
Acupuncture in patients with allergic rhinitis: a pragmatic randomized trial

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Background: Acupuncture is widely used in patients with allergic rhinitis, but the available evidence of its effectiveness is insufficient.

Objective: To evaluate the effectiveness of acupuncture in addition to routine care in patients with allergic rhinitis compared with treatment with routine care alone.

Methods: In a randomized controlled trial, patients with allergic rhinitis were randomly allocated to receive up to 15 acupuncture sessions during a period of 3 months or to a control group receiving no acupuncture. Patients who did not consent to random assignment received acupuncture treatment. All patients were allowed to receive usual medical care. The Rhinitis Quality of Life Questionnaire (RQLQ) and general health-related quality of life (36-Item Short-Form Health Survey) were evaluated at baseline and after 3 and 6 months.

Results: Of 5,237 patients (mean [SD] age, 40 [12] years; 62% women), 487 were randomly assigned to acupuncture and 494 to control, and 4,256 were included in the nonrandomized acupuncture group. At 3 months, the RQLQ improved by a mean (SE) of 1.48 (0.06) in the acupuncture group and by 0.50 (0.06) in the control group (3-month scores, 1.44 [0.06] and 2.42 [0.06], respectively; difference in improvement, 0.98 [0.08]; $P < .001$). Similarly, quality-of-life improvements were more pronounced in the acupuncture vs the control group ($P < .001$). Six-month improvements in both acupuncture groups were lower than they had been at 3 months.

Conclusions: The results of this trial suggest that treating patients with allergic rhinitis in routine care with additional acupuncture leads to clinically relevant and persistent benefits. In addition, it seems that physician characteristics play a minor role in the effectiveness of acupuncture treatment, although this idea needs further investigation.

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INTRODUCTION

Despite advances in conventional therapy, a remarkable number of patients with allergic rhinitis are turning for relief to complementary medical treatments.^{1,2}

Acupuncture is widely used for the treatment of allergic rhinitis²; however, several studies on its efficacy in patients with allergic rhinitis have yielded inconclusive results.^{3–8} For example, Xue et al⁵ and Ng et al⁸ demonstrated that acupuncture is effective in reducing subjective allergic rhinitis symptom scores, whereas Magnusson et al⁷ found that acupuncture was not superior to sham acupuncture in reducing clinical

symptoms and concluded that acupuncture should be further evaluated in larger randomized studies.

In Germany, acupuncture is mainly administered by physicians. Before 2000, acupuncture was partly paid by some health insurance companies. Under increasing budgetary pressure, the Federal Committee of Physicians and Health Insurers recommended in 2000 that large research initiatives on acupuncture should be conducted for chronic diseases. In 2000, because of increasing budgetary pressure, the Federal Committee of Physicians and Health Insurers recommended that large research initiatives should be conducted on acupuncture in the treatment of chronic diseases.⁹ Subsequently, acupuncture could only be reimbursed by insurance companies if the patients participated in one of the these studies.

The primary objective of the present study was to investigate the effectiveness of acupuncture in addition to routine care in patients with allergic rhinitis compared with routine care alone. In addition, we investigated whether the effects of acupuncture differ in randomized and nonrandomized patients, whether the treatment effects last for a longer period, and whether specific patient and physician characteristics are associated with particular treatment outcomes. The effectiveness of acupuncture in allergic rhinitis was not demonstrated in pragmatic trials before. However, after reviewing the results of the prior trials on the efficacy of acupuncture in allergic rhinitis,^{3–8} our hypothesis was that acupuncture in

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addition to routine care is more effective than routine care alone in patients with allergic rhinitis.

METHODS

Design

In accordance with German federal regulations, the participating health insurance companies covered 100% of the acupuncture costs for patients who agreed to randomization and 90% of the costs for patients who participated in the study but did not agree to randomization. The Acupuncture in Routine Care Study was a multicenter randomized controlled trial plus a nonrandomized cohort (Fig 1). Patients who agreed to randomization were allocated to an acupuncture group that received immediate acupuncture treatment or to a control group that received delayed acupuncture treatment after 3 months. Patients who declined to be randomized were included in a third arm and also received immediate acupuncture treatment (nonrandomized acupuncture group). The study period per patient was 6 months: a 3-month treatment phase followed by 3 months of follow-up.

The protocol of this study was approved by the local ethics review boards. The study was performed according to common guidelines (Declaration of Helsinki, which consists of ethical principles for the medical community regarding human experimentation, and Good Epidemiologic Practice, which proposes minimum practices and procedures that should be considered to help ensure the quality and integrity of data used in epidemiologic research, <http://www.dundee.ac.uk/iea/GoodPract.htm>). All study participants provided written informed consent.

