Takagi award-winning paper

Effect of Acupuncture Treatment in Patients with Bronchial Asthma

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Abstract

[AIM] Acupuncture has traditionally been used in Japan in the treatment of bronchial asthma and is being increasingly applied. Although there are many published studies on acupuncture and asthma, few meet the scientific criteria necessary to prove the effectiveness of acupuncture. This study, therefore, presents the clinical results of acupuncture treatment for adult bronchial asthma.

[Design] Single-subject research design (N-of-1 method).

[Setting] Department of Internal Medicine, Acupuncture and Moxibustion Center, Meiji University of Oriental Medicine, Japan.

[Participants] Six patients of both genders (mean age, 49.0 years) with moderate to severe persistent bronchial asthma.

[Intervention] Six patients received 10 sessions of acupuncture treatment (one time per week for 10 weeks). The basic combination of meridian points for the treatment of the patients were LU 1 (*Zhongfu*), LU 5(*Chize*), LU 9 (*Taiyan*), CV 4 (*Guanyuan*), CV 12 (*Zhongwan*), BL 13 (*Feishu*), BL 20 (*Pishu*), and BL 23 (*Shenshu*).

[Measurements] Primary outcome was the symptom of asthma at the end of the 10 treatment periods. Secondary outcomes were Visual Analogue Scale of dyspnea (DVAS), respiratory function, Peak Expiratory Flow Rate (PEFR), blood, the use of asthma drugs. The effect of the intervention on eosinophils in blood was assessed.

[Main results] Late effects of asthma patients showed significantly better results, compared with base line on outcome measures after the 10 weeks. In this study, symptoms of asthma and dyspnea VAS in patients with asthma were significantly improved by acupuncture.

[Conclusion] This study indicated that acupuncture was effective for asthma symptoms and respiratory function.

Key words: *Bronchial asthma, Acupuncture, Lung function, Steroid, Single case study*

Ⅰ. Introduction

Bronchial asthma is a condition characterized by increasing airway hypersensitivity and reversible obstruction of bronchial airways due to various stimulations. Its main symptoms are episodic wheezing or dyspnea. In patients with severe symptoms of asthma, their daily lives and social lives are disturbed. Airway obstruction is induced by inflammation of airways such as spasms in bronchial smooth muscle, airway edema, or increases in airway secretion and it is thought to be a chronic inflammatory disorder of airways[1]. For the treatment of asthma, inhaled and oral corticosteroids are administered, which are generally accepted to be the most effective therapeutic drugs for bronchial asthma. There are, however, some patients with bronchial asthma who do not respond to corticosteroids[2].

Acupuncture is a traditional medicine that has been

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applied to respiratory diseases for a long time and has recently been used for chronic bronchitis and emphysema as well as bronchial asthma[3]. In particular, some cases of acupuncture treatment for bronchial asthma have been reported, and Fung et al.[4] reported that acupuncture treatment was effective in preventing exercise-induced asthma. In a systematic review performed by Martin et al.[5], however, no obvious evidence was shown because there were differences in the methods of acupuncture treatment between each report. There is no consistent observation on the effect of acupuncture treatment for bronchial asthma.

We, therefore, provided acupuncture treatment in conjunction with medication for patients with bronchial asthma who could not fully control it by inhaled or oral corticosteroids and evaluated the effect of acupuncture treatment for symptoms of asthma and respiratory functions using a single-subject research design (N-of 1, single case study).

Ⅱ. SUBJECTS AND METHODS

1. Subjects

Subjects were six patients (two males and four females, mean age 49.0 ± 18.0 years) from asthma patients treated as outpatients in the Department of Internal Medicine, Meiji University of Oriental Medicine Hospital and the Acupuncture and Moxibustion Center, Meiji University of Oriental Medicine during the period from August of 1997 to January of 2002, whose symptoms could not be fully controlled by orally administered or inhaled corticosteroids in conjunction with standard treatment such as orally administered theophylline and inhaled or orally administered β_2-agonists.

