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A Nasally Applied Cellulose Powder in Seasonal Allergic Rhinitis in Adults with Grass Pollen Allergy: A Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study

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Key Words
Allergic rhinitis · Barrier protection · Cellulose powder · Clinical trial · Grass pollen

Abstract
Background: A nasally applied cellulose powder is increasingly used in many countries as a remedy for allergic rhinitis. In 2009, a 4-week study in birch pollen-allergic children showed a reduction in nasal symptoms. The best effect occurred on days with lower pollen counts. The present study in grass pollen-allergic adults used the same basic design. ***Methods:*** In May 2013, a double-blind, placebo-controlled study was conducted in 108 patients with allergic rhinitis due to grass pollen (18–40 years of age). SMS on mobile phones were used as reminders of treatment and reporting of symptom scores. ***Results:*** We found significant reductions in severity scores for sneezing, runny nose, stuffy nose and symptoms from eyes and lower airways, both separately and together (all $p < 0.001$). Reflective opinion of effect and guess on treatment at follow-up visits (both $p < 0.001$) confirmed a high efficacy. No clinically significant adverse effects were reported. ***Conclusions:*** The product provided significant protection against all seasonal allergic rhinitis symptoms from both upper and lower airways during the grass pollen season in an adult population. The magnitude and scope of efficacy support the use of the product as an early choice in the treatment of allergic rhinitis.
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Introduction

Allergic rhinitis is a very common chronic condition. In the United States alone, it affects 65 million people [1]. The prevalence of allergic rhinitis increases with age [2], peaking in teenagers and young adults, and allergy to pollen is a predominant cause [3]. The adverse consequences for the individuals include impacts on their educational career [4] and substantial suffering [5]. A range of remedies and treatments is available on prescription and over the counter. Nasal steroid sprays are considered most efficacious but many sufferers are reluctant to take them due to fear of adverse effects.

An inert cellulose powder (Nasaleze®) has been on sale as a medical device against hay fever in Europe since 1994. It is applied in the nostrils by a simple puffer device. The mechanism of action of the cellulose is through a reaction

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with moisture on the mucous membrane, which forms a gel layer. This protective barrier on the nasal mucosa helps to prevent the contact between inhaled allergen and mucosal cells [6].

A double-blind, placebo-controlled study of birch pollen-allergic children in Sweden showed a significant alleviation of runny nose and total nasal symptoms [7]. The best effect was seen on days with pollen counts defined as low or moderate. Our hypothesis was that the trial product in the given dosage should be even more efficacious in grass pollen allergy, a more common problem in a global perspective. In contrast to birch pollen, which is dispersed during a limited period of often intense flowering, grass pollen is often present in the air for several months, and days with low-moderate values generally predominate [7, 8]. The present study aimed to assess the efficacy of the powder in grass pollen rhinitis in young adults on the European continent using the same basic design as the Swedish study in children.

Methods

Research Design

The study was performed at the University Clinics of Kharkov and Dnepropetrovsk, Ukraine, in May 2013, which are urban areas situated in a region dominated by semiarid grassland, which is to a large degree converted into agricultural land. The growing season starts in April, and grass flowering mainly occurs in May and June. A power calculation based on the study in children [7] corresponded to the number of subjects obtained. Subjects 18–40 years of age (n = 108) were recruited locally among the patients already followed at respective clinics. All of them had a history of typical nasal symptoms of seasonal allergic rhinitis (SAR) during late spring to early summer. At the first appointment, patient history was scrutinized and severity was assessed. To exclude severe disease, we did not accept patients with previous use of nasal steroids or an assessed current need for nasal steroids. Subjects should not have perennial symptoms or a history of asthma. They were tested with a blood sample for ImmunoCAP specific IgE for timothy grass pollen and birch pollen, with >0.35 kU/ml counted as positive. A positive test for timothy grass pollen was required for inclusion.

The patients were randomly assigned to active or placebo groups using an identical device to be puffed in each nostril 3 times daily. The nasal powders were supplied in plastic containers, which deliver the powder from a nozzle when squeezed. The exact amount delivered is not standardized and the variation in the patterns of deposition in the nose is not known. The placebo was a lactose powder with the same particle size, appearance and the same tinge of mint taste as the cellulose powder.

After emergency contacts with the investigators, rescue medication could be obtained. It consisted of oral antihistamine, loratadine (10-mg tablets) and sodium cromoglycate eye drops. Each subject obtained oral and written instructions about the SMS. The SMS reporting of symptoms started with a 3-day run-in period before the treatment and continued during the 4-week treatment period during the grass pollen season.