Patients and Physicians

Patients insured by one of the participating social health insurance funds who received a diagnosis of allergic rhinitis were recruited after contacting a participating physician. If patients requested acupuncture or if the physician considered acupuncture to be an adequate treatment, the patients were informed about the study. To be included in this study, patients had to meet the following criteria: age of 18 years or older, clinical diagnosis of seasonal and/or perennial allergic

rhinitis with symptoms that required treatment, insured by one of the health insurance companies that participated in this large acupuncture research initiative, and written informed consent. The exclusion criteria were all forms of nonallergic rhinitis. Patients who met the inclusion criteria, provided informed consent, and signed an agreement for randomization were eligible for study.

The physician contacted the randomization center by telephone and reported the group allocation. To determine who was assigned to each group, we used blocks of 10, and the random list was generated with a commercial software program (SAS; SAS Institute Inc, Cary, North Carolina). Patients who declined randomization were included in the nonrandomized acupuncture group. Patients were only included in the study if we received both the physician baseline questionnaire and the patient consent form after randomization. Physicians interested in participating in the study were required to have at least an A-diploma, which represents 140 hours of certified acupuncture education. This education and other training include wide variations in style and acupuncture technique.

Interventions

Each patient in the randomized and nonrandomized acupuncture groups received up to 15 acupuncture sessions during the first 3 months and no acupuncture between 3 and 6 months. The control group was not allowed to use any kind of acupuncture during the first 3 months. In all 3 treatment groups, the patients were allowed to use any additional conventional treatments as needed. Each patient could be treated individually, and the number of needles and the acupuncture points used were chosen at the physicians' discretion. Following the restrictions made by the health insurance companies, only needle acupuncture (with disposable 1-use needles) was allowed, whereas other forms of acupuncture treatment (eg, laser acupuncture, electroacupuncture, moxibustion) were not permitted. In addition, only manual needle stimulation was allowed.

Outcome Measurements

On successful inclusion in the study, patients completed standardized questionnaires (including sociodemographic characteristics) at baseline and then again after 3 and 6 months. The primary outcome measure to evaluate the effectiveness of acupuncture in seasonal allergic rhinitis was the Rhinitis Quality of Life Questionnaire (RQLQ) score 3 months after treatment initiation. The RQLQ^{10,11} measures the influence of allergic rhinitis symptoms on the quality of life and contains 28 items in 7 domains (sleep, non-hay fever symptoms, practical problems, nose symptoms, eye symptoms, activity, and emotional function in everyday life). The analysis of the RQLQ is based on a sum score (range, 0–6), with low values indicating higher disease-specific quality of life. Changes in score from the RQLQ of greater than 0.5 were considered clinically significant.¹¹

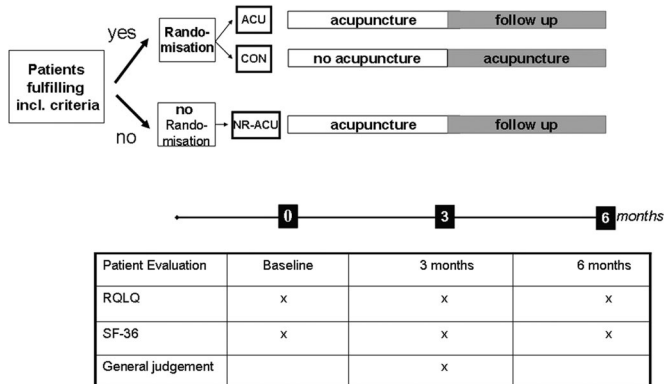


Figure 1. Study design.

As a secondary outcome, we used the reduction of the RQLQ score from baseline in terms of percentages. If the RQLQ score increased for an individual patient during the follow-up, the percentage was calculated by using the maximum possible loss and given a negative sign. We decided to use the percent reduction and not the absolute reduction on the RQLQ score because the latter correlated substantially with baseline ($r = -0.60$ vs $r = 0.31$). Patients who demonstrated a reduction in RQLQ score of at least 20% (change in score from the RQLQ of >0.5 was considered of clinical importance) were considered to be treatment responders. All patients without data were counted as nonresponders. As further secondary outcome parameters, we used the 36-Item Short-Form Health Survey (SF-36)^{12,13} component scales to evaluate the quality of life as it relates to one's general health and the success of acupuncture on one's general health after 3 months. The component scales evaluate health-related quality of life, which is influenced by allergic rhinitis and the success of treatment after 3 months on a 10-point scale (0, no success and completely unsatisfied; 10, complete success and very satisfied). Adverse effects were evaluated with the use of patient and physician questionnaires after 3 months. Data about cointerventions (conventional, complementary, and alternative treatments) were provided by the social health insurance funds.

