

An Analysis of the Clinical Benefits of Hydroxyl Ag Titan Sheet (HATS) in 12 Adults with Hay Fever

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Abstract Background / Objective: The prevalence of hay fever in Japan is a little over 40 percent. Effective treatments for hay fever have been sought in order to prevent not only decreases in affected individuals' quality of life, but also labor losses and increases in healthcare costs. The purpose of this study is to verify the clinical efficacy of composite Hydroxyl Ag Titan Sheet (HATS), a new, proprietary treatment for hay fever, developed by adding silver to the photocatalytic effect of titanium oxide and by using hydroxyapatite. Research Method: The research subjects were seven women and five men, with an average age of 47.6 years. The method of the research was to compare each respective subject's time when not using the treatment to their time while using it. We verified the data by comparing the subjective clinical efficacy of both HATS not using and HATS using periods. Each period was 5 days. Specifically, additive-free non-woven fabric not treated with HATS were made into string shapes 1 cm wide x 5 cm and inserted intranasally for 40 minutes from 9:00 AM for five consecutive days henceforth, the HATS non-using group. Five days later, non-woven fabric containing henceforth HATS using group was used in the same manner as with the control group, and an evaluation was performed by comparing the therapeutic value, for each groups against hay fever symptoms before and after for each five day period. The institution carrying out the research was a medical institution in Tokyo. The research period was November 1st, 2015 to May 30th, 2016. Results: Both HATS using and HATS non-using group were compared for the severity of three symptoms; nasal inflammation sneezing, nasal mucus, nasal, and nasal obstruction. Sneezing was scored at 2.25, nasal mucus at 3.03 and nasal obstruction at 3.08. Improvements in symptoms were observed in the HATS using group compared with HATS non-using. The HATS using group showed significant improvement 24 hours after treatment. The value for sneezing went to 1.42, nasal mucus to 2.17, and nasal obstruction to 2.00. This effect was significant maintained throughout the five days compared with the HATS non-using group. Additionally, neither subjective nor clinical side effects were observed. Conclusions: There was no improvement in symptoms observed for the HATS non-using group during five day period. In the HATS using group, however, subjective and clinical improvement without any side effects were shown. In order to make practical use of HATS treatment as a simple home care therapeutic approach, there will be a need to verify the absence of side effects. Randomized, controlled intervention studies, along with research into long-term effects is needed.

Keywords Silver hydroxyapatite (HATS), Photocatalysis, Hay fever, Subjective symptoms

1. Preface

Rhinitis that results from hay fever is an archetypal type I allergic reaction that emerges in the nasal mucosa. A 2005 national epidemiologic study using ECRHS found that the frequency of nasal allergies, including hay fever, was 47.2% in adults [1]. In addition, it is estimated that over 40% of Japanese suffers from allergic rhinitis including Japanese cedar hay fever and this rate is expected to increase [2].

The main symptoms of allergic rhinitis are sneezing, rhinorrhea, and nasal congestion, which are effectively linked to concomitant symptoms including of factory

disorder, sleep disorder, and a reduction in concentration. As a result, it is being recognized as a major disease which impacting Quality of Life (QOL).

It is important also to view allergic rhinitis from the perspective of how it decreases worker productivity. For example, Lamb [3] et al. reports that productivity loss as a result of allergic rhinitis is 2.3 hours per day and corresponds to 3.6 days of absence from work per year. Also, it is reported that the average loss of productivity value per person as result of allergic rhinitis and hay fever is \$593 per year. This is reported to be more of an economic loss than loss caused by high stress, headaches, depression, arthritis or rheumatism, anxiety disorder, respiratory infection, high blood pressure, diabetes, asthma, and cardiovascular disease. Studied in Japan supported these findings. Ogino [4] outlines the reality of the impacts on labor productivity in hay fever patients and reports that a significant correlation has been

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recognized between labor productivity and QOL or symptom severity. Additionally, Okamoto [5] has done preliminary calculations on economic loss connected to allergic rhinitis brought on by nasal congestion. These calculations estimate that the economic loss resulting from reduced productivity in patients with allergic rhinitis brought on by nasal congestion amounts to 4.3966 trillion yen per year, and the economic loss resulting from traffic accidents caused by sleep disorder amounts to 160.1 billion yen, for a total estimate exceeding medical fees of 4.5567 trillion yen in economic loss. With these factors in mind, improving symptoms with appropriate treatments and preventing a reduction in QOL will be useful in improving labor productivity loss.

