
◎原 著

Spa therapy and bronchial hyperresponsiveness in elderly patients with asthma

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Summary : Clinical effects of spa therapy were examined in 150 patients with asthma in relation to bronchial hyperresponsiveness and patient age. 1. The efficacy rate of spa therapy was larger as the patient age was higher: the rate was 73.3% in patients under age 49, 81.8% in those between the ages of 50 and 59, 86.4% in those between the ages of 60 and 69, and 90.6% in those over age 70. The mean of efficacy rates was 83.3% in all subjects.

2. The bronchial hyperresponsiveness (BH) was lower as patient age was higher: the BH in patients between the ages of 60 and 69 and in those over age 70 was significantly lower compared to the BH in those under age 49 ($p < 0.001$).

3. Clinical effects of spa therapy tended to be lower in patients with increased bronchial hyperresponsiveness. The bronchial hyperresponsiveness showed a tendency to decrease after spa therapy in whom the therapy was effective, however, the BH did not change in patients with slight or no efficacy during spa therapy.

key words : spa therapy, asthma, bronchial hyperresponsiveness, patient age

Introduction

In recent years, the number of elderly patients with asthma has been increasing. Bronchial asthma is a disease characterized by bronchial hyperreactivity to various stimuli, in which IgE-mediated allergic reaction mainly participate even in elderly patients with asthma as a major factor affecting the pathophysiology of the airways¹⁾. The IgE-mediated allergy has been reported to change qualitatively and

quantatively with aging^{2,3)}. Our previous studies have shown that bronchial reactivity to methacholine and the release of histamine from leucocytes tend to decrease with aging⁶⁾.

It has been shown that spa therapy is effective in bronchial asthma: the therapy improves clinical symptoms⁷⁾, and ventilatory function^{8,9)} in patients with asthma, particularly the disease accompanied by hypersecretion and bronchiolar obstruction^{10,11)} as the direct action of the therapy. Bronchial hyperresponsi-

veness is improved by spa therapy¹²⁾. The therapy is also effective for elderly patients with asthma¹³⁾. Furthermore, suppressed function of adrenocortical glands is also improved by spa therapy as the indirect action of the therapy^{14, 15)}. However, the efficacy of spa therapy on asthma is affected by several factors such as patient age, disease severity, and bronchial hyperresponsiveness. In this study, the effects of spa therapy on asthma were discussed in relation to bronchial hyperresponsiveness and patient age.

Subjects and Methods

The subjects in this study were 150 patients (81 females and 69 males) with asthma. Their mean age was 57.7 years (range 21-77 years). All subjects were admitted at Misasa Medical Branch and had complex spa therapy¹⁶⁾ for 1-3 months. The subjects were divided into three groups according to efficacy of spa therapy; marked, moderate, and slight or no efficacy. The efficacy of spa therapy was evaluated by comparing their symptoms before and after undergoing spa therapy. Spa therapy was judged as being effective for patients whose efficacy was marked and moderate. The subjects were also classified into four groups according to their age: 0-49, 50-59, 60-69, and 70+ years.

Bronchial responsiveness to methacholine before spa therapy was compared with the value after the therapy. Suppression of bronchial hyperresponsiveness by spa therapy was expressed as an improvement rate (IR), which was calculated as following formula:
$$\text{improvement rate(IR)} = \frac{\text{C min of methacholine after spa therapy}}{\text{C min before the therapy} + \text{C min after the therapy}}$$
 Higher value of IR suggest that spa therapy suppressed bronchial hyperresponsiveness more strongly.

Bronchial reactivity to methacholine was examined by a Astograph (TCK6100H, Chest Co) when the subjects were attack-free. Various concentrations of methacholine (49, 98, 195, 390, 781, 1563, 3125, 6250, 12500 $\mu\text{g/ml}$) were prepared for bronchial challenge according to the method used by Chai et al¹⁷⁾. An increase of total respiratory resistance (Rrs) after methacholine inhalation was observed by the oscillation method. A methacholine concentration causing a significant increase in Rrs was assessed as Cmin (minimum concentration). All medications were stopped 12 hours prior to the examination.