Statistical Analyses

Confirmatory testing of the primary and secondary outcomes (using SPSS statistical software, version 11.5; SPSS Inc, Chicago, Illinois) were based on the intention-to-treat population, using the maximal available data set. Sensitivity analyses were performed for the primary outcome by using various hot deck methods or regression-based multiple imputation. The test procedure was performed to maintain a global significance level of $\alpha = .05$. Using covariance analysis, we tested the null hypothesis: mean RQLQ score after 3 months of acupuncture = mean RQLQ score after 3 months of control against a 2-directional alternative, based on the t test of the study group difference after adjustment for baseline. To be able to detect a difference of 0.5 point in the RQLQ score with a power of 90% in this study consisting of 527 patients per group, both the control and acupuncture groups would need to have a mean RQLQ score of 4.0 with an SD of 2.5.¹⁰

To identify factors that affect improvements in the RQLQ score and for a better understanding of the patient selection, we fitted linear mixed models for the RQLQ score to the data of all study patients (using the procedure MIXED in SPSS 11.5). Mixed models were chosen to comply with the potential cluster structure of the data because several patients were included by the same physician and thus may reveal more similarity in their responses to treatment than patients treated by different physicians. Mixed models correct for these cluster effects by giving more conservative P values than simple regression models. As potential regressors, we prespecified several characteristics of the physicians (age, years of pro-

fessional experience, type of acupuncture diploma, hours of acupuncture training, years of acupuncture experience, diagnosis in the context of traditional Chinese medicine, and percentage of practice time with acupuncture treatment) and of the patients (sex, age, less or more than 10 years of education, baseline physical and mental quality-of-life scores, RQLQ score, the duration of complaints before the study, and the study group to which each patient was assigned) before the study started. For the final model, we selected significant variables in a stepwise backwards procedure, based on likelihood ratio tests. The corresponding P values are reported. In addition, we considered the selected regressors as potential modifiers of the acupuncture effect and added the corresponding interaction terms to the model, backwards selecting if they were significant. Differences between physicians were judged on the basis of Wald tests of the between-physicians variance component. All reported P values are based on 2-directional alternatives to the respective null hypotheses.

RESULTS

Study Population and Treatment

Between December 2000 and August 2001, a total of 5,324 patients with allergic rhinitis were recruited for the study by 2,274 study physicians (Fig 2 for patient selection). A total of 1,068 patients had accepted randomization and were allocated to acupuncture or control group. Eighty-seven patients (48 acupuncture, 39 control) could not be included in the analysis because the study office did not receive the consent form or the patients did not receive the study intervention. The remaining 5,237 patients (487 acupuncture, 494 control, and 4,256 nonrandomized-acupuncture) were included in the analysis. After 3 months, data were available for 91.5% of the patients (458 acupuncture, 444 control, and 3,888 nonrandomized acupuncture).

The randomized groups were comparable with regard to baseline characteristics, with the exception of significant differences for previous cortisone treatment (Table 1). Between the randomized and the nonrandomized acupuncture groups, however, significant differences were found regarding symptom duration, duration of disease, concomitant asthma, acupuncture in the last 12 months, RQLQ score and all subscores, and mental health of SF-36. Patients in the acupuncture groups received a mean (SD) of 9.9 (3.0) acupuncture sessions (randomized acupuncture, 10.3 [2.6]; nonrandomized acupuncture, 9.9 [3.0]; $P = .06$). Most patients (75%) received 5 to 10 sessions, whereas 19% received more than 10 sessions and 6% received fewer than 5 sessions.

Randomized Comparisons

Contrary to reports in the literature, some items of the RQLQ score were not well accepted by the German patients. Even at baseline, in one-third of the patients, at least 1 of the 28 items was missing. We thus decided to replace isolated missing values. If up to 2 of the items were incomplete, maximum likelihood estimates were imputed to be able to calculate a

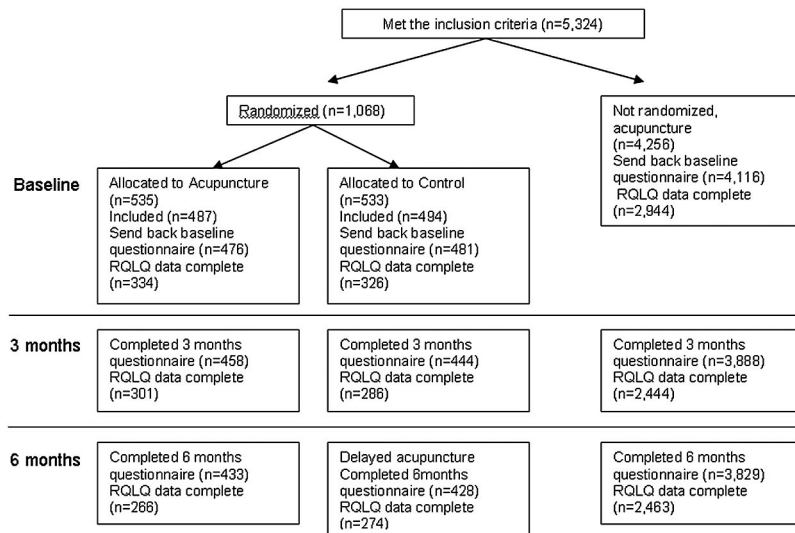


Figure 2. Trial flowchart. RQLQ indicates Rhinitis Quality of Life Questionnaire.