Japan's total annual medical expenses surpassed 40 trillion yen in 2014. The total annual cost of chemotherapy treatments for all types of cancer is 750 billion yen; the cost of treatment for allergic diseases is roughly the same. Moreover, the total economic loss from sick days and hospital visits as a result of allergic disease is estimated to be approximately 800 billion yen. This figure comes from individual annual medical expenses of 20,000 yen for approximately 40 million patients with allergic rhinitis as well as hay fever. Consequently, it is expected that an appropriate method of preventative treatment will be developed.

In considering the medical costs of allergic rhinitis and hay fever together with economic loss, a big task in this research is to view the issue both medically and economically in developing appropriate methods of prevention and new medical treatments.

Methods of treatment for allergic rhinitis and hay fever up until now have been divided into 4 categories. The first of these methods is to avoid antigens through air purification and wearing a mask; physically removing allergen exposure from the body. The second is pharmacotherapy, using antihistamines and steroids that control the activation of mastocytes as an allergic reaction within the body. The third method is immunotherapy that is representative of hyposensitization therapy. Finally, neurectomies have come to be used as a surgical treatment.

The method used in this study, an independently developed composite photocatalytic material sheet (Hydroxyl Ag Titan Sheet 「HATS」) made by adding silver

to the photocatalytic effects of titanium oxide and using hydroxyapatite, is an originally developed item that applies previously developed catalytic functions. HATS falls under the first treatment method mentioned above, as it controls the outbreak of hay fever by inhibiting bodily exposure to allergenic materials including pollen, mites, as well as viruses and germs using the redox method to physically and chemically degenerate and decompose the materials.

The goals of this research are to confirm the safety of preventative treatment through HATS, to clarify the clinical effects of non-woven fabric using HATS after using threads that do not include HATS, to investigate the mechanisms involved, and to verify the possibility of using it as a self-medication at home.

If this new HATS method has no major side effects and, further, is shown to be effective, we can expect it to be significant not only as a scientific basis for simple and easy self-medication at home that will certainly improve individual QOL, but also as a means of improving public health by stabilizing medical expenses and improving labor productivity.

2. Research Target, HATS Hay Fever Treatment Mechanisms, and Its Safety and Clinical Evaluation Methods

2.1. Research Target

The target persons of this study were those who, during the hay fever season of March to May, experienced sneezing, runny nose, and nasal congestion almost daily, and who, based on the Japan Allergy Society's 2013 nasal allergy examination guidelines, had been scored in the 3 to 4 point hay fever range by otolaryngology specialists and exhibited strong symptoms for a period of three or more years. The participants were a group of 5 men and 7 women, selected from a consenting group of 26 to 53 year olds who have been resistant to medical treatment, having had no definite clinical effects from prior medical treatments. The average age was 47.6 years old (Table 1).

Table 1. Clinical background of the 12 subjects

	Age										Total
	26	33	34	38	44	45	47	49	50	53	
Sex	0	0	0	0	0	1	1	1	1	1	5
	0.0%	0.0%	0.0%	0.0%	0.0%	20.0%	20.0%	20.0%	20.0%	20.0%	100.0%
Female	1	1	1	1	2	0	0	0	1	0	7
	14.3%	14.3%	14.3%	14.3%	28.6%	0.0%	0.0%	0.0%	14.3%	0.0%	100.0%
Total	1	1	1	1	2	1	1	1	2	1	12
	8.3%	8.3%	8.3%	8.3%	16.7%	8.3%	8.3%	8.3%	16.7%	8.3%	100.0%



Figure 1. Study design to show the subjective clinical effect of HATS compared with the non-HATS

