Allergic rhinitis (AR) has been referred to as "the most common IgE-mediated allergic disease" with prevalence estimates in the temperate country ranging up to 20%. It has been ranked as the fifth most prevalent chronic disease in these areas. Epidemiological studies have demonstrated that allergic rhinitis is on the increase. It is more recognized that the western lifestyle in both the indoor and outdoor environment, is a risk factor for increased sensitization and ultimately allergic diseases. I am reporting here a present status of AR in Korea including my experience and a work we are doing now.

**DISTRIBUTION OF THE PATIENTS WITH AR IN KOREA**

In 1992, Korean academy of allergy and asthma established recommendable allergen to perform the skin tests: D. pteronissius, D. farinae, Cat and dog dander, Pollens (tree, grass, weed), Fungi (alternaria, aspergillus, penicillium) and insect (cockroach). We have studied the distribution of offending allergens in the patients who were diagnosed as AR at Kyung Hee university hospital from April, 1984 to August, 1998. They were 6856 in number and 3236 (47.4%) were allergic to House dust, 5392 (78.65%) to house dust mite (D. farinae), 1376 (20.07%) to cockroach, 658 (9.6%) to dog hair and 521 (7.6%) to cat hair. Only 328 (4.78%) patients were seasonal 3).

Recently Korea rural areas have been industrialized and many factories have moved to the country side. These areas are not safe to allergy any more. Our data also demonstrated that there was no difference of prevalence rate between big cities and country sides. Three months between early fall to early winter are peak season. And the number of patients is increasing from later 3 grades of the elementary school.

**HERBAL MEDICINE AS A MODALITY TREATMENT IN ALLERGIC RHINITIS**

The treatment of allergic rhinitis (AR) has been improved by our increasing understanding of the
underlying pathophysiology of the allergic response. A number of the patients can be treated with a variety of drugs, but without achieving an adequate response. Hence there remains a need to develop new therapeutic agents for better prevention and treatment of allergic disorders. Some of herbal medicine has been used in patients with chronic respiratory disease like allergic rhinitis, bronchial asthma. Recently an attempt has been made to prove the efficacy of herbal extracts for treating AR. Now we are evaluating the effects of some herbal medicine mahuangbujaseshin tang (MBST) and soshihotang (SST) on animal allergic model and patients with AR.

The ex vivo effect of the MBST and SST on histamine release from rat mast cells

Since traditional herbal medicine MBST and SST have included allergic rhinitis and bronchial asthma, the effects of these medicines were evaluated on histamine release and the intracellular Ca²⁺ response in mast cells ex vivo. A single dose of MBST and SST dissolved in 2 ml of distilled water was administered orally to each group of Wistar rats. Groups of four rats each were administered doses of 0.5, 1.0, 5.0 or 10g, 1kg, control rats were only administered 2 ml distilled water. Several hours after administration of SST or MBST in distilled water, rats were killed. Tyrode's solution was injected into the peritoneal cavity, peritoneal cells, including mast cells, were collected by aspiration. These cells were layered on metrizamide solution and the mast cells were harvested. The suspension of mast cells was incubated with or without MBST or SST and DNP-As was added to this suspension. After stopping the reaction histamine contents of the supernatant and pellet were determined. Mast cells treated with or without MBST or SST were incubated with Ca²⁺ indicator dye. Fluorescence intensities excited at 340 and 380 nm were measured with spectrofluorometer. MBST at 4h and SST at 3h after oral administration inhibited histamine release from rat mast cell significantly. The inhibitory effect was seen dose-dependent. Both medicines of MBST and SST blocked the effect on antigen induced Ca²⁺ response of the mast cells.

Dynamic study of structural change of rat mast cells after treatment of MBST

Mast cells are known to play an important role in the immediate-type allergic reaction, which is the major mechanism for causing allergic rhinitis and bronchial asthma. The bridging of surface IgE receptors by antigens elevates intracellular free Ca²⁺ concentration, leading to release of the chemical mediators, including histamine, leukotrienes, and prostaglandins. We studied structural change of mast cells of immunized wistar rat. Rat were immunized with DNP-As and MBST was administrated orally to each animal. The mast cells were collected from the pleural and the peritoneal cells by gradient method with metrizamide solution. The suspension of the mast cells prepared with Tyrode's was incubated and DNP-As was added to this suspension. Microscopical structural change was examined by dynamic study of movie with 30 sec to 30 min interval slice. The surface of the mast cells was covered by MBST. And it was impossible that the granules were expelled out from the cells when they were stimulated with DNP-As. This result suggests that MBST is effective to the allergic model of rat as mast cell stabilizer.