The generation of leukotrienes B4 (LTB4) and C4 (LTC4) by peripheral leucocytes was assessed by a method previously described¹⁸⁾.

Buffy coat was separated by adding a quarter volume of 6% dextran and followed by being left 1 hour at room temperature. After the number of the cells was adjusted to 5×10^6 cells/ml in Tris ACM, Ca ionophore A23187 (1 μg) was added to the cell suspension. The mixed solution was incubated for 15 min at 37°C, and centrifuged at 3000 rpm for 30 min after the addition of 4 times volume of pre-chilled ethanol (finally 80% ethanol). Supernatant was taken into the syringe filter (Toyo Roshi Co, Japan), and dried up to solid. The solid was dissolved with 250 μl of 50% ethanol. The HPLC analysis for LTB4 and LTC4 was performed by a method described by Lam et al¹⁹⁾. The results were expressed as ng/ 5×10^6 cells.

Statistically significant differences of the mean were estimated using the unpaired Student's t test. A p value of <0.05 was regarded as significant.

Results

Figure 1 shows clinical effects of spa therapy in patients with asthma classified by

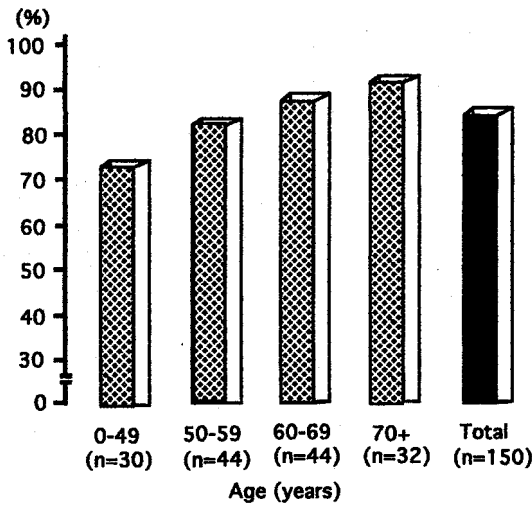


Fig. 1. Clinical effects of spa therapy on bronchial asthma in relation to patient age.

age. The efficacy rate of spa therapy in all subjects was 83.3%. The effects of spa therapy was larger in patients over the age of 70 (90.6%) than in those under the age of 49 (73.3%). Bronchial hyperresponsiveness (BH) to methacholine tended to decrease with aging. The BH in patients between the ages of 60 and 69 ($p < 0.001$) and in those over age 70 ($p < 0.001$) was significantly lower than the reactivity in those under age 49 (Fig. 2).

Any significant correlations were not observed between clinical effects of spa therapy and bronchial hyperresponsiveness in patients under age 49 (Fig. 3-a) and in those between the ages of 50 and 59 (Fig. 3-b), however, bronchial hyperresponsiveness was larger in patients with slight or no efficacy than in those with moderate efficacy in both age groups. The bronchial hyperresponsiveness was generally low in patients between the ages of 60 and 69 (Fig. 3-c) and over age 70 (Fig. 3-d), and the reactivity in patients with moderate efficacy was lower than the

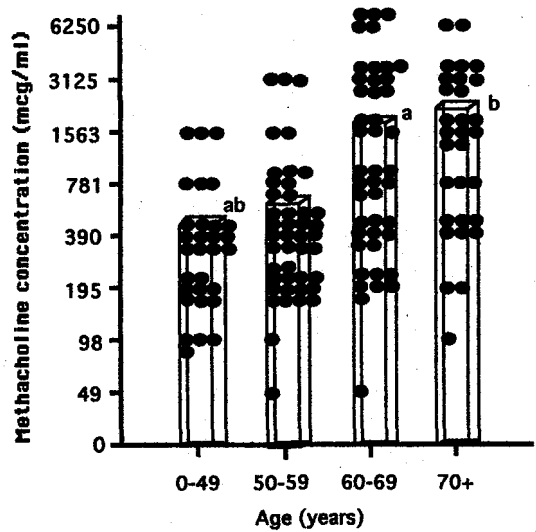


Fig. 2. Bronchial hyperresponsiveness to methacholine in patients with asthma and patient age. a and b, $p < 0.001$.