Table 1. Baseline Characteristics of the Study Population

Characteristics	Randomized groups			Randomized vs nonrandomized groups			Total (N = 5,237)
	Acupuncture (n = 487)	Control (n = 494)	P value ^b	Randomized (n = 981)	Non randomized (n = 4,256)	P value ^b	
Female, No. (%)	307 (63)	321 (65)	.16	628 (64)	2,593 (61)	.08	3,221 (61.5)
Male, No. (%)	180 (37)	173 (35)		353 (36)	1,663 (39)		2,016 (31.5)
Age, mean (SD), y	39.0 (11.5)	39.4 (12.3)	.68	39.2 (11.9)	39.7 (11.6)	.22	39.6 (11.6)
>10 Years of school, No. (%)	282 (60)	284 (60)	.88	566 (60)	2,461 (61)	.42	3,027 (61)
AR symptom duration, mean (SD), mo	6.6 (3.4)	6.9 (3.5)	.22	6.7 (3.8)	5.8 (3.1)	<.001	5.9 (3.2)
Duration of disease, mean (SD), y	11.9 (9.3)	12.1 (9.4)	.66	12.0 (9.4)	13.1 (9.8)	.002	12.8 (9.7)
Concomitant asthma, No. (%)	126 (26)	122 (25)	.71	248 (25)	1,310 (31)	.001	1,558 (29.7)
Previous cortisone treatment, No. (%)	250 (51)	212 (43)	.009	462 (47)	1,894 (45)	.16	2,356 (45.0)
Previous histamine blocker treatment, No. (%)	432 (89)	438 (89)	>.99	870 (89)	3,821 (90)	.27	4,691 (89.7)
Acupuncture in last 12 months, No. (%)	54 (11)	57 (12)	.81	111 (12)	745 (18)	<.001	856 (16.9)
RQLQ global score, mean (SD)	3.1 (1.1)	3.1 (1.1)	.60	3.1 (1.1)	3.4 (1.1)	<.001	3.3 (1.1)
RQLQ subscores, mean (SD)							
Sleep	2.4 (1.5)	2.4 (1.5)	.51	2.4 (1.5)	2.7 (1.5)	<.001	2.6 (1.5)
Non-hay fever symptoms	2.7 (1.2)	2.6 (1.3)	.25	2.6 (1.3)	2.8 (1.2)	<.001	2.8 (1.2)
Practical problems	3.9 (1.5)	4.0 (1.6)	.72	3.9 (1.5)	4.2 (1.4)	<.001	4.2 (1.4)
Nasal symptoms	3.4 (1.4)	3.2 (1.5)	.35	3.3 (1.5)	3.7 (1.4)	<.001	3.6 (1.4)
Eye symptoms	2.4 (1.7)	2.2 (1.7)	.22	2.3 (1.7)	2.9 (1.7)	<.001	2.8 (1.7)
Activities	3.7 (1.6)	3.6 (1.7)	.58	3.7 (1.6)	4.1 (1.5)	<.001	4.0 (1.5)
Emotional	2.4 (1.3)	2.3 (1.4)	.23	2.3 (1.3)	2.6 (1.3)	<.001	2.5 (1.3)
Physical health (SF-36), No. (%)	48.9 (8.9)	49.3 (8.5)	.55	49.1 (8.7)	48.9 (8.4)	.44	48.9 (8.5)
Mental health (SF-36), No. (%)	45.0 (10.0)	45.2 (9.7)	.12	45.5 (9.9)	44.8 (10.5)	.04	44.9 (10.4)

Abbreviations: AR, allergic rhinitis; RQLQ, Rhinitis Quality of Life Questionnaire; SF-36, 36-Item Short-Form Health Survey.

^a Lower values indicate less pain.

^b Exploratory *P* values are from 2-sided *t* tests or χ^2 tests.

sum score for these patients. If more than 2 domains were missing, the corresponding subscores were treated as missing, and no sum score was calculated.

The development of the RQLQ score in both the randomized groups is depicted in Figure 3. In the primary analysis at 3 months, the RQLQ improved by a mean (SE) of 1.48 (0.06)

in the acupuncture group and by 0.50 (0.06) in the control group (3-month scores were 1.44 [0.06] and 2.42 [0.06], respectively; difference, 0.98 [0.08]; *P* < .001).

This improvement was robust in the sensitivity analyses for missing data (smallest difference between acupuncture and control group, 0.79 [0.08]; *P* < .001). The proportion of

responders was 69.6% in the acupuncture group compared with 34.8% in the control group ($P < .001$).

In the RQLQ score and its subscales, the 3-month improvement (percent reduction) was significantly more pronounced in the acupuncture group than in the control group (Table 2). Similar results were found for quality of life (on both SF-36 component scores (Table 3).

During the 3 months after randomization, additional prescribed medication due to allergic rhinitis was used significantly ($P = .01$) less often by patients in the acupuncture group (59%) compared with patients in the control group (68%). However, no differences were found between the acupuncture and control groups with regard to the number of patients who took additional complementary or alternative treatment (acupuncture, 16% of patients; control, 17%; $P = .61$).

