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Original article

# A comparison between mometasone furoate nasal spray and intranasal glycyrrhetic acid in patients with allergic rhinitis: a preliminary study in clinical practice

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**Abstract.** Allergic rhinitis (AR) is caused by an IgE-mediated inflammatory reaction consequent to the exposure to the causal allergen. Glycyrrhetic acid (GlyAc) is a natural compound extracted from the liquorice that exerts anti-inflammatory activity. This real-life study compared intranasal GlyAc, present in a medical device containing also glycerol and mannitol, with mometasone furoate nasal spray (MFNS) in 50 adult outpatients with AR. Both treatments lasted 2 months. Endoscopic signs, perception of symptom severity, assessed by VAS, and nasal function measured by rhinomanometry were evaluated at baseline (T0), after one (T1) and two (T2) months. The intergroup analysis showed that at T1 there was no significant difference between groups about the use of decongestants and antihistamines, turbinate hypertrophy and pale mucosa, perception of olfaction and snoring. At T2 there was no significant difference between groups about use of relievers, all endoscopic signs, and perception of nasal discomfort, nasal obstruction, olfaction, and snoring. The intragroup analysis showed that in MFNS group there was a significant change during the entire period of treatment for all parameters except watery rhinorrhea (sign) and ocular discomfort; in GlyAc group there was a significant change during the entire period of treatment for all parameters. In conclusion, this preliminary study, conducted in clinical practice, evidenced that intranasal CysAC plus mannitol was able to significantly improve nasal endoscopic signs, perception of symptoms, and nasal function in patients with AR. Therefore, GlyAc could be a reasonable therapeutic option to control allergic inflammation. (www.actabiomedica.it)

**Key words:** glycyrrhetic acid, mannitol, mometasone furoate, allergic rhinitis, topical treatment, clinical practice

## Introduction

Allergic rhinitis (AR) is caused by a type 2 inflammation characterized by functional defect of allergen-specific T regulatory cells, T helper 2 cell polarization, and eosinophilic mucosal infiltration (1). Also, AR is frequently associated with comorbidity, such as conjunctivitis and asthma (2). Allergic inflammation causes typical AR symptoms, including itching, sneezing, watery rhinorrhea (anterior and posterior), and nasal obstruction. In particular, nasal obstruction is a very bothersome symptom that may also induce nasal discomfort, reduced olfaction and disturbed sleep, and, lastly, significantly impairs quality of life (QoL) and daily activities (3, 4).

As allergic inflammation is the mainstay of AR symptoms, anti-inflammatory drugs are the most effective treatment option (5). Intranasal corticosteroids

are widely used with effective and safe outcomes (6). In this regard, mometasone furoate nasal spray (MFNS) is one of the most used intranasal corticosteroids, as a matter of fact MFNS quickly reduces allergic inflammation and relieves AR symptoms (7). Even though the safety profile of intranasal corticosteroids is substantially fair, there is popular dislike of them, the so-called corticosteroid phobia (8). Therefore, non-steroidal anti-inflammatory drugs have been developed to remedy this disappointment. In this regard, it has been discovered that a natural compound, derived from the *Glycyrrhiza glabra*, exerts anti-inflammatory activity, inhibiting extracellular high mobility group protein box 1 (HMGB1), such as an alarmin involved in inflammation (9). Glycyrrhizin is a glycoside alkaloid present in *Glycyrrhiza glabra* roots and is composed of one molecule of glycyrrhetic acid (GlyAc), the active component, and two molecules of glucuronic acid. GlyAc has no cytotoxicity, even at high concentration, and good pharmacological tolerance (10). GlyAc significantly reduced HMGB1 levels in nasal lavage fluid of AR children and HMGB1 *in vitro* release from cultured eosinophils, and increased eosinophilic apoptosis (11). These anti-inflammatory effects resulted in improved mucociliary clearance as demonstrated in patients with CRSwNP (12). GlyAC also improved nasal symptoms in children with AR and adults with nasal congestion (13, 14). GlyAc is presently available as a multicomponent medical device containing also mannitol, effective anti-edema osmotic molecules.