Three times a day the patients were reminded by SMS to take their nasal puffs and were asked to confirm the intake by a response SMS. In the evening, they were asked about the severity of symptoms during the preceding day from the nose, eyes and lower airways and to answer with a figure from 1 to 6, corresponding to (1) *no trouble at all*; (2) *little trouble*; (3) *moderate trouble*; (4) *rather much trouble*; (5) *much trouble* and (6) *very much trouble*. For the nose, scoring of sneezing, running nose and blocked nose were reported. For the eyes and lower airways, only a concluding figure was used.

In the registration, a question on the use of rescue medication was added daily.

At a concluding appointment after the treatment period, the subjects were asked about their global opinion of the efficacy: *no effect*, *good effect* or *very good effect*. They were also asked whether they believed they had obtained the active substance or placebo. Adverse events including discomfort related to the treatment were affirmed or denied.

Pollen Counts

Daily average grass pollen concentration was recorded with a nonstandard volumetric spore trap, which was situated on a balcony in an urban environment near the center of Kharkov.

Statistical Methods

For each question, the mean score was calculated for the whole 28-day period for every subject. Mean values for the sum of all scores as well as the sum of the nasal scores were also calculated. The scores from the two treatment groups were then compared using t tests. The group comparison of reflective opinions and the guess on obtained medication at the follow-up visit were assessed using the χ^2 test.

The study was approved by the local ethics committees at the respective hospitals.

Results

For the study, 108 patients were recruited. One subject in the placebo group withdrew during the 1st day of treatment because of nasal irritation and was the only patient not included in the full analysis set. One further subject in each group was tainted with protocol violations but analyses with exclusion of these did not cause discernible changes of the results. Therefore, all analyses presented were based on the full analysis set of the population. The group characteristics (table 1) were equivalent except for a slightly higher age in the active group. Less than half of the participants in both groups had a positive test for birch pollen in addition to the grass pollen allergy. There were more female than male subjects.

An excellent compliance was obtained in that the subjects had a very good adherence to the requirements of the study, such as reporting their symptoms. Missing replies

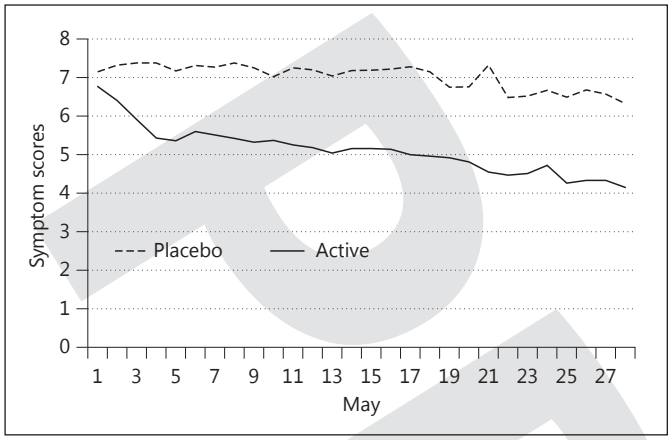

Fig. 1. Sum of nasal symptoms day by day in the respective groups (full analysis set, n = 107). Significance of daily group differences: May 1, nonsignificant, May 2, $p < 0.05$, May 3–28, $p < 0.001$.

were not replaced but just omitted. Still, no analysis was based on less than 50 answers from the placebo group and 51 from the active group. The severity scoring during May 1–28 is shown in table 2. The mean scores were generally in the low range. Over the entire 4 weeks, there was a highly significant reduction in all symptoms from the nose, eyes and lower airways in the active group compared to the placebo group both for separate symptoms, total nasal symptoms, and all symptoms from upper and lower airways taken together.

Total nasal scores each day are shown in figure 1. The fluctuations in severity were relatively small. A 3-day run-in served as a technical adjustment period and no more than 66 subjects participated any day; the scores were virtually identical in the two groups. The following 3 days, the difference between the groups increased markedly, followed by a slightly increasing divergence between the groups with duration of treatment. Except for the 1st day, the group differences were significant (day 3 and later, all $p < 0.001$).

At the follow-up visit, the global appreciation of treatment was in strong and significant favor of the active treatment (table 3). The subjects also guessed which treatment they had received; guessing that the active treatment was received was 10 times more common in the active group than in the placebo group (table 4).