According to the classification of severity of asthma symptoms[6], five cases were classified as severe persistent asthma (Step 4) and one case as moderate persistent asthma (Step 3). In the respiratory function tests (performed during the periods without attacks), VC was 2.7 ± 0.7 L, %VC was 97.0 ± 33.6%, FVC was 2.4 ± 0.4 L, FEV_1 was 1.7 ± 0.4 L, FEV_1% was 72.0 ± 10.8%,

Table 1-1. Characteristics of patients

Case No.	Age/Sex	Disease duration (Months)	Classification	Acupuncture start time
1	48/F	48	Step 4	1997/9/29
2	30/F	156	Step 4	1999/7/28
3	66/M	12	Step 4	1999/2/8
4	60/M	6	Step 4	1998/8/5
5	66/F	108	Step 4	1997/8/5
6	24/F	96	Step 3	2001/7/23
Mean ± SD	49.0 ± 18.4	71.0 ± 59.1	-	

Table 1-2. Respiratory functions of each patient at the start of acupuncture treatment
VC: Vital Capacity, FVC: Forced Vital Capacity, FEV1: Forced Expiratory Volume in 1 second, PEFR: Peak Expiratory Flow Rate

Case No.	Respiratory function test						PEFR (L/min) On rising time	PEFR (L/min) At bedtime
	VC (L)	%VC (%)	FVC (L)	FEV1 (L)	FEV1% (%)	V25 (L/S)		
1	2.6	98.3	2.4	1.8	75.0	0.6	250	300
2	3.1	107.5	2.6	1.5	57.6	0.3	270	270
3	3.2	98.7	3.0	2.2	72.5	0.6	250	300
4	2.7	82.3	2.4	2.1	87.5	0.8	300	450
5	3.4	149.1	1.8	1.1	61.1	0.2	120	170
6	1.5	46.0	2.0	1.5	75.0	0.4	220	300
Mean ± SD	2.7 ± 0.7	97.0 ± 33.6	2.4 ± 0.4	1.7 ± 0.4	72.0 ± 10.8	0.5 ± 0.2	235.0 ± 62.2	298.0 ± 89.7

V 25 was 0.5 $\pm$ 0.2 L/S, peak flow values (PEFR) (on rising) was 235.0 $\pm$ 62.2 L/MIN, and PEFR (at bed-time) was 298.0 $\pm$ 89.7 L/min. Characteristics and classification of severity of asthma symptoms and respiratory functions before acupuncture treatment of the six patients are shown in Table 1 (1-1, 1-2), 2.

Before performing this study, the six patients were informed of the purpose of the study and the research protocol, and we obtained their consent in written form. This clinical study was performed with the approval of the Ethics Committee of Meiji University of Oriental Medicine.

2. Methods of acupuncture treatment
1) Setting the acupuncture treatment period (Table 3)

In order to evaluate the effect of the treatment, we set two periods according to a single-subject research design (N-of 1, single case study)[7]. One was Period A in which acupuncture treatment was performed in conjunction with standard medication and the other was Period B in which acupuncture treatment was not performed but standard medication was performed. Only Period A was repeated. The acupuncture treatment was performed once a week. In Period A, ten acupuncture treatments were provided. In Period B, only medication was provided for the same number of treatment days as those of

Period A. When remarkable exacerbations of asthma were observed in a patient and he/she wished to receive acupuncture treatment during Period B, the next Period A was started at that point.

2) Choice of meridian points and methods of treatment

Meridian points for the treatment of patients in the present study were those shown to be effective for patients with bronchial asthma and those that were shown to be effective in various reports5,8,9]. The basic combination of meridian points for the treatment were Taiyan (LU 9), Chize (LU 5), Zhonghu (LU 1), Zhongwan (CV 12), Guanyuan (CV 4), Feishu (BL 13), Pishu (BL 20) and Shenshu (BL 23). Depth of insertion was about 10 mm to 30 mm at all meridian points, which depended on body habitus of the patients. At Taiyan, from the peripheral cite to the central cite, transverse insertion was performed, and at other meridian points, perpendicular insertion was performed. For acupuncture stimulation, manual twisting after insertion was performed for about ten seconds and the needles retained for ten minutes after patients recognized needle sensation (de qi). When patients suffered from anorexia, insomnia, generalized fatigue or lumbago, those were treated as well. For those treatments, disposable stainless needles (Seirin Corp.), 40 mm in length and 0.16 to 0.20

Table 2 Severity of bronchial asthma by clinical findings

Classification	Step 1 Mild intermittent	Step 2 Mild persistent	Step 3 Moderate persistent	Step 4 Severe persistent
Definitions	· Asthma, coughing, and/ or dyspnea occurs once or twice per week · Symptoms are intermittent and short · Symptoms occur once or twice at night per month	· Symptoms occur 2 or more times per week · Daily life and sleep may be disturbed twice or more per month · Symptoms occur at night twice or more per month	· Chronic symptoms · Inhalation medicine β_2-agonists taken as needed almost every day · Daily life and sleep are disturbed once or more per week. · Symptoms occur at night once or more per week	· Often getting worse even with medical treatment · Symptoms are lasting · There is a limit in everyday life · Frequent symptoms at night · Taking oral corticosteroids continuously

Table 3 Evaluation schedule

	1- 10	11- 20	21- 30
	Period A1	Period B	Period A2
	at startat, at end		at startat, at end
Asthma diary	○ - ○	○ - ○	○ - ○
Dyspnea VAS	○ ○		○ ○
Respiratory functions test	○		○
Blood test	○		○
PEFR	○ - ○	○ - ○	○ - ○

mm in diameter, were used.