Nonrandomized Comparisons

At 3 months, improvement was similar in the nonrandomized acupuncture group compared with the randomized acupuncture group (RQLQ score: mean [SE], 1.71 [0.02] to 1.51 [0.02] and 1.71 [0.05] to 1.51 [0.05]; difference, 0.006; 95% confidence interval, -0.107 to 0.118 ; $P = .92$). The proportion of responders was 69.6% in the randomized acupuncture group compared with 67.6% in the nonrandomized acupuncture group ($P = .38$). No significant differences were found between randomized and nonrandomized patients in the 3-month improvements from baseline (percent reduction) (Table 3).

Factors Affecting the Size of the 3-Month RQLQ or Quality of Life (SF-36)

Several confounding factors affected the 3-month RQLQ score. According to the multivariate analysis consistently in all treatment groups and independent of treatment, RQLQ

score reduction was significantly more pronounced in patients with better education ($P < .001$), better physical ($P < .001$) or mental ($P < .001$) quality-of-life scores, and when the RQLQ at baseline was more pronounced ($P < .001$). RQLQ score reduction did not differ significantly among physicians ($P = .36$).

After the confounding variables were accounted for and despite their presence, the additional percent reductions of RQLQ score due to randomized acupuncture were estimated to be 29.6% (difference between acupuncture vs control: 95% confidence interval, 25.9%–33.3%; $P < .001$) and thus slightly less pronounced than the unadjusted estimates (Table 3).

No significant acupuncture effect modifier was found. However, a trend was seen toward a stronger acupuncture effect in educated people ($P = .054$). The physician's acupuncture qualification (eg, hours of training, years of experience) had no significant influence on the effect of the treatment.

Durability of Acupuncture Effects During 6 Months

The 6-month follow-up results observed in the acupuncture groups are given in Table 4. The 6-month improvements in the randomized and nonrandomization groups were only slightly lower than they had been at 3 months. The 6-month response rates in the randomized and nonrandomized acupuncture groups were 68.8% and 71.8%, respectively ($P = .17$).

Delayed Acupuncture

Delayed acupuncture resulted in a slight but significantly smaller general RQLQ improvement after 6 months compared with early acupuncture (Table 4). After delayed acupuncture, the improvement in RQLQ seen in control patients after 6 months was comparable to those improvements observed after 3 months in patients who had been randomized to immediate acupuncture therapy.

Adverse Effects

In 10.8% of patients, 529 adverse effects were reported after acupuncture (minor local bleeding or hematoma, 69%; pain, eg, needling pain, 9%; local infections at needle insertion place, 4%; vegetative symptoms, 2%; and other, 16%). No life-threatening adverse effects were reported.

DISCUSSION

Patients with allergic rhinitis treated with acupuncture in addition to routine care showed significant improvements in disease-specific and general quality of life compared with patients who received routine care alone. Physician characteristics, such as the level of formal acupuncture training or certification, did not influence treatment outcomes.

To our knowledge, the present study is by far the largest randomized trial of acupuncture in allergic rhinitis to date, including approximately 7.5% of physicians specialized in acupuncture in Germany. The study took a pragmatic ap-

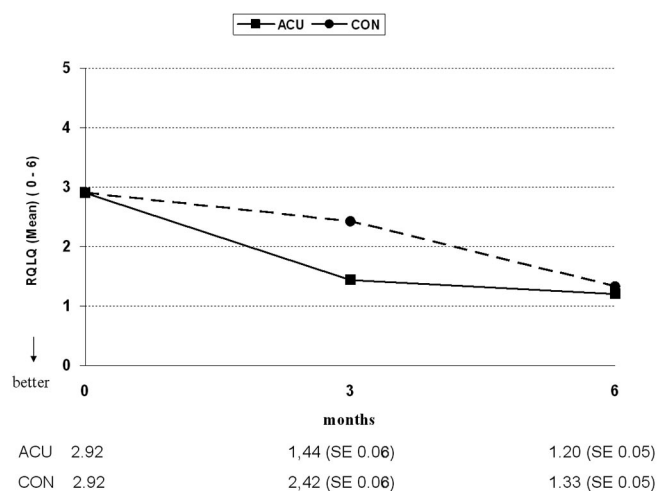


Figure 3. Development of Rhinitis Quality of Life Questionnaire (RQLQ) score (means and SE) in the 2 randomized treatment groups (ACU indicates acupuncture group; CON, control group: patients with no acupuncture in the first 3 months).

