

## clinical investigations

# Short-term Acupuncture Therapy Is of No Benefit in Patients With Moderate Persistent Asthma\*

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**Study objectives:** Acupuncture traditionally has been used to treat asthma. Nevertheless, only a few controlled studies have been performed to determine the efficacy of this treatment. Our study aimed to determine the efficacy of acupuncture in patients with moderate persistent asthma.

**Methods:** Twenty-three patients with moderate persistent asthma who had been treated only with inhaled  $\beta_2$ -agonists were randomly assigned to receive four sessions of real acupuncture (RA) or sham acupuncture (SA) in a blinded manner. After a washout period of 3 weeks, the patients were crossed over. Monitoring included FEV<sub>1</sub>, methacholine challenge, daily peak flow (PF) variability, and the keeping of an asthma diary.

**Results:** Twenty of 23 patients completed the study. There was no significant change in FEV<sub>1</sub> following treatment. The mean ( $\pm$  SE) FEV<sub>1</sub> values before and after the RA were  $73 \pm 4\%$  and  $73 \pm 3\%$ , respectively (not significant [NS]). FEV<sub>1</sub> values before and after SA were  $70 \pm 3\%$  and  $70 \pm 3\%$ , respectively (NS). There was also no change in provocative methacholine concentration causing a 20% fall in FEV<sub>1</sub> (PC<sub>20</sub>) before and after treatment. The mean PC<sub>20</sub> values before and after RA were  $0.92 \pm 0.42$  mg/mL and  $1.16 \pm 0.51$  mg/mL, respectively ( $p = 0.71$ ), while the PC<sub>20</sub> values before and after SA were  $1.47 \pm 0.83$  mg/mL and  $1.11 \pm 0.79$  mg/mL, respectively ( $p = 0.59$ ). There was no change in the mean PF variability before and after the RA ( $1.6 \pm 3.1\%$  and  $1.8 \pm 2.3\%$ , respectively [NS]). The PF variability before and after SA were  $3.6 \pm 2.8\%$  and  $2.8 \pm 3.4\%$ , respectively (NS). No significant difference was demonstrated for symptom scores or for the use of  $\beta_2$ -agonist inhalers (RA,  $6.7 \pm 3.4$ ; SA,  $8.1 \pm 3.6$ ;  $p = 0.58$ ).

**Conclusion:** In patients with moderate persistent asthma, a short course of acupuncture treatment resulted in no change in lung functions, bronchial hyperreactivity, or patient symptoms.

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**Key words:** acupuncture; asthma; methacholine challenge

**Abbreviations:** CAM = complementary/alternative medicine; NS = not significant; PC<sub>20</sub> = provocative concentration of a substance causing a 20% fall in FEV<sub>1</sub>; PF = peak flow; RA = real acupuncture; SA = sham acupuncture; TCM = traditional Chinese medicine

The use of complementary/alternative medicine (CAM) is increasing,<sup>1</sup> and many physicians either refer patients for CAM treatment or practice CAM themselves.<sup>2</sup> Furthermore, acupuncture was recently<sup>1</sup>

approved for practice by the British Medical Association,<sup>3</sup> and most medical schools in the United States

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offer elective courses in CAM.<sup>4</sup> Traditional Chinese medicine (TCM) has claimed the ability to favorably influence the course and symptoms of bronchial

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asthma. However, the published data on this subject are controversial. To date, real acupuncture (RA) has been shown to have an immediate effect<sup>5-7</sup> but not a lasting effect on asthma.<sup>8-10</sup> Methacholine challenges<sup>11</sup> and exercise,<sup>12</sup> but not histamine challenges,<sup>13</sup> have been shown to be affected by RA. However, most studies performed to date were not controlled or crossover in design.<sup>14</sup> Immunomodulatory changes in lymphocyte subsets and cytokines have been shown to be affected by acupuncture.<sup>15</sup> Furthermore, these studies have been criticized by CAM therapists because treated subjects received “nonpersonalized” therapy. Using a sham, controlled, crossover-designed study, we evaluated the influence of a short and intensive course of personalized acupuncture on patients with moderate persistent asthma.

## MATERIALS AND METHODS

### Study Design

Patients with moderate persistent asthma who were > 18 years of age and were attending the outpatient clinic at the Institute of Pulmonology at Hadassah University Hospital were screened for participation in the study. Inclusion criteria were the following: use of inhaled  $\beta_2$ -agonists, as required only; FEV<sub>1</sub> values between 70% and 85% of the predicted value, as calculated with respect to age and height; and at least 12% improvement in FEV<sub>1</sub> after the administration of  $\beta_2$ -agonist medication. Patients were not eligible for the study if they had been treated for asthma in an emergency department within 1 month before the study, had been hospitalized for asthma within 3 months before the study, had an upper respiratory tract infection within 6 weeks before the study, or had received therapy with corticosteroids (oral or inhaled) within 1 month prior to the study.

