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## Complex spa therapy and airway inflammation in bronchial asthma

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**Abstract :** Efficacy of complex spa therapy was studied in 55 patients with bronchial asthma. Complex spa therapy was effective in 47 (85.5%) of the 55 patients with bronchial asthma : marked efficacy was observed in 15 (27.3%), moderate in 32 (58.2%), slight in 6 (10.9%) and no efficacy in 2 patients (3.6%). Improvement of clinical symptoms and findings by complex spa therapy was more clearly observed in patients with an increased proportion of BAL lymphocytes, neutrophils and eosinophils. These findings suggest that complex spa therapy more affects cell infiltration in the airways than bronchoconstriction induced by chemical mediators. Improvement of ventilatory function represented by FEV1.0% value was higher in patients with a low proportion of BAL neutrophils, suggesting that patients with increased number of BAL neutrophils require longer complex spa therapy than those without BAL neutrophilia.

**Key words :** complex spa therapy, airway inflammation, bronchial asthma

### Introduction

Bronchial asthma is a disease characterized by transient dyspnea with wheezing, which is caused mainly by IgE-mediated allergic reactions. In the condition, bronchial response to inhalant allergens can be divided into two phases : immediate asthmatic reaction (IAR) and late asthmatic reaction (LAR)<sup>1,2)</sup>. In IAR, chemical mediators, such as histamine

and leukotrienes released from tissue mast cells play an important role<sup>3-6)</sup>. In addition to these humoral factors in IAR, in the stage of LAR cellular components in the airways have been noted in the mechanism of onset of bronchial asthma. Thus, airway inflammation is now widely accepted as a pathological feature of bronchial asthma<sup>7-9)</sup>. The increased severity of airway inflammation makes therapy of bronchial asthma more

difficult.

Our previous studies have shown that spa therapy (swimming training in a hot spring pool and/or inhalation with iodine salt solution)<sup>10-13</sup> and complex spa therapy (swimming training + inhalation with iodine salt solution + fango therapy)<sup>14,15</sup> are effective for bronchial asthma; improvement of ventilatory function<sup>16-18</sup>, improvement of subjective and objective symptoms, and improvement of suppressed function of adrenocortical glands<sup>19,20</sup>.

In the present study, the efficacy of complex spa therapy was evaluated on patients with bronchial asthma with regard to airway inflammation, by observing improvement of clinical symptoms and finding, and ventilatory function.

### Subjects and Methods

The subjects of this study were 55 patients (28 females and 27 males) with bronchial asthma. Their mean age was 55.6 years (range, 22-73 years), and the mean serum IgE level was 451 IU/ml (range, 6-2197

Table 1. Complex spa therapy

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#### Swimming training in a hot spring pool

Swimming training was carried out for 30 min a day and 5 times a week.

#### Inhalation of iodine salt solution

Inhalation of 1.0 ml iodine salt solution (KI 134 mg/l, NaCl 14.664 g/l) was performed twice a day.

#### Fango therapy

Fango taken from Ningyo pass and heated to 70-80°C was packed with cloth (40-43°C). The back of patients was covered with the fango, and warmed for 30 min 5 times a week.

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IU/ml). They were all admitted to our hospital and received complex spa therapy comprised of swimming training in a hot spring pool, inhalation therapy with an iodine salt solution and fango therapy for one to three months (Table 1). All of them were non-smokers.

Efficacy of spa therapy was assessed as marked, moderate, slight or of no value by evaluating improvement of clinical symptoms and findings, and reduction of drugs used to control asthma attacks. The therapy was regarded as effective when marked and moderate efficacy was shown.

Marked efficacy: their asthma attacks had disappeared and reduction of antiasthmatic drugs, particularly glucocorticoids, was attained by spa therapy.

Moderate efficacy: their asthma attacks were clearly improved, but they had occasional dyspnea with wheezing, or reduction of drugs used for asthma was not attained in spite of improvement of symptoms.

Slight efficacy: their asthma attacks were slightly improved, but they often had dyspnea with wheezing, and the dose of drugs used for asthma was not reduced by spa therapy.

