Efficacy and safety of a new mometasone furoate nasal spray formulation in patients with acute rhinosinusitis: a randomized clinical trial

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ABSTRACT

Common inflammatory airway disorders, such as seasonal and perennial allergic rhinitis, acute sinusitis, and nasal polyposis, can have a significant impact on patient health and quality of life. Intranasal corticosteroids are recommended as part of treatment plans for each of these illnesses because they reduce inflammation and thus symptoms. In order to compare the efficacy and safety of a new nano formulation of mometasone furoate nano-nasal spray (MF-NNS) with a commercially available nasal spray called mometasone furoate nasal spray (MFNS) for the treatment of allergic rhinitis, 20 rhinitis patients were enrolled in this randomized controlled trial (10 to 50 years). Patients were given 50 mcg MF-NNS doses in the morning and evening. This regimen was administered as a nasal spray for a 3-week efficacy and safety phase. The primary endpoints changed from baseline in the subjects' congestion as determined by the physicians' assessment of allergic rhinitis. Analysis of variance was used to evaluate all efficacy end points. More clinical trials have shown that MF-NNS reduces both objective and subjective markers of inflammation in adults, adolescents, and children.

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Introduction

When the human nasal mucosa is exposed to natural allergens, an Ig-E-mediated immune response occurs, which can lead to a chronic inflammatory illness such as allergic rhinitis (AR). AR symptoms can be either seasonal or ongoing.[1] Patients with persistent AR symptoms experience sporadic or ongoing symptoms caused by allergens such as animal saliva and cockroach, dust mite, and mould dander. Sneezing, postnasal drip, rhinorrhea, nasal irritation, nasal congestion, and rhinorrhea are all symptoms of AR. Patients also experience non-nasal symptoms such as red, itchy, or watery eyes.[2] One of the most common and frequently troublesome symptoms is nasal congestion, which is linked to sleep disturbances that can impair cognitive performance, reduce health-related quality of life, and cause psychosocial dysfunction.[3]

Seasonal allergens, such as molds or pollen, cause an IgE-mediated reaction, resulting in seasonal allergic rhinitis.[4] Contact with allergens on a regular or infrequent basis causes a variety of disorders, including perennial allergic rhinitis. Dust mites, molds, insects (cockroaches), and animal dander are the most common indoor allergens[5] In seasonal and perennial allergic rhinitis, the nasal mucosa is heavily infiltrated with inflammatory cells such as eosinophils and basophils, and mast cells release inflammatory mediators such as histamines, prostaglandins, and leukotrienes.[6] Nasal

congestion is a common complaint among patients suffering from allergic rhinitis. Eye symptoms include scleral redness, tearing, burning, and itching.[7]

AR treatment's main goals are to prevent or reduce symptoms as safely and efficiently as possible.[8] Intranasal corticosteroids, in addition to appropriate preventive measures, are regarded as the first-line treatment for chronic AR because they reduce both the early and late stages of the immune response.[9] These medications inhibit the production and release of cytokines, block the release of Ig-E-mediated mediators from mast cells and basophils, and reduce the number of both pro-inflammatory cells. Furthermore, their ability to reduce nasal secretions and mucous membrane permeability aids in the relief of AR symptoms.[10] The goal of this study is to assess the efficacy and safety of mometasone furoate nano-nasal spray (MF-NNS) 50-µg doses administered once daily in the morning in the treatment of rhinitis patients. MF-NNS was a newly prepared nano nasal spray made from polymers[11] that was chemically tested and approved by all means and found to be within USP 42 specifications.

Materials and Methods

In this prospective, randomized clinical trial, the first and last visits served as the study's two points of measurement. The final visit was scheduled 3 weeks ±5 days after the initial exam. This trial included a 3-week efficacy and safety phase. During the study, the primary effectiveness measure was the mean change in the physician-evaluated total nasal symptom score (TNSS) from baseline to day 21. Other efficacy variables in the phase include subject-evaluated TNSS, individual nasal symptoms, and total symptom score (TSS, non-nasal and nasal symptoms, summed). During the open-label phase of the improvement period, doctors reviewed the overall state of PAR. Adverse events (AEs) were recorded throughout.

Ethical standard

This study was carried out in accordance with the Helsinki Declaration and was approved by the Rashid Latif Medical and Pharmacy College and Hospital's ethics committee in Lahore, Pakistan (RLCP-ID: CT-RLCP-000133-2022).