Ⅲ． EVALUATION METHODS

1. Symptoms of asthma

Patients recorded their asthma symptoms everyday in an asthma diary[10] developed by the Bronchial Asthma Severity Criteria Review Committee and their symptoms for a week were scored (asthma score).

2. Dyspnea

Severity of dyspnea was evaluated by a 100 mm Visual Analogue Scale (VAS) of which the right end (100 mm) indicates the worst dyspnea imaginable, while the left end (0 mm) indicates no dyspnea, both at the beginning and at the end of the period A.

3. Respiratory functions

Vital capacity was measured with a spirograph before Period A 1 began and when Period A 2 ended. Forced expiratory vital capacity, flow volume for a second and V̇ 25 were measured by Flow Volume.

PEFR was also measured by peak flow meters (Vitalograph Ltd., Ireland). PEFR was measured at rise time and bedtime everyday. It was measured three times at each rise time and bedtime, and the highest value was recorded in the asthma diary.

4. Administration doses of corticosteroids

Changes of administration doses of oral and inhaled corticosteroids were evaluated four times before the beginning and at the end of each Period A.

5. Statistical analysis

Data on asthma attack scores and VAS are expressed as means ± standard errors, while PEFR was expressed as mean ± standard deviation. Changes in the asthma attack scores, VAS and PEFR were analyzed with one factor ANOVA, which was followed by Fisher's PLSD multiple comparisons if necessary. Differences were considered statistically significant when the value was less than 0.05.

Ⅳ． RESULTS

There were no withdrawals due to remarkable adverse events or no interruption according to a doctor's judgment.
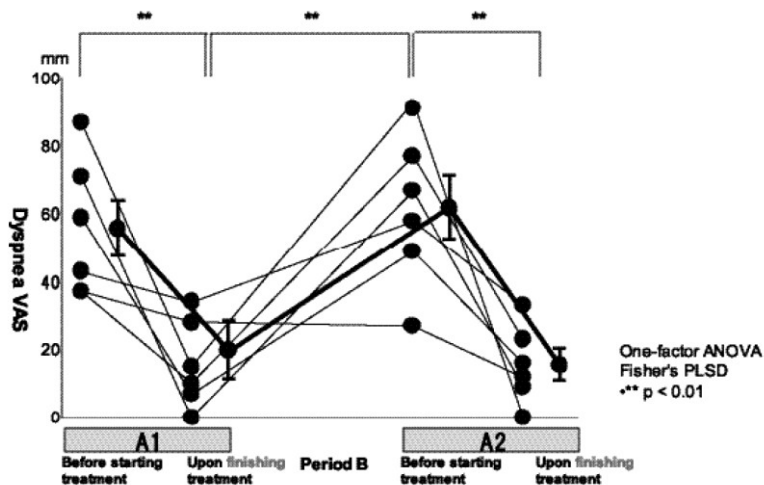

Figure 1 Changes in asthma attack score before and after acupuncture
Changes in asthma attack score during each period are shown. The vertical axis indicates asthma scores evaluated by an asthma diary. The horizontal axis indicates length of treatment periods. Consistent with periods of acupuncture treatment, symptoms of asthma attacks were significantly improved.
Period A: period with acupuncture
Period B: period of treatment without acupuncture
One-factor ANOVA Fisher's PLSD *: $p < 0.05$, **: $p < 0.01$
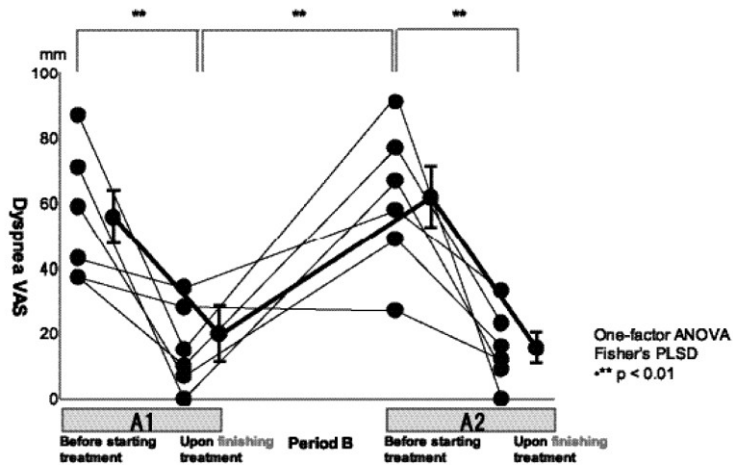
Figure 2 Changes in subjective experiences of dyspnea accompanying asthma symptoms before and after acupuncture