There were only a few signs of adverse events reported during the treatment period (active group 1) or at the follow-up visit (placebo group 4, active group 5); almost all of these concerned nasal irritation and none was severe or serious. Correspondingly, only 1 patient in each group

Table 1. Group characteristics for the full analysis set

Characteristics	Placebo	Active	Total
Mean age, years	24.5	29.3	26.9
Positive test for pollen, n			
Birch	24 (45.3%)	23 (42.6%)	47 (43.9%)
Timothy grass	53 (100%)	54 (100%)	107 (100%)
Gender, n			
Female	34 (64.2%)	34 (63%)	68 (63.6%)
Male	19 (35.8%)	20 (37%)	39 (36.4%)

Table 2. Total of symptoms scored retrospectively at night for 4 weeks

Question	Placebo (n = 53)	Active (n = 54)	p value
Sneezing	2.31	1.65	<0.001
Runny nose	2.37	1.75	<0.001
Blocked nose	2.32	1.76	<0.001
Eye symptoms	2.18	1.59	<0.001
Lower airways	1.92	1.44	<0.001
Sum of nasal symptoms	6.99	5.16	<0.001
Sum of all symptoms	11.1	8.19	<0.001

Table 3. Global opinion about the effect of treatment reported at follow-up

Opinion	Placebo, n	Active, n
No effect	28 (52.8%)	4 (7.4%)
Good effect	12 (22.6%)	32 (59.3%)
Very good effect	1 (1.9%)	15 (27.8%)
Don't know	12 (22.6%)	3 (5.6%)
Group differences, $p < 0.001$.		

Table 4. Patient's guess about treatment received reported at follow-up

Guess	Placebo, n	Active, n
Active	4 (7.5%)	44 (81.5%)
Placebo	26 (49.1%)	4 (7.4%)
Don't know	23 (43.4%)	6 (11.1%)
Group differences, $p < 0.001$.		

received emergency medication in terms of antihistamine tablets, and none received eye drops.

Pollen Counts

The daily average grass counts were low and never exceeded 25 grass pollen grains/m^3. The situation of the trap was not optimal to monitor the regional pollen load adequately, but the results confirm the presence of grass pollen in the air throughout the study period.

Discussion

Since 1994, this British remedy for hay fever has been on sale as a medical device and it has been increasingly used in many parts of the world. In various previous studies, the inert cellulose powder has been free from clinically significant adverse effects [7, 9, 10], making the product particularly attractive for over-the-counter use and self-medication. A previous double-blind, placebo-controlled study of birch pollen-allergic children in Sweden showed a significant alleviation of runny nose and total nasal symptoms [7]. In a previous study on adults with grass pollen rhinitis, there was a reduction in rescue medication but no decrease in symptom scores [9]. The dosage of the trial product in this study varied, however, and was generally lower than in the Swedish study in children as well as in the present study.

The use of SMS on mobile phones for reminders and reporting of symptom scores was an original feature in the Swedish children's study that we wanted to test in another clinical context. The continuous and instantaneous reporting of symptom scores into a database speeds up the study procedure and allows a continuous supervision of the study progress on an individual level. This use of mobile phones implies a further development of e-diaries, a methodology with clear benefits compared to paper records in terms of compliance and data safety [11]. The high response rate in symptom reporting and other aspects of the study may be due to both the interactive design and, as we were told, a strong historical tradition of compliance in the area.

Population

The study population was drawn from patients presenting to university hospital clinics. All subjects in the study had a laboratory-confirmed allergy to grass pollen of mild/moderate severity; exclusion criteria were a history of asthmatic or perennial symptoms at inclusion or previous use or assessed need of nasal steroids.

Dosage

The fixed dose of 3 times daily was the same as in the Swedish children's study and is based mainly on clinical experience. For the period of most intense pollen exposure, it may have been somewhat insufficient, but for the more moderate exposure that is most common during grass pollen seasons in many temperate areas [7, 8] it may be more adequate. Another reflection is whether the evening dose really was necessary when the daily pollen exposure was finished; morning and afternoon dosage may have been sufficient. On the other hand, the inert nature of the product allows for considerable dosage increase on demand.