No efficacy: their asthma attacks and the dose of drugs used for asthma did not change after spa therapy.

Spa effects were clinically evaluated one month after their discharge from our hospital.

Bronchoalveolar lavage (BAL) was performed in all subjects by previously reported methods<sup>21,22</sup>. Informed consent for the BAL examination was obtained from all study subjects. The aspirate obtained by a bronchofiberscope were centrifuged at 1200 rpm for 10 min at 4°C after filtration through a

sterile steel mesh, and the resultant cell pellet was resuspended in Tris ACM which comprises 1ml of 0.1M Ca, 0.5ml of 0.1M Mg and 98.5ml of Tris A buffer (TRIZMA pre-set crystal, pH 7.7, Sigma Chemical Co. St. Louis, Mo, USA, 0.3275 g + KCl 0.0372 g + 3% albumin 5ml + H<sub>2</sub>O 100 ml)<sup>20</sup>. Smear preparations made with the cell suspension were stained with May Giemsa. A differential cell count was performed on 500 cells, excluding epithelial cells. The results were expressed as a percentage of the total cells.

Ventilatory function tests were carried out on all subjects during an attack-free stage, using a Box Spiro 81-S (Chest Co). In this study, the ventilatory parameter, FEV1.0% value was compared in relation to spa efficacy.

Serum IgE levels were measured by the radioimmunosorbent test (RIST).

**Results**

Of 55 patients with bronchial asthma, marked efficacy was observed in 15 (27.3%), and moderate efficacy in 32 patients (58.2%). Thus, spa efficacy was clearly found in 47 patients with bronchial asthma (85.5%) (Fig. 1).

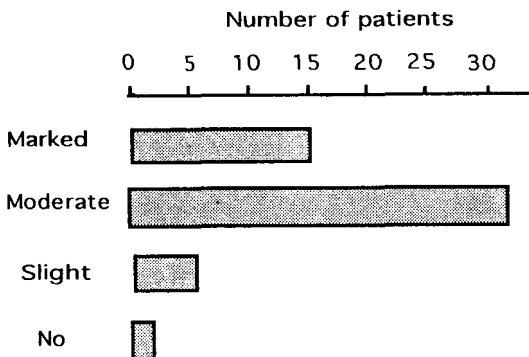


Fig. 1. Clinical effects of complex spa therapy on patients with bronchial asthma

A correlation between efficacy of spa therapy and proportion of lymphocytes in bronchoalveolar lavage (BAL) fluid was studied in all subjects. The mean proportion of BAL lymphocytes was 19.2 ± 16.4% (mean ± SD) in 15 patients on whom spa therapy showed a marked efficacy, 18.1 ± 12.6% in 32 with moderate efficacy, 14.8 ± 11.2% in 6 with slight efficacy, and 9.1 ± 3.5% in 2 without efficacy. The mean proportion of BAL lymphocytes was higher in patients on whom spa therapy showed a marked and moderate efficacy than in those on whom it showed slight efficacy and no efficacy, but no significant difference was found between them (Fig. 2).

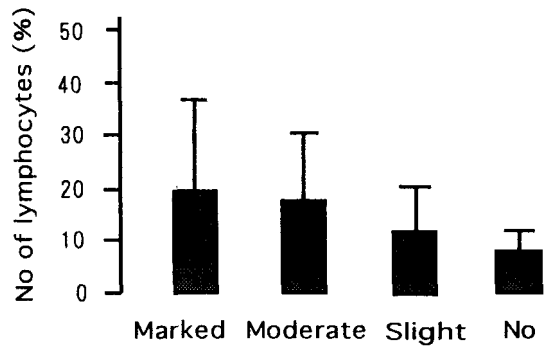


Fig. 2. Correlation between efficacy of complex spa therapy and number of BAL lymphocyte

BAL neutrophil count was higher in patients with marked (14.0 ± 22.1%) and moderate efficacy (8.2 ± 10.8%) than in those with slight efficacy (2.2 ± 0.8%) and without efficacy (0.8 ± 0.5%). A high proportion of BAL neutrophils of more than 10% was observed only in the patients with marked and moderate efficacy. The BAL neutrophil count was not increased in patients on whom spa therapy was ineffective,

but the difference between effective and ineffective groups was not significant (Fig. 3).