2.2. The New Medical Treatment, HATS Characteristics and Hay Fever Treatment Mechanisms

HATS, a new medical treatment method for hay fever, is an independently developed composite photocatalytic material sheet using silver added to the photocatalytic effects of titanium oxide and using hydroxyapatite. The principle behind HATS is based on a 1967 research report by Fujishima Akira that showed that when titanium oxide was exposed to light, it would become water and hydrogen, then decompose into water [6]. In contrast to the previously utilized photocatalysis of titanium oxide, which brought about free radicals through reflecting light and causing the movement of electrons within the titanium oxide, HATS uses anatase-type titanium oxide that has properties equivalent to that of photocatalysis. A special characteristic of HATS is that it improves the adsorption of oxidation-reduced, denatured odor components, pollen proteins, and viruses. Moreover, the HATS used in this study was made by thermally bonding 10g of hydrated silver titanium into every square meter of 100% unwoven fabric. It is a technology that maintains a porousness of a molecular level of over 99 nanometers; too small for permeation into the human body. HATS is HAT melded into unwoven fabric.

The HATS mechanism is one in which an electron hole h^+ is produced on the surface of titanium dioxide by energy from silver. Following that, there is a moisture reaction and activated oxygen (OH^-) is produced. Then it reacts with O_2 , producing superoxide (O_2^-) and converting mainly into water. Titanium dioxide has the function of oxidizing microbes, mold, and antigen proteins via exposure to visible spectrum light. It has unlimited functionality as a catalytic actor in the oxidative decomposition of antigen proteins, altering water, carbon dioxide and other molecules. Hydroxyapatite absorbs microbes broken down by free radicals including pollen, mold, proteins and germs, and viruses as well as the selective absorption of proteins. Hydroxyapatite, through absorption and more efficient titanium dioxide, simplifies the breakdown of all types of proteins that can become antigens.

2.3. The Safety of HATS

The titanium oxide used as a catalyst in HATS was approved as a food additive in 1983 by the Ministry of Health and Welfare. However, because HATS is made up of new hydroxyapatite and mixed silver powder in addition to titanium oxide, safety confirmation tests including 1) oral acute toxicity tests, 2) human patch tests 3) primary irritation skin tests, 4) skin sensitization tests 5) cytotoxicity tests were entrusted to and conducted by respective specialist

institutions [7, 8].

1) The oral acute toxicity test was conducted on rats by the Mitsubishi Safety Laboratory KK and was a result reported to be safe on August 8th, 1999. 2) The human patch test was conducted on 25 individuals by the Japan Hair Science Association and was a result reported to have few irritative effects on December 4th, 2002. 3) The primary irritation skin test was conducted, in accordance with OECD Guidelines for the Testing of Chemicals, on 3 rabbits by Japan Food Research Laboratories and was as a result reported to have no recognizable irritative effects on June 13th, 1999. 4) The skin sensitization test was conducted by the Japan Hair Science Association through observation of 13 adult men and 13 adult women who wore closed bandages for 48 hours, and was as a result reported to have a low potential to cause irritative effects. 5) The cytotoxicity test was conducted on V79 cells by the Toxic Materials Research Division of the Mitsubishi Safety Laboratory KK. It was reported on January 20th, 2003 that the test revealed cytotoxicity in which its IC_{50} was 53.5%.

2.4. Clinically Observed HATS Clinical Effectiveness Indicators

The clinically observed effectiveness indicators for HATS treating hay fever are on three main symptoms, sneezing, runny nose, and nasal congestion. This is based on the Nasal Allergy Examination Guidelines outlined by the Japan Allergy Society in 2013. The clinical condition of these symptoms were self-reported on record sheets by patients when first waking in the morning. Reports on the severity of sneezing, runny nose, and nasal congestion were "None" (0), "Light" (1), "Somewhat Heavy" (2), "Heavy" (3), and "Very Heavy" (4).

2.5. Research Methods for Clarifying Clinical Treatment Effectiveness

A 1cm x 5cm thread of unwoven fabric without HATS was inserted into the nasal cavity for 40 minutes from 9:00am for 5 consecutive days. Next, an unwoven fabric with HATS added was introduced and examined with the same 5 day study as conducted with the fabric without HATS.