Efficacy

There was a strong and highly statistically significant reduction in all symptom scores analyzed both separately and together. The scoring was also relatively low in the placebo group, which might depend both on the severity of the disease and the pollen exposure. The relief of ocular and bronchial symptoms is considered secondary to the nasal effects in line with the concepts of 'united airways' [12] and naso-ocular reflex [13]. It might be that a certain threshold of nasal disease is necessary in order to elicit the secondary organ effect and that the very low level of nasal symptoms in the active group largely remained below this hypothetical threshold.

The reflective opinion on the effect and guess on treatment obtained was similarly convincing and corroborates the picture of a pronounced clinical effect.

The symptom reduction was larger than in the corresponding study in Swedish children with birch pollen allergy both in terms of absolute scores and relative reduction [7]. One apparent difference between the studies was the pollen seasons. The Swedish birch pollen season in 2009 was intense [7] and the grass pollen load in Kharkov during the present study was light, a fact that probably also explains the small day-by-day fluctuation in mean symptom scores in the present study compared to those reported in other studies [7, 14, 15].

In the study of children in 2009, there was an increased efficacy in periods with lower pollen counts, which can be interpreted in support of the opinion that the product is most appropriate for mild/moderate disease. Maintaining relative freedom from nasal symptoms may be of particular importance for this kind of treatment. Any breakthrough of nasal symptoms may readily reduce the potential action of the product; a blocked nose may obstruct the deposition, a sneezing and runny nose may throw it out. There are no restrictions other than convenience in the

concurrent use of other remedies [7]. Such combinations may in certain severity grades be necessary to maintain the wanted and optimal freedom from symptoms.

Another aspect of the efficacy is demonstrated in the day-by-day view of nasal symptom scores. There is an apparent long-term increase in efficacy, which may support the general advice to start the treatment early, sometimes even before the pollen season has begun.

Nasal steroid sprays are recommended as the first choice in the international ARIA (Allergic Rhinitis and Its Impact on Asthma) guidelines [16]. These guidelines, however, do not discuss non-pharmacological products, probably due to the scarcity of studies of acceptable scientific quality in this context. The degree of symptom reduction in the present study is comparable with a usual result in placebo-controlled studies of nasal steroids and oral antihistamines [17, 18]. Hence, considering the complete absence of significant adverse effects and, with a reservation for the huge imbalance in the number of studies performed compared with intranasal steroid treatment, we suggest that this kind of barrier protection may be tried as an early choice in the treatment of SAR, particularly in the mild/moderate stages of the disease, corresponding to the selected contingent in the present study; our inclusion criteria selected cases with mild/moderate disease, and the degree of severity also comprised the majority of patients with allergic rhinitis [4].

Furthermore, the ARIA guidelines state that allergen avoidance should be part of the management strategy [16]. From a biomedical point of view, the use of cellulose powder is an avoidance measure acting locally on a crucial point of the pathogenetic chain. For many sufferers, a number of psychosocial adverse effects are related to general environmental measures. If this can be averted by the use of a handy spray it may be very valuable. There are other effects of allergen exposure which are related to natural tolerance induction or protection from sensitization [19]. Reduction of the amount of environmental allergen exposure may reduce such a potentially beneficial development. The use of this product implies a targeted avoidance measure for the intranasal route, but it allows all other mucosal allergen exposure. Therefore, theoretically, it may disturb a natural tolerance induction less than gross environmental measures would.

Other Non-Pharmacologic Treatments

There are other local nasal treatments acting physically. The best known is intranasal irrigation with saline [20]. A gel formulation from seawater using a barrier concept was efficacious against allergic rhinitis in an experimental setting [21]. Another product based on the barrier principle, an oil emulsion, has shown a protective effect in a pollen challenge study but with a mode of treatment not feasible for clinical conditions [22]. The magnitude and scope of efficacy in the present study, however, prevails in comparison.

Pollen Exposure

The choice of grass pollen in this study was partly because it is probably the most common allergen in SAR in Europe and globally. Based on the profile in children with a better effect of the product in periods of lower birch pollen exposure and the many days with low/moderate pollen counts that are common during the generally long grass pollen seasons [7], we also expected a high efficacy in grass pollen SAR. The pollen counts from the non-standard volumetric spore trap were low and never exceeded 25 grass pollen grains/m^3. The construction of the trap and its location, however, were not optimal to register the regional pollen load adequately, but the counts confirmed the presence of grass pollen in the air throughout the study period.

