

# **Title of the study**

**Mometasone Furoate Nasal Spray in Italian Children With  
Seasonal Allergic Rhinitis: a Comprehensive Assessment**

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# Study Protocol and Statistical Analysis Plan

The present study recruited children suffering from SAR during the pollen season. They had a poor control of SAR despite antihistaminic treatment (cetirizine 2.5 mg bid in preschoolers or 5 mg bid in schoolers). SAR diagnosis was performed according to validated criteria. Allergy was defined if nasal symptom history was consistent with documented sensitization.

Inclusion criteria were: age range 4-12 years, SAR diagnosis, Total Symptoms Score (TSS)  $\geq$  6, and written informed consent of both parents or legal guardians. Exclusion criteria were: perennial AR, rhinitis due to other causes, concomitant acute or chronic rhinosinusitis, nasal polyps, asthma comorbidity, current use of topical or systemic corticosteroids, antihistamines, antileukotrienes, inadequate washout of them, nasal anatomic defect, respiratory infections in the last two weeks, participation in other clinical studies in the previous month, documented hypersensitivity to the study product or its excipients, and trip planned outside of the study area.

The study was conducted in a third-level pediatrics department located in Southern Italy. The study procedure was approved by the local Ethics Committee (Prt n 408, 20/06/2019).

Children were randomly (ratio 1:1) subdivided into two groups: the active group treated with MFNS (Mometasone group) and the control group treated with isotonic saline. For both groups, the schedule was for one spray into each nostril (MFNS 50 mcg/spray) twice a day for 21 days.

The participants were evaluated at baseline (T0), after 7 (T1) and 21 (T2) days, and 30 days (T3) after treatment discontinuation.

During the study, systemic or intranasal antihistamines, other corticosteroids, leukotriene antagonists, and sodium cromoglicate were prohibited.

The primary endpoint of this study was the change in eosinophilic infiltrate, assessed by nasal cytology, after the treatment. The secondary objectives were the nasal mast cell and neutrophil count, symptom severity, and QoL changes during the study.

Nasal cytology is a well-defined methodology. The procedure included sampling, processing, and microscope reading. Sampling required collecting cells from the surface of the middle portion of the inferior turbinate by a sterile disposable curette. The procedure was performed under anterior rhinoscopy, with an appropriate light source, and it was painless. The sample obtained was immediately smeared on a glass slide, air-dried, and stained with May-Grünwald-Giemsa (MGG) for 30 minutes. Next, the stained sample was read at optical microscopy, with a 1000x objective with oil immersion. The count of eosinophils, neutrophils, and mast cells was expressed as a mean of 10 microscopic fields.

The validated Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) consists of 23 questions in 5 domains (nasal symptoms, ocular symptoms, practical issues, limitation of activities, other symptoms) that are answered on a 7-point scale (0-6), where 0 represents the absence of problems and 6 the greatest symptom distress. Children will complete the questionnaire together with a parent at baseline and during the study. A Total Score was calculated as the mean of the 5 domains.

Total symptom score was the sum of 3 domains: i) nasal symptoms (TNSS) included itching, sneezing, rhinorrhea, nasal congestion; ii) ocular symptoms (TOSS): itching, hyperemia of the conjunctiva, tearing; and iii) throat symptoms (TTSS): itching, coughing. With the help of their parents, patients scored symptoms severity on a 4-point scale: 0 = absent or irrelevant, 1 = mild, 2 = moderate, 3 = severe. Total symptom score was assessed at 12 hours (TTS 12h) and two weeks (TTS 2W) before the visits. TSS represents the doctor's point of view of symptom severity.

A visual analogic scale (VAS) measured the parental perception of symptom severity (0=no symptom; 10=very severe symptoms).

Safety was assessed on the incidence of adverse events for each treatment and physical examination.

The statistical analysis included different tests. Shapiro-Wilk test was performed to investigate continuous variables distribution. Differences between the active and control group were tested with Mann-Whitney U test for independent samples. Longitudinal changes for continuous variables were investigated by Wilcoxon signed-rank test for paired samples. Delta changes in questionnaires scores were calculated for each group as T1-T0 scores for the control group, T2-T0 scores, and T3-T0 scores for the mometasone group. Differences in delta changes between groups were investigated by Mann-Whitney U test. Chi-square test and Fisher exact test were performed for differences in categorical variables. A  $p \leq 0.05$  was considered statistically significant. Data were expressed as median (interquartile range) or as a percentage as appropriate. All analyses were performed with SAS® on Demand for Academics (Cary, NC: SAS Institute Inc.)