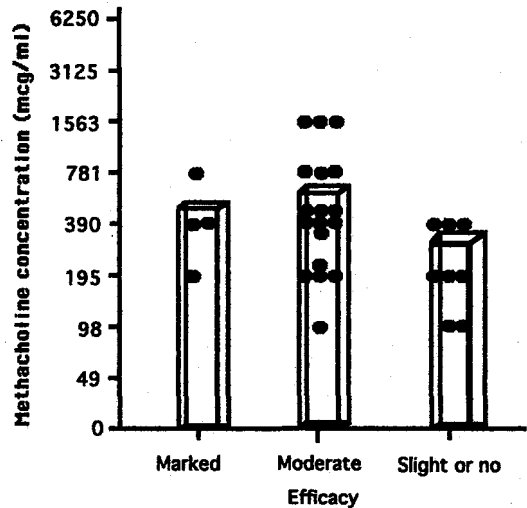


Fig. 3-a. Clinical effects of spa therapy on patients with asthma under the age of 49 years in relation to bronchial hyperresponsiveness

reactivity in those with slight or no efficacy. Bronchial hyperresponsiveness decreased after spa therapy in patients with marked

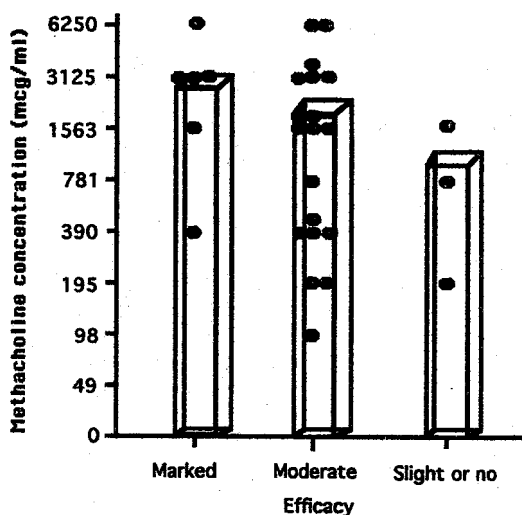
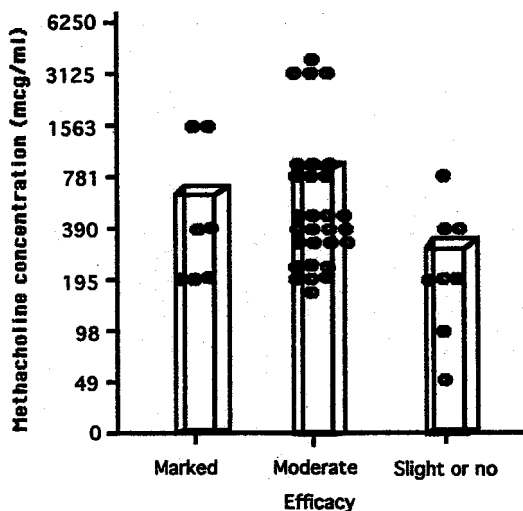


Fig. 3-b. Clinical effects of spa therapy on patients with asthma between the ages of 50 and 59 years in relation to bronchial hyperresponsiveness

Fig. 3-d. Clinical effect of spa therapy on patients with asthma over the age of 70 years in relation to bronchial hyperresponsiveness