Changes in subjective experiences of breathing difficulty accompanying asthma symptoms before the start and at the end of acupuncture treatment are shown. The vertical axis indicates strength of subjective breathing difficulty evaluated by VAS, and the horizontal axis indicates one series from the period before and after acupuncture treatment. Subjective experience of breathing difficulty accompanying asthma symptoms was significantly improved at the end of the acupuncture treatment in comparison with that before the start in each series of treatment.
Period A: period with acupuncture
Period B: period of treatment without acupuncture

1. Changes in asthma attacks (Fig.1)

Asthma scores before the start of Period A 1 were 30.0 ± 8.1 and those at the end of the period were significantly improved to 4.7 ± 3.1 ($p < 0.01$). The values before the start of Period A 2, however, significantly increased to 21.6 ± 6.5 ($p < 0.05$). Asthma scores at the end of Period A 2 significantly improved to 1.5 ± 0.8 ($p < 0.05$). Conditions of asthma attacks significantly improved from 30.0 ± 8.1 before the start of Period A 1 to 1.5 ± 0.8 at the end of Period A 2 ($p < 0.01$).

### 2. Effect of acupuncture on dyspnea (Fig. 2)

Severity of dyspnea measured with VAS before the start of Period A 1 was 55.7 ± 20.4 mm, which significantly improved to 19.7 ± 21.0 mm at the end of period A 1 ($p < 0.01$). VAS values significantly improved from 57.8 ± 25.7 mm before the start of Period A 2 to 15.5 ± 11.5 mm at the end of Period A 2 ($p < 0.01$). The values before the start of Period A 1 and at the end of period A 2 significantly improved from 55.7 ± 20.4 to 15.5 ± 11.5 mm ($p < 0.01$).

3. Changes in PEFR on rising before and after the period of acupuncture treatment (Fig. 3-1)

Mean value of PEFR on rising significantly increased from 235.0 ± 62.2 L/min before the start of Period A 1 to 325.8 ± 83.1 L/min at the end of Period A 1 ($p < 0.05$). The mean value at the end of Period A 1 was 325.8 ± 83.1 L/min and decreased to 244.2 ± 45.4 L/min before the start of Period A 2 ($p = 0.053$). The mean value before the start of Period A 2 increased from 244.2 ± 45.4 to 323.3 ± 77.6 L/min at the end of Period A 2 ($p = 0.059$). The mean value before the start of Period A 1 significantly increased from 235.0 ± 62.2 L/min to 323.3 ± 77.6 L/min at the end of Period A 2 ($p < 0.05$).

