Efficacy and safety of medical device Nasaval in prevention and treatment of persistent allergic rhinitis in adults and children

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Summary

This paper describes the findings of an open non-comparative clinical study of efficacy and safety of an ultra-disperse cellulose preparation in prevention and treatment of persistent allergic rhinitis (AR).

Introduction

Allergic rhinitis is a condition characterized by allergic inflammation, resulting from contact of allergens with nasal mucosa and associated with one or more of the following symptoms:

1. Nasal congestion
2. Nasal discharge
3. Sneezing
4. Nasal itching (1).

AR is one the most widespread allergic diseases. Not infrequently, it precedes other allergic disease, such as atopic dermatitis and bronchial asthma. Active manifestations of AR have a significant impact on the patient's quality of life, interfere with sleep and rest, and decrease capacity for work.

Methods of preventing and treating AR, which are currently available in an allergist's armamentarium, are not completely effective, are time-consuming, costly and associated with a number of side effects. The challenge of finding adequate means to prevent and treat AR is further aggravated in children and pregnant women, due to the lack of evidence confirming the safety of such medications in these categories of patients.

The usage of ultra-disperse cellulose may become a method of choice to prevent and treat AR.

After the registration and approval of microcellulose powder for medical application in Russian Federation, this open non-comparative study was conducted in 2009 to investigate the effectiveness and safety of medical device Nasaval in prevention and treatment of allergic rhinitis.

Study design

Forty eight patients with persistent allergic rhinitis were included into the study. The group consisted of 25 adults and 23 children of both genders, aged 2 to 62 years. The patients were examined weekly over the observation period of 4 weeks. Children were accompanied by their parents during their visits to the trial centre. At study enrollment, the patients were asked for their verbal and written informed consent, according to a form developed for this study in

accordance with the Helsinki Declaration. One of the parents was requested to sign the consent form for an under-aged child.

In accordance with the study protocol, an individual record form was filled out for each patient and included passport data, initial case history and examination findings as well as the findings of follow up visits during the course of the study.

- The patients received one puff Nasaval into each nostril 3 times a day over the course of 4 weeks. In case of insufficient effect they were allowed to use the preparation more frequently.
- The patients visited the investigator weekly, i.e. 4 times during the study period. The severity of AR symptoms and the tolerability of the product were assessed during each visit.
- The patients filled out a quality of life questionnaire and a visual analogue scale during initial and final visits.
- The effectiveness of treatment was assessed by investigator together with the patient (in case of children together with the parents) during the final visit.
- The patients were maintaining a diary with daily records of severity of AR symptoms, any side effects and need for other medications.

Subjects

Patients, who were enrolled into the study, came to the initial visits with a confirmed diagnosis of AR, supported by the findings of allergen tests and rhinoscopy.

Figure1. Charasteristics of the study group.

Parameter	**Adults n=25**	**Children n=23**
Age	**18 to 62 years Mean - 40.2 years.**	**2 to 18 years Mean - 10.8 years**
Duration of AR	**13.8 years (2-40)**	**5.75 years (1-15)**
Bronchial asthma	**68%**	**24%**
Atopic dermatitis	**-**	**8%**
Pollenosis	**64%**	**79%**
Epidermal allergy	**82%**	**79%**
Nutritional allergy	**36%**	**33%**
Family history of allergy	**68%**	**92%**
Drug allergy	**23%**	**12%**

Figure 1 demonstrates that most of the subjects had several concomitant types of allergy. Household and epidermal types of sensibilization were most common. The presence of various allergy types was revealed by history taking and allergen tests. Concomitant bronchial asthma, nutritional or drug allergy was observed in many of the subjects. Nutritional and medicamentous types of sencibilization were commonly manifesting as nettle rash, and sometimes as asthmatic attacks. Most of the subjects had a family history of allergy. Therefore, AR was associated with

other atopic conditions in most subjects of the study group. The sencibilization spectrum of the study group is presented in Figure 2.

Figure 2. Forms of sencibilization found in study subjects during allergen tests.

Types of allergens	**Adults (n=25), %**	**Children, (n=23), %**
Dermatophag. Pteron. Dermatophag.Farine	**100**	**100**
Pollen	**64**	**79**
Thereof:		
Trees	**79**	**89**
Cereals	**43**	**74**
Weeds	**21**	**52**
Allergy to 2 or 3 types of pollen:	**57**	**68**
Epidermal allergy	**82**	**79**
Thereof:		
Cat	**94**	**89**
Dog	**50**	**79**
Horse	**11**	**21**
Hamster		**5**
Allergy to 2 or more epidermal allergens:	**50**	**68**

With regard to the data in Figure 2, the following conclusions may be drawn. Firstly, all subjects enrolled in the study were sensitized to house dust mite allergens. Secondly, house dust mite allergy was frequently concomitant with epidermal and pollen allergies. The structure of sensibilization types was virtually similar in children and adults. A combination of household allergy with sensibilization to cat epidermis and tree pollen was very frequent in all age groups.