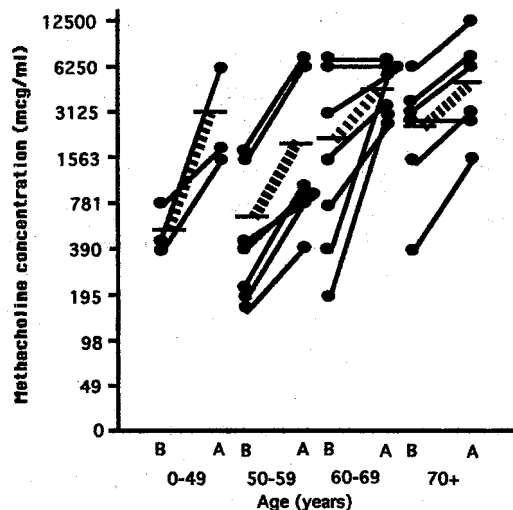
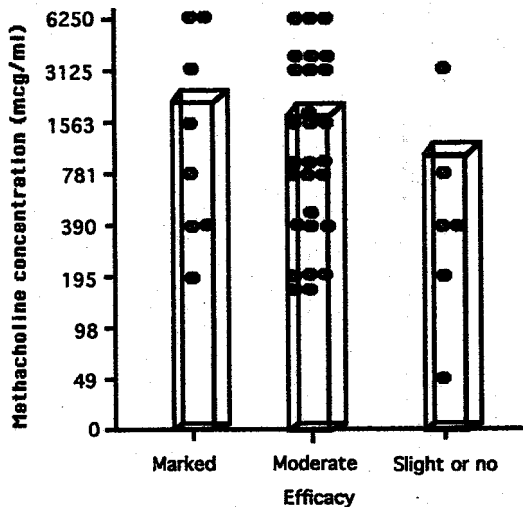


Fig. 3-c. Clinical effects of spa therapy on patients with asthma between the ages of 60 and 69 years in relation to bronchial hyperresponsiveness

Fig. 4-a. Comparison of bronchial hyperresponsiveness before (B) and after spa therapy (A) in asthmatics with marked efficacy in relation to patient age. Improvement rate (IR) : 0.86 (0-49 years), 0.78 (50-59 year s), 0.65 (60-69 years), and 0.65

efficacy, compared with the initial value before the therapy. The improvement rate (IR)(expressed by Cmin of methacholine

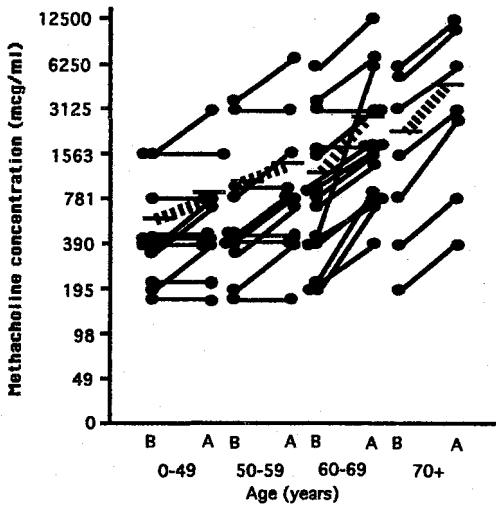


Fig. 4-b. Comparison of bronchial hyperresponsiveness before (B) and after spa therapy (A) in asthmatics with moderate efficacy in relation to patient age. Improvement rate (IR) : 0.58 (0-49 years), 0.62 (50-59 years), 0.79 (60-69 years), and 0.67 (70+ years)