The evaluation method was also conducted so as to avoid a placebo effect and determine the true clinical value of HATS. This was achieved by conducting a 5 day foundational study in advance where hats was not added to the thread. The effectiveness of the HATS added thread on the three major symptoms of nasal inflammation was self-reported every day for five days. Because the 5 day study on those who did not use threads with HATS yielded almost no visible changes, the mean score of the 5 day period was determined and set as the base score. All comparisons to the 5 day study with HATS added were statistically verified using a corresponding t-test. The statistical significance value was set at 5%.

The study was conducted by a medical institution in the

Tokyo Metropolis from November 1st, 2015 to May 30th, 2016.

In keeping with ethical considerations, the participants in this study were able to stop their use of HATS if they felt that their symptoms were worsening too much. The decision to suspend use could be made freely if the participant felt that they were not receiving any benefits from usage.

Though all 12 participants saw an effect through using HATS, 1 participant reported a sense of discomfort in the nasal mucous cavity from the 4th day of the study and was unable to do the clinical self-evaluation. This study was further conducted with ethical consideration in compliance with the Helsinki Declaration.

3. Results of the Study

In regards to the day by day breakdown of using HATS over the 5 day period, we conducted a statistical examination of the general effects on the three main symptoms of nasal inflammation--sneezing, runny nose, and nasal congestion--as well as the 5 day average values for unwoven fabric without HATS, and for all combinations of daily scores from days 1 to 5 in those who used HATS.

The results of the study 3-1. The effects of unwoven fabric with and without HATS over each day of the 5 day period, 3-2. Comparison of the effectiveness of unwoven fabric with and without HATS in treating the symptoms of nasal inflammation over the 5 day period, and 3-3. Daily breakdown of the clinical effectiveness of HATS in treating hay fever over the 5 day period.

3.1. The Effects of Unwoven Fabric with and without HATS over Each Day of the 5 Day Period

Concerning the effects of unwoven fabric with and without HATS over each day of the 5 day period, we analyzed the clinical self-awareness scores of the 3 main symptoms of nasal inflammation--sneezing, runny nose, and nasal congestion-- of the 12 participants.

There were no changes in symptoms in using fabric without HATS. The average scores were: sneezing (2.33), runny nose (3.03), and nasal congestion (3.05) (Table 2). In contrast, an effect was seen from the 1st day in using fabric with HATS, with the scores being: sneezing (1.42), runny nose (2.17), and nasal congestion (2.00), with the effects growing more pronounced each time they were tracked (Table 2).

3.2. Comparison of the Effectiveness of Unwoven Fabric with and without HATS in Treating the Symptoms of Nasal Inflammation over a 5 Day Period

We compared the effectiveness of unwoven fabric with HATS over a 5 day period to the average scores of those without HATS over a 5 day period. The results showed that all 12 cases saw improvement in their symptoms after 24 hours of using HATS. The efficacy of using HATS was not

limited to the 1st of use. From the 2nd to 5th days after beginning use, we observed a statistically significant ($P < 0.05$) improvement in the 3 main symptoms of nasal inflammation, namely, sneezing, runny nose, and nasal congestion. (Table 2, 3)

3.3. Daily Breakdown of the Clinical Effectiveness of HATS in Treating hay Fever over the 5 Day Period

We verified the efficacy of unwoven fabric with HATS by checking the improvement in symptoms for each major symptom after each day of the study.

The sneezing scores after each day were 1.42, 1.42, 1.00, 0.83, 0.73, a continuous improvement every day (Table 2, Figure 2).

Next, we verified all of the comparisons, namely, comparing day 1 to day 2, day 1 to day 3, day 1 to day 4, and day 1 to day 5. Similarly, we compared day 2 to the other days, day 3 to the other days, day 4 to the other days, and day 5 to the other days; verifying and combining each possible comparison. (Table 4).

As a result, we found statistical significance in the case of sneezing when comparing day 1 to day 5 and day 2 to day 5. This implies that the efficacy of HATS is easy to see after day 1. As for runny nose, by comparing day 1 to day 4 and day 1 to day 5 and 2 to day 3 and day 2 to day 4 and day 2 to day 5, we found that these changes were statistically significant. As for runny nose, by comparing day 1 to day 4 and day 1 to day 5 and 2 to day 3 and day 2 to day 4 and day 2 to day 5, we found that these changes were statistically significant. This implies that improvement in runny nose due to HATS can be easily seen after the 3rd or 4th day. As for nasal congestion, we found statistical significance in comparing day 1 to day 3, 1 to day 4, 1 to day 5, and day 2 to day 4, day 2 to day 5. (Table 4).