Conclusions

We could demonstrate that the efficacy of a cellulose powder in the treatment of birch pollen SAR proven in children was even more pronounced in grass pollen SAR in adults, both in terms of magnitude and scope of symptom reduction. All nose, eye and lower airway symptoms were substantially alleviated. As grass pollen allergy is a very common condition all over the world, we believe that this product will provide an increasingly significant contribution to the scope of treatments available today.

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PROOF

过敏与免疫学档案 2014;163:313–318

纤维素粉末用于治疗成人草花粉引起的季节性过敏性鼻炎的双盲安慰剂对照试验

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关键词：过敏性鼻炎；隔离屏障；纤维素粉末；临床试验；草花粉

摘要

背景：越来越多的国家使用纤维素粉末用于治疗过敏性鼻炎。2009 年，我们对桦树花粉过敏儿童作了一个 4 周疗程的试验，结果表明，纤维素粉末能够有效改善过敏性鼻炎引起的症状，其中在低水平花粉计数时期，改善效果最显著。本试验，我们采用 2009 年针对儿童试验的基本设计，对草花粉过敏的成人进行试验研究。

方法：2013 年 5 月，对草花粉过敏的 108 名患者（18-40 岁）进行双盲安慰剂对照试验，患者通过手机短信的方式报告症状积分。

结果：纤维素粉末可以显著减少打喷嚏、流鼻涕、鼻塞以及眼部和呼吸道中的症状积分和症状总积分（P<0.001）。随机访问调查方式也证实了纤维素粉末的显著疗效（P<0.001）。试验中，没有任何关于副作用的报告。

结论：纤维素粉末能够显著改善季节性过敏性鼻炎引起的各种症状，从纤维素粉末对过敏性鼻炎症状改善的范围和程度来看，建议患者最好在患病早期就使用纤维素粉末。

简介

过敏性鼻炎是一种非常普遍的疾病，在美国，就有 6500 万过敏性鼻炎患者。过敏性鼻炎患者随着年龄的增长而增加，目前，青少年时期也成为患病高峰期。过敏性鼻炎主要是由花粉引起的，给患者带来了长期的痛苦。医院或者药房可以买到相应的治疗药物，类固醇类的鼻喷剂被认为是最有效的，但许多患者考虑到它的副作用，很少购买。

惰性纤维素粉末从 1994 年起作为枯草热治疗的医疗器械在欧洲上市。它是一种简单的鼻喷器械。纤维素粉末的作用机制是粉末进入鼻腔后与水汽结合，在鼻粘膜表面形成凝胶，也即在过敏原和鼻粘膜间形成一道隔离屏障，阻挡过敏原等颗粒进入机体。

在瑞典，对桦树花粉过敏儿童的双盲安慰剂对照试验表明，纤维素粉末能够显著缓解过敏性鼻炎引起的症状，其中在低水平或者中等水平花粉计数时期，改善效果最为显著。现在的假设是纤维素粉末对改善草花粉过敏症状，疗效更加显著。桦树花粉传播时间短，花粉计数水平高，而草花粉有几个月的传播时间，花粉计数水平在低、中等水平。现在的研究目的是采用 2009 年针对儿童试验的基本设计，对草花粉过敏的成人进行试验，来评价纤维素粉末的治疗效果。

方法

研究设计

2013 年 5 月，在半干旱乌克兰地区的哈尔科夫和第聂伯罗彼得罗夫斯克大学诊所，我们开始本试验。本地区的草生长季始于四月，开花季主要在五月和六月。检验效能的计算同儿童试验设计一样，基于受试者的数量。本试验招募到 108 名本地受试者（18-40 岁），被诊断已患有过敏性鼻炎，而需要首先确认的是，每位受试者必须有季节性过敏性鼻炎（SAR）典型症状史。本试验没有招募过敏性鼻炎特别严重而需要使用或正在使用类固醇类鼻喷剂的患者，以及具有常年性哮喘病史的患者。受试者经过 CAP 检测系统测试，确认血样中提牧草和桦树过敏原相应的特异性抗体含量，含量大于 0.35kU/mL 的，表示为阳性患者。本试验要求受试者必须患有提牧草过敏引起的过敏性鼻炎。

患者被随机分配到治疗组和安慰剂组。我们使用相同的塑料瓶包装治疗剂和安慰剂，使用时通过挤压瓶身使粉末进入鼻腔。患者在使用过程中无法知悉使用

的是哪种产品。本试验要求患者每天使用 3 次，每次使用的剂量大小没有规定。安慰剂为乳糖粉末，具有同纤维素粉末相同的颗粒大小、外观以及薄荷味特征。

必要时，患者联系研究者之后可以使用急救药物，如口服的抗组胺药氯雷他定（10mg/片）和滴眼剂咳乐钠。患者在试验 3 天前及试验 4 周期间通过手机短信方式发送症状报告。

