Efficacy of the Plasma Cluster® Device in Asthmatic and/or Allergic Rhinitis Patients with House Dust Mite Allergy: A Prospective Observational Pilot Study

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ABSTRACT: **Background:** Mite allergy is an indoor allergen responsible for most respiratory allergies in the western world. Environmental control can modify disease activity in these patients.

Objectives: To examine the benefit of the Plasma Cluster® device (Sharp, Japan) for inactivating and removing mites from the environment of patients diagnosed with either mite-sensitive perennial allergic rhinitis or mite-sensitive allergic asthma.

Methods: Patients with AR (n=30) or AA (n=10) were enrolled into a prospective open observational 8 week study. The first 2 weeks involved initial evaluation, the following 4 weeks consisted of active usage of the device, and the last 2 weeks were designated for follow-up. Symptom scores (recorded daily by patients and during visits by physicians) were recorded and analyzed.

Results: Patients with AR experienced a significant ($P < 0.05$) reduction in nasal discharge, post-nasal drip, nasal congestion, nasal itching, watery eyes, itchy eyes, headache, itchy ears, night disturbances and an improvement in general well-being during the last 2 days of the study compared to baseline. Patients with AA reported significant ($P < 0.05$) reduction in dyspnea, wheezing and the need to avoid dust mites. There was a significant ($P < 0.05$) improvement in mean peak expiratory flow rate at study closure compared to baseline.

Conclusions: Short-term usage of the Plasma Cluster® device resulted in considerable clinical improvement and increased peak expiratory flow rate in patients with AR or AA. The findings of this pilot study warrant longer and controlled studies to determine the value of this device in the treatment of various allergic disorders. *IMAJ* 2009;11:74–77

KEY WORDS: mite, allergic rhinitis, allergic asthma, plasma cluster

In 1925, twenty years after von Pirquet coined the term "allergy" and Wolff-Eisner demonstrated a link between asthma and hypersensitivity, Storm van Leeuwen [1] proposed enclosing asthmatic patients in an allergen-proof chamber or moving them to high altitudes to reduce allergen exposure. Eighty years later, after clinical trials of these and other allergen avoidance interventions, there remains substantial uncertainty and controversy regarding which modality should be recommended to patients with asthma or allergic rhinitis [2-5]. Dust mite allergens, which play an important role in causing and aggravating asthma and rhinitis in many parts of the world, have been a major focus of trials of allergen avoidance. The two strategies proposed by Storm van Leeuwen have been studied as a means of reducing mite allergen exposure among asthmatic patients allergic to dust mite, with reportedly beneficial effects. Among the currently discussed mite allergen avoidance interventions, encasement of the mattress and pillows in allergen-impermeable covers combined with frequent hot water washing of bedding seem to be the most practical and effective approach to reduce allergen exposure in the bedroom [6].

Many devices have been proposed to improve the plight of allergy sufferers, among which the use of high efficiency particle arrest filters seems to be the most efficient in reducing the numbers of bedroom mites [7-9], although its ability to alleviate allergy symptoms was less convincing [10]. More recently, a new device was introduced by the Japanese manufacturer, Sharp. In addition to HEPA and carbon filters, this device also contains a unit that distributes both negative and positive ions into the air. This device was shown in many studies to inactivate bacteria, viruses, mites and molds [11-14]. This multicenter prospective pilot study evaluated the clinical benefit of using the Plasma Cluster® ions (Sharp, Japan) device for alleviating symptoms in both mite-sensitive allergic rhinitis and mite-sensitive asthma sufferers.

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AR = allergic rhinitis
AA = allergic asthma

HEPA = high efficiency particle arrest

PATIENTS AND METHODS

This multicenter study involved 11 allergy treatment facilities in Israel. The study patients had been treated in these centers for at least 1 year prior to their participation in the study. None of the patients was receiving immunotherapy and there was no change in their medications during the entire study and follow-up period. All of the AA patients were considered to have mild-to-moderate degree asthma as defined by the GINA (Global Initiative for Asthma) guidelines and none was taking oral corticosteroids.

Informed consent was obtained from each patient following the study's approval by the ethics committee of each institution. Each center recruited four patients with AR and between one and four patients with AA. Some of the patients had both AR and AA. The centers were located throughout the country and included patients in the central, northern and southern parts of Israel. The study was conducted during different seasons so that the results could be considered not to have been influenced by seasonal changes.

The study cohort consisted of 19 males and 14 females with AR whose ages ranged between 22 and 63 years (mean 35 ± 12) and 5 males and 7 females with AA whose ages ranged between 22 and 45 years (mean 28 ± 9). Six patients had both AR and AA. None of the patients had any other chronic illness. Skin tests were done by prick and included mites, grasses, weeds, epidermals and molds. Each patient had at least one positive prick-skin test to a mixture of mites (*Dermatophagoides pteronyssinus* and *D. farinae*).