The effects of HATS on runny nose and nasal congestion, specifically the significant effects have been seen from day 3 or after day 4, implies that a certain number of days will be required before the these effects manifest.

3.4. Side Effects of HAT Infused Unwoven Fabric

In considering the side effects of using HATS, we divided and verified during insertion of just the unwoven fabric along with the insertion of HATS through self reported symptoms and the degree of change in hematology. As a result, we found that for both the HATS use and non-use groups, the nasal congestion of all 12 participants had worsened 30 minutes after insertion. Three participants experienced slightly more sneezing. Additional side effects including pain, lacrimation, increased congestion, bleeding, olfactory disorder, numbness of the lips, and tingling in the nasal cavity were not reported. One of the 12 participants ceased observations due to discomfort in the nasal cavity from the 4th day of the study.

There was no statistically significant change in IgE or eosinophil when comparing the blood tests of the 12 participants. This indicates that clinical effects in using

HATS are limited to the inside of the nasal cavity and there are no full body immunoreactions resulting from use.

Table 2. Discriptive analysis of 5 days of HATS nonusing and 5 days of HATS using

		N	Minimum	Maximum	Average	SD
non-using group	sneezing 1 day	12	0	4	2.33	1.15
	sneezing 2 day	12	0	4	2.42	1.08
	sneezing 3 day	12	0	4	2.33	1.15
	sneezing 4 day	12	0	4	2.33	1.15
	sneezing 5 day	12	0	4	2.25	1.14
	sneezing average	12	0	4	2.33	1.11
using group	sneezing 1 day	12	0	3	1.42	1.00
	sneezing 2 day	12	0	3	1.42	1.08
	sneezing 3 day	12	0	2	1.00	0.60
	sneezing 4 day	12	0	2	0.83	0.72
	sneezing 5 day	12	0	2	0.73	0.65
non-using group	nasal mucus 1 day	12	2	4	3.00	0.95
	nasal mucus 2 day	12	1	4	3.00	1.04
	nasal mucus 3 day	12	2	4	3.08	0.90
	nasal mucus 4 day	12	1	4	3.00	1.04
	nasal mucus 5 day	12	2	4	3.08	0.90
	nasal mucus average	12	1.6	4	3.03	0.95
using group	nasal mucus 1 day	12	1	4	2.17	0.94
	nasal mucus 2 day	12	1	3	1.92	0.79
	nasal mucus 3 day	12	0	3	1.50	0.90
	nasal mucus 4 day	11	0	3	1.45	1.04
	nasal mucus 5 day	11	0	3	1.36	1.03
non-using group	nasal obstruction 1 day	12	1	4	3.00	0.85
	nasal obstruction 2 day	12	1	4	3.08	0.90
	nasal obstruction 3 day	12	1	4	3.08	0.90
	nasal obstruction 4 day	12	1	4	3.08	0.90
	nasal obstruction 5 day	12	1	4	3.00	0.85
	nasal obstruction average	12	1	4	3.05	0.84
using group	nasal obstruction 1 day	12	1	3	2.00	0.85
	nasal obstruction 2 day	12	0	3	1.83	0.83
	nasal obstruction 3 day	12	0	3	1.33	0.89
	nasal obstruction 4 day	11	0	2	1.09	0.70
	nasal obstruction 5 day	11	0	3	0.82	1.08

Table 3. HATS subjective clinical effect compared with the 5 days average of HATS nonusing