4. Changes in PEFR at bedtime before and after the period of acupuncture treatment (Fig. 3-2)

Mean value of PEFR at bedtime increased from 263.3 ± 62.5 L/min before the start of Period A 1 to 331.7 ± 88.4 L/min at the end of period A 1. The mean value at the end of Period A 1 was 331.7 ± 88.4 L/min and decreased to 273.3 ± 78.1 L/min before the start of Period A 2. The mean value before the start of Period A 2 increased from 273.3 ± 78.1 L/min to 326.7 ± 85.0 L/min
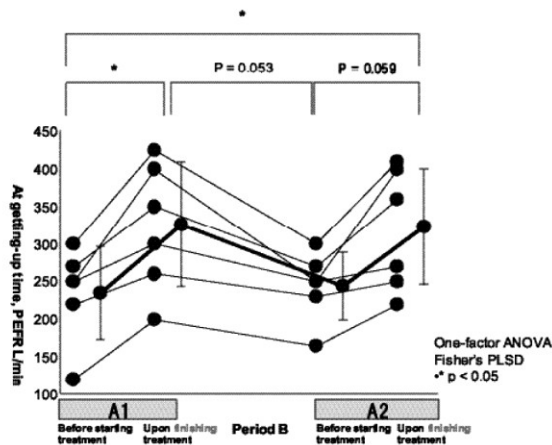
Figure 3-1 Changes in PEFR on rising before and after the period with acupuncture
Changes of mean values in PEFR on rising significantly increased ($p < 0.05$) from 235.0 ± 62.2 L/min before the start of Period A1 to 325.8 ± 83.1 L/min at the end of Period A1. The mean value at the end of Period A1 was 325.8 ± 83.1 L/min and was decreased to be 244.2 ± 45.4 L/min before the start of Period A2 ($p = 0.053$). The mean value before the start of Period A2 increased from 244.2 ± 45.4 to 323.3 ± 77.6 L/min at the end of Period A2 ($p = 0.059$). The mean value before the start of Period A1 significantly increased from 235.0 ± 62.2 to 323.3 ± 77.6 L/min at the end of Period A2 ($p < 0.05$).
Period A: period with acupuncture
Period B: period of treatment without acupuncture
PEFR: Peak Expiratory Flow Rate
One-factor ANOVA Fisher's PLSD   *:$p < 0.05$
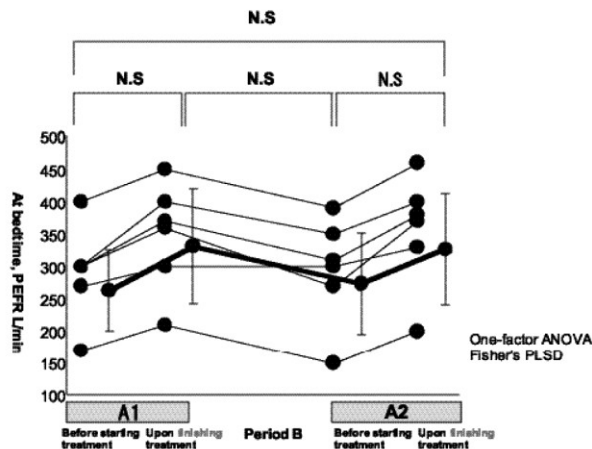
Figure 3-2 Changes in PEFR at bedtime before and after the period with acupuncture (Fig.3-2)
Mean value of PEFR at bedtime increased from 263.3 ± 62.5 L/min before the start of Period A1 to 331.7 ± 88.4 L/min at the end of Period A1. The mean value at the end of Period A1 was 331.7 ± 88.4 L/min and decreased to 273.3 ± 78.1 L/min before the start of Period A2. The mean value before the start of Period A2 increased from 273.3 ± 78.1 to 326.7 ± 85.0 L/min at the end of Period A2. The mean value before the start of Period A1 increased from 263.3 ± 62.5 to 326.7 ± 85.0 L/min at the end of Period A2.
Period A: period with acupuncture
Period B: period of treatment without acupuncture
PEFR: Peak Expiratory Flow Rate
One-factor ANOVA Fisher's PLSD

at the end of period A 2. The mean value before the start of Period A 1 increased from 263.3 ± 62.5 L/min to 326.7 ± 85.0 L/min at the end of Period A 2.

5. Respiratory function tests (Table 4-1)

In four cases (#2, #4, #5, and #6) out of six, respiratory function tests were performed before and after acupuncture treatment. Before the start of Period A 1 and at the end of Period A 2, cases in which improvement of more than 20% was seen in each respiratory function test were one case out of four for VC, two cases out of four for FVC, three cases out of four for FEV_1 and three cases out of four for $\dot{V}$ 25.

6. Changes in eosinophil counts in the peripheral blood (Table 4-2)

Hematological examinations were performed in five out of six patients before and after the period of acupuncture. There were three patients (#3, #5, and #6) who showed more than a standard value of eosinophils (below 5%) before the start of Period A. However, at the end of Period A, cases 3, 5 and 6 showed decreases in the eosinophil counts from 6.6% to 1.1%, 9.8% to 4.5%, and 18.9% to 10.4%, respectively. In addition, for case 1, there was a decrease from 0.8% to 0.3%, although the change was observed within the normal limits.

Table 4-1 Changes in respiratory function tests
 In changes of each respiratory function test before the start of Period A 1 and at the end of Period A 2, cases in which improvement of more than 20% was seen in each respiratory function test: one out of four cases for VC, two out of four cases for FVC, three out of four cases for FEV_1 and three out of four cases for $\dot{V}$ 25.
 VC: Vital Capacity, FVC: Forced Vital Capacity, FEV_1: Forced Expiratory Volume in 1 second, PEFR: Peak Expiratory Flow Rate

| Case No. | Respiratory function test | | | | | | | | | |
| | VC(L) | | FVC(L) | | FEV_1(L) | | FEV_1%(%) | | $\dot{V}$ 25(L/S) | |
	Before starting A 1	Upon finishing A 2	Before starting A 1	Upon finishing A 2	Before starting A 1	Upon finishing A 2	Before starting A 1	Upon finishing A 2	Before starting A 1	Upon finishing A 2
1	-	-		-	-	-		-	-	-
2	3.1	3.0	2.6	2.6	1.5	1.8	57.6	70.4	0.3	0.6
3	-	-		-	-	-		-	-	-
4	2.7	2.5	2.4	2.2	2.1	1.8	87.5	83.6	0.8	0.8
5	3.4	2.4	1.8	2.6	1.1	1.7	61.1	65.1	0.2	0.4
6	1.5	3.3	2.0	2.9	1.5	2.0	75.0	70.0	0.4	0.8
Mean± SD	2.7± 0.8	2.8 ± 0.4	2.2 ± 0.4	2.6 ± 0.3	1.6 ± 0.4	1.8±0.1	70.3± 13.7	72.3± 7.9	0.5± 0.3	0.7± 0.2