研究者每天发送手机短信确认患者当天是否用药。晚上，患者报告前一天症状的改善程度，症状包括鼻部症状（打喷嚏、流鼻涕、鼻塞）以及眼部和呼吸道症状。症状积分 1-6 分分别表示为：1-无症状，2-轻度症状，3-中度症状，4-症状明显，5-症状非常明显，6-症状极其明显。患者如有使用急救药物，也需要登记报告。

4 周试验后，患者需要对受试产品作一个整体的效用评价，包括无效、有效、非常有效 3 种评价，以及产品不良事件的报告。

花粉计数

在哈尔科夫市中心附近的阳台上，使用非标准孢子捕获法，每日记录草花粉浓度。

统计方法

计算每位患者 28 天试验的单个症状的平均分，所有症状的总的平均分以及鼻部症状总的平均分。两组试验比较使用 t 检验法，随机访问调查方式产品比较使用 x^2 检验法。

结果

本试验招募了 108 位患者，其中一个安慰剂组的患者，在第一天的试验中由于鼻腔刺激原因而退出本试验；有一位受试者违反了协议规定，但分析结果没有明显改变，因此也包含在本试验的整体数据分析中。患者的一些基本资料见表 1。从表 1 中可以看出，治疗组的平均年龄比安慰剂组稍微高一点，每组将近一半的患者是桦树花粉过敏人群，每组患者人群中女性要比男性多。

表 1. 患者人群基本情况

基本情况（n=107）	安慰剂组（n=53）	治疗组（n=54）	全部
平均年龄	24.5	29.3	26.9
过敏原检测			
桦树	24（45.3%）	23（42.6%）	47（43.9%）
提牧草	53（100 %）	54（100%）	107（100%）
性别			
女性	34（64.2%）	34（63%）	68（63.6%）
男性	19（35.8%）	20（37%）	39（36.4%）

参与试验的患者全部按照协议进行，保证了数据的准确性。安慰剂组中每天每个症状的积分报告都超过 50 份，治疗组中每天每个症状的积分报告都超过 51 份。5 月 1 号至 5 月 28 号，患者各症状积分情况见表 2。从表 2 可以看出，症状的平均分数都在较低的水平，而治疗组相对于安慰剂组，所有症状都有非常显著地改善。

表 2. 患者在 4 周期间各症状平均积分情况

症状	安慰剂组（n=53）	治疗组(n=54)	P 值
打喷嚏	2.31	1.65	<0.001
流鼻涕	2.37	1.75	<0.001
鼻塞	2.32	1.76	<0.001
眼部症状	2.18	1.59	<0.001
呼吸道	1.92	1.44	<0.001
鼻部症状总和	6.99	5.16	<0.001
所有症状总和	11.1	8.19	<0.001

患者每天的平均鼻部症状积分总和见图 1。从图 1 可以看出，两组症状积分波动程度相对较小，相比之下，治疗组症状积分波动更明显。5 月 1 日前 3 天的调整时期，两组的症状积分基本相同，5 月 1 日后，两组的症状积分产生明显差异，也即除了 5 月 1 日第一天以外，其他日期都产生了差异显著（第 3 天及之后，所有 P 值<0.001）。