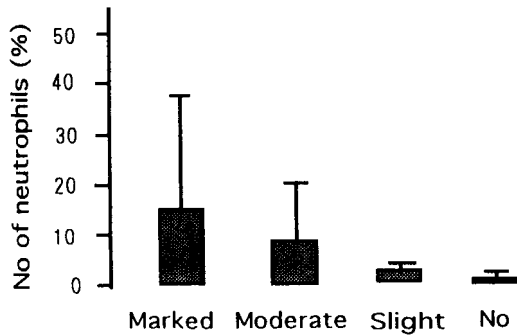


Fig. 3. Correlation between efficacy of complex spa therapy and number of BAL neutrophils

The proportion of BAL eosinophils was also increased in patients with marked ( $10.5 \pm 10.8\%$ ) and moderate efficacy ( $7.2 \pm 8.4\%$ ) compared to those with slight efficacy ( $1.8 \pm 1.3\%$ ) and without efficacy ( $4.8 \pm 5.1\%$ ). A high proportion of BAL eosinophils of more than 10% was found in 10 (21.3%) of the 47 patients on whom spa therapy was effective and 1 (12.5%) of the 8 patients on whom it was ineffective, but the difference between effective and ineffective groups was not significant (Fig. 4).

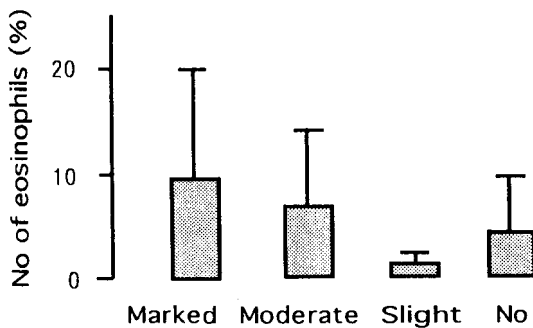


Fig. 4. Correlation between efficacy of complex spa therapy and number of BAL eosinophils

Ventilatory function was improved by complex spa therapy. A correlation between improvement of FEV<sub>1.0</sub>% and proportion of BAL cells was examined. The proportion of BAL neutrophils was lower in patients with improvement of FEV<sub>1.0</sub>% value of more than 30%, while there was less improvement of FEV<sub>1.0</sub>% as the BAL neutrophil number was increased, but the difference was not significant (Fig. 5).

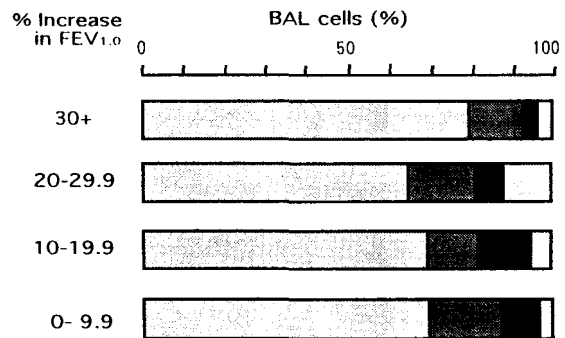


Fig. 5. Correlation between improvement of FEV<sub>1.0</sub> value by complex spa therapy and proportion of BAL cells. (■): macrophages, (■): lymphocytes, (■): neutrophils, (□): eosinophils.

## Discussion

It is well known that IgE antibodies participate in the mechanism of onset of asthma<sup>3-6</sup>) In immediate asthmatic reaction (IAR) that occurs within 30 min after inhalation with an allergen, chemical mediators, such as histamine and leukotrienes are released from tissue mast cells, and cause pathophysiological changes in the airways: bronchoconstriction, bronchial wall edema, and mucus hypersecretion. In contrast, in late asthmatic reaction (LAR), cellular components, such as lymphocytes, neutrophils and eosinophils are accumulated in the local

allergic reaction sites<sup>24-27</sup>). Airway inflammation has been suggested to be more important in adult patients with bronchial asthma, since it can be observed even in mild asthma<sup>28,29</sup>, and it increases the complexity and severity of asthma. Thus, it is important for physicians to examine the degree of airway inflammation in patients with bronchial asthma for treatment of the disease.