On the basis of this background, the current study compared MFNS with GlyAc in patients with AR in clinical practice.

## Patients and methods

The present study was conducted as prospective and randomized study. Globally, 50 outpatients (27 males; mean age 37.9 ± 10.72 years) suffering from AR were enrolled. AR diagnosis was performed, according to validated criteria (15). Briefly, nasal symptom history had to be consistent with documented sensitization, i.e. allergic symptoms should occur after exposure to the sensitizing allergen.

Inclusion criteria were: i) age range between 18 and 65 years, ii) both genders, iii) AR diagnosis, iv) presence of nasal symptoms since at least one month, documented by a run-in period, and v) written informed consent. Exclusion criteria were: i) presence of concomitant chronic nasal diseases, ii) any acute upper respiratory tract infections, iii) presence of massive occlusive nasal polyposis, iv) diagnosis of cystic fibrosis or Kartagener syndrome, v) immune diseases and/or immunodeficiency (congenital or acquired), vi) clinical conditions (systemic diseases or other) that may interfere with the evaluation of the safety and efficacy of the products under investigation.

The primary endpoint was the demonstration of non-inferiority of GlyAc in comparison with MFNS about the perceived symptoms (including nasal discomfort, nasal obstruction, rhinorrhea, itching, sneezing, post-nasal drip, olfaction, snoring, bronchial and ocular discomfort, quality of life, quality of sleep, and impact on daily activities) measured by a standard Visual Analogue Scale (VAS).

The secondary endpoints were the changes of: i) the nasal endoscopy findings (including turbinate hypertrophy, watery rhinorrhea, post-nasal drip, and pale mucosa), ii) the nasal airway resistance assessed by Active Anterior Rhinomanometry (AAR) in basal condition and after decongestant test (3), iii) the impact of the treatment on the quality of life, quality of sleep and ability to perform daily activities, iv) the tolerability and the compliance, and v) any possible adverse event.

Patients were randomly (1:1 ratio) subdivided in two groups: MFSN Group (2 puffs for nostril once daily for 60 days) and GlyAc Group (2 puffs for nostril twice a day for 60 days). The patients were evaluated at baseline (T0), after 30 (T1) and 60 (T2) days.

Patients could take as rescue medication intranasal decongestants and/or systemic antihistamines, their use was recorded and assessed.

The study protocol was approved by the Ethics Committee of the Clinical Republican Hospital of Chisinau.

### *Statistical analysis*

Continuous variables were given as means with standard deviations and categorical variables as num-

ber of subjects and percentage values. Turbinate hypertrophy, watery rhinorrhea, and post-nasal drip were dichotomised as absent or present.

To evaluate the statistical significance of the clinical characteristics across the three time-point (T0, T1, and T2), an intra-group analysis was performed. In particular, continuous variables were analysed using Friedman's test, while categorical variables were analysed by the Cochran's Q test. Thereafter to decide which groups are significantly different from each other, the post-hoc tests were performed using the Wilcoxon or the McNemar test for continuous or categorical variables, respectively.

An inter-group analysis was performed comparing data between the two treatment groups of patients at the three time-point. In particular, the Wilcoxon test and the Pearson's Chi-squared Test (Fisher's Exact test where appropriated) were used for continuous and categorical variables, respectively.

Owing to the exploratory design of this study, adjustment for multiple testing was performed using Bonferroni method only in the post-hoc tests. Differences, with a p-value less than 0.05, were selected as significant and data were acquired and analysed in R v3.6.2 software environment.

## Results

All outpatients completed the study. The compliance was good in all patients. The tolerability was good in 79% of MFNS patients and 92% of GlyAc patients. No clinically relevant adverse events were reported.

*Inter-group analysis*

The descriptive statistics of demographic and clinical variables in the two groups is reported in Table 1.

At baseline, the two groups were not homogeneous for two endoscopic signs, post-nasal drip and pale mucosa (both more frequent in GlyAc group), for the nasal resistances (higher in GlyAc group), and for the perceived symptom of ocular discomfort (more severe in GlyAc group).

