

New developments in the prevention and treatment of seasonal allergic rhinitis in children.
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Summary

An open-label, comparative, randomised study of the effectiveness and safety of using microdispersed cellulose powder (Nasaleze) to treat allergic rhinitis in children over a period of 6 weeks from April to June 2009 was carried out.

50 children aged between 4 and 14 with diagnosed seasonal allergic rhinitis (SAR) were observed. 30 children were given microdispersed cellulose powder. 20 children were put into a comparison group (control group) and received symptomatic treatment. The objective and subjective symptoms of SAR were assessed prior to treatment and at 2, 4 and 6 weeks after first using the product.

A positive result was observed in 26 patients (86.4%) from the first few days of using microdispersed cellulose powder. The product was not effective in 2 children (6.6%) with moderate to severe SAR and these children were also treated with nasal corticosteroids. 2 children (6.6%) experienced increased sneezing and their treatment with the product was stopped.

Children who received Nasaleze during the pollen season reduced the frequency of their intake of antihistamines, decongestants and topical steroids.

Introduction:

Allergic rhinitis is an illness which affects the mucous membrane of the nasal cavity and which then leads to allergic inflammation, with a high rate of occurrence in children. Allergic rhinitis often combines with bronchial asthma and can be the first sign of the development of an allergic process in the respiratory tracts. The development of allergic rhinitis, as a rule, combines with paranasal sinus involvement and is characterised by stuffiness of the nose, profuse mucous secretions and itching. A rhinoscopy can determine pronounced oedema of the mucous membrane, which can continue even after taking vasoconstrictive products, as well as a white or greyish tinge to the mucous [1]. A late diagnosis of allergic rhinitis and the delayed prescription of adequate and targeted treatment may lead to serious ENT complications.

Depending on the progress and deterioration of allergic rhinitis, children may experience intermittent (seasonal) and persistent (perennial) allergic rhinitis.

Seasonal allergic rhinitis in children is most often caused by the effect of pollen from trees, grasses and weeds as well as mould fungi on the child's body. The particular features of seasonal rhinitis include the frequency with which the illness intensifies. Allergic illnesses which develop in connection with sensitisation to plant pollen are called pollinosis (from the English word pollen).

An important link in the pathogenesis of pollinosis is genetically-determined increased IgE synthesis, including specific and anti-pollen IgE. The illnesses are most frequent during the season when the most widespread plants in the area are in flower.

Allergic rhinitis can be seen in the first year of a child's life, but is more frequent after 1-2 years as a result of the repeated influence of the allergens. The appearance of pollinosis is normally diagnosed in children over 3. The illness rate is higher during school age. The illness is often diagnosed late, with the clinical symptoms being regarded as signs of ARVI, infectious rhinitis, antritis or conjunctivitis.

The clinical symptoms of the illness recur year on year at the same time of year. There are *immediate symptoms* of rhinitis (itchiness, sneezing, rinorrhea and oedema of the mucous membrane), which are seen straight after contact with the allergen, and *symptoms of chronic rhinitis* (constant oedema, reduced sense of smell, and nasal hyperreactivity), which are caused by the development of chronic inflammation.

The main forms of pollinosis are *rhinitis, sinusitis, conjunctivitis and bronchial asthma*. This latter type often only develops in children after a few seasons of intensifying rhinoconjunctivitis.

Treatment of allergic rhinitis is complex and the first step is eliminating contact with the allergens. During the pollen season, in order to eliminate contact with the allergens, it is recommended that windows and doors be kept closed, an internal air conditioning system used, and time spent outdoors limited. It is often impossible to implement many of these measures with children.

Medicinal treatment has gradually increased as the severity of AR itself has increased: antihistamines - H1 HISTAMINE receptor blockers (claritin, acrius, telfast, kestin) some of which may be used in the form of a nasal spray (allergodil); mast cell stabilisers (kromoglin nasal spray, nasal inhaled corticosteroids (nasonex, flixonase, tafen). Highly effective allergen-specific immune therapy.