Efficacy evaluations

Subjects were evaluated during therapy based on their severe nasal rhinitis symptoms over the previous 12 hours. Symptoms were recorded twice a day on diary cards provided by the doctor to each patient: when they first appeared before dosing in the morning and about 12 hours later in the evening. The outcomes or symptoms were noted and recorded in the patient's file. The study drug's initial dose was administered at the study center under the supervision of the investigator or a designee (hospitals). The doctor assessed the severity of the symptoms at the baseline (day 1) and day 21 visits. Rhinorrhea (nasal discharge/runny nose or postnasal drip), stuffiness/congestion, itching, and sneezing are all nasal symptoms. Non-nasal symptoms include itching or burning eyes, watering or tears, ocular redness, and ear or tongue irritation.

Safety evaluation

At the start of each session, a physician evaluated all subjects' adverse events. The subjects' overall health status was monitored based on examinations until the final visit. All adverse events (AEs) were recorded in the patients' medical records and on a case report form.

Eligibility criteria

The study included children and adults of any age who had a diagnosis of rhinitis sicca, symptoms of dry nose caused by the use of specific drugs, or who were receiving concurrent treatment for allergies or rhinosinusitis. Patients were evaluated if they displayed any of the following important symptoms: a dry nose is characterized by crusting, itching, sneezing, pain in the nose, an anterior/runny nose, thick nasal discharge, impaired nasal breathing or nasal obstruction, impaired sense of smell, impaired sleep, and the desire to clear one's throat.

Only symptoms classified as mild or severe, or at least twice as moderate or strong, were eligible for inclusion in the analyses. Patients rated their symptoms on a 0-3 ordinal scale (0=none, 1=mild, 2=moderate, and 3=strong). In order to provide a realistic picture of typical therapy and therapeutic output, no additional inclusion or exclusion criteria were defined beyond those in the Instruction for Use. Patients were instructed to use 1-2 sprays per day, according to the manufacturer's instructions. Different dosing recommendations had to be noted in the case report form. With each spray, 0.10 mL of solution was released (Figure 1).

Criteria

Inclusion criteria were: i) children and adults aged 10 to 50 with rhinitis; and ii) the ability and willingness to understand and provide informed consent.

Exclusion criteria included: i) current pregnancy; ii) current hospitalization; iii) inability to complete online questionnaires or follow study requirements; iv) kidney failure or dialysis, severe liver disease or cirrhosis; v) any parathyroid disorders; and vi) previous SARS-CoV-2 infection.

Statistical analysis

Databases, double entries, checks for outstanding values, and locks are created when EXCEL software is used for data management. To conduct statistical analysis, SPSS 25.0 software is used. A planned study has a 90% chance of detecting a difference between MF-NNS and commercial mometasone furoate nasal spray (MFNS) nasal spray. Given that the study had more than 20 participants.

Results

The study includes 20 patients aged 10 to 50 years old who were given 50 mcg/dose of MFNS and MF-NNS. Demographic and clinical characteristics were comparable between the two groups. One subject (4%) out of ten who received MFNS did not complete the study or had the same gap in his doses. Two subjects who received MF-NNS refused to continue in the study due to other health issues. Three subjects were dropped from the curriculum. MF-NNS subjects had a significantly greater reduction in symptoms endpoint of physician-evaluated change in TNSS from baseline to day 21 than MFNS subjects. Similarly, significant improvements in MF-NNS were discovered. Improvement was increased in subjects who took MF-NNS for 21 days. Throughout the study, subjects were evaluated by physicians for overall rhinitis conditions in two groups: those who received MFNS and those who received MF-NNS. Subjects treated with MF-NNS had significantly better overall rhinitis at baseline than those treated with MFNS. Throughout the study, both groups showed a general trend toward continued improvement in the physician-evaluated overall condition of rhinitis. Furthermore, the degree of improvement increased with therapy duration (Tables 1-4).

Safety

The frequency of adverse events (AEs) was comparable between the MFNS and MF-NNS groups, and the majority of AEs were deemed to be of mild or moderate severity and unrelated to therapy throughout both times. 15% and 16% of patients receiving MFNS or MF-NNS, respectively, experienced adverse events (AEs) that were thought to be possibly, probably, or definitely related to the treatment. During the period, the most frequently reported treatment-related AEs for

Table 1. Patients' profile.

Characteristics	N
Age in years (average)	
Mean ± standard deviation	39
Range	10-50
Gender	
Male	12
Female	8
Body mass index	
Mean ± standard deviation	25
Diabetes as native disease	4
HIV	0
Hypertensive	5