At T1, there was no significant difference between groups about the use of decongestants and antihistamines, turbinate hypertrophy and pale mucosa, perception of olfaction and snoring. Patients in MFNS group had significantly less frequently watery rhinorrhea, post-nasal drip, and lower resistances, than patients treated with GlyAc.

At T2, there was no significant difference between groups about use of relievers, all endoscopic signs, and perception of nasal discomfort, nasal obstruction, olfaction, and snoring. Patients treated with MFNS had significantly lower resistances, and lower perception of symptom severity of rhinorrhea, itching, sneezing, post-nasal drip, ocular discomfort, quality of life, quality of sleep, and impact on daily activities, than patients in GlyAc group.

*Intra-group analysis*

MFSN group: there was a significant change during the entire period of treatment for all parameters except watery rhinorrhea (sign) and ocular discomfort (Table 2). The post-hoc analysis showed that there were some parameters that did not significantly change at T1 and/or T2 in comparison with baseline values as reported in detail in Table 2.

GlyAc group: there was a significant change during the entire period of treatment for all parameters (Table 3). The post-hoc analysis showed that there were some parameters that did not significantly change at T1 and/or T2 in comparison with baseline values as reported in detail in Table 3.

## Discussion

Type 2 inflammation sustains signs, symptoms and functional impairment in AR patients. For this reason, intranasal corticosteroids are an effective therapeutic option as are able to improve clinical feature and restore nasal function. The International guidelines state that intranasal corticosteroids are usually safe (15). However, many doctors, and also patients, discourage a prolonged use for potential side effects. GlyAc could be a promising alternative to corticosteroids as has been demonstrated to be effective and safe (10-14). A previous study compared GlyAc with intranasal budesonide (11). The findings showed that

**Table 1**: Demographic data and inter-group analysis at the three time points. Characteristic: variable taken into account; p-value: test p-value (see the text for abbreviations and further details)