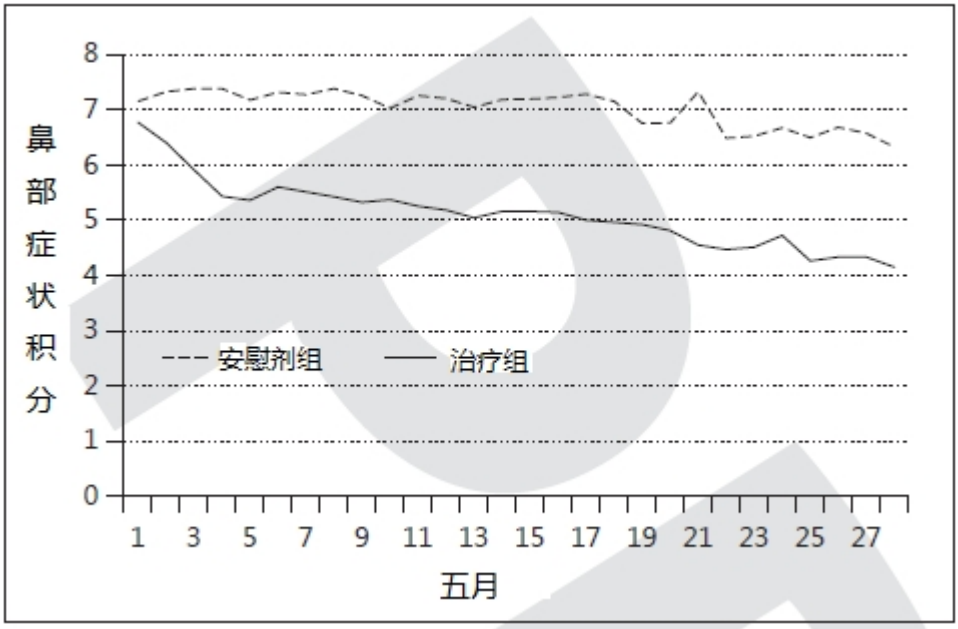

图 1.患者每天平均鼻部症状积分总和（n=107），每日显著性差异情况：5 月 1 日，没有显著性差异；5 月 2 日，P<0.05；5 月 3 日-28 日，P<0.001。

在随机访问调查中，治疗组中绝大部分患者对受试产品疗效持肯定态度(见表 3)。治疗组中认为产品是纤维素粉末的人数比认为是安慰剂的人数多了 10 倍（见表 4）。

表 3. 随机访问调查中，患者对各自受试产品治疗效果的意见

意见	安慰剂组（n=53）	治疗组(n=54)
无效	28（52.8%）	4（7.4%）
有效	12（22.6%）	32（59.3）
非常有效	1（1.9%）	15（27.8）
不知道	12（22.6%）	3（5.6%）
组间差异，P<0.001		

表 4. 随机访问调查中，受试者对受试产品类别的判断

判断	安慰剂组（n=53）	治疗组(n=54)
纤维素粉末	4（7.5%）	44（81.5%）
安慰剂	26（49.1%）	4（7.4%）
不知道	23（43.4%）	6（11.1%）
组间差异，P<0.001		

试验过程中，几乎没有不良事件的报告，偶有轻微地鼻腔刺激报告，其中也只有一个患者在试验过程中使用了急救抗组胺药物。

花粉计数

试验过程中，每天的平均花粉计数值较低，在每平米 25 个草花粉粒以下。花粉计数较难监控，但计数结果也反映一定的真实性。

讨论

该粉末从 1994 年起作为医疗器械在英国上市，用于治疗枯草热疾病，现在越来越多的国家开始使用它。多方面的研究试验证明，该粉末对鼻腔不会照成不良影响，因此消费者可以在药店或者网站自己购买获得。在瑞典，对桦树花粉过敏儿童的双盲安慰剂对照试验表明，纤维素粉末能够显著缓解过敏性鼻炎引起的症状。之前也有报道纤维素粉末可以有效减少过敏性鼻炎成人患者急救药物的使用量。

使用手机短信，可以提供研究者原始的数据，进一步的发展可以使用手机电子日记的方式，患者对症状有一个连续地、实时地记录，形成的整体数据库可以加快研究的进程，研究者对患者的监管也更加高效。

患者

本研究从大学医院诊所招募到受试者，每一位受试者都通过实验确认存在中等程度的草花粉过敏疾病，本试验没有招募过敏性鼻炎特别严重而需要使用或正在使用类固醇类鼻喷剂的患者，以及具有常年性哮喘病史的患者。

用量

主要是基于之前产品使用的临床经验，同在瑞典对桦树花粉过敏儿童的双盲安慰剂对照试验一样，每天固定使用 3 次。对于花粉计数水平高的时期，也许每

天 3 次使用量还不足够，但对于花粉计数水平中等或以下的时期，每天 3 次的使用量已足够。另一方面是考虑晚上的那次使用是否必要，因为受试者主要是在白天接触花粉过敏原，然而，纤维素粉末惰性、天然的性质，允许受试者可以增加产品的使用量。

功效

纤维素粉末可以非常显著地减少打喷嚏、流鼻涕、鼻塞以及眼部和呼吸道中的过敏症状积分和症状总积分。和其他研究报道试验相比，安慰剂组的患者症状积分也相对较低，这和受试者人群草花粉过敏程度不是特别严重相吻合。本试验中，也统计了眼部和支气管症状的改善效果，因为考虑到“同一气道”的概念，即眼部和支气管症状的产生也许就是从鼻部症状的发生开始的。