When interviewed, all patients participating in the study complained of the symptoms of actively manifesting AR of various severity grades: sneezing, nasal and nasopharyngeal itching, eyelid itching, nasal discharge, impaired nasal breathing. All symptoms were assessed for severity grading:

0. Absent (no symptoms)
1. Mild (symptoms do not influence the lifestyle)
2. Moderate (symptoms have a moderate impact on everyday lifestyle)
3. Severe (symptoms have a significant impact on the patient's lifestyle and interfere with normal everyday activities).

Findings

Figures 3 and 4 demonstrate the improvement of AR symptoms in both adults and children in the course of regular administration of disperse cellulose powder.

Figure 3. Evolution of AR symptoms in the course of 4 week treatment with Nasaval in adults.

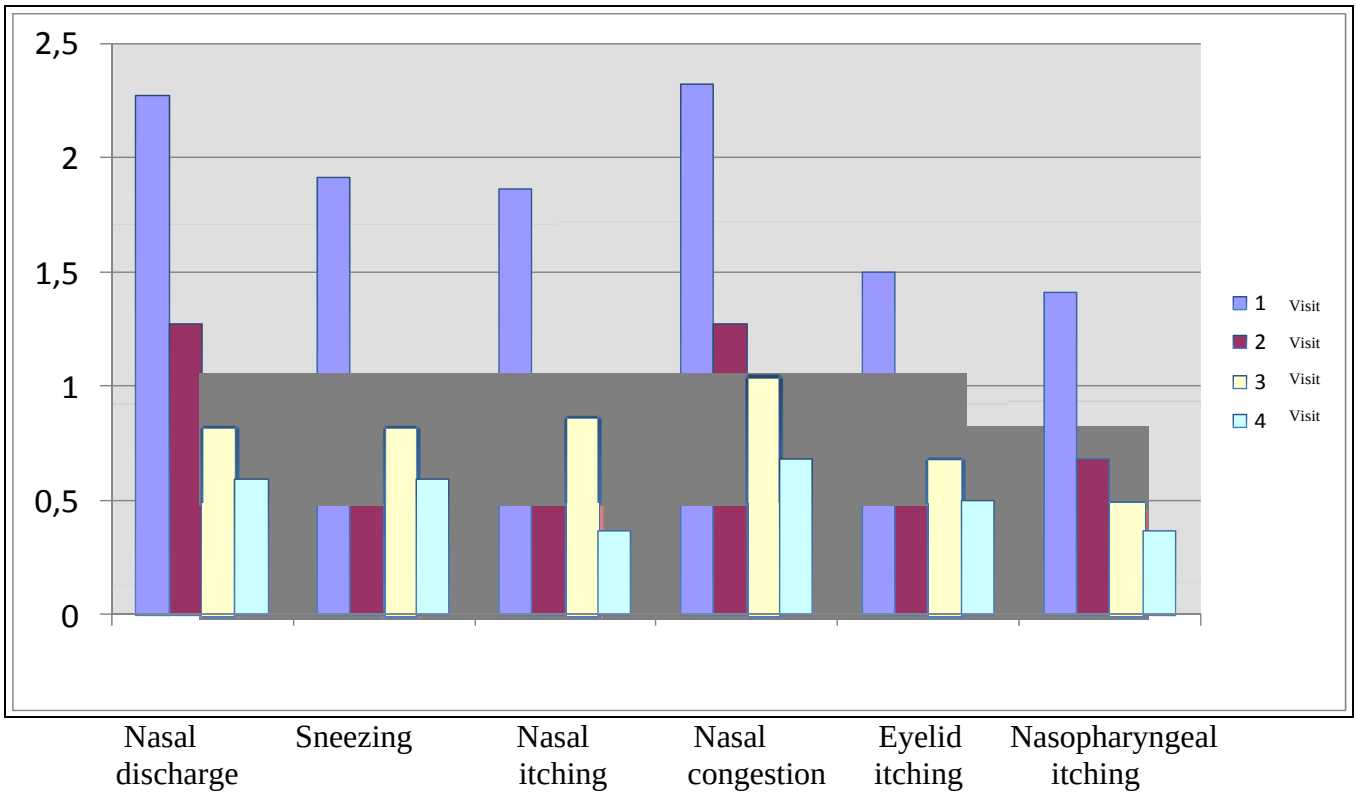
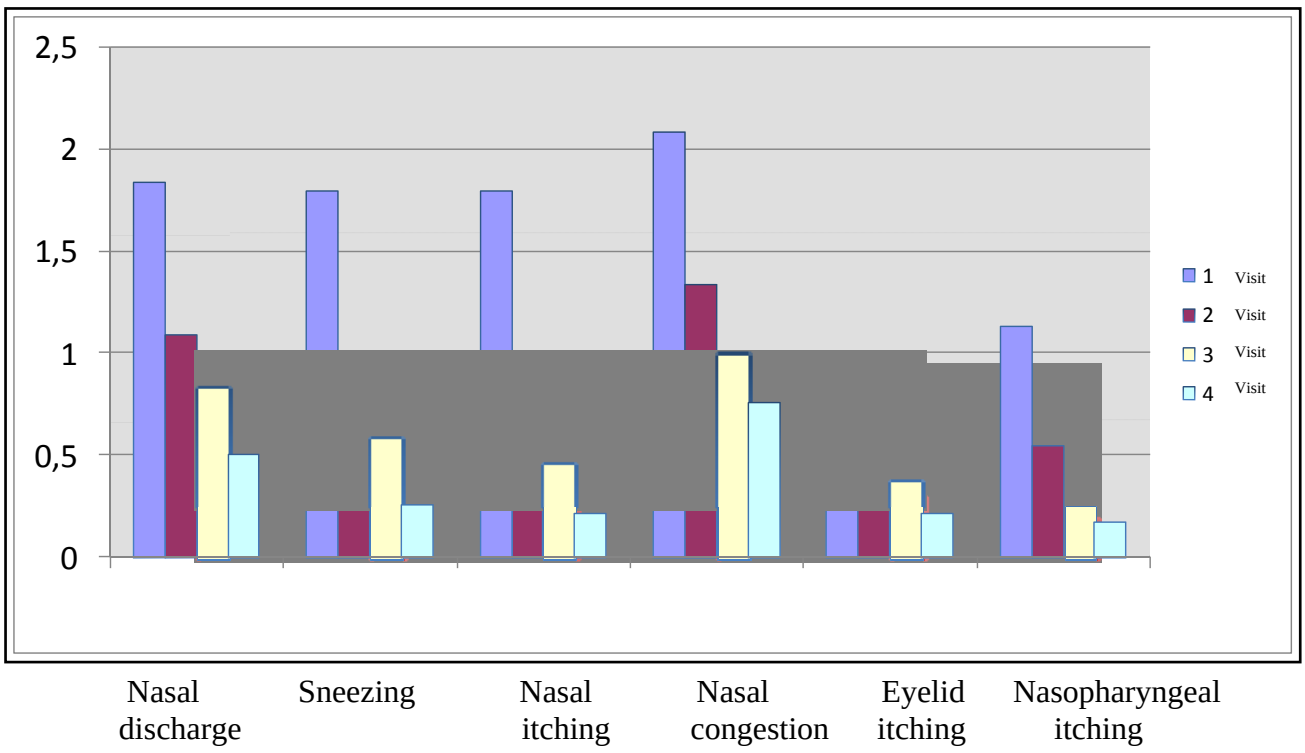


Figure 4. Evolution of AR symptoms in the course of 4 week treatment with Nasaval in children.



Analysis of the data presented in Figures 3 and 4 demonstrates that the effects of microcellulose had an early onset. Improvement of all AR symptoms was observed already in the first week of therapy, and was especially significant by the end of the study period, both in children and in adults.

The following case record illustrates this trend: A 25-year old woman was diagnosed with perennial moderate allergic rhinitis 20 years ago. Allergy tests confirmed allergy to house dust mite and pollen of cereals and weeds. Family history includes allergic rhinitis in father and brother. Improvement of AR symptoms in the course of 4-week therapy with microcellulose powder is presented in Figure 5.

Figure 5. Effects of Nasaval therapy on symptom scores in a 25 year old patient.