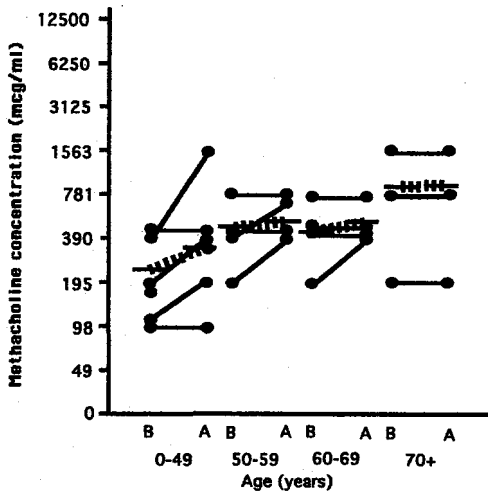


Fig. 4-c. Comparison of bronchial hyperresponsiveness before (B) and after spa therapy (A) in asthmatics with slight or no efficacy in relation to patient age. Improvement rate (IR) : 0.59 (0-49 years), 0.57 (50-59 years), 0.53 (60-69 years), and 0.50 (70+ years)

after spa therapy/Cmin before the therapy + C Cmin after the therapy) was considerably high from 0.65 to 0.86 in patients with marked efficacy. In these patients, the IR was higher in younger subjects under age 59 than in subjects between ages of 60 and 69 and over age 70 (Fig. 4-a). In patients with moderate efficacy of spa therapy, the IR was from 0.58 to 0.79, which was relatively low compared with the values in patients with marked efficacy. The IR in these patients was higher in subjects between ages of 60 and 69 and over age 70, compared with the value in younger subjects under age 59 (Fig. 4-b). The IR of bronchial hyperresponsiveness by spa therapy was very low from 0.50 to 0.58 in patients with slight or no efficacy. The IR was not different among four age groups (Fig. 4-c).

The generation of LTB₄ by leucocytes was higher in patients with marked efficacy and with moderate efficacy than in those with

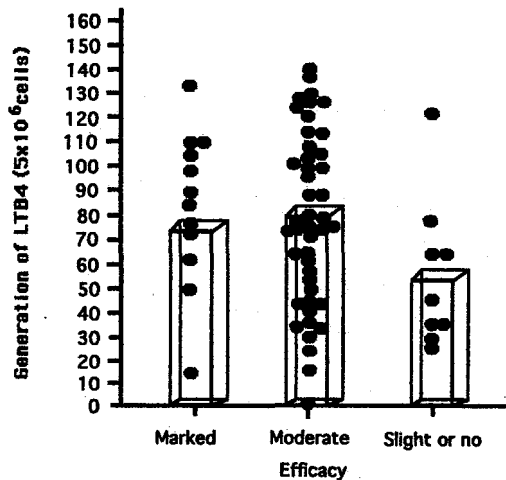


Fig. 5. Clinical effects of spa therapy and generation of leukotriene B₄ by peripheral leucocytes in patients with asthma.

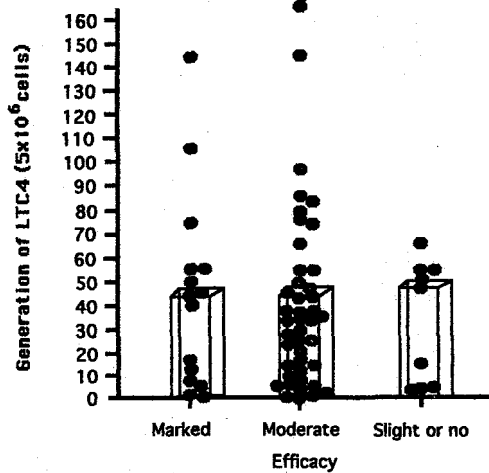


Fig. 6. Clinical effects of spa therapy and generation of leukotriene C 4 by peripheral leucocytes in patients with asthma.

slight or no efficacy, however, these differences were not significant (Fig. 5). The mean value in the generation of LTC₄ was not different among three groups divided by spa efficacy, however, some of patients with marked and moderate efficacy showed higher value in the LTC₄ generation (Fig. 6).