Patients were randomly assigned to receive 1 week of either RA or sham acupuncture (SA) [four sessions] in a blinded manner (*ie*, both the patient and evaluator were blinded). To avoid a lasting effect of acupuncture treatment, a washout period of at least 3 weeks was designed. Groups then were crossed over, and patients who had received RA received SA, and vice versa (Fig 1). Spirometry testing and methacholine challenges were performed at the beginning and end of each course of RA or SA. Throughout the study, the patients recorded morning and evening peak flow (PF) values, recorded their use of daily  $\beta_2$ -agonist inhalers, and completed a quality-of-life questionnaire.

Patients were withdrawn from the study if they missed an

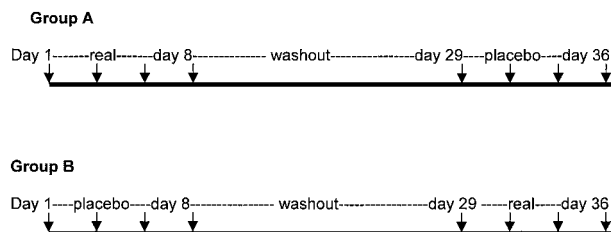


FIGURE 1. Study design.

acupuncture session or in the event of a worsening of asthma that required treatment with inhaled or oral corticosteroids.

The protocol was approved by the institutional review board, and written informed consent was obtained from all participants. The study was conducted between July 1998 and June 1999.

### Acupuncture

Acupuncture sessions were performed by a certified and experienced acupuncture therapist. Sterile, single-use acupuncture needles (Suzhou Medical Instruments Factory; Suzhou, China) were used.

For RA, the first and last sessions were designed to treat acute attacks of asthma, while the second and third sessions were designed to treat the root of the asthma, as diagnosed by TCM, and were personalized for each patient.<sup>16</sup> The depth and angle of the needle insertion were specifically determined depending on the selected point.<sup>17</sup> *De qi* was achieved in all points. SA was performed at places other than acupuncture points on the back, shoulders, and extremities at an angle of 10° to 30° and was directed to the subcutaneous tissue.

Each acupuncture session lasted 20 to 30 min, and the needles were manipulated once or twice during each session in both groups.

### FEV<sub>1</sub>

Spirometry was performed using a compact spirometer (Vitalograph Ltd; Buckingham, UK). Patients were encouraged to perform at least three maneuvers during each measurement to meet American Thoracic Society criteria for acceptability and reproducibility. The highest FEV<sub>1</sub> value from each set of measurements was used for analysis.

### Methacholine Challenge

A methacholine solution (Spectrum Chemical Corp; Gardena, CA) was prepared in doubling concentrations ranging from 0.03 to 8 mg/mL. Solutions were administered via a nebulizer chamber (Hudson RCI; Temecula, CA) with an airflow rate of 5 L/min for 2 min, and the FEV<sub>1</sub> was measured 3 min after each dose. The dose was successfully doubled until a provocative concentration causing a fall in FEV<sub>1</sub> of 20% (PC<sub>20</sub>) from baseline was obtained and the PC<sub>20</sub> value could be calculated. The PC<sub>20</sub> was computed from the methacholine dose-response curve (*ie*, the change in FEV<sub>1</sub> in relation to the methacholine concentration) by linear interpolation on a log scale.

### Data Recorded at Home

The patients recorded asthma symptoms, medication consumption, and peak expiratory flow results in an asthma diary. Each patient was supplied with a new mini-Wright peak flowmeter (Clement Clarke International Ltd; London, UK) and was instructed in its use. Only those able to use the meter reliably were included in the study. The patients were asked to measure their peak expiratory flow twice daily at home, in the morning and in the evening before taking any medication, and to record the best of three attempts. Daily PF variability was calculated using the following equation:

$$\frac{\text{evening PF} - \text{morning PF}}{(\text{evening PF} + \text{morning PF})/2}$$

and the result was presented as a percentage.

Each patient was supplied with an asthma diary that is used in

our clinic; the number of wheeze episodes was recorded and a score was given for exercise tolerance (0, normal exercise tolerance; 3, severe difficulty during exercise). The dose of any medication received and the number of doses per hour also were recorded. Short-acting inhaled bronchodilators were used as rescue medication during the course of the study.

### Statistical Analysis

PC<sub>20</sub> values were transformed into a logarithmic scale for the statistical analysis. A mixed-model analysis of variance was done using a software package (SAS, version 6.12 [PROC MIXED program]; SAS Institute; Cary, NC). A p value of ≤ 0.05 was considered to be statistically significant.