THE DEVICE

The Plasma Cluster® ions device was donated by Sharp, Osaka, Japan. As described by Nishikawa's group and others [11-14], this technology consists of a multi-electrode array that produces positive and negative ions surrounded by a water shell [15]. The ion density is 10,000 pcs/cm. The respective hydrated ions are deposited on microparticles such as bacteria or odor-causing molecules, which they decompose and deactivate chemically [16]. The amount of ozone generated by the device is less than 0.01 ppm, which is significantly less than the standard (0.05 ppm) for industrial operations and consumer electronics.

STUDY DESIGN

Each patient was seen at least four times during the 8 week study. On the first visit, he/she was interviewed by the investigator, followed by a history intake, physical examination, spirometry (in cases of AA) and initial peak expiratory flow measurement. Each measurement was repeated three times and the best of the three was selected for data analysis. The patient filled in a questionnaire, which included 30 different symptoms (adapted from Juniper and Guyatt [8]). AA patients were given a symptoms diary and instructed to complete it twice daily, using a severity score of 0–3, recording the amount of puffs of albuterol taken to relieve symptoms, and recording PEFR as measured at home twice a day and throughout the study period.

Symptoms were recorded for a total period of 8 weeks: 2 weeks as a run-in period without the device, 4 weeks with the device placed in the bedroom and close to the patient's bed, and an additional 2 weeks following removal of the device. The patients performed spirometry and filled in a symptoms score at each clinic visit.

STATISTICAL ANALYSIS

The data were analyzed by a statistician who recorded the information of each patient and statistically compared the results by the *t*-test for the comparison of two periods and ANOVA for changes throughout whole periods. Significance was established at $P < 0.05$.

RESULTS

Thirty of the original 33 AR patients completed the AR protocol, while 10 of the original 12 AA patients completed the AA protocol. The data on these 43 patients were included in the statistical analysis.

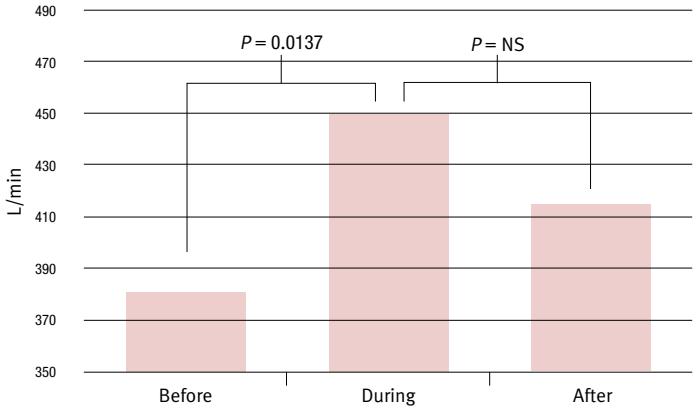
As seen in Table 1, there was a significant improvement at the end of the fourth week with the device compared to baseline, but there was no significant difference for the same parameters between baseline scores and those recorded at the end of the first phase (i.e., 2 weeks of observation). There was good agreement between the patients' reports and the physicians' assessments in terms of improved symptoms ($P < 0.05$). Improvement was also seen during the 2 weeks after removing the device, although to a lesser degree than

Table 1. Parameters reported to have significantly improved with the use of the Plasma Cluster® device

Parameters	*P*
Nasal discharge	0.002
Postnasal drip	0.06
Nasal congestion	0.002
Nasal tching	0.01
Watery eyes	0.04
Itchy eyes	0.05
Headache	0.05
Itchy ears	0.08
Night disturbances	0.05
General feeling (last 2 days of study)	0.02

PEFR = peak expiratory flow rate

Figure 1. Effect of the Plasma Cluster® device on peak expiratory flow rate before, during and after removal of the Plasma Cluster® device



during the period of its active use. The mean score of improvement was 5.1 ± 3.2 (on a scale of 0–10). Almost two-thirds of the patients (19/30, 63%) scored an improvement > 5.

The AA patients reported a significant reduction ($P < 0.05$) in dyspnea, wheezing, and the need to avoid dust mite. They also had a significant improvement ($P = 0.0137$) in mean PEFR at the end of the treatment period compared to the observational phase. There was a significant difference between the average daily PEFR measurements for each period ($P < 0.005$ ANOVA)[Figure 1].

No significant change was noted in the spirometric measurements obtained during visits to the physician's office. There was good agreement between patients' symptoms, diary entries and the physicians' report of asthma status.

DISCUSSION

Mite allergy is responsible for the majority of respiratory allergies in western societies [3-6,8-10]. Many devices and suggestions are offered to affected individuals in an attempt to reduce or inactivate the widespread indoor allergen. Most of the relevant studies evaluated the effect of environmental control on asthma, but only a few investigated nasal symptoms.