Sympton		mean value	SD Standaed deviation	95% confidence intervals		P
				Lower limit	Upper limito	
sneezing	average - 1 day after	0.917	0.624	0.520	1.313	0.000
	average - 2 day after	0.917	0.967	0.303	1.531	0.007
	average - 3 day after	1.333	1.145	0.606	2.061	0.002
	average - 4 day after	1.500	1.263	0.697	2.303	0.002
	average - 5 day after	1.709	1.067	0.992	2.426	0.000
nasal mucus	average - 1 day after	0.867	1.167	0.125	1.608	0.026
	average - 2 day after	1.117	1.130	0.399	1.834	0.006
	average - 3 day after	1.533	1.394	0.647	2.419	0.003
	average - 4 day after	1.491	1.355	0.581	2.401	0.004
	average - 5 day after	1.582	1.260	0.735	2.428	0.002
nasal obstruction	average - 1 day after	1.050	0.879	0.492	1.608	0.002
	average - 2 day after	1.217	1.025	0.565	1.868	0.002
	average - 3 day after	1.717	1.189	0.961	2.472	0.000
	average - 4 day after	1.945	1.194	1.144	2.747	0.000
	average - 5 day after	2.218	1.495	1.214	3.223	0.001

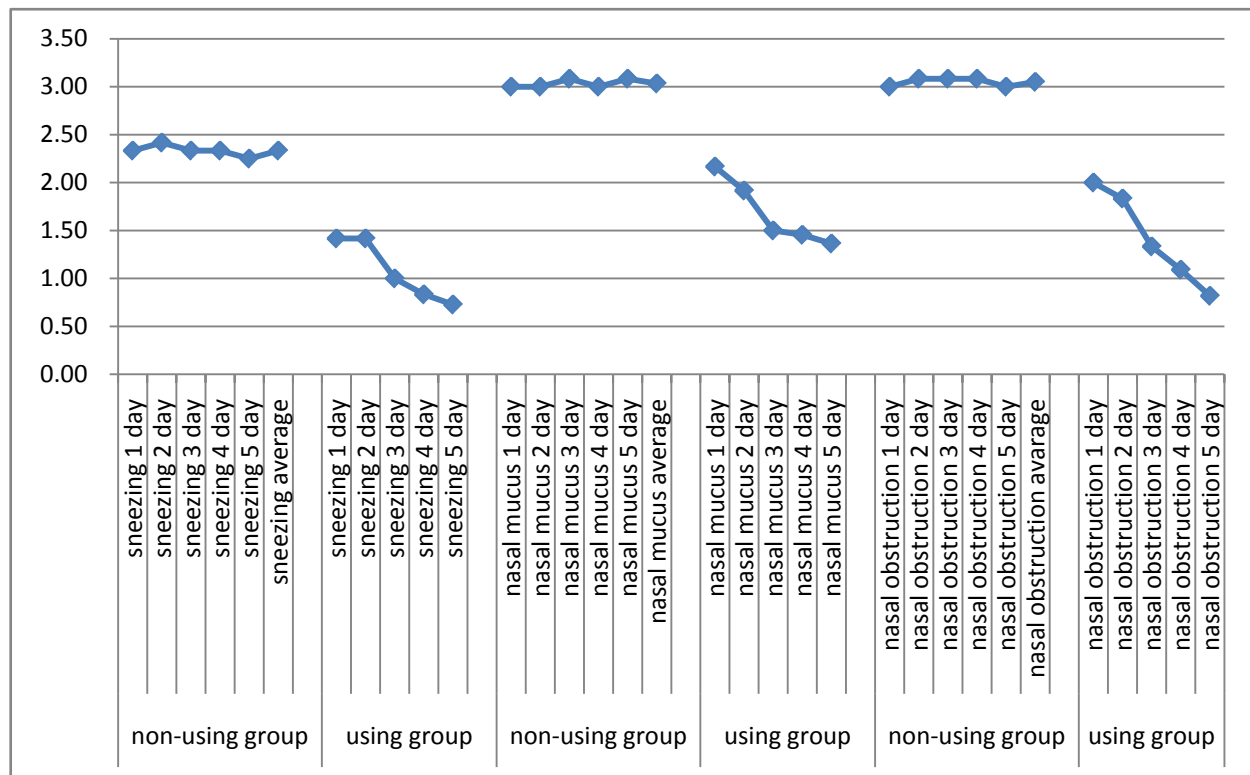
**Figure 2.** Subjective and clinical improvement in the HATS using group compared with HATS nonusing group