	Nasal discharge	**Sneezing**	**Nasal itching**	**Nasal congestion**	**Ocular itsching**	**Nasopharingeal Itching**
Initial symptoms	**3**	**2**	**2**	**2**	**1**	**0**
Study week 1	**2**	**1**	**1**	**1**	**0**	**0**
Study week 2	**1**	**1**	**2**	**1**	**0**	**0**
Study week 4	**1**	**0**	**0**	**1**	**0**	**0**
0. Absent (no symptoms) 1. Mild (symptoms do not influence the lifestyle) 2. Moderate (symptoms have a moderate impact on everyday lifestyle) 3. Severe (symptoms have a significant impact on the patient's lifestyle and interfere with normal everyday activities).						

Overall assessment of the outcomes of 4-week therapy with Nasaval was conducted during the final visit. The investigator assessed the overall efficacy of cellulose micropowder together with the patient. The patients' judgement was based on their sensation of the symptoms, while the investigators analyzed the evolution of AR symptoms, visual scale scores, and the findings of the quality of life questionnaires. The results are summarized in Figure 6.

Figure 6. Assessment of the efficacy of Nasaval.

Effectiveness	Adults (% of all adult subjects)	Children (% of all pediatric subjects)	Total (% of all subjects)
Very good	45	38	41
Good	50	62	57
Moderate	5	-	2
No effect	-	-	-

As it can be noted from the data in Figure 6, therapy with microcellulose powder was effective in varying degrees in all patients participating in the study. The majority of both adults and children (in the latter case the feedback was as a rule collected from the parents) assessed the efficacy of the product as good or very good.

Effectiveness of treatment is further confirmed by the improvement in quality of life of the patients treated with Nasaval. The questionnaire, which was used to assess quality of life of AR patients before and after 4 weeks of treatment with cellulose powder is presented in Figure 7.

Figure 7. AR patient quality of life questionnaire.

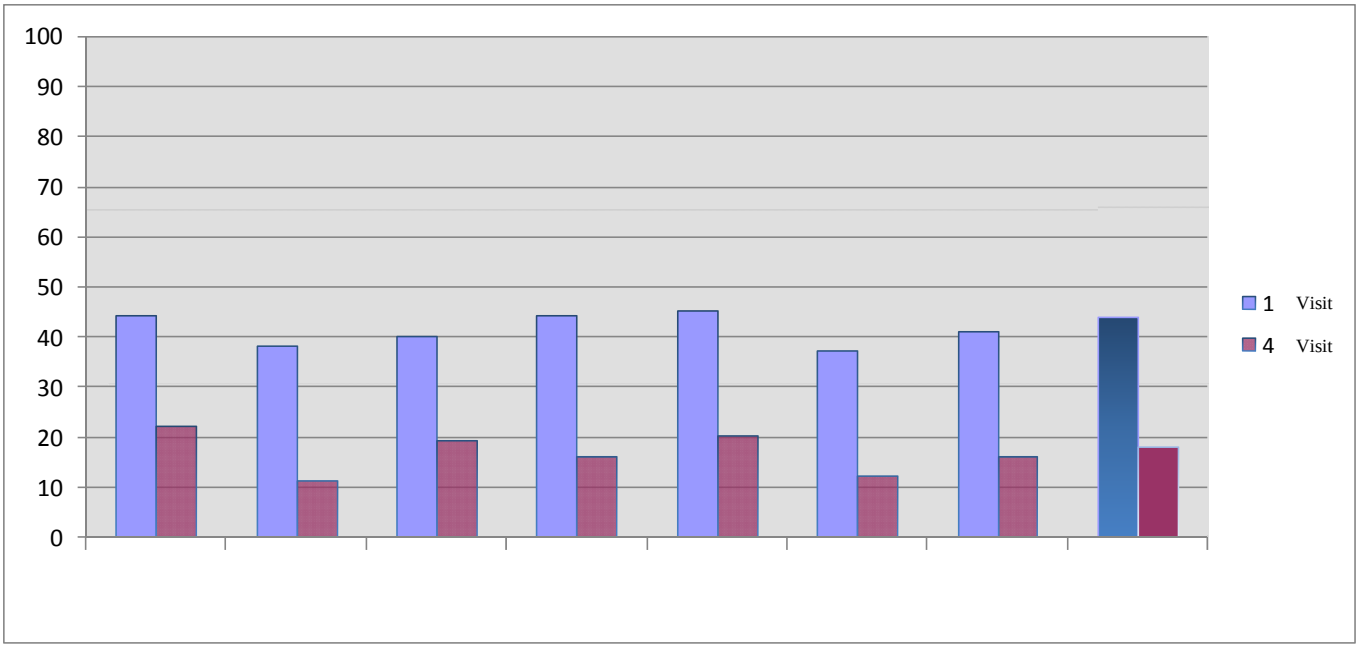
Types of activity	1.Usual activities at home and at work; 2. Communication; 3. Outdoor activities
Sleep	4. Difficult to fall asleep 5. Awaking during the night 6. Difficult to wake up
General symptoms	7. Fatigue 8. Thirst/dryness in the mouth 9. Decreased capacity for work 10. Sluggishness 11. Concentration problems 12. Headache 13. Depression
Practical problems	14. Must always carry tissues 15. Must rub nose and eyes 16. Must blow the nose all the time
Nasal symptoms	17. Nasal congestion 18. Nasal discharge 19. Sneezing 20. Postnasal drip
Ocular symptoms	21. Itching in the eyes 22. Epiphora 23. Pain 24. Swelling around the eyes
Emotional condition	25. Frustration, anger 26. Impatience, anxiety. 27. Irritation 28. Uneasiness.