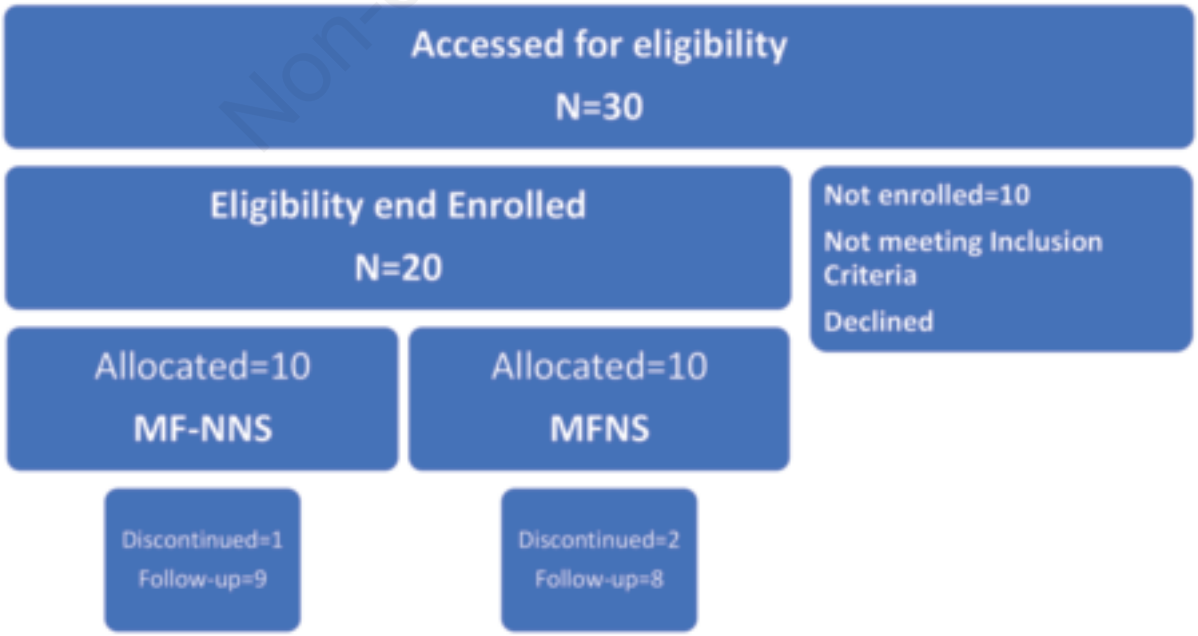

Figure 1. Subject flow chart throughout the study. MF-NNS, mometasone furoate nano-nasal spray.

MFNS and MF-NNS were: epistaxis, seven for MFNS (4%) and nine for MF-NNS (5%); headache, six for MFNS (3%) and five for MF-NNS (3%); sneezing, five for MFNS (3%) and seven for MF-NNS (4%); and coughing, three for MFNS (2%) and five for MF-NNS (3%).

Discussion

Perennial AR can begin in childhood and may be a precursor to allergies or respiratory conditions later in life. Because they are administered directly to the nasal mucosa, intranasal corticosteroids are an effective treatment for PAR in children. Their anti-inflammatory effects reduce nasal itching, sneezing, rhinorrhea, and nasal congestion.[12,13] The current study found that MF-NNS was significantly more effective

Table 2. Adverse events reported during the 21-day study period.

Variable	N	
Discontinuation of treatment	3	
Adverse events	**MF-NNS (9)**	**MFNS (8)**
Fatigue	1	1
Nausea	1	0
Headache	4	6
Insomnia	4	2
Pruritus	2	2
Anemia	0	0
Cough	3	7
Arthralgia	1	1

MF-NNS, mometasone furoate nano-nasal spray; MFNS, mometasone furoate nasal spray.

Table 3. Baseline and outcome ratings for the initial and final endoscopic examinations (on an ordinal scale of 0-3, expressed as mean standard deviation).

	Dryness of nasal mucus		Redness of nasal mucosa		Edema of nasal mucosa		Crusting/itching	
	Baseline	Outcome	Baseline	Outcome	Baseline	Outcome	Baseline	Outcome
MF-NNS	2.16±0.95	1.41±0.23	1.71±1.72	1.32±1.22	1.12±1.12	1.82±1.35	2.12±1.35	1.52±1.10
MFNS	2.72±0.15	1.89±0.21	1.61±1.82	1.92±1.02	2.15±1.92	2.85±1.33	1.19±1.35	1.92±1.30

MF-NNS, mometasone furoate nano-nasal spray; MFNS, mometasone furoate nasal spray.

Table 4. Characteristics.

Parameters	**Characteristics, n=20**		
Age	10-50		
Male sex, n (%)	12 (60)		
Female sex n (%)	8 (40)		
Diabetes, n (%)	4 (34)		
Hypertension, n (%)	5 (24)		
Median laboratory values before	**MF-NNS (9)**	**MFNS (8)**	**SD**
ALT, U/L	Between 15-30	Between 15-30	0.31
AST, U/L	Between 21-58	Between 21-58	0.25
ALP, IU/L	Between 69-90	Between 69-90	0.24
CPR, mg/L	Between 7-10	Between 7-10	0.12
LDH, U/L	Between 147-208	Between 147-208	0.26
IgE (kUA/L)	Between (0.70-3.49)	Between (0.70-3.49)	0.30
Median laboratory values after 21days treatment	**MF-NNS (9)**	**MFNS (8)**	**SD**
ALT, U/L	Between 18-31	Between 18-31	0.22
AST, U/L	Between 26-50	Between 26-50	0.46
ALP, IU/L	Between 63-90	Between 63-90	0.13
CPR, mg/L	Between 7-14	Between 7-14	0.45
LDH, U/L	Between 137-210	Between 137-210	0.23
IgE (kUA/L)	Between (0.70-3.49)	Between 3.50-17.49	0.42