Table 4. HATS subjective clinical effect comparing 5 days with each other

comparision	mean value	SD Standaed deviation	95% confidence intervals		P
			Lower limit	Upper limito	
sneeing 1 day to 2 day	0.000	.603	-.383	.383	1.000
sneeing 1 day to 3 day	.417	.900	-.155	.989	.137
sneeing 1 day to 4 day	.583	.996	-.050	1.216	.067
sneeing 1 day to 5 day	.818	.751	.314	1.323	.005
sneeing 2 day to 3 day	.417	.793	-.087	.920	.096
sneeing 2 day to 4 day	.583	.996	-.050	1.216	.067
sneeing 2 day to 5 day	.818	.874	.231	1.405	.011
sneeing 3 day to 4 day	.167	.389	-.081	.414	.166
sneeing 3 day to 5 day	.273	.467	-.041	.587	.082
sneeing 4 day to 5 day	.091	.302	-.112	.293	.341
nasal mucus 1 day to 2 day	.250	.965	-.363	.863	.389
nasal mucus 1 day to 3 day	.667	1.155	-.067	1.400	.071
nasal mucus 1 day to 4 day	.545	.522	.195	.896	.006
nasal mucus 1 day to 5 day	.636	.809	.093	1.180	.026
nasal mucus 2 day to 3 day	.417	.515	.089	.744	.017
nasal mucus 2 day to 4 day	.545	.688	.084	1.007	.025
nasal mucus 2 day to 5 day	.636	.809	.093	1.180	.026
nasal mucus 3 day to 4 day	.182	.405	-.090	.454	.167
nasal mucus 3 day to 5 day	.273	.467	-.041	.587	.082
nasal mucus 4 day to 5 day	.091	.539	-.271	.453	.588
nasal obstruction 1 day to 2 day	.167	.718	-.289	.623	.438
nasal obstruction 1 day to 3 day	.667	.985	.041	1.292	.039
nasal obstruction 1 day to 4 day	.818	.982	.159	1.478	.020
nasal obstruction 1 day to 5 day	1.091	1.044	.389	1.793	.006
nasal obstruction 2 day to 3 day	.500	1.000	-.135	1.135	.111
nasal obstruction 2 day to 4 day	.727	.786	.199	1.255	.012
nasal obstruction 2 day to 5 day	1.000	1.095	.264	1.736	.013
nasal obstruction 3 day to 4 day	.091	.539	-.271	.453	.588
nasal obstruction 3 day to 5 day	.364	.674	-.089	.817	.104
nasal obstruction 4 day to 5 day	.273	.647	-.162	.707	.192

4. Considerations

4.1. Future Developments of HAT Melded into Unwoven Fabric for the Treatment of Hay Fever

With the goal of clarifying the clinical effectiveness of HATS over time as a new method of treating hay fever, we conducted an additional 5 day study in which the 12 participants reported the clinical efficacy of HATS, divided into the period without HATS use and the period with HATS use.

As a result, we saw a dramatic improvement in symptoms in all 12 cases. Additionally, statistically significant differences were detected in the point values for sneezing, runny nose, and nasal congestion when comparing groups after use of HATS to the not using HATS period.

Although improvement in sneezing was seen after day 1 of using HATS, it took several days to see symptom improvement in nasal congestion.

Though neither subjective nor clinical side effects were seen, one participant had to cease observation of HATS after the 4th day due to a feeling of discomfort in the nasal cavity.

Because no objective changes were found in blood tests for allergic reactions, the possibility that there are no immunoreactions from use is implied.

Fujii et al. [10] report that there has been a trend over the last 10 years. Nishibata et al. [11] report that the amount of Japanese cedar and hinoki cypress pollen in the air has doubled incidences of Japanese cedar hay fever over the decades since 1985. Also, Kusuki et al. [12] have indicated that the Japanese cedar hay fever incidence rate has increased in children as well. In this sense, hay fever is a major health challenge for every generation.