Since 2002 many countries have been using inert cellulose that creates a natural barrier in the nasal cavity. This protects the respiratory tracts against allergens entering the mucous membrane of the nose and the further penetration of the allergen with it then turning into an allergic reaction, in particular, allergic rhinitis [1-7].

Nasaleze is a microdispersed cellulose powder in a spray dispenser which protects the mucous membrane of the nose against pollutants and air allergens: plant pollen, everyday allergens, epidermal animal and bird allergens, and other microparticles which enter the nasal cavity when breathing in [2].

Prof. Richard Lewis at the Worcestershire Royal Hospital in Great Britain believes that the vast majority of microdispersed cellulose particles are too big to enter the human respiratory system when inhaled through the nose. When the microcellulose particles come into contact with any moist surface, including the mucous membrane of the nasal cavity, they absorb water and turn into a gel. The gel is removed through normal mucociliary clearance, which cleans away the normal secretions of the respiratory system.

The action mechanism is caused by the fact that the cellulose consists of long polymer chains which attach to intramolecular links. By including hydrophilic groups, it gradually swells and becomes easily soluble by the polymer in water.

The product is issued in the form of a dry spray in a special 500 mg bottle that dispenses the exact dose. It can be used as often as necessary. Recommended dose: one spray in each nostril 3-4 times a day (every 5-6 hours). It is recommended that Nasaleze be re-sprayed every time the nose is blown in order to restore the protective layer. Any nasal products used in the treatment of SAR should be used 10-15 minutes before the use of Nasaleze spray. The use of Nasaleze is also recommended before coming into contact with an allergen.

Previous research has shown a high level of effectiveness of microdispersed cellulose powder in the prevention and treatment of SAR.

Research into the drug in 102 patients with SAR [3] showed that Nasaleze was effective in 77% of patients (the average effectiveness rating on a 5-point scale was 3.8, where 5 represents no symptoms and full control). The symptoms were alleviated 0.1 – 3 hours after first using the product. Most patients rated Nasaleze spray as an effective treatment and prevention method for SAR. When using the product, patients noticed fewer side effects when compared with many other pharmaceutical products [3].

A double-blind, placebo-controlled study into the use of inert cellulose powder in adult patients for the alleviation of the symptoms of SAR was carried out in Great Britain. 97 adult patients with pollinosis took part in the study during the active pollen season [5]. The results show that when using inert cellulose powder, the need to use medicinal products to treat SAR is reduced.

The Aivazis V study [6] found that there was a significant decrease in the mucociliary clearance time when using Nasaleze spray in children with SAR, which may be connected with the regeneration and normalisation of the ciliated epithelia. Mucociliary clearance of the mucous membrane is the first line of defence of the nasal ciliated epithelium against inhalable particles such as allergens, pollutants and viruses. Cellulose strengthens the mucous membrane of the nose, which allows for the filtration of allergens and the inhalation of fresh air only into the lungs.

Volunteers took part in research into the symptoms of SAR, PEFn and PIFn respiratory functions and ECPs (eosinophil cationic proteins) after the provocation of a measured dose of grass pollen that was introduced into the nose via a micro-spoon [7].

The symptoms were analysed before the provocation and 24 hours afterwards. The microdispersed cellulose drug prevented the development of the symptoms of SAR (rhinitis, itching in the nose), and improved the PIFn, PEFn and ECP indexes when compared with the placebo group.

In Russia microdispersed cellulose was registered and given a marketing authorisation in 2009. The authors (T.V. Zakhazhevsckaya, I.V. Sidorenko, V.K. Treskunov and A.V. Karaulov) carried out an open-label non-comparative study to assess the effectiveness and safety of Nasaleze spray in the prevention and treatment of allergic rhinitis. 48 patients took part in the study (25 adults and 23 children aged between 2 and 62) with persistent AR. The patients were observed for a period of 4 weeks [4]. It was found that Nasaleze reduces the intensity of the symptoms of allergic rhinitis during the first week of use and improves the quality of life of patients with allergic rhinitis when used more than twice.

We carried out an open-label, comparative, randomised study of the effectiveness and safety of using microdispersed cellulose powder (Nasaleze) in the preventative treatment of seasonal allergic rhinitis in children over a period of 6 weeks from April to June 2009.