The Plasma Cluster® ion device was recently introduced as a tool capable of improving the quality of life of individuals sensitive to indoor allergens [11-16]. The molecular structures of the device were identified as $H_3O+(H_2O_m)$ and $O_2-(H_2O_n)$ (m, n ≥ 0) as the major ions [13,14], while ozone and the other ions were negligible [11-13]. Kawamoto et al. [17] recently demonstrated that the use of the Plasma Cluster® ion device significantly reduced the allergenic activity of Japanese cedar pollens in the lab. The rate of decrease in *in vitro* antigenic activities and *in vivo* allergenic activities was proportional to the densities of the device caused by changing the input voltage [17].

Previous research on the use of negative ion generators that electrostatically precipitated airborne dust and allergens has shown little or no evidence of any clinical benefits [18]. Warner and co-authors [19] reported that ionizers could not be recommended for use in homes of asthmatic subjects with the intent to alleviate their symptoms, but that a significant abatement of airborne allergen concentrations may be useful as part of an allergen avoidance regimen. Ionizers and/or air filtration units did not reduce the levels of mite allergens in indoor environments, since the largest amounts of these allergens remained in settled dust [20].

Our data demonstrated an improvement in symptom scores as reported by the patients as well as in the physicians' evaluations of patients who suffer from mite-sensitive respiratory allergies. This is shown for both nasal and airway disease. Importantly, some of the nasal symptoms also continued to improve after removal of the device. The same outcome was seen in the PEFR results, although the difference did not reach statistical significance. We assume that this benefit could be due to the suppression of mucosal inflammation occurring as the result of inactivating dust mite.

Although this is an observational and not a blinded study, it has the advantage of having included a phase of observation prior to the application of the device and another phase 2 weeks following the cessation. Using the device for a longer period might have had a stronger and more long-lasting effect, and a larger group of patients in the asthmatic arm could probably strengthen the results.

More than a dozen clinical trials of allergen-proof encasings [6-8] have been published; they were at least 3 months in duration and they measured mite allergen levels in bedding. All of these trials reported reduced allergen concentrations, varying in efficacy from 39 to 99.9% reduction in mite allergen levels.

HEPA filters and HEPA filter vacuum cleaners can effectively reduce environmental levels of pet-derived allergens in indoor environments, but there are no convincing data [21,22] that environmental control measures can reduce asthma morbidity to acceptable levels in patients with pet-allergic asthma who continue to live with a pet to which they are allergic. The use of chemicals in removing dust mite was shown in a few studies to be effective [23,24] – a method hard to apply in daily life. Fewer studies have looked at allergen avoidance for other indoor allergens. Avoidance of cockroach allergen was the focus of several interventional studies, but reductions in allergen levels were not obtained, and no clinical benefits were seen in the trials that reported clinical outcomes. A recent study of an intensive 6 month extermination and cleaning intervention showed that substantial reductions in cockroach allergen levels in infested apartments can be obtained, but clinical outcomes were not assessed. Exposure

to mold can aggravate the asthma of sensitized persons, and case reports have described the clinical benefits of eliminating indoor exposure for such individuals. The potential clinical effect of interventions to reduce indoor residential exposure to fungi, however, has not been evaluated in clinical trials.

The use of Plasma Cluster® ion devices holds much promise to inactivate the antigenicity and allergenicity of a variety of airborne allergens without elevation of ozone concentrations in domestic surroundings. This device deactivates the immunoglobulin E antibody binding sites of the allergen on the molecular level and thus prevents the allergen from combining with the IgE antibody.

According to the time/dose-dependent experiments by Digel et al. [25], the inhibiting effects of this device on the multiplication of different bacteria (Staphylococcus, Enterococcus, Micrococcus and Bacillus) became apparent within the first few minutes and led to an irreversible 99.9% destruction of these bacteria within the following 2–8 hours of exposure. The destructive effect of the device corresponded to membranal damage of the bacteria. Their study revealed changes in the bacterial surface protein composition induced by the device. In contrast, neither DNA nor cytoplasm protein damage was detected electrophoretically. The antimicrobial action of the device seems to occur because of chemical modification of the surface proteins of bacteria. *In situ* hydroxyl-radical formation on the surface of bacteria was proposed as the leading mechanism of the protein damage caused by the device. At the same time, DNA damage seems not to be involved in the antibacterial action of the device.

Our findings should encourage further research to confirm the benefits of the Plasma Cluster® ion device under natural conditions in domestic environments. The data obtained from such studies would broaden the knowledge on the effects of airborne plasma-generated cluster ions and help to produce more efficient air-cleaning devices.

Acknowledgments
Esther Eshkol is thanked for editorial assistance.

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IgE = immunoglobulin E