resolution of disease-related impairment of a patient's quality of life can be interpreted as the most desirable outcome for an allergic episode. This interpretation is supported, e.g. by the mean standardized mental component score of the SF-36 at study completion, which showed an improvement in mental well-being *in the treatment group*. Similar effects have been found recently in a study of

acupuncture in the treatment of patients with Crohn's disease (31).

There were only minor adverse events during the study. Liver and renal function was monitored as a precautionary measure, as liver dysfunction and renal failure have been associated with the use of CHM in isolated cases (18–20). No clinically relevant changes in transaminases or creatinine were found between baseline and end-point.

As noted above, we used a semi-standardized therapy combining acupuncture and CHM and limited treatment for all patients to 6 weeks. A completely individualized therapy, as is more common in TCM (9, 16), might have resulted in a better long-term outcome, as was demonstrated in a prior study on the efficacy of CHM in the treatment of irritable bowel syndrome (32). Long-term therapy of more than 6 weeks, starting before the pollen-season, has also been recommended (16). The main reason for these methodological restrictions was to ensure that the conditions and circumstances of treatment are as homogeneous as possible. However, because most patients had received some form of anti-allergic treatment prior to the study, complete homogeneity was, of course, unattainable.

We tested for the credibility of both interventions, as has been recommended previously by others in the field of acupuncture research (26). We were unable to detect substantial differences between the two treatment groups, which indicates that, for patients, blinding to therapy vs control treatment was complete.

Another methodological difficulty is the fact that treatment in the control group was not entirely inactive. According to TCM principles, control patients were treated with herbs (*although different from the treatment group*) which influence the so-called 'spleen'-orbis (33). Additionally, sham acupuncture has yet to be confirmed as a valid placebo and thus is still a matter of controversy. Even needles that do not penetrate the skin produce a physical sensation with unspecific effects (34). In general, blinding of the acupuncturists is impossible. In addition to spontaneous improvement, the psychological support which is provided by the therapeutic setting itself likely influences symptom severity over time. Because the drugs used in CHM are typically administered as a decoction consisting of dried, raw herbs, it is difficult from a methodological viewpoint to ensure controlled, placebo-based therapy. In some Western studies, CHM is provided as tablets (35), capsules (32) or in a powdered form (suspended in boiled water and taken as a decoction) (14), which makes double-blinding possible.

Despite the finding that acupuncture combined with CHM has significant clinical benefits in AR (this study) as well as in irritable bowel syndrome (32), the underlying mechanisms of action still remain largely unexplored. Acupuncture appears to modulate the immune system, by causing shifts in lymphocyte subpopulations towards an increased number of CD3⁺ and CD4⁺ cells, and by modulating the cytokine patterns towards a decrease of

interleukin (IL)-6 and IL-10 and an increase of IL-8 (36). Acupuncture also appears to stimulate the release of certain hormones [e.g. adrenocorticotrophic hormone (ACTH), β -endorphin, substance P and somatostatin] (37, 38) and to change the activity of the autonomic nervous system, while CHM has a complex composition for which anti-inflammatory, antibacterial and immunological effects have been described (39–42).

Conclusion

This is the first controlled, randomized, single-blinded study using acupuncture plus a Chinese herbal remedy administered according to TCM diagnostic principles in patients with mild-to-moderate allergic seasonal rhinitis. We could show that this treatment was efficacious in improving global severity rating and in affecting disease-related quality of life parameters after 6 weeks of treatment when compared with sham needling plus a

non-specific herbal formulation. However, no effect of active treatment on individual symptom severity could be shown. Taking into account the above-mentioned limitations of the study, we conclude that acupuncture plus Chinese herbal formulations may offer relief in patients with seasonal AR. Our findings support further investigations of acupuncture and CHM in this and other diseases.

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