50 children aged between 4 and 14 with diagnosed seasonal allergic rhinitis (SAR) were observed. 30 children were given microdispersed cellulose powder. 20 children were put into the comparison group and received symptomatic treatment. The objective and subjective symptoms of SAR were assessed prior to treatment and at 2, 4 and 6 weeks after first using the product. Nasaleze was used in accordance with the dosage recommendations: one spray into each nostril 3-4 times a day (every 5-6 hours). The patients were advised to re-spray Nasaleze every time they blew their nose or when likely to come into contact with an allergen, in order to restore the protective layer.

All of the patients taking part in the study were diagnosed with SAR. During the observation period, both groups were allowed to use concomitant antihistamines and GKS nasal sprays 15-20 minutes before using the microdispersed cellulose powder.

The objective and subjective symptoms of SAR were assessed prior to treatment and at 2, 4 and 6 weeks from first using Nasaleze. The results were recorded in the "Patient observation diary".

The average age of the patients in groups 1 and 2 was 8.3 ± 3.2 and 8.7 ± 3.7 respectively. The average duration of the illness was 3.1 ± 0.87 and 2.8 ± 1.0 years. Both groups showed a similar sensitisation to allergens: sensitisation to pollen allergens alone covered 50% of the children, for 38.4% of the children the symptoms of allergic rhinitis developed not only from plant pollen but from other allergens such as household dust and pet allergens.

Children with mild SAR accounted for 73.3% of the first group and 78% of the second group, while children with moderate to severe symptoms accounted for 20% of the first group and 22% of the second group.

Five children in the main group (16.7%) and four children (20%) in the control group suffered from bronchial asthma as well as seasonal allergic rhinitis.

20 children (76%) in the main group and 10 children (50%) in the control group had a significant family history of allergic illnesses, including seasonal allergic rhinitis.

None of the patients had received treatment for SAR prior to the start of the observation period.

The patients visited the doctor 4 times every 2 weeks (Table 1).

Table 1 Case monitoring timetable for the patients per visit.

Study	Visit 1	Visit 2	Visit 3	Visit 4
Informed consent	X			
Questionnaire	X			
Collection of medical records	X			
Patient examination	X	X	X	X
Symptoms of seasonal allergic rhinitis (on a point scale: 0 - no symptoms, 1 - low level of intensity, 2 - moderate level of intensity, 3 - severe)	X	X	X	X
Treatment adjustment		X	X	X
Assessment of adverse events		X	X	X
General doctor and patient assessment		X	X	X

Results of the study and discussion:

2 weeks after first taking microdispersed cellulose powder (Nasaleze), the main group noticed a definite drop in all SAR symptoms: rinorrhea decreased from 1.8 ± 0.4 to 0.8 ± 0.6 points; sneezing – from 1.5 ± 0.6 to 0.5 ± 0.6 ; itching in the nose from 1.2 ± 0.5 to 0.4 ± 0.5 ; blocked nasal passages from 1.8 ± 0.5 to 0.7 ± 0.6 ($p < 0.001$) (Fig. 1.2). The majority of patients (73%) noticed a distinct improvement in their condition by the fifth day of using Nasaleze. Fig. 1-4.

During the next 2 weeks, 12 children's (40%) symptoms disappeared completely.

The remaining children noticed a decrease in their SAR symptoms: rinorrhea - to 0.6 ± 0.6 points; blocked nasal passages - to 0.5 ± 0.6 ; sneezing and itching in the nose remained unchanged ($p > 0.5$)

6 weeks after first using Nasaleze spray the SAR indicators remained at their previous level.

Fig. 1 The course of SAR symptoms (rinorrhea, sneezing).