Our previous studies have shown that spa therapy is more effective in patients over the age of 40, and in those with type I b and type II asthma<sup>30</sup>. However, there are few reports about the relationship between spa effects and airway inflammation. In this study, we examined how airway inflammation affects the efficacy of complex spa therapy (swimming training in a hot spring pool + inhalation therapy with iodine salt solution + fango therapy).

The findings we obtained in this study showed that the efficacy of complex spa therapy on bronchial asthma correlates to a certain extent with the degree of airway inflammation: spa therapy is more effective when there are larger number of BAL cells such as lymphocytes, neutrophils and eosinophils. The percentage of BAL lymphocytes was more than 20% in 18 (38.3%) of the 47 patients on whom spa therapy was markedly or moderately effective, while a high percentage of BAL lymphocytes was found in only 1 (12.5%) of the 8 patients on whom it had little or no effect. The findings indicate that complex spa therapy is more effective on patients with a high percentage of BAL lymphocytes. In contrast, proportion of BAL lymphocytes was lower in patients with slight ( $14.8 \pm 11.2\%$ ) or no efficacy ( $9.1 \pm 3.5\%$ ) than in those with marked ( $19.2 \pm 16.4\%$ ) or moderate efficacy (18.1

$\pm 12.6\%$ ).

The proportion of BAL neutrophils was higher in patients with marked or moderate efficacy. A high percentage of BAL neutrophils (more than 10%) was observed in 12 (25.5%) of 47 patients with spa efficacy, but not in any of patients on whom spa therapy was ineffective. Spa therapy showed a marked or moderate efficacy with a larger number of BAL eosinophils: a high percentage of BAL eosinophils (more than 10%) was observed in 10 (21.3%) of the 47 patients on whom spa therapy was effective and in only one (12.5%) of the 8 patients on whom it was ineffective. These findings demonstrate that the increase in number of BAL neutrophils and eosinophils, as well as lymphocytes, correlates with the efficacy of spa therapy.

Improvement of ventilatory function by spa therapy was different depending on airway inflammation, particularly on the proportion of BAL neutrophils. FEV1.0% value was more improved by spa therapy in patients with a low proportion of BAL neutrophils than in those with a high proportion of the cells. There were no correlations between improvement of FEV1.0% values by complex spa therapy and the proportion of BAL lymphocytes. These results suggest that patients with a high proportion of BAL neutrophils require complex spa therapy for longer time than those with a low proportion of BAL neutrophils.

The results obtained here show that treatment for bronchial asthma including complex spa therapy is affected by airway inflammation, and that the therapy should be devised according to the kind of inflammatory cells increased in number in the airways, particularly an increase in number of BAL

neutrophils.

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### 気管支喘息における複合温泉療法と気道炎症反応

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気管支喘息55例を対象に, 複合温泉療法(温泉プール水泳訓練+ヨードゾル吸入+鈹泥湿布療法)を試み, その臨床効果と気道炎症反応との関連について, 若干の検討を加えた。

1. 複合温泉療法の臨床効果では, 著効15例(27.3%), 有効32例(58.2%), やや有効6例, 無効2例であり, 明らかに有効と判断された症例は, 55例中47例(85.5%)であった。2. 複

合温泉療法は, 気管支肺胞洗浄液(BALF)中の細胞成分(リンパ球, 好中球, 好酸球など)が多い症例, すなわち気道炎症反応がより強い症例により有効であった。このことは, 複合温泉療法が, 単純性の(化学伝達物質による)気管支攣縮よりも, 気道炎症反応をともなった病態により強く影響を及ぼすことを示している。

3. 複合温泉療法による換気機能の改善(1秒量)は, BAL液中の好中球数が少ない症例においてより高度であった。このことは, BAL液中に高度な好中球増多が見られる症例に対しては, より長期的な複合温泉療法が必要であることを示しているものと考えられた。

キーワード: 複合温泉療法, 気道炎症反応, 気管支喘息