With this in mind, the main strong point of this treatment is the possibility of improving a condition that has been intractable for the past 20 to 30 years by treating it in a matter of days. Even with nasal congestion, which often fails to improve through prior treatments, there is a visible effect after several days of treatment. Also, one special characteristic of this treatment is the absence of side effects affecting the central nervous system that can be seen from pharmaceutical drugs, namely drowsiness. Moreover, it is possible to use this treatment on children for whom medical therapies such as laser treatments, that require anesthesia, and TCA treatments are difficult to acceptable. There is similarly a high possibility of using it in the elderly and the infirm. Moreover, because costly medical surgeries are not necessary, this process can also be used in developing countries. Its low cost makes HATS a possible method of medical treatment and relief at home. Moving forward, we also anticipate future evidence that the range of conditions in which this can be used as a preventative treatment can be expanded, as there was also a case in which itching due to allergic conjunctivitis had vanished. In this way, it is implied that, compared to medical drugs, the treatment can be used to treat allergic rhinitis from new angles. The fact that good results from the treatment can be produced without necessarily visiting the hospital and without significant medical facilities and equipment, means that the burden on patients will be minimal, a benefit for both patients and medicine overall.

4.2. The Clinical Efficacy Mechanisms of HAT Melded into Unwoven Fabric for the Treatment of Hay Fever

In grasping the physical properties of HATS, we move to estimate the mechanisms behind its clinical effectiveness in the treatment of hay fever.

The physical properties of HATS are such that electrons in the titanium oxide are excited by the energy of the silver ions. These moving electrons lead to electron holes in the proteins. These holes then react with the surrounding enclosures, generating super radicals and reactive oxygen species. The way in which these super radicals and reactive oxygen species break down the lipids of cell walls into water are indicated by the photocatalytic principles of anatase-type titanium.

Keeping this principle in mind, the super radicals and reactive oxygen species that are generated by unwoven

fabric with HAT break down the pollen proteins within the nasal mucosa; the proteins of the antigens of pollen, mites, and house dust through the power of oxidation-reduction. This physically prevents the allergic reaction in the nasal mucosa and prevents the incidence of rhinitis symptoms. In fact, it has been reported that HAT, when added to fabrics such as hand towels, is capable of destroying germs such as staphylococcus aureus and pathogenic escherichia coli as well as preventing their growth on such fabrics. [9]

Hay fever, as an example of an I-type allergic disease, based on the reaction between the antibody IgE cell walls of mastocytes MC and antigens, brings about an excitement in the chemical mediators of the mucosal tissue by releasing specific granules MC. Through unwoven fabric with HATS, we estimate that its medical effectiveness on symptoms of rhinitis is due to the contact between unwoven fabric with HAT powder and the nasal mucosa. When this occurs, we assume that the proteins of the pollen antigens on the surface of the nasal mucosa are denatured and broken down by getting rid of the antigenicity of the allergens and reducing the number of antigens, reducing contact with allergic immune cells. As such, we estimate the high possibility that this treatment can avoid antigen-antibody allergic reactions as well as prevent an immunoreaction in advance. Moreover, we suppose the possibility that even the very small number of immune response receptors in the nasal concha are denatured and the immunoreaction caused by the information exchange between the antigen-presenting cells and the antigens is rendered inactive.

4.3. Future Development and Research Challenges of the Effectiveness of HATS in Treating Hay Fever

This study was the first in the world to the effectiveness of HATS as a medical treatment in adults and we anticipate that reproduction studies will further verify and generalize its effectiveness. Moreover, if the detailed mechanisms and long term safety of using HATS can be established and it can be used as a medical treatment at home, it would contribute greatly to stabilizing medical expenses in the future.

The task for research on the efficacy of HATS moving forward will be to verify the presence of long term side effects along with clarifying the mechanisms behind its clinical effectiveness on a molecular level. In addition, it is necessary to clarify the cytokine kinetics of TH2, eosinophil infiltration, the presence of multilayeration in nasal mucosa, mucin production, serum IgE, and IL-4, IL-33 for cellular kinetics on the pathological level.

Also, for the future development of HATS, in order to be able to utilize it as a simple method of home care, we expect that the targets persons of future studies will be more numerous and more varied in age. Verification of long term effects and side effects along with additional randomized comparison studies, should also be included in future HATS development.

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