Discussion

Spa therapy has been performed for the treatment of patients with asthma and chronic obstructive pulmonary disease (COPD)²⁰. Bronchial asthma can be classified into three types according to clinical symptoms: Ia. simple bronchoconstriction type, Ib. bronchoconstriction + hypersecretion type, and II. bronchiolar obstruction type²¹⁻²³. Our previous studies have demonstrated that spa therapy is effective for patients with asthma^{6,12,24-28} and those with COPD, particularly pulmonary emphysema²⁹⁻³¹. Regarding clinical asthma

types, spa therapy is more effective in patients with type Ib and II than in those with type Ia⁷. Clinical effects of spa therapy on asthma are comprised of the direct action for airways and the indirect action for adrenocortical glands^{14,15}, autonomic nerve system³², and so on. Furthermore, spa therapy is shown to have suppressive action of bronchial hyperresponsiveness¹⁰, which is one of the characteristics of asthma. It has been shown that spa therapy is also effective for asthma patients in the elderly¹³. In the present study, the efficacy of spa therapy on bronchial asthma was examined in relation to bronchial hyperresponsiveness and patient age.

Clinical effects of spa therapy on asthma were to a certain extent related to patient age. In general, spa efficacy was larger as patient age was higher: efficacy rate (73.3%) in patients under age 49 was lower than the rate (90.6%) in those over age 70. Bronchial hyperresponsiveness to methacholine decreased as patient age was higher: the bronchial hyperresponsiveness in patients over age 70 and in those between the ages of 60 and 69 was significantly lower than the responsiveness in those under age 49. These results demonstrated that spa therapy was more effective in older patients with low bronchial responsiveness.

A correlation between bronchial hyperresponsiveness and spa efficacy was observed in all age groups: spa efficacy was lower in patients with increased bronchial hyperresponsiveness. However, bronchial hyperresponsiveness tended to decrease after spa therapy in asthma patients, particularly in those with marked and moderate efficacy of spa therapy. In the patients with marked efficacy, improvement rate (IR) by spa therapy, expressed by the formula (IR = C min of methacholine after

spa therapy /Cmin before the therapy + Cmin after the therapy) was higher in patients under age 49 (0.86) and in those between the ages of 50 and 59 (0.78) compared to the IR in those between the ages of 60 and 69 (0.65) and over age 70 (0.65). The results might suggest that improvement of bronchial hyperresponsiveness by spa therapy was larger in younger patients with marked efficacy. In contrast, in patients with moderate efficacy, the IR was larger in subjects between the ages of 60 and 69 (0.79) and over age 70 (0.67) in those under age 49 (0.58) and between the ages of 50 and 59 (0.62). Bronchial hyperresponsiveness did not change by spa therapy in patients with slight and no efficacy.

In our previous studies showed that spa therapy was more effective in patients with increased generation of leukotienes B4 (LTB4) and C4 (LTC4) by leucocytes²⁹). However, any significant correlation between generation of leukotrienes B4 (LTB4) and C4 (LTC4) by leucocytes and spa efficacy was not observed in this study.

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高齢者気管支喘息における気道過敏性と温泉療法

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150例の気管支喘息症例を対象に、気道過敏性と年齢との関連のもとに温泉療法の効果が評価された。

1. 温泉療法では、年齢が高くなるほどその有効率も高くなるという傾向が見られ、49才以下

の症例では73.3%、50-59才の症例では81.8%、60-69才の症例では86.4%、70才以上では90.6%であり、全症例の平均有効率は73.3%であった。

2. 気道過敏性は、年齢が高くなるほど低下する傾向が見られ、60-69才および70才以上の症例の気道過敏性は、49才以下の症例と比べ有意に低い値を示した($P < 0.001$)。

3. 温泉療法の臨床効果は、気道過敏性が強くなるにつれて低下する傾向が見られた。また、温泉療法の著効例や有効例では、治療により気道過敏性が低下してくるが、やや有効例や無効例では、気道過敏性はほとんど変化しないことが示された。