Assessment scale:
0 – not disturbing
1 – almost undisturbing 3 – moderately disturbing 5 – very significantly disturbing
2 – slightly disturbing 4 – significantly disturbing 6 – extremely disturbing

The questionnaire covers various aspects of the patient's life, his/her physical an emotional condition and other factors, which may be negatively affected by AR.

The findings of the questionnaires are analyzed in Figure 8.

Figure 8. Assessment of quality of life by the patients before and after therapy with Nasaval. (Scale of assessment: 100 % - Maximal impact of the disease on quality of life.)



It can be observed from the data in Figure 8, that quality of life of AR patients improved more than twofold in the course of treatment with microcellulose powder.

Both patients and investigators assessed the tolerability of Nasaval. This assessment is summarized in Figure 9.

Figure 9. Tolerability of Nasaval

Tolerability	Adults (% of total adult subjects)	Children (% of total pediatric subjects)
Very good	95	87
Good	5	9
Moderate	-	4
Poor	-	-
Description of unwanted effects	• Formation of crusts in the nose during 4 first days of therapy – 2 patients; • Burning in the nose – 1 patient	• Burning in the nose – 1 patient • Itching in the nose, sneezing for 1 hour after administration – 1 patient

As a rule, both children and adults reported good or very good tolerability of microcellulose powder. Occasional unwanted effects included: formation of crusts in the nose, burning in the nose, sneezing. These symptoms occurred in isolated cases and did not lead to discontinuation of therapy.

Conclusions

1. Nasaval reduces the severity of AR symptoms already in the first week of treatment.
2. Nasaval therapy is associated with a more than twofold improvement in the quality of life of AR patients
3. Therefore, Nasaval is an effective and safe method of prevention and treatment of allergic rhinitis both in adults and children.
4. Microcellulose powder is capable of creating a natural safe barrier protecting the airways from contact with allergens and oxidating pollutants.

Literature

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医疗器械 Nasaleze 用于预防和治疗成人和儿童常年性过敏性鼻炎的有效性和安全性

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*关键词：*常年性过敏性鼻炎，Nasaleze，超分散纤维素粉末，临床试验

小结：

本文描述了超分散纤维素制剂预防和治疗常年性过敏性鼻炎（AR）的有效性和安全性的开放式非比较临床研究发现。

简介：

过敏性鼻炎的疾病特点是鼻粘膜接触过敏原引起的过敏性炎症，有下面一个或多个症状：

1. 鼻充血
2. 鼻涕
3. 喷嚏
4. 鼻痒

AR 是最普遍的过敏性疾病之一。AR 先于其他过敏性疾病如异位性皮炎和支气管哮喘并不少见。AR 的积极表现是明显影响患者生活质量，干扰睡眠和休息和降低工作能力。

过敏症专科医生的全套配备中现有的预防和治疗 AR 的方法并不完全有效，且费时、昂贵，伴有很多副作用。在儿童和孕妇寻找适当的预防和治疗 AR 的方法的挑战更加难，因为缺少证据确定这些药物在这类患者的安全性。

超分散纤维素的使用可成为预防和治疗 AR 的一个方法。

在微纤维素粉末作为医用在俄罗斯联邦注册和批准后，2009 年进行了该开放式非比较性研究以调查医疗设备 Nasaleze 在预防和治疗过敏性鼻炎的有效性和安全性。

研究设计

48 名常年性过敏性鼻炎患者参加本研究，25 名成人，23 名儿童，男女都有，年龄 2-62 岁。在 4 周观察期内每周检测患者一次。患儿来试验中心时由父母陪伴。根据 Helsiniki 宣言，研究登记时，根据本研究制定的表格，患者要求书面和口头知情同意。未达到法定年龄的儿童，由其父亲或母亲签署知情同意书。