| Characteristic | Time T0 | | | Time T1 | | | Time T2 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Treatment | | P-value | Treatment | | P-value | Treatment | | P-value |
| | *MFSN* | *GlyAc* | | *MFSN* | *GlyAc* | | *MFSN* | *GlyAc* | |
| **Age** | 37.98 (9.34) | 37.83 (12.03) | 0.7932 | | | | | | |
| **Gender** *Male* | 11 (45.83%) | 16 (61.54%) | 0.4070 | | | | | | |
| *Female* | 13 (54.17%) | 10 (38.46%) | | | | | | | |
| **Decongestants use** | 9 (37.5%) | 8 (30.77%) | 0.7666 | 2 (8.33%) | 4 (15.38%) | 0.6688 | 1 (4.17%) | 3 (11.54%) | 0.6105 |
| **Systemic antihistamines use** | 7 (29.17%) | 7 (26.92%) | 0.9999 | 2 (8.33%) | 3 (11.54%) | 0.9999 | 0 (0%) | 2 (7.69%) | 0.4906 |
| **SIGNS** | | | | | | | | | |
| **Turbinate Hypertrophy** | 24 (100%) | 26 (100%) | 0.9999 | 24 (100%) | 26 (100%) | 0.9999 | 14 (58.33%) | 14 (53.85%) | 0.7827 |
| **Watery Rhinorrhea** | 14 (58.33%) | 21 (80.77%) | 0.1239 | 11 (45.83%) | 21 (80.77%) | **0.0176** | 7 (29.17%) | 10 (38.46%) | 0.5592 |
| **Post-nasal Drip** | 12 (50%) | 21 (80.77%) | **0.0359** | 11 (45.83%) | 20 (76.92%) | **0.0404** | 7 (29.17%) | 10 (38.46%) | 0.0996 |
| **Pale mucosa** | 18 (75%) | 25 (96.15%) | **0.0451** | 15 (62.5%) | 21 (80.77%) | 0.2109 | 7 (29.17%) | 8 (30.77%) | 0.9999 |
| **NASAL AIRFLOW** | | | | | | | | | |
| **Inspiratory Resistance** | 0.96 (0.33) | 1.3 (0.25) | **0.0001** | 0.55 (0.27) | 1.04 (0.18) | **<0.0001** | 0.39 (0.16) | 0.64 (0.18) | **<0.0001** |
| **Expiratory Resistance** | 1.05 (0.34) | 1.49 (0.16) | **<0.0001** | 0.61 (0.26) | 1.14 (0.21) | **<0.0001** | 0.46 (0.17) | 0.65 (0.21) | **0.0001** |
| **Nasal Decongestant Test Insp.** | 0.59 (0.27) | 0.95 (0.1) | **<0.0001** | 0.41 (0.18) | 0.74 (0.16) | **<0.0001** | 0.34 (0.16) | 0.42 (0.17) | **0.0285** |
| **Nasal Decongestant Test Exp.** | 0.66 (0.28) | 1.03 (0.1) | **<0.0001** | 0.44 (0.18) | 0.79 (0.15) | **<0.0001** | 0.38 (0.15) | 0.46 (0.2) | **0.0489** |
| **SYMPTOMS** | | | | | | | | | |
| **VAS Nasal Discomfort** | 5.29 (3.79) | 6.34 (2.74) | 0.5264 | 2.74 (2.63) | 3.82 (2.02) | **0.0456** | 0.95 (1.66) | 1.67 (2.3) | 0.2801 |
| **VAS Nasal Obstruction** | 7.3 (2.28) | 7.36 (1.57) | 0.9534 | 2.65 (1.61) | 3.85 (1.51) | **0.0030** | 0.85 (1.38) | 1.54 (1.99) | 0.1413 |
| **VAS Rhinorrea** | 5.47 (3.52) | 6.88 (1.98) | 0.2171 | 1.78 (1.9) | 3.54 (1.57) | **0.0006** | 0.37 (0.8) | 1.77 (1.96) | **0.0009** |
| **VAS Itching** | 3.74 (3.83) | 4.71 (3.36) | 0.3959 | 0.9 (1.48) | 2 (1.82) | **0.0165** | 0.01 (0.04) | 0.88 (1.17) | **<0.0001** |
| **VAS Sneezing** | 5.17 (3.48) | 5.7 (2.86) | 0.5588 | 1.1 (1.68) | 2.72 (2.11) | **0.0055** | 0.04 (0.18) | 1.36 (1.67) | **0.0001** |
| **VAS Post-nasal Drip** | 3.93 (3.56) | 6.02 (2.11) | 0.0682 | 1.54 (1.53) | 3.15 (2.14) | **0.0033** | 0.27 (0.66) | 1.55 (1.86) | **0.0005** |
| **VAS Olfaction** | 2.48 (2.67) | 1.33 (2.22) | 0.0892 | 0.93 (1.29) | 0.62 (1.11) | 0.3006 | 0.38 (0.75) | 0.22 (0.49) | 0.5625 |
| **VAS Snoring** | 1.92 (2.48) | 1.32 (2.35) | 0.3841 | 0.8 (1.2) | 0.87 (1.67) | 0.5656 | 0.25 (0.53) | 0.37 (0.84) | 0.7580 |
| **VAS Bronchial Discomfort** | 0.58 (1.53) | 1.01 (2.41) | 0.9152 | 0.55 (1.4) | 1.05 (2.52) | 0.9152 | 0.34 (1.06) | 0.9 (2.19) | 0.9394 |
| **VAS Ocular Discomfort** | 0.9 (2.16) | 2.28 (2.64) | **0.0246** | 0.3 (1.03) | 0.98 (1.53) | **0.0414** | 0 (0) | 0.34 (0.81) | **0.0265** |
| **VAS Quality of Life** | 7.78 (2.35) | 6.9 (2.11) | 0.1320 | 2.3 (1.74) | 3.79 (1.76) | **0.0021** | 0.82 (1.4) | 1.78 (1.97) | **0.0179** |
| **VAS Quality of Sleep** | 7.97 (2.23) | 7.05 (2.06) | 0.0756 | 2.33 (1.97) | 3.69 (1.75) | **0.0030** | 0.8 (1.42) | 1.67 (1.92) | **0.0318** |
| **VAS Impact on Daily Activities** | 7.82 (2.44) | 6.57 (2.24) | 0.0644 | 1.98 (1.83) | 3.33 (1.87) | **0.0056** | 0.69 (1.29) | 1.63 (2.12) | **0.0481** |