Table 2. Disease-Specific Quality of Life (RQLQ) and Secondary Outcomes for the 3 Treatment Groups (Means and Standard Deviations) After 3 Months

Outcomes	Randomized groups				Acupuncture groups		
	Acupuncture, mean (95% CI)	Control, mean (95% CI)	Acupuncture vs control		Nonrandomized, mean (95% CI)	Nonrandomized vs randomized	
			Δ (95% CI)	P value ^b		Δ (95% CI)	P value ^b
RQLQ ^a							
Global score	1.5 (1.4–1.6)	2.4 (2.3–2.5)	–0.9 (–1.1 to –0.8)	<.001	1.5 (1.5–1.6)	0.1 (–0.1 to 0.2)	.35
Sleep	1.3 (1.2–1.4)	2.1 (1.9–2.2)	–0.8 (–1.0 to –0.6)	<.001	1.3 (1.3–1.4)	0.0 (–0.1 to 0.1)	.79
Non-hay fever symptoms	1.5 (1.4–1.6)	2.3 (2.2–2.4)	–0.8 (–1.0 to –0.6)	<.001	1.5 (1.4–1.5)	–0.0 (–0.2 to 0.1)	.44
Practical problems	2.2 (2.0–2.3)	3.3 (3.1–3.5)	–1.2 (–1.4 to –0.9)	<.001	2.4 (2.3–2.4)	0.2 (0.1 to 0.4)	.01
Nasal symptoms	1.6 (1.5–1.8)	2.7 (2.6–2.9)	–1.1 (–1.3 to –0.9)	<.001	1.7 (1.7–1.8)	0.1 (–0.1 to 0.2)	.34
Eye symptoms	1.0 (0.9–1.1)	1.9 (1.7–2.1)	–0.9 (–1.1 to –0.7)	<.001	1.1 (1.1–1.2)	0.1 (–0.0 to 0.3)	.052
Activities	1.6 (1.4–1.7)	2.8 (2.5–3.1)	–1.0 (–1.3 to –0.8)	<.001	1.6 (1.5–1.6)	–0.0 (–0.2 to 0.1)	.83
Emotional	1.1 (1.0–1.2)	1.9 (1.8–2.0)	–0.8 (–1.0 to –0.6)	<.001	1.1 (1.1–1.1)	0.0 (–0.1 to 0.1)	.83
Quality of life (SF-36)							
Physical component score	51.8 (51.1–52.4)	48.4 (47.6–49.3)	3.3 (2.2–4.4)	<.001	52.2 (51.9–52.4)	0.4 (–0.3 to 1.1)	.25
Mental component score	48.4 (47.5–49.3)	45.3 (44.3–46.3)	3.0 (1.7–4.4)	<.001	49.1 (48.8–49.4)	0.7 (–0.1 to 1.6)	.10
General judgment							
Satisfaction by treatment	8.3 (8.1–8.5)	7.1 (6.8–7.4)	1.2 (0.8–1.5)	<.001	8.4 (8.3–8.4)	0.1 (–0.1 to 0.3)	.36
Success of treatment	7.5 (7.2–7.7)	5.9 (5.6–6.3)	1.5 (1.1–1.9)	<.001	7.6 (7.5–7.7)	0.2 (–0.1 to 0.4)	.23

Abbreviations: CI, confidence interval; RQLQ, Rhinitis Quality of Life Questionnaire; SF-36, 36-Item Short-Form Health Survey.

^a Lower values indicate better status.

^b P values are from 2-sided *t* tests.

Table 3. Disease-Specific Quality of Life (RQLQ) and Secondary Outcomes for the 3 Treatment Groups: 3-Month Changes From Baseline

Outcomes	Randomized groups				Acupuncture groups		
	Acupuncture group, mean (95% CI), % reduction	Control group, mean (95% CI), % reduction	Acupuncture vs control		Nonrandomized group, mean (95% CI), % reduction	Nonrandomized vs randomized	
			Δ (95% CI)	P value		Δ (95% CI)	P value
RQLQ	48.6 (45.2–52.0)	16.8 (12.6–21.0)	31.8 (16.5–37.2)	<.001	50.8 (49.6–52.0)	2.2 (–1.4 to 5.8)	.23
RQLQ secondary outcomes ^a							
Sleep	44.0 (39.9–48.0)	16.3 (11.9–20.8)	27.7 (21.7–33.7)	<.001	47.0 (45.6–48.4)	3.0 (–1.2 to 7.2)	.16
Non-hay fever symptoms	41.5 (38.0–45.0)	13.6 (9.5–17.8)	27.9 (22.4–33.2)	<.001	45.6 (44.4–46.9)	4.2 (0.4–8.0)	.03
Practical problems	40.2 (36.0–44.4)	10.4 (5.6–15.2)	29.8 (23.5–36.1)	<.001	40.5 (39.0–41.9)	0.3 (–4.2 to 4.8)	.90
Nasal symptoms	45.9 (42.0–49.7)	13.1 (8.3–18.0)	32.7 (26.6–38.9)	<.001	49.7 (48.4–51.0)	3.8 (–0.3 to 7.9)	.07
Eye symptoms	51.8 (47.6–55.9)	18.4 (13.4–23.5)	33.3 (26.8–39.9)	<.001	54.3 (52.9–55.7)	2.5 (–1.9 to 7.0)	.24
Activities	50.7 (46.3–55.2)	17.6 (12.2–22.9)	33.1 (26.2–40.1)	<.001	55.0 (53.5–56.5)	4.3 (–0.3 to 8.9)	.06
Emotional	52.8 (48.6–57.0)	20.7 (6.0–25.4)	32.1 (25.8–38.4)	<.001	54.7 (53.3–56.2)	1.9 (–2.5 to 6.3)	.39
Quality of life (SF-36) ^b							
Physical component score	2.8 (2.1–3.5)	–1.1 (–1.9 to –0.3)	3.8 (2.8–4.9)	<.001	3.3 (3.1–3.6)	0.6 (–0.2 to 1.4)	.15
Mental component score	3.3 (2.3–4.2)	–0.3 (–1.3 to 0.6)	3.6 (2.3–4.9)	<.001	4.4 (4.0–4.7)	1.1 (0.1–2.1)	.03