根据研究方案，每个患者填写个体记录及其护照资料、初始病史、检查结果和研究过程中的随访发现。

- 4 周中患者每天 3 次向每个鼻孔喷入一次 Nasaleze。如果效果不够，他们可以多次使用该制剂。
- 患者每周拜访调查者一次，即整个研究期 4 次。每次拜访评估 AR 症状的严重性和产品的耐受性。
- 患者填写生活质量调查问卷，最初和最后的拜访要做视觉模拟量表。
- 在最后一次拜访时由研究者和患者（如果是儿童，与其父母）一起评估治疗的有效性。

- 患者日记记录 AR 症状的严重性、任何副作用和其他药物的使用。

试验对象

参加本研究的患者初诊根据过敏原测试和鼻窦镜结果确定 AR 诊断。

图 1 研究人群特点

参数	成人 n=25	儿童 n=23
年龄	18-62 岁，平均 40.2 岁	2-18 岁，平均 10.8 岁
AR 的持续期	13.8 岁（2-40）	5.75 岁（1-15）
支气管哮喘	68%	24%
异位性皮炎	-	8%
花粉症	64%	79%
动物表皮过敏	82%	79%
食物过敏	36%	33%
过敏家族史	68%	92%
药物过敏	23%	12%

图 1 显示大多数试验对象伴有多种过敏性疾病。尘螨或动物表皮过敏最常见。询问病史和过敏原测试显示存在各种过敏原类型。许多试验对象也观察到支气管哮喘、食物或药物过敏。食物和药物过敏常表现为荨麻疹，有时表现为哮喘发作。大多数试验对象有过敏的家族史。因此，研究组的大多数患者 AR 与其他特应性疾病有关。研究组的过敏范围见图 2。

图 2 研究对象过敏试验显示的过敏范围

过敏原类型	成人（n=25），%	儿童（n=23），%
屋尘螨 粉尘螨	100	100
花粉 其中： 树 禾本 野草	64 79 43 21	79 89 74 52
2 种或 3 种花粉过敏	57	68
表皮过敏 其中： 猫 狗 马 仓鼠	82 94 50 11	79 89 79 21 5
2 个或更多表皮过敏原过敏	50	68

关于图 2 的数据，得到如下结论。首先，参加研究的所有试验对象对尘螨过敏原过敏。其次，尘螨过敏常伴有动物表皮和花粉过敏。儿童和成人过敏类型的结构事实上相似。尘螨过敏连带猫表皮和花粉过敏在所有年龄组都很常见。