**Table 2.** Intra-group analysis in MFSN group at the three time points. Characteristic: variable taken into account; p-value: test p-value (see the text for abbreviations and further details)

| Characteristic | Time T0 | Time T1 | Time T2 | p-value | Post-hoc analysis | | |
|---|---|---|---|---|---|---|---|
| | | | | | T0 vs T1 | T1 vs T2 | T0 vs T2 |
| **Compliance** | | | | 0.9999 | | | |
| *good* | | 24 (100%) | 24 (100%) | | | | |
| **Tolerability** | | | | 0.9999 | | | |
| *good* | | 22 (91.67%) | 19 (79.17%) | | | | |
| *fairly good* | | 2 (8.33%) | 5 (20.83%) | | | | |
| **Decongestants use** | 9 (37.5%) | 2 (8.33%) | 1 (4.17%) | **0.0008** | **0.0469** | 0.9999 | **0.0234** |
| **Systemic antihistamines use** | 7 (29.17%) | 2 (8.33%) | 0 (0%) | **0.0076** | 0.3750 | 0.9999 | **0.0469** |
| **SIGNS** | | | | | | | |
| **Turbinate Hypertrophy** | 24 (100%) | 24 (100%) | 14 (58.33%) | **<0.0001** | 0.9999 | **0.0059** | **0.0059** |
| **Watery Rhinorrhea** | 14 (58.33%) | 11 (45.83%) | 7 (29.17%) | 0.0581 | | | |
| **Post-Nasal Drip** | 12 (50%) | 11 (45.83%) | 3 (12.5%) | **0.0013** | 0.9999 | 0.0645 | **0.0352** |
| **Pale Mucosa** | 18 (75%) | 15 (62.5%) | 7 (29.17%) | **0.0010** | 0.9999 | **0.0234** | **0.0103** |
| **NASAL AIRFLOW** | | | | | | | |
| **Inspiratory Resistance** | 0.96 (0.33) | 0.55 (0.27) | 0.39 (0.16) | **<0.0001** | **<0.0001** | **<0.0001** | **<0.0001** |
| **Expiratory Resistance** | 1.05 (0.34) | 0.61 (0.26) | 0.46 (0.17) | **<0.0001** | **0.0001** | **<0.0001** | **0.0001** |
| **Nasal Decongestant Test Insp.** | 0.59 (0.27) | 0.41 (0.18) | 0.34 (0.16) | **<0.0001** | **<0.0001** | **<0.0001** | **<0.0001** |
| **Nasal Decongestant Test Exp.** | 0.66 (0.28) | 0.44 (0.18) | 0.38 (0.15) | **<0.0001** | **<0.0001** | **<0.0001** | **<0.0001** |
| **SYMPTOMS** | | | | | | | |
| **VAS Nasal Discomfort** | 5.29 (3.79) | 2.74 (2.63) | 0.95 (1.66) | **<0.0001** | 0.0848 | 0.0794 | **0.0013** |
| **VAS Nasal Obstruction** | 7.3 (2.28) | 2.65 (1.61) | 0.85 (1.38) | **<0.0001** | **0.0262** | **0.0143** | **<0.0001** |
| **VAS Rhinorrhea** | 5.47 (3.52) | 1.78 (1.9) | 0.37 (0.8) | **<0.0001** | **0.0157** | 0.8538 | **0.0001** |
| **VAS Itching** | 3.74 (3.83) | 0.9 (1.48) | 0.01 (0.04) | **<0.0001** | **0.0035** | **<0.0001** | **<0.0001** |
| **VAS Sneezing** | 5.17 (3.48) | 1.1 (1.68) | 0.04 (0.18) | **<0.0001** | **0.0074** | 0.0724 | **<0.0001** |
| **VAS Post-nasal Drip** | 3.93 (3.56) | 1.54 (1.53) | 0.27 (0.66) | **<0.0001** | **0.0051** | 0.7815 | **<0.0001** |
| **VAS Olfaction** | 2.48 (2.67) | 0.93 (1.29) | 0.38 (0.75) | **<0.0001** | **0.0121** | 0.4667 | **<0.0001** |
| **VAS Snoring** | 1.92 (2.48) | 0.8 (1.2) | 0.25 (0.53) | **0.0001** | **0.0392** | 0.0828 | **<0.0001** |
| **VAS Bronchial Discomfort** | 0.58 (1.53) | 0.55 (1.4) | 0.34 (1.06) | **0.0498** | **0.0001** | **<0.0001** | **<0.0001** |
| **VAS Ocular Discomfort** | 0.9 (2.16) | 0.3 (1.03) | 0 (0) | 0.0545 | | | |
| **VAS Quality of Life** | 7.78 (2.35) | 2.3 (1.74) | 0.82 (1.4) | **<0.0001** | **<0.0001** | **0.0085** | **0.0037** |
| **VAS Quality of Sleep** | 7.97 (2.23) | 2.33 (1.97) | 0.8 (1.42) | **<0.0001** | **<0.0001** | **0.0067** | **0.0030** |
| **VAS Impact on Daily Activities** | 7.82 (2.44) | 1.98 (1.83) | 0.69 (1.29) | **<0.0001** | **0.0001** | **0.0088** | **0.0003** |