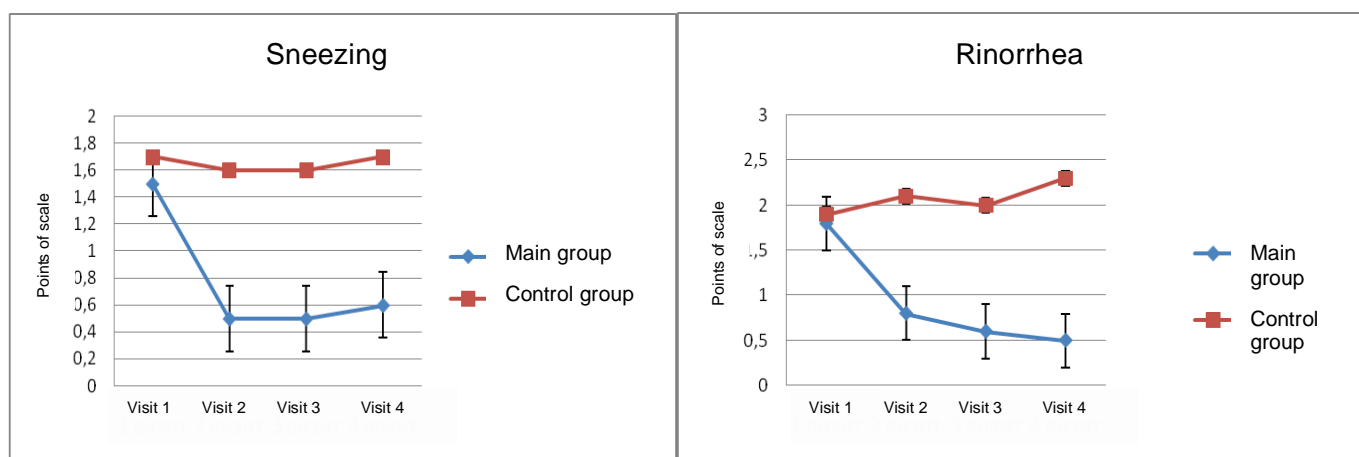
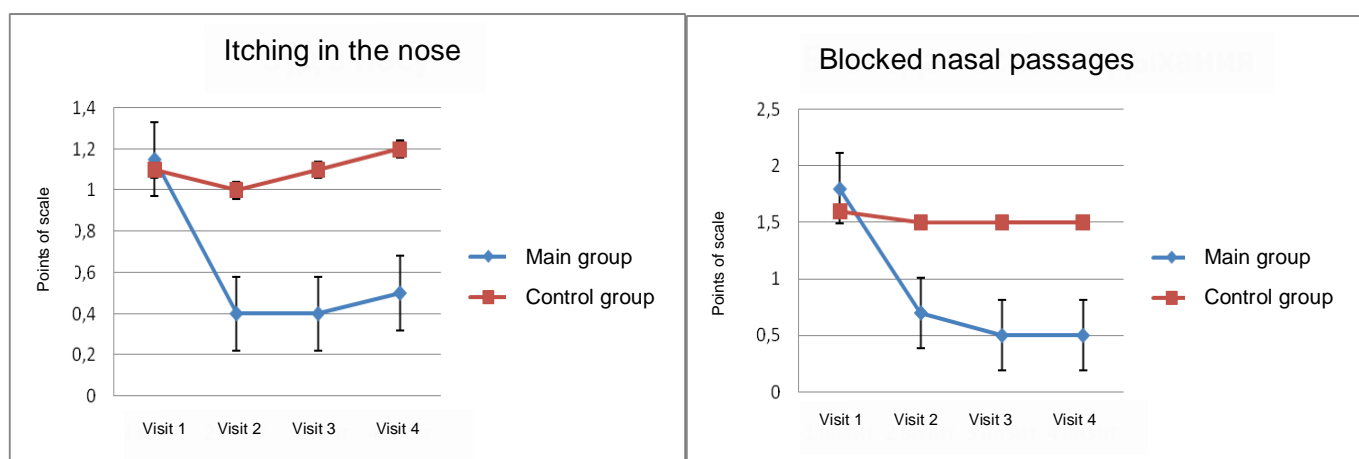
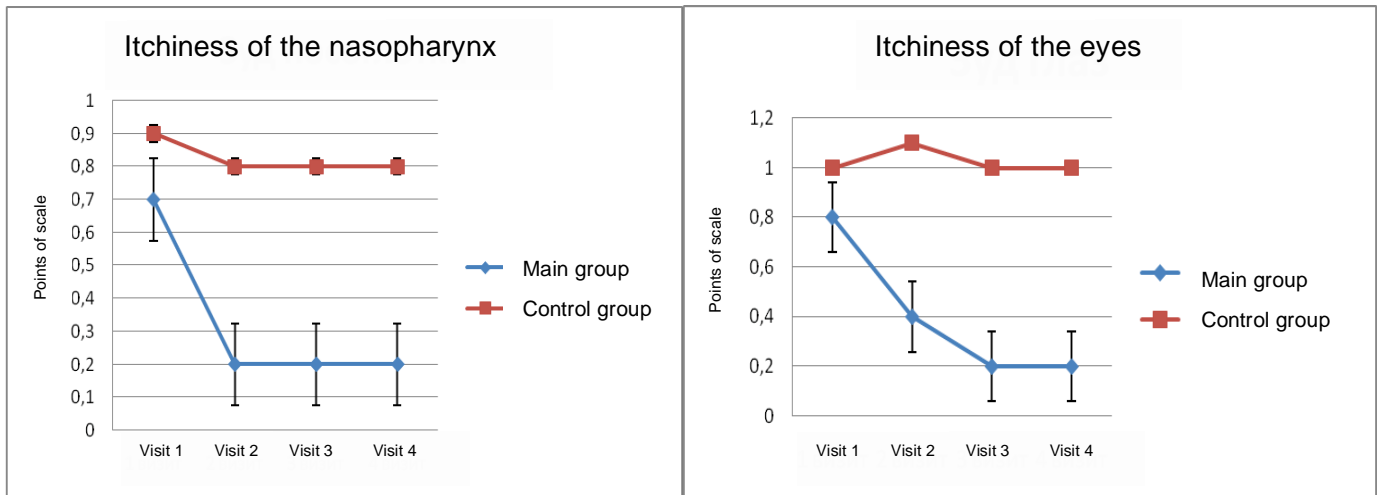