面谈时，参与本研究的所有患者主诉 AR 主要表现的症状的各种严重程度：喷嚏、鼻和鼻咽痒、眼睑发痒、鼻流涕、鼻呼吸障碍。所有症状评估严重程度分级：

0．缺失（没有症状）
1．轻度（症状没有影响生活方式）
2．中度（症状中度影响日常生活方式）
3．严重（症状严重影响患者生活方式，干扰正常日常活动）

发现

图 3 和 4 显示成人和儿童在定期使用纤维素散粉的过程中 AR 症状的改善。

图 3 成人 Nasaleze 4 周治疗期间 AR 症状的发展

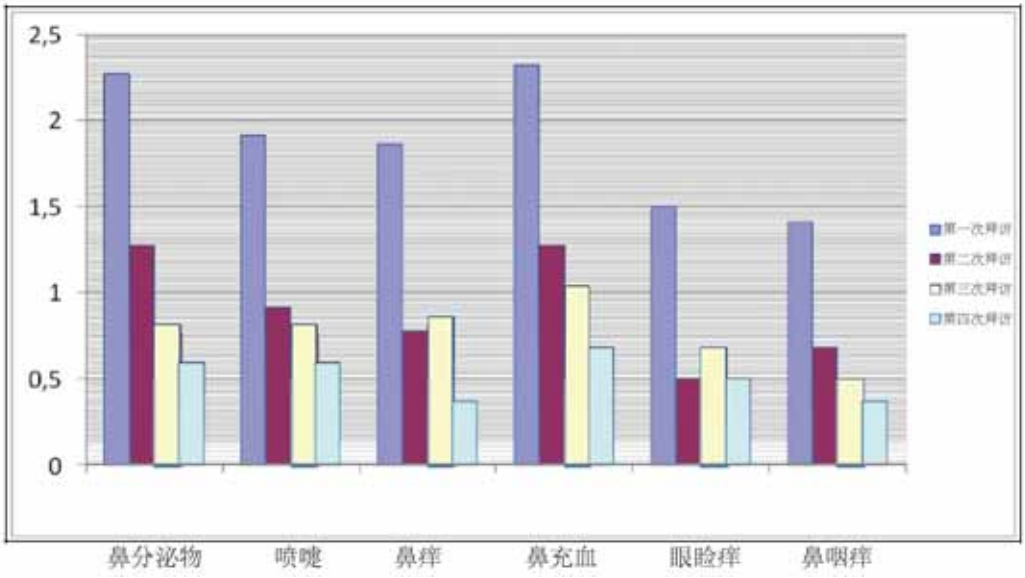

图 4 儿童 Nasaleze 4 周治疗期间 AR 症状的发展

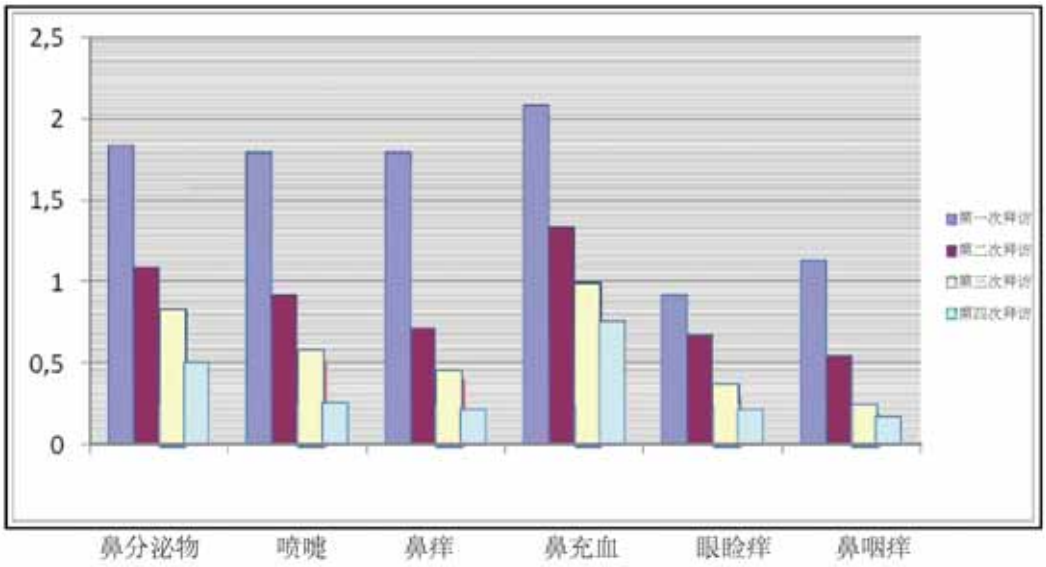

图 3 和 4 的数据分析显示微纤维素的作用刚用就有。不论是成人还是儿童，治疗的第一周就已经观察到所有 AR 症状的改善，尤其明显的是研究结束时。

下面病例记录显示了这种趋势：25 岁女性 20 年前诊断为中度常年性过敏性鼻炎。过敏测试确认对尘螨和禾本科和野草花粉过敏。家族史包括父亲及兄弟有过敏性鼻炎。图 5 显示了其用微纤维素的 4 周治疗期 AR 症状的改善。

图 5 25 岁患者 Nasaleze 治疗对症状评分的作用

	鼻分泌物	喷嚏	鼻痒	鼻充血	眼痒	鼻咽痒
初始症状	3	2	2	2	1	0
研究 1 周	2	1	1	1	0	0
研究 2 周	1	1	2	1	0	0
研究 4 周	1	0	0	1	0	0
0．缺失（没有症状） 1．轻度（症状没有影响生活方式） 2．中度（症状中度影响日常生活方式） 3．严重（症状严重影响患者生活方式，干扰正常日常活动）						

最后一次拜访时进行 Nasaleze 4 周治疗结果的总评估。研究者和患者一起评估纤维素微粉末的总效果。患者的判断是根据他们症状的感觉，而研究者是分析 AR 症状的发展、目视量表评分和生活质量调查问卷的发现。结果总结在图 6。

图 6 Nasaleze 效果的评估

效果	成人 （所有成人对象的%）	儿童 （所有儿童对象的%）	总计 （所有对象的%）
很好	45	38	41
好	50	62	57
中度	5	-	2
没作用	-	-	-