**Table 3.** Intra-group analysis in GlyAc group at the three time points. Characteristic: variable taken into account; p-value: test p-value (see the text for abbreviations and further details)

| Characteristic | Time T0 | Time T1 | Time T2 | p-value | Post-hoc analysis | | |
|---|---|---|---|---|---|---|---|
| | | | | | T0 vs T1 | T1 vs T2 | T0 vs T2 |
| **Compliance** | | | | 0.9999 | | | |
| *good* | | 26 (100%) | 26 (100%) | | | | |
| **Tolerability** | | | | 0.9999 | | | |
| *good* | | 24 (92.31%) | 24 (92.31%) | | | | |
| *fairly good* | | 2 (7.69%) | 2 (7.69%) | | | | |
| **Decongestants use** | 8 (30.77%) | 4 (15.38%) | 3 (11.54%) | 0.1482 | | | |
| **Systemic antihistamines use** | 7 (26.92%) | 3 (11.54%) | 2 (7.69%) | **0.0150** | 0.1365 | 0.9519 | 0.0760 |
| **SIGNS** | | | | | | | |
| **Turbinate Hypertrophy** | 26 (100%) | 26 (100%) | 14 (53.85%) | **<0.0001** | 0.9999 | **0.0016** | **0.0016** |
| **Watery Rhinorrhea** | 21 (80.77%) | 21 (80.77%) | 10 (38.46%) | **<0.0001** | 0.9999 | **0.0029** | **0.0029** |
| **Post-Nasal Drip** | 21 (80.77%) | 20 (76.92%) | 9 (34.62%) | **<0.0001** | 0.9999 | **0.0029** | **0.0015** |
| **Pale Mucosa** | 25 (96.15%) | 21 (80.77%) | 8 (30.77%) | **<0.0001** | 0.3750 | **0.0029** | **<0.0001** |
| **NASAL AIRFLOW** | | | | | | | |
| **Inspiratory Resistance** | 1.3 (0.25) | 1.04 (0.18) | 0.64 (0.18) | **<0.0001** | **0.0025** | **<0.0001** | **0.0025** |
| **Expiratory Resistance** | 1.49 (0.16) | 1.14 (0.21) | 0.65 (0.21) | **<0.0001** | **0.0162** | **<0.0001** | **0.0061** |
| **Nasal Decongestant Test Insp.** | 0.95 (0.1) | 0.74 (0.16) | 0.42 (0.17) | **<0.0001** | **<0.0001** | **<0.0001** | **<0.0001** |
| **Nasal Decongestant Test Exp.** | 1.03 (0.1) | 0.79 (0.15) | 0.46 (0.2) | **<0.0001** | **0.0001** | **<0.0001** | **0.0001** |
| **SYMPTOMS** | | | | | | | |
| **VAS Nasal Discomfort** | 6.34 (2.74) | 3.82 (2.02) | 1.67 (2.3) | **<0.0001** | 0.9999 | **0.0055** | **<0.0001** |
| **VAS Nasal Obstruction** | 7.36 (1.57) | 3.85 (1.51) | 1.54 (1.99) | **<0.0001** | 0.9999 | **0.0055** | **<0.0001** |
| **VAS Rhinorrhea** | 6.88 (1.98) | 3.54 (1.57) | 1.77 (1.96) | **<0.0001** | 0.9999 | **0.0015** | **<0.0001** |
| **VAS Itching** | 4.71 (3.36) | 2 (1.82) | 0.88 (1.17) | **<0.0001** | 0.9737 | **0.0052** | **0.0006** |
| **VAS Sneezing** | 5.7 (2.86) | 2.72 (2.11) | 1.36 (1.67) | **<0.0001** | 0.6531 | **0.0424** | **0.0001** |