MF-NNS, mometasone furoate nano-nasal spray; MFNS, mometasone furoate nasal spray; ALP, alkaline phosphate, ALT alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; LDH, lactase dehydrogenase; LFT, liver function test, SD, standard deviation.

than MFNS in relieving rhinitis symptoms in subjects aged 10-50 years, as evidenced by reductions from baseline over a 3-week period. Individual nasal symptom scores decreased significantly more with MF-NNS than with MFNS over days 1-21, supporting these findings. According to doctors and subjects, the general state of rhinitis and response to treatment improved during MF-NNS treatment. These variables showed a trend of further improvement over a three-month treatment period for both MF-NNS recipients and those receiving MFNS during the research period. The findings of this study support the findings of a dose range study in subjects aged 10 to 50 years with seasonal AR. Patients whose MF-NNS intake at 50 µg/day was significantly more effective than MFNS in lowering the doctors estimated rate. Doctors have reported a greater improvement in symptoms when using MF-NNS. There were no reported deaths or life-threatening adverse events. Subjects experienced no serious adverse events. Only three subjects discontinued treatment for reasons unrelated to ADR, one from group MFNNS and two from group MF-NS. No clinically significant changes in laboratory parameters, vital signs, or limited physical examinations were observed in any treatment group. The trials were completed by 17 subjects in total.

Conclusions

At the end of the trial, MF-NNS doses of 50 mcg given once daily significantly reduced rhinitis grade, with differences reaching statistical significance with commercial medications. Mometasone furoate nasal spray and MF-NNS were both tested for 21 days, and MF-NNS showed statistically greater improvements in congestion than baseline. MF-NNS reduces nasal symptoms such as nasal blockage and congestion, making it an effective and well-tolerated treatment for seasonal rhinitis in both adults and children.

References

1. Drazdauskaitė G, Layhadi JA, Shamji MH. Mechanisms of allergen immunotherapy in allergic rhinitis. Curr Allergy Asthma Rep 2021;21:1-17.
2. Baena-Cagnani CE, Patel P. Efficacy and long-term safety of mometasone furoate nasal spray in children with perennial allergic rhinitis. Curr Med Res Opin 2010;26:2047-55.
3. González-Núñez V, Valero AL, Mullol J. Impact of sleep as a specific marker of quality of life in allergic rhinitis. Curr Allergy Asthma Rep 2013;13:131-41.
4. Nielsen GD, Hansen JS, Lund RM, et al. IgE-mediated asthma and rhinitis I: a role of allergen exposure? Pharmacol Toxicol 2002;90:231-42.
5. Skoner DP. Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. J Allergy Clin Immunol 2001;108:S2-S8.
6. Eifan AO, Durham SR. Pathogenesis of rhinitis. Clin Experi Allergy 2016;46:1139-51.
7. Berkowitz R, Roberson S, Zora J, et al. (eds). Mometasone furoate nasal spray is rapidly effective in the treatment of seasonal allergic rhinitis in an outdoor (park), acute exposure setting. Allergy & Asthma Proceedings; OceanSide Publications: 1999.
8. Scadding GK. Optimal management of allergic rhinitis. Archiv Dis Childhood 2015;100:576-82.
9. Carr WW, Ratner P, Munzel U, et al. (eds). Comparison of intranasal azelastine to intranasal fluticasone propionate for symptom control in moderate-to-severe seasonal allergic rhinitis. Allergy & Asthma Proceedings; 2012.
10. Komi DEA, Mortaz E, Amani S, et al. The role of mast cells in IgE-independent lung diseases. Clin Rev Allergy Immunol 2020;58:377-87.
11. Far J, Abdel-Haq M, Gruber M, Abu Ammar A. Developing biodegradable nanoparticles loaded with mometasone furoate for potential nasal drug delivery. ACS Omega 2020;5:7432-9.
12. Williamson I, Benge S, Barton S, et al. Topical intranasal corticosteroids in 4-11 year old children with persistent bilateral otitis media with effusion in primary care: double blind randomised placebo controlled trial. BMJ 2009;339.
13. Salib R, Drake-Lee A, Howarth P. Allergic rhinitis: past, present and the future. Clin Otolaryngol Allied Sci 2003;28:291-303.