Table 4-2 Changes in blood chemistry data
 In the changes of blood chemistry data before the start of Period A 1 and at the end of Period A 2, the proportion of eosinophils was decreased in four out of five cases.

| Case No. | Blood test | | | | | |
| | WBC (mm3) | | Eosinophilic (%) | | CRP | |
	Before starting A 1	Upon finishing A 2	Before starting A 1	Upon finishing A 2	Before starting A 1	Upon finishing A 2
1	3990	5060	0.8	0.3	0.0	0.1
2	-	-	-	-	-	-
3	7660	6600	6.6	1.1	0.1	0.0
4	9630	9860	0.9	2.2	0.0	0.6
5	4370	3520	9.8	4.5	0.0	0.1
6	6040	4720	18.9	10.4	0.0	0.1
Mean± SD	6338 ± 2348	5952 ± 2445	7.4 ± 8.0	3.7 ± 4.1	0.02 ± 0.04	0.18 ± 0.2

7. Changes in administration doses of inhaled and oral corticosteroids (Table 5)

Before the start and at the end of the Period A, the doses of oral corticosteroids were reduced in three (#1, #2, #3) out of four patients as were the doses of inhaled corticosteroids in two (#2, #5) out of five patients.

Due to the deterioration of asthma attacks during Period B, doses of oral and inhaled corticosteroids needed to be increased in three out of four cases (#1, #2, and #3) and two (#2, #5) out of five patients, respectively.

Before the start of and at the end of the Period A, the doses of oral corticosteroids were reduced in three (#1, #2, and #4) out of four patients and the doses of inhaled corticosteroids were reduced in three out of five patients (#1, #2, and #3)

8. Changes in severity of asthma (Table 5)

At the end of Period A, the severity of asthma symptoms were improved in six patients compared with that before the start of Period A, as asthma attacks were ameliorated. However, due to deterioration of asthma attacks in five patients during Period B, exacerbations of asthma were observed before the start of Period A 2 in three out of five patients. At the end of Period A 2, severity was improved in five patients compared with that before the start of Period A 2. When compared with the state before the start of Period A 1, improvement in the severity was observed in six patients at the end of Period A 2.

Ⅴ. DISCUSSION

1. Study design and clinical effect

To evaluate the effect of acupuncture treatment from the viewpoint of Evidence Based Medicine (EBM), it is desirable to prove the effect of acupuncture treatment in a setting of a randomized controlled trial (RCT). There are, however, difficulties in performing an RCT study with control groups in practical and clinical settings, since most patients want acupuncture treatment in actual clinical acupuncture scenes. Accordingly, in the proof of the effect of acupuncture treatment, this study utilized a single-subject research design (N-of-1), in which the clinical effect could be assessed without a control group. In the single case study used here, it was thought that the clinical effect could be assessed by obtaining reproducible data from a single patient who repeated two periods alternately, Periods A and B.

With this single case study of six patients in an improved state of asthma during Period A, five patients who showed exacerbations of asthma when entering into Period B showed improvement in asthma symptoms when entering Period A 2 again. Moreover, all cases with the administration of corticosteroids in the total observation period showed improvement in asthma symptoms when treated with acupuncture, indicating that this improvement was obtained due to the effect of acupuncture treatment, and not to either the drug effects or a self-remitting natural course. We considered, by

Table 5 Changes in corticosteroids and severity
At the end of Period A1, compared with the start of Period A1, oral corticosteroids were interrupted in three cases and inhaled corticosteroids were reduced in two cases due to improved asthma attacks. In Period B, oral corticosteroids were resumed in three cases due to deterioration of asthma attacks and the doses of inhaled corticosteroids were increased in two. However, at the end of Period A 2 compared with the start of Period A2, oral corticosteroids were stopped in three cases due to improvement of asthma attacks and the doses of inhaled corticosteroids were reduced in three cases.