## RESULTS

Twenty of 23 patients completed the study. Three patients discontinued the study due to pulmonary infection (one patient), the inability to fulfill study requirements (one patient), and loss to follow-up (one patient).

### FEV<sub>1</sub>

Nineteen patients were available for analysis (Fig 2). No significant difference was observed in FEV<sub>1</sub> measurements made before and after acupuncture therapy. The mean (± SE) FEV<sub>1</sub> values measured before and after 1 week of RA (n = 19) were 73 ± 4% predicted and 73 ± 3% predicted, respectively (p = 1), and the mean FEV<sub>1</sub> values measured before and after 1 week of SA (n = 19) were 70 ± 3% predicted and 70 ± 3% predicted, respectively (p = 0.98) [Fig 2]. A comparison of the late effects of RA (n = 10) and SA (n = 9) on FEV<sub>1</sub> measured 3 weeks after the last treatment also was

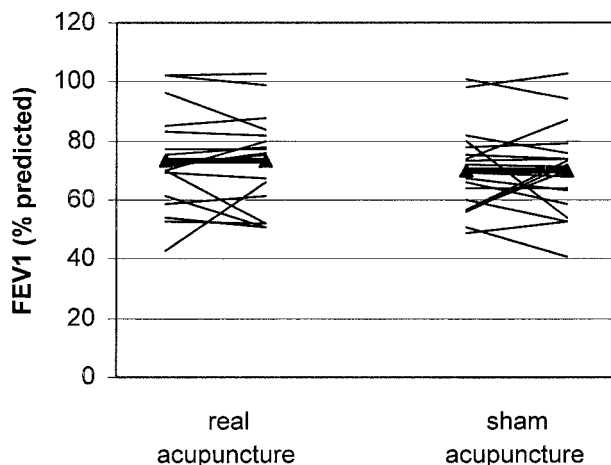


FIGURE 2. FEV<sub>1</sub> measured before and after RA and SA. The thick lines represent mean values.

not significant (NS) [70 ± 6% predicted and 70 ± 5% predicted, respectively; p = 0.46].

### PC<sub>20</sub>

There was no significant change in PC<sub>20</sub> following RA (0.92 ± 0.42 mg/mL; n = 20) compared to that following SA (1.16 ± 0.51 mg/mL; n = 20; p = 0.71). In the control SA group (n = 20), no effect was seen (before, 1.47 ± 0.83 mg/mL; after, 1.11 ± 0.79 mg/mL; p = 0.59) [Fig 3].

There was no delayed benefit for PC<sub>20</sub> by RA (measurement at the end of the RA sessions, 1.16 ± 0.51 mg/mL; measurement 3 weeks later, 2.48 ± 1.61 mg/mL; n = 10) or by SA (measurement at the end of the SA sessions, 1.11 ± 0.79 mg/mL; measurement 3 weeks later, 0.83 ± 0.36 mg/mL; p = 0.24; n = 10).

### PF Variability

The mean daily PF variability before and after RA (n = 14) was 1.6 ± 3.1% and 1.8 ± 2.3%, respectively (NS). The mean daily PF variability before and after SA (n = 14) was 3.6 ± 2.8% and 2.8 ± 3.4%, respectively (NS). No late effect of RA or SA on daily PF variability was demonstrated (p = 0.82).

### Patient Symptoms and Medication Use

Most of the patients did not report wheezing. The mean number of wheezing episodes per day was 0.22 and 0.24, respectively, during the RA (n = 11) and SA (n = 11) treatments. The mean daily exercise tolerance score was 0.15 and 0.21, respectively, in the RA and SA periods (n = 11). No significant difference was demonstrated in the weekly consumption of β<sub>2</sub>-agonist inhalers (during RA, 6.7 ± 3.4 puffs per week [n = 15]; during SA, 8.1 ± 3.6 puffs per week [n = 15]; p = 0.58).

## DISCUSSION

The chronicity of bronchial asthma and the fear of steroid therapy cause many patients to seek alternative methods of treatment such as acupuncture, herbal medicine, and massage therapy. TCM is based on the principle that a balance between two forces (yin and yang) is the key to health. An imbalance of either force results in a state of disease. Balance can be restored by various methods, including exercise, massage, acupuncture, and herbal therapy. Tradition together with centuries of personal experience have added considerable weight to this theory. Claims for the ability of acupuncture and herbal medicine to influence the course and symp-