从图 6 中资料可以看出微纤维素粉末治疗在本研究的所有患者有不同程度的效果。成人和儿童（后者是从父母那收集的反馈）的大多数评估该产品的效果是好或很好。

治疗的有效性需进一步由 Nasaleze 治疗患者生活质量改善来确认。图 7 显示了用于评估 AR 纤维素粉末治疗 4 周前后患者的生活质量调查问卷。

图 7 AR 患者生活质量调查问卷

活动类型	1．家里和工作日常活动； 2．交流； 3．户外活动
睡觉	4．难入睡； 5．半夜醒来； 6．难以唤醒
一般症状	7．疲劳 8．口渴/口干 9．工作能力下降 10．呆滞 11．注意力集中问题 12．头痛 13．抑郁
实际问题	14．必须总是带手机纸 15．必须擦鼻和眼睛 16．必须吹鼻子
鼻症状	17．鼻充血 18．鼻分泌物 19．喷嚏 20．鼻涕倒流
眼部症状	21．眼痒 22．泪溢 23．痛 24．眼周肿胀
情感障碍	25．沮丧，愤怒 26．急躁，焦虑 27．刺激 28．不安

评估量表：

0- 不影响

1- 几乎不影响　　3- 中度影响　　5- 影响非常明显

2- 轻度影响　　4- 明显影响　　6- 影响极其明显

调查问卷包括 AR 负面影响的患者生活、他/她身体和精神状况和其他因素的各个方面。

图 8 分析了调查问卷的发现。

图 8 Nasaleze 治疗前后患者生活质量的评估（评估量表：100%-疾病对生活质量的最大影响）

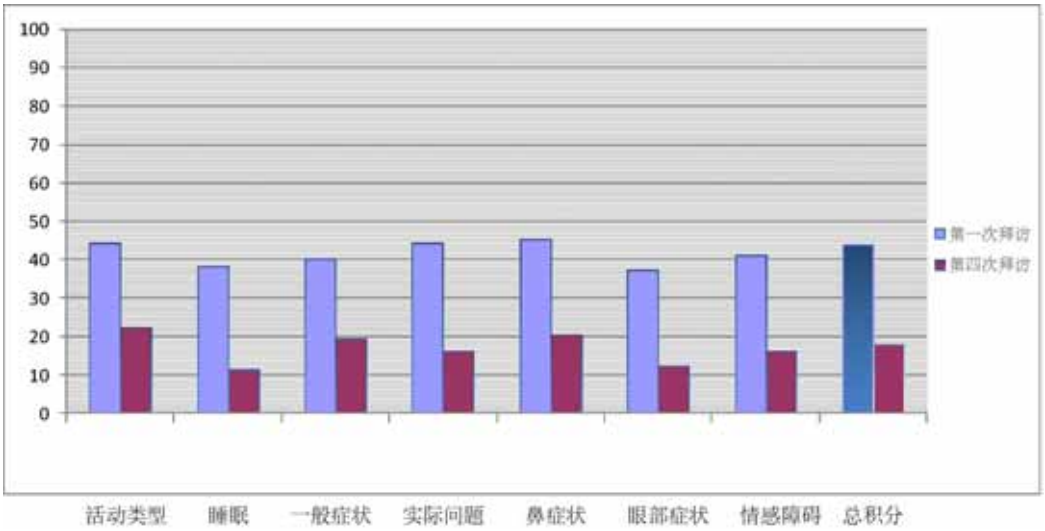

图 8 的资料显示微纤维素粉末治疗过程中 AR 患者的生活质量提高了 2 倍多。

患者和研究者评估了 Nasaleze 的耐受性。评估总结在图 9。

图 9 Nasaleze 的耐受性

耐受性	成人（总成人对象的%）	儿童（总儿童对象的%）
很好	95	87
好	5	9
中度	-	4
差	-	-
不良作用描述	◆ 治疗开始前 4 天鼻部形成结痂-2 例 ◆ 鼻部烧灼感-1 例	◆ 鼻部烧灼感-1 例 ◆ 使用后鼻痒鼻痒、喷嚏 1 小时-1 例

通常儿童和成人报告微纤维素粉末有好或很好的耐受性。偶有不良作用包括：鼻部形成结痂、鼻部烧灼感、喷嚏。这些症状发生在孤立情况下，并不导致停止治疗。

结论

1． Nasaleze 在治疗的第一周就降低了 AR 症状的严重性；
2． Nasaleze 治疗改善了 AR 患者生活质量两倍多；
3． 因此，Nasaleze 是预防和治疗成人和儿童过敏性鼻炎的有效安全方法；
4． 微纤维素粉末可产生天然安全屏障保护气道免于接触过敏原和氧化污染物。

文献

见原文。