Abbreviations: CI, confidence interval; RQLQ, Rhinitis Quality of Life Questionnaire; SF-36, 36-Item Short-Form Health Survey.

^a Lower values indicate better status.

^b For quality of life (SF-36), the values are change in baseline vs 3 months.

proach, aiming to evaluate acupuncture in a manner that would reflect as closely as possible the conditions of routine medical practice (needle acupuncture and manual stimulation) and maximize external validity. We used internationally established and accepted outcome parameters to evaluate patients with allergic rhinitis.^{10,11} The study had high fol-

low-up rates; furthermore, we used conservative methods to deal with missing data. The additional inclusion of patients who declined randomization allowed for investigating any potential selection effects. By including patients who declined randomization, we also accounted for any selection bias that may have been present in this study design.

Table 4. Disease-Specific Quality of Life (RQLQ) and Secondary Outcomes for the Randomized Groups: 6-Month Changes From Baseline

Outcomes	Randomized groups				Acupuncture groups		
	Acupuncture group, mean (95% CI), % reduction	Control group, mean (95% CI), % reduction	Control vs acupuncture		Nonrandomized group, mean (95% CI), % reduction	Nonrandomized vs randomized	
			Δ (95%CI)	P value		Δ (95% CI)	P value
RQLQ	56.5 (53.0–60.1)	51.4 (47.7–55.1)	5.2 (0.1–10.3)	.047	62.1 (61.0–63.2)	5.6 (2.0–9.1)	.002
RQLQ secondary outcomes ^a							
Sleep	49.1 (44.7–53.5)	48.4 (44.1–52.7)	0.7 (–5.4 to 6.9)	.81	56.7 (55.3–58.1)	7.6 (3.1–12.1)	.001
Non-hay fever symptoms	46.8 (42.8–50.8)	42.1 (38.1–46.0)	4.7 (–0.9 to 10.4)	.10	52.8 (51.5–54.1)	6.0 (1.9–10.1)	.004
Practical problems	47.9 (43.4–52.3)	42.9 (38.1–47.6)	5.0 (–1.5 to 11.5)	.13	51.4 (49.8–52.9)	3.5 (–1.3 to 8.3)	.15
Nasal symptoms	55.1 (51.1–59.1)	47.8 (43.4–52.2)	7.3 (1.4–13.2)	.02	61.2 (60.0–62.5)	6.1 (2.1–10.2)	.003
Eye symptoms	56.9 (52.6–61.3)	51.4 (46.8–56.1)	5.5 (–0.9 to 11.8)	.09	64.8 (63.4–66.3)	7.9 (3.5–12.4)	<.001
Activities	62.6 (58.2–67.0)	57.3 (52.8–61.8)	5.3 (–1.0 to 11.6)	.10	68.5 (67.1–69.9)	5.9 (1.5–10.3)	.008
Emotional	62.5 (58.2–66.9)	54.2 (49.7–58.7)	8.3 (2.1–14.5)	.009	65.4 (63.9–66.8)	2.8 (–1.6 to 7.2)	.21
Quality of life (SF-36) ^b							
Physical component score	3.0 (2.3–3.9)	2.0 (1.2–2.8)	1.1 (–0.1 to 2.2)	.06	3.7 (3.4–4.0)	0.6 (–0.2 to 1.5)	.14
Mental component score	3.6 (2.6–4.6)	3.4 (2.5–4.3)	0.2 (–1.2 to 1.6)	.76	4.2 (3.9–4.6)	0.6 (–0.5 to 1.7)	.29

Abbreviations: CI, confidence interval; RQLQ, Rhinitis Quality of Life Questionnaire; SF-36, 36-Item Short-Form Health Survey.

^a Lower values indicate better status; control group also received acupuncture.

^b For quality of life (SF-36), the values are change in baseline vs 3 months.