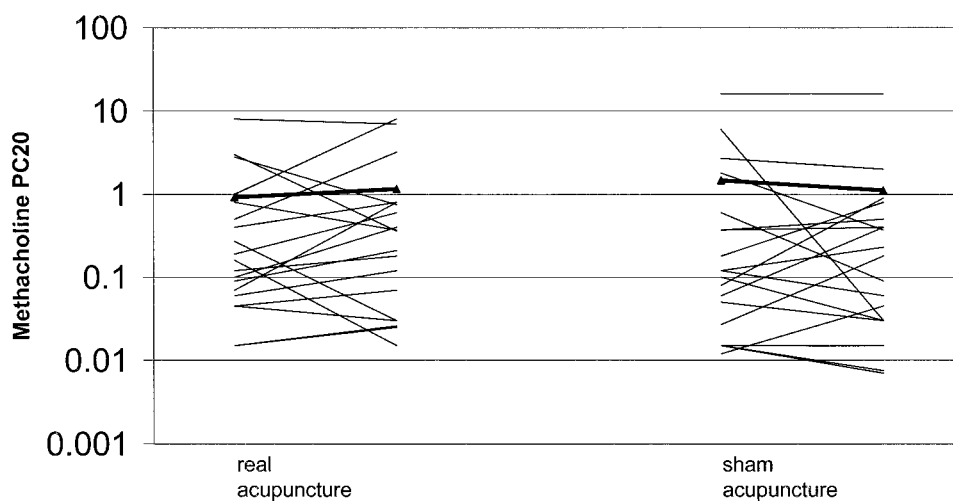


FIGURE 3. The methacholine PC<sub>20</sub> before and after RA and SA. Values are presented in a logarithmic scale. Thick lines represent the mean values.

toms of bronchial asthma exist in the Chinese medical literature.<sup>16,18,19</sup> However, the published data on this subject are scanty and controversial. A short-term effect of acupuncture on bronchial asthma was shown by Yu and Lee<sup>5</sup> and later by Virsik et al.<sup>6</sup> Both studies demonstrated that RA compared to SA results in an improvement in FEV<sub>1</sub> during an acute asthma attack. Takishima et al<sup>7</sup> found that acupuncture caused a short-term reduction in airway resistance. A sustained or long-lasting effect of acupuncture has not been demonstrated, although such treatment has been reported to improve the patient's well-being significantly.<sup>8,9</sup> Sham controlled studies on the effect of acupuncture on the results of bronchial provocation tests are also inconsistent. Tashkin et al<sup>11</sup> tested the efficacy of acupuncture in 12 patients with mild-to-moderate bronchial asthma (some had been treated with systemic steroid therapy). These patients were treated immediately following methacholine challenge with RA (using fixed acupuncture points), SA, saline solution inhalation, or isoproterenol inhalation. The dose of methacholine was predetermined to cause a 30% reduction in airway conductance. RA, but not SA, reduced the bronchial hyperreactivity that had been induced by methacholine inhalation. The demonstrated effect was weaker than that with isoproterenol inhalation. In a study by Fung et al,<sup>12</sup> RA had no effect on air flows in 19 patients with exercise-induced asthma. However, following exercise challenge, both RA and SA caused a significant reduction in the fall of FEV<sub>1</sub>, although RA had a greater effect. In contrast to exercise or methacholine challenge, no effect of RA was demonstrated in a study using histamine challenge.<sup>13</sup> Most previous studies used a heterogeneous

group of patients in regard to steroid, theophylline, and other bronchoprotective treatments and in regard to smoking habits. Pulmonary function tests were not performed at the same time of day for the treatment and control groups. An additional problem encountered in studies of CAM and acupuncture as a whole is related to the fact that, in contrast to the case in Western medicine, in Chinese medicine bronchial asthma can be diagnosed by more than five different syndromes.<sup>16</sup> Each syndrome involves a different treatment and prognosis. This is the source for criticism made by the CAM therapists who maintain that a nonpersonalized treatment (*ie*, non-syndrome-specific treatment) is bound to achieve a lack of response in the patient. However, in our study, we attempted to overcome this pitfall by providing personalized treatment.

In our study, RA did not affect PC<sub>20</sub>, FEV<sub>1</sub>, PF variability, or weekly consumption of  $\beta_2$ -agonists. In our study, the lack of effect by RA on bronchial asthma may be due to the relatively small number of patients. However, not even a trend of improvement was observed by acupuncture treatment. It is also possible that the intervention was too short, although TCM claims an effect after even a single session of acupuncture.<sup>16</sup> TCM claims that at times an effect may be apparent only at some time after the RA treatment.<sup>8</sup> Our study does not support the hypothesis, because 3 weeks post-RA, no beneficial effect was demonstrated on the results of pulmonary function tests.

Our study was performed in a selected group of patients with moderate persistent asthma who had not been treated with inhaled or systemic corticosteroid therapy. It is possible that acupuncture may

have a favorable effect on patients with more severe asthma, although this would need to be addressed in a separate study.

In this study, we evaluated the influence of a short and intensive course of acupuncture on patients with persistent asthma in a blinded, crossover, and syndrome-specific manner. At this stage, the available data do not support or justify the use of a short, intensive course of acupuncture to treat patients with asthma.

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