Fig. 2 The course of SAR symptoms (itching in the nose, blocked nasal passages).



They also noticed a decrease in other allergic manifestations. Two weeks after the start of the study, itchiness of the eyes decreased from 0.8 ± 0.7 to 0.4 ± 0.5 points; itchiness of the nasopharynx decreased from 0.8 ± 0.8 to 0.2 ± 0.4 points ($p < 0.001$). After 4 weeks it had decreased to 0.2 ± 0.3 points (Fig. 3).

Fig. 3 The course of SAR symptoms (itchiness of the eyes, itchiness of the nasopharynx).



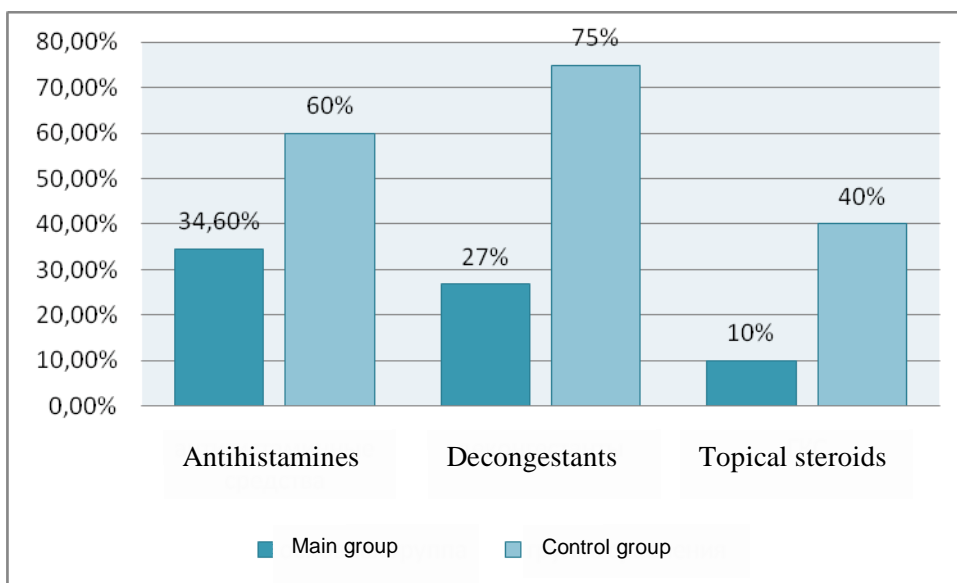
When using Nasaleze spray, 9 children (34.6%) occasionally took antihistamines, 7 children (26.9%) took decongestants and 3 children (10%) took topical glucocorticosteroids.