Clearly, this kind of approach also has methodologic limitations. In our study, neither physicians nor patients were blinded to treatment. Although the main outcome measure was evaluated independently by the patients, a bias resulting from nonblinding to the intervention cannot be ruled out. Also, a selection bias attributable to the participating physicians because of positive attitudes about acupuncture and affiliation with the insurance groups funding the study cannot be ruled out. In addition, trial physicians may have had a personal or financial interest in producing positive results in favor of acupuncture, which could have influenced the results of the trial. To minimize social acceptability bias, all questionnaires were sent directly from and to the coordinating research institute. Furthermore, only needle acupuncture was allowed in this trial, and the specifics of acupuncture treatment and any cointerventions were left to the discretion of the physicians, which means that patients' treatment regimens were highly variable. Because concomitant medication (eg, cortisone) was not documented or analyzed in the treatment groups, we are unable to provide information about its use. Our inclusion criteria were broad, which resulted in a heterogeneous patient sample and, potentially, some cases of diagnostic misclassification. In addition, our study design and methods did not allow us to distinguish between patients with seasonal allergic rhinitis and those with perennial allergic rhinitis. However, because of the randomization procedure used in this trial, an equal distribution of patients with seasonal allergic rhinitis and those with perennial allergic rhinitis in both randomized groups can be assumed; as a result, the specificity of allergic rhinitis type is unlikely to have influenced the overall effect size of treatment.

Finally, our patients had a highly positive attitude toward acupuncture treatment. This attitude, empathy toward the treating physician, and other aspects of acupuncture as a complex medical intervention might have contributed to the beneficial effects observed in our trial. Also, patients who participated in our trial were reimbursed by their health insurance companies. It is therefore conceivable that patient expectation and financial incentives increased the nonspecific effect of acupuncture treatment. Although these issues might be considered limitations from an experimental perspective, the study design was chosen to reflect general medical practice as closely as possible.

To evaluate changes in allergic rhinitis symptoms, it would have been helpful to use a disease-specific symptom score based on daily symptoms, such as the Allergic Rhinitis Symptom Questionnaire (ARSQ). However, we decided not to include a disease-specific symptom score in the outcome measure because we had observed inconsistencies between the RQLQ and the ARSQ in our previous trial⁵ and because it would have been difficult to use a detailed diary in such a large, pragmatic, multicenter trial. This pragmatic study cannot answer the question of whether the effects observed may be at least in part due to a placebo effect.

In patients who consented to randomization, treatment outcomes after acupuncture were similar to those in patients who declined randomization. A patient's self-selection in randomized studies of complementary and alternative medicine could be a relevant problem.¹⁴ Therefore, to control for selection bias, the use of study designs that also include nonrandomized patients appears to be desirable. In our study, approximately 3 in 4 eligible patients refused randomization,

perhaps because of the disadvantage of having a 50% chance of a 3-month delay before starting acupuncture treatment. These patients were included in the nonrandomized acupuncture group. No significant differences were found in respect to both baseline characteristics and treatment outcomes between randomized and nonrandomized patients. Further support for the observation that results of randomized trials and nonrandomized observational studies could yield similar results is derived from other publications.¹⁵

In both randomized and nonrandomized patients, the improvements in the RQLQ score were clinically relevant.^{10,11} In addition, an important finding of our study is that improvements seen immediately after completion of 3 months of treatment continued for at least another 3 months.

This pragmatic study cannot answer the question of whether the effects observed may be at least in part due to the placebo effect. A further limitation of our study design is that the treatment group received a form of add-on, whereas the standard group received routine care alone. Because there was, as a result, no control for the add-on acupuncture group, our positive findings must be interpreted with caution. This being said, the results of earlier controlled trials have shown acupuncture to have beneficial treatment effects in patients with allergic rhinitis. However, the results of sham-controlled trials in patients with allergic rhinitis were inconsistent.^{4–8} However, a trend was seen in favor of acupuncture in the trials that investigated the efficacy in a larger study population, including a recently published randomized controlled trial in 80 patients with persistent allergic rhinitis.^{3,5,6,8} In addition, 2 recently published reviews on the efficacy of acupuncture in allergic rhinitis yielded inconsistent results.^{16,17} To our knowledge, no study has investigated the effectiveness of acupuncture in allergic rhinitis while comparing acupuncture with a control group receiving routine care and delayed verum treatment.

Our finding that the formal qualification of the physician and the years of acupuncture experience had no significant influence on treatment outcome was supported by other trials of the present acupuncture research initiative^{18–20} and could be interpreted as a further indication that formal acupuncture training has only a limited role for the treatment effect. However, these results should be interpreted with caution and not as a well-supported conclusion because this finding was not the main focus of the study and the indicators in the present study might not adequately reflect the quality of a physician's treatment. Our study provides further evidence that acupuncture is a safe intervention. This finding is in agreement with previous large surveys and trials.^{21–23}

In conclusion, the results of this pragmatic trial suggest that treating patients with allergic rhinitis in routine care with additional acupuncture leads to clinically relevant benefits. Further trials that include sham acupuncture groups should be conducted to investigate the specificity of the treatment effect. Acupuncture can be considered an effective and safe treatment option for patients with allergic rhinitis.

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