The effect of MBST in the patency on nasal passage in the Guinea pig

One of the characteristic features of AR is the extreme reactivity of the nasal mucosa to specific antigen and non-specific stimuli5)6). Patients with AR develop a greater swelling of nasal mucosa in response to a wide variety of stimuli than healthy subjects. Histamine, peptid LTs, platelet activating factor were known to induce obstruction in allergic reaction in the nose. The leukotriens (LTC4 and LTD4), enhanced permeability, and lead to fluid extravasation and tissue edema7). They were considered to involve the development of the late reaction8). The purpose of this investigation has been to adapt a method based on acoustic reflection to the study of Hartly guinea pig (GP) nose and to measure change in the size of nasal airway volume after instillation LTD4 in GP by acoustic rhinometry. They were non-sensitized or sensitize and this procedure was under-
went after oral administration of MBST or SST. GPs sensitized with oral albumine were divided into two groups. GPs of each group were administered orally MBST (experimental group) and saline for 2 weeks. Thereafter they were subdivided into 2 groups: LTD4 instilled group and saline instilled group. LTD4 or saline were instilled in both nasal cavities and acoustic rhinometry measurement were performed three times on each side 30 min. before and 3 and 6h after instillation of LTD4 or saline. The nasal cavity volume between the nostril and 2cm into the nasal cavity was calculated by computer for each measurements. Nasal patency of each animal was evaluated with the sum of the volume of the right and left nasal cavities. Changes in volume after the instillation were expressed as the percentage from the values before the instillation. In the sensitized GP, the value of nasal patency abruptly decreased at 30 min after instillation and recovered to the value at 3h after the instillation in non-treated GPs. The nasal patency then decreased again significantly at 6h after the instillation. On the other hand, the value did not change up to 6hr after the instillation in MBST treated GPs. Among the nonsensitized group, nontreated GPs showed similar findings of biphasic phenomenon and MBST treated GPs failed to change their patencies up to 6h after the instillation of LTD4. The results we obtained this study suggests that MBST can be effective on allergic reaction of GP as leukotriene inhibitor.

Evaluation of the effects of herbal medicines on patients with allergic rhinitis

The purpose of this study was to evaluate the effectiveness of MBST and SST. Eligible patients were made male and female, 18 to 65 years of age. Each patient signed an informed consent before any procedures were performed. Diagnostic criteria used to select patients with AR were as follows: a minimum 2-year history of AR, a positive reaction to allergic work-up (skin testing, RAST or MAST, nasal provocation test), and rhinitis symptoms (nasal congestion, rhinorrhea, and sneezing) of at least moderate severity as evaluated by the patient. Patients were excluded from the study if they present-ed with nasal polyps, obstructive nasal defect, acute or chronic sinusitis, a respiratory or systemic infection with 4wks immediately preceding screenng, or past adverse reaction to nasal or systemic glucocorticoids.

The patient were divided into 2 groups: MBST group and SST group. MBST group indicated patients administrated orally MBST for 1wk or 2wks and SST group indicated patients administrated SST. We studied the effects of MBST and SST with double-blind, randomized, placebo-controlled group study, and also studied change of nasal patency after challenge of antigen. The efficacy measures included relief of combined nasal symptoms (symptom severity index, SSI) and percent improvement from last dose of baseline to day 14 and endpoint (day 28). The patients were introduced to write their symptom severity on patient diary (nasal obstruction, rhinorrhea, sneezing). The nasal cavity volume was measured by acoustic rhinometry (AR). The nasal patency of each subject was evaluated with the sum of the volume of the right and the left nasal cavities. Changes in volume after antigen challenge were expressed as the percent change from the values before the challenge. AR was performed before administration of medicine, on day 14 and 28.

SSI was significantly decreased from treatment wk 2 in MBST group. In SST group, patients who took the medicine for 2wks showed significant decrease SSI from treatment wk 2 and patients who took for 1wk showed significant decrease on treatment wk 4. Both of MBST and SST group showed significant increase the percent improvement from last dose of base line to wk 2 and wk 4. Two week administration of MBST and SST showed better effect than 1wk administration. The percent volume change after antigen challenge was remarkably decreased in patients who took MBST and SST for 2 wks.

This results indicated that the herbal medicine of MBST and SST were effective to the patients with allergic rhinitis.

DISCUSSION AND CONCLUSION

Prior to the discovery and availability of H1-blocking agents, the only way of reducing symptoms caused
by aeroallergens was to avoid these allergens; however, this approach had sharp limitations in the cast of pollen, mold spores, and house-dust allergens. The great clinical allergists early in the twentieth century identified important aeroallegens, prepared allergen extracts, and devised safe and effective treatment regimens involving their use.10

Antihistamines are currently the most frequent used medication for the treatment of AR. Although second-generation, relatively non-sedating antihistamines have surpassed sales of the relatively sedating, first-generation antihistamines in the treatment of AR, many first-generation antihistamines are available and continue to be used frequently as self medication. And the nasal glucocorticoids, generally considered the most effective pharmacologic treatment for AR, have been available for more than 30 years.

There have been several kinds of new trials of treatment AR: leukotriene antagonist, anti-IgE antibody, anti-ICAM antibody, Th1 cytokine transfer, and DNA base immunization. Recently herbal medicine (or alternative medicine) can be considered to be a part of the treatments. The efficacy of herbal medicines in the treatment of AR has not been extensively studied.

We evaluated efficacy of herbal medicine, MBST and SST in allergic model and patients with AR. Our data from the animal studies suggest that these medicines are effective in animal models as mast cell stabilizer in rat and leukotriene antagonist in GP. We also performed double-blind study with MBST and SST. Our data demonstrate that both of MBST and SST are effective to the patient with AR up to 1 month after last dose. And 2 wk administration is more effective than 1 wk administration in controlling symptom of AR. Detail and long term effect of the medicines is need to further study. However, the herbal medicine of MBST and SST show us a possibility to be effective in patients with AR.

References


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