The product was not effective for 2 children (6.6%) with moderate to severe SAR and these children were also treated with nasal corticosteroids. 2 children (6.6%) experienced increased sneezing and their treatment with the product was stopped.

On the whole, the majority of parents and doctors (86.4%) assessed the microdispersed cellulose powder as highly effective for the preventative treatment of seasonal allergic rhinitis.

In the comparison group the symptoms remained constant for the entire observation period, which required the frequent administration of antihistamines for 8 children (60%), decongestants for 15 children (75%), and 8 patients (40%) sometimes used topical steroids (Fig. 4).

Fig. 4 Frequency of use of medical products to treat SAR.



Microdispersed cellulose powder thus had a noticeable effect on the symptoms of allergic rhinitis (rinorrhea, sneezing, itchy nose, blocked nasal passages, itchy eyes, itchy nasopharynx).

Conclusion:

It has thus been proven that microdispersed cellulose powder has a positive effect on the preventative treatment of SAR in children.

The marked effect of microdispersed cellulose on SAR symptoms definitely decreased but to a lesser extent for symptoms such as itchy eyes and nasopharynx.

It was proven that children who received Nasaleze during the pollen season had their intake of antihistamines, decongestants and topical steroids reduced.

The preventative use of Nasaleze spray when coming in contact with a known allergen (cat, dog and other animals) significantly decreased the development of allergic reactions.

It has been proven that it is advisable to use Nasaleze spray for the preventative treatment of seasonal allergic rhinitis.

Discussion:

The treatment of allergic rhinitis up to now has been based on the use of products which act either as membrane stabilisers, which prevent the degranulation of immune cells, or as histamine receptor blockers. The use of most of these drugs is restricted by age and length of treatment. The new product, Nasaleze, is a modern way of controlling the symptoms of and treating allergic rhinitis. This inert cellulose powder, when administered in the nostrils, forms a gel-like substance which is similar to the normal mucous membrane in the nose which, when it comes into contact with a moist surface (always present in the nasal cavity), prevents the release by airborne allergens of vasoactive substances from mast cells. This can be seen not only as an effective measure to prevent the initial immunological reaction, but as a chance to reduce the symptoms of allergic rhinitis which have already been observed.

Nasaleze is a natural and safe product which does not contain any chemical substances and which has proven effective in previous studies. [1-7].

It is important that the microdispersed cellulose powder is well-tolerated, safe and easy to use, and may be used in children of any age, starting from the very young.

In this study, Nasaleze facilitated the classification of SAR symptoms during the first few days after the start of inhalation. The children's medical records contained a lot of SAR symptoms over a long period which required the use of different pharmacological products with a certain range of side effects. 86.4% of the children experienced a definite reduction in the symptoms of SAR and the frequency of use of additional treatment methods decreased. The product was not effective in 2 patients with moderate to severe SAR. 2 patients stopped participating in the study on account of increased sneezing which could be classed both as an intensification in SAR symptoms and as a side effect of the product. This study showed that inert cellulose powder administered to the nasal cavity prevents the development of an allergic reaction to plant pollen and other irritants in children. Treatment using cellulose powder should be started as early as possible and continued throughout the entire season when there is increased pollen in the air; the number of applications per day may be increased as necessary. Children noticed a positive blocking effect of Nasaleze spray when coming into contact with pets, allowing them to minimise their allergic reaction.

Regular use of inert cellulose powder in the nostrils may effectively prevent and alleviate the symptoms of SAR.

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