| Case No. | A 1 Period | | | | | | Period A 2 | | | | | |
| | Before starting | | | Upon finishing | | | Before starting | | | Upon finishing | | |
	Predonisolone (mg/day)	Inhalation (μ g/day)	Classification	Predonisolone (mg/day)	Inhalation (μ g/day)	Classification	Predonisolone (mg/day)	Inhalation (μ g/day)	Classification	Predonisolone (mg/day)	Inhalation (μ g/day)	Classification
1	20	BDP 800	Step 4	Stop	BDP 800	Step 3	10	BDP 800	Step 3	Stop	BDP 400	Step 2
2	5	BDP 800	Step 4	Stop	BDP 400	Step 2	5	BDP 800	Step 3	5	BDP 200	Step 1
3	5	FP 800	Step 4	Stop	FP 800	Step 2	15	FP 800	Step 4	Stop	FP 400	Step 1
4	5	-	Step 4	5	-	Step 2	5	-	Step 3	Stop	-	Step 1
5	-	BDP 800	Step 4	-	BDP 600	Step 2	-	BDP 800	Step 2	-	BDP 800	Step 1
6	-	BDP 400	Step 3	-	BDP 400	Step 2	-	BDP 400	Step 2	-	BDP 400	Step 2

using the single-subject research design (N-of-1) in a single case study, that it could evaluate the effect of acupuncture treatment for asthma.

2. Clinical effects of acupuncture treatment

The patients with bronchial asthma studied here improved their asthma symptoms and VAS during Period A (acupuncture treatment period). Moreover, there were improvements in the airway obstruction in the assessment of FEV_1 and PEFR, and improvements in bronchial asthma were observed not only from the subjective symptoms but also from the findings of objective examinations.

As in the past, due to obstructive ventilation impairment caused by the constriction of bronchial smooth muscle, bronchial asthma is characterized by decreases in respiratory function tests, such as FEV_1, PEFR and $\dot{V}$ 25. Particularly, FEV_1 reflects the airflow of the central airway of the respiratory tract, while $\dot{V}$ 25 reflects the airflow of the peripheral airway. From the data in this study, improvements in the obstructive ventilation impairment was observed by acupuncture treatment in three (#2, #5, #6) out of four patients in the assessable respiratory function test who showed increases in FEV_1 and $\dot{V}$ 25 at the end of Period A. Alternatively, in case #4 who had a common cold since one day before the last examination day and showed a slightly positive C-reactive protein (CRP: < 0.5), respiratory function was decreased due to upper respiratory inflammation.

Additionally, PEFR at rise time and bedtime in all cases was improved at the end of Period A. Because PEFR indicates the maximal expiratory flow volume in reflection of airflow of the central airway, the value is significantly lowered in patients with asthma symptoms. Furthermore, PEFR values on rising being lower than that at bedtime suggest a possible asthma attack from night to morning time. All cases examined in this study had an asthma attack at night and five of six cases showed lower PEFR on rising compared with that at bedtime (Table 1). However, with the continuous performance of acupuncture, the difference of the average values of PEFR at rise time and bedtime was decreased at every endpoint of Period A. The frequency of asthma attacks at night was decreased in many cases. Moreover, the patients commented that the absence of nighttime attacks led to sound sleep and physical relaxation. These findings in respiration function, in which an asthma attack was improved during Period A, indicated the ef-

fect of acupuncture. Alternatively, in Period B (period without acupuncture), five of six cases showed deterioration of asthma attacks. Of five with deterioration, three (#1, #2, and #3) needed extra-outpatient visits other than regular visits. In addition, more use of short-acting inhalation β_2-agonists (bronchial dilatation drugs) was commented by all of these five patients. These results, in which a combined usage of this type of acupuncture (choice of meridian points, time of treatment) improved asthma attacks but the 10 week course of acupuncture allowing deterioration of asthma attacks, suggested that acupuncture has an immediate, but little lasting, effect on asthma attacks. In the guideline at present [11], bronchial asthma is regarded as a disease that is not cured, but controlled symptomatically over long periods of time. As the guideline focuses mainly on drug therapy such as inhaled corticosteroids, it may be desirable that acupuncture combined with drug therapy should be continued for a certain period of time even after achieving improvement or disappearance of asthma attacks. Further study is, however, needed on how long acupuncture should be continued.

The therapeutic mechanism of acupuncture to bronchial asthma has been speculated as a bronchial dilatation action through the autonomic nerve afferent pathway from a somatic visceral reflex stimulated by acupuncture, as well as relaxation of bronchial smooth muscle through the autonomic nervous system[12]. Sugiura et al.[13] reported that bronchial asthma patients treated with acupuncture showed sedation and relaxation of constricted bronchial smooth muscle for one hour after acupuncture, which accompanied an improvement in respiratory resistance. Similarly, this study, in which relief of dyspnea as well as improvements in FEV_1 and $\dot{V}$ 25 were experienced in patients, suggested a possibility that acupuncture induced sedation and relaxation of the bronchial smooth muscle constriction state.