同样地，随机访问调查方式也证实了纤维素粉末显著的改善效果。

本试验中受试者症状改善程度比对桦树花粉过敏儿童试验更加显著，绝对症状积分也更小。两者明显的区别是花粉计数水平不一样，桦树花粉过敏儿童试验中，花粉计数水平很高，而本试验的草花粉计数水平较低。这也很好地解释了本试验同其他试验报道相比，每天的平均症状积分波动不大的原因。

在 2009 年，从桦树花粉过敏儿童试验中可以了解到，低花粉计数水平时期，纤维素粉末疗效更加显著。这也许可以理解为纤维素粉末对中等症状过敏性鼻炎患者的治疗效果最佳。因为保持相对平和的鼻炎症状也许对纤维素粉末的治疗非常重要，任何一个鼻炎症状的发生都有可能降低纤维素粉末的治疗效果，如鼻塞也许导致纤维素粉末的堆积，打喷嚏和流鼻水也许导致一部分纤维素粉末流失。纤维素粉末和其他药物协同使用非常方便，鼻炎症状特别严重的患者可以考虑这种方式，这样可以保持相对平和的鼻炎症状，使产品发挥最大的疗效。

从每天平均鼻部症状积分图上可以了解到纤维素粉末对过敏性鼻炎症状有一个持续地治疗改善效果。这样可以建议过敏性鼻炎患者提早使用产品，甚至在花粉季节还未开始就可以开始使用。

“过敏性鼻炎及其对哮喘的影响（ARIA）2010”治疗指南中，类固醇类鼻喷剂被推荐为治疗过敏性鼻炎的第一选择药物，然而治疗指南没有考虑无药理学的治疗产品，也许因为在这个领域，无药理学产品缺乏可接受的的研究报道。通过目前的研究报道可以看出，纤维素粉末对过敏性鼻炎症状的改善程度可以跟类固醇

类鼻喷剂和抗组胺类口服药物相媲美。因此，考虑到纤维素粉末相比之下完全没有副作用的因素，我们建议它可以作为治疗过敏性鼻炎的早期选择产品，特别是中等过敏性症状的患者。

进一步地，“过敏性鼻炎及其对哮喘的影响（ARIA）2010”治疗指南中阐释了过敏原的隔离是治疗过敏性鼻炎的一部分，从生物医学的角度看，纤维素粉末的使用，是过敏性鼻炎致病链中阻隔过敏原发病体的关键因素。许多患者对产品的不良影响因素认知也包含环境方面的因素，因此，便利地鼻腔喷剂更易被患者所接受。人体受花粉过敏原刺激会激发机体产生免疫耐受诱导作用和致敏的保护作用，降低人体对花粉过敏原的接触也许也会降低人体对这种潜在机能的发展，然而纤维素粉末只针对一部分过敏原的阻隔，因此，它不会降低机体的防护机能，其他过敏原可以发展机体激发相应的防护潜能。

其他非药物治疗方法

其他非药物靶向治疗过敏性鼻炎的方法中，生理性盐水鼻腔冲洗剂最为熟知，可以缓解过敏性鼻炎的症状。其他基于阻隔原理的产品，如油乳胶，也有一个很好的保护效果，然而产品使用非常不便。总体地，从目前对过敏性鼻炎症状改善的范围和程度来看，纤维素粉末相比其他产品更占优势。

花粉过敏原

本试验选择草花粉过敏原是基于其在欧洲和全球过敏性鼻炎中是最为普遍的过敏原。从桦树花粉过敏儿童试验中可以了解到，低等、中等花粉计数水平时期，纤维素粉末疗效更加显著。而从整个长的花粉季时期可以看出大部分天数是低、中等花粉计数水平时期。试验过程中，每天平均花粉计数值较低，在每平米25个草花粉粒以下。花粉计数较难监控，但计数结果也反映一定的真实性。

结论

通过试验证明，纤维素粉末能够全面改善桦树花粉过敏儿童的过敏性鼻炎症状，也能够全面改善草花粉过敏成人的过敏性鼻炎症状，鼻部、眼部、呼吸道部位的症状都得到了显著地改善。草花粉过敏原在全球都非常普遍，我们相信纤维素粉末能够发挥越来越大的作用。

致谢