Bronchial asthma has been recognized as a chronic inflammatory disorder as research of the pathophysiology of bronchial asthma advances. Particularly, it has been proved that cytokine networks involving eosinophils at the center induces release of cytotoxic eosinophil-specific granules to the airway that generate inflammation in the airway, leading to edema at the bronchial mucosa or submucosa, increased production of mucus, constriction of bronchial smooth muscle, and airway obstruction. Therefore, airway inflammation through the

eosinophil-centered cytokine network plays an important role in causing the attack of bronchial asthma.

In this study, two courses of acupuncture treatment (during Period A and Period B) showed improvement in asthma attacks in patients and decreased eosinophil counts in blood in four out of five cases, which could be measured (#1, #3, #5, and #6). We[15] also provided acupuncture treatment for patients who have both bronchial asthma (severe persistent asthma) and chronic obstructive pulmonary disease (COPD), once a week for ten weeks and observed that the acupuncture treatment improved asthma attacks and decreased eosinophil counts in blood and Eosinophil Cationic Protein (ECP), a cytotoxic protein induced by eoshinophils, as a result. These findings indicate a possibility that one of therapeutic mechanisms of acupuncture treatment for patients with bronchial asthma may be involved in improving eosinophilic inflammation. However, until this point, among clinical reports[3,16] on acupuncture treatment for bronchial asthma, there are no reports that acupuncture treatment decreased eoshinophils specifically. Because there is no definitive evidence of the possibility that acupuncture treatment may improve eosinophilic inflammation of airways even though the possibility has been suggested, we consider that we will need to review the effect of acupuncture treatment on this point,

3. Doses of corticosteroids

At present, according to NIHLBI Guidelines for the Diagnosis and Management of Asthma[17], corticosteroids for bronchial asthma are described to be the most effective anti-asthma drugs, and are extensively used as an improvement drug for acute symptoms or long-term prevention drug. Inhaled corticosteroids are considered to be most effective for patients with persistent asthma, from moderate persistent (step 2) to severe persistent (step 4). Oral corticosteroids are recommended when patients do not respond to inhaled corticosteroids. There are, however, some patients with asthma who are controlled poorly with these steroids[2]. For such patients, the dose of corticosteroids is increased in accordance with a clinical guideline and the side effects of these drugs may cause problems. Inhaled corticosteroids have relatively few side effects compared with oral steroids because they are inhaled to airways directly, but there are still some side effects[10]. In this study, subjects were patients with asthma whose symptoms were controlled poorly even after they were

administered persistent inhaled and oral steroids or bronchodilators. Acupuncture treatment for these patients who did not fully responded to certain doses of steroids, improved their asthma symptoms in all cases in this study, which suggested that one course of (ten sessions) acupuncture treatment has efficient effects on improvement of asthma symptoms. Mitchell et al.[19] also performed a clinical examination on 31 patients with mild to moderate asthma, in which an acupuncture treatment group and fake group were randomly assigned. It was reported that after eight acupuncture treatments for 12 weeks, asthma attacks and PEFR were improved significantly and doses of inhaled steroids could be decreased. This result was similar to our findings in the present study.

According to medication therapy response to severity in the Asthma Prevention and Management Guideline[6], when symptoms are not controlled by ongoing treatment, another more strict treatment should be provided. In Japan, we take a step-up approach in the treatment with corticosteroids in which doses of steroids are increased when defined doses of corticosteroids according to grades of severity offer little effect. As for the cases in this study, patients had been administered normal doses of corticosteroids without improvement in asthma attacks and doses had to be increased. We provided acupuncture treatment on these patients in combination with medication and observed the disappearance of asthma attacks in two out of six cases and improvement in four out of six cases at the end of the second course of acupuncture treatment. This made it possible for doses of steroids to be reduced or cut (Table 5). It was suggested that patients who have difficulties in controlling asthma symptoms with only medication can be controlled by acupuncture treatment in combination with medication.

Acknowledgements

VI. CONCLUSION
1. Acupuncture treatment was provided for six patients with bronchial asthma who were controlled poorly even with standard medication including corticosteroids.

2. In all cases, improvement or disappearance of asthma symptoms was observed in accordance with length of the acupuncture treatment

3. At the end of the acupuncture treatment, improvement of respiratory function and decrease in eosinophil counts were observed along with improvement of asthma symptoms. In four out of six cases, doses of corticosteroids could be reduced.

4. As a result of acupuncture treatment provided for patients with bronchial asthma, who were controlled poorly with medication, acupuncture treatment was considered to be effective in improving asthma attacks, subjective symptoms, and respiratory function of the patients.

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