| **VAS Post-nasal Drip** | 6.02 (2.11) | 3.15 (2.14) | 1.55 (1.86) | **<0.0001** | 0.999 | **0.0043** | **<0.0001** |
| **VAS Olfaction** | 1.33 (2.22) | 0.62 (1.11) | 0.22 (0.49) | **<0.0001** | **0.0163** | **<0.0001** | **0.0008** |
| **VAS Snoring** | 1.32 (2.35) | 0.87 (1.67) | 0.37 (0.84) | **<0.0001** | **0.0203** | **<0.0001** | **0.0005** |
| **VAS Bronchial Discomfort** | 1.01 (2.41) | 1.05 (2.52) | 0.9 (2.19) | 0.1266 | | | |
| **VAS Ocular Discomfort** | 2.28 (2.64) | 0.98 (1.53) | 0.34 (0.81) | **<0.0001** | 1.0000 | 0.2238 | **<0.0001** |
| **VAS Quality of Life** | 6.9 (2.11) | 3.79 (1.76) | 1.78 (1.97) | **<0.0001** | **0.0014** | 0.9999 | **<0.0001** |
| **VAS Quality of Sleep** | 7.05 (2.06) | 3.69 (1.75) | 1.67 (1.92) | **<0.0001** | **0.0010** | 0.9999 | **<0.0001** |
| **VAS Impact on Daily Activities** | 6.57 (2.24) | 3.33 (1.87) | 1.63 (2.12) | **<0.0001** | **0.0050** | 0.9999 | **<0.0001** |

both treatments significantly improved clinical parameters and reduced inflammatory biomarkers, namely HMGB1.

The present study was designed to compare GlyAc with another popular intranasal corticosteroid, such as MFNS, in a real-life setting, such as in outpatients visited at a rhinologic clinic.

The inter-group comparison demonstrates that there was no significant difference between corticosteroid treatment and GlyAc about the use of relievers, such as decongestants and antihistamines. This outcome is clinically important as demonstrates that both treatments were able to control AR. Moreover, there was no significant different also for the turbinate hypertrophy, watery anterior and posterior (post-nasal drip) rhinorrhea, such as the visible discharge in the nasal cavity, and pale mucosa: these endoscopic signs mean the intensity of inflammatory reaction. So, these findings establish that both MFNS and GlyAc reduce inflammatory phenomena. On the contrary, there was a significant difference between groups about the effect on nasal resistances, but it has to be noted that these differences were present even at baseline. Consequently, the clinically relevant information may derive only by the intragroup analysis. Concerning the subjective perception of symptom severity, assessed by VAS, MFNS significantly reduced the symptom perception even after one month for many parameters. However, the significant difference disappeared for some symptoms, including nasal discomfort, nasal obstruction, olfaction, snoring, and bronchial discomfort, at the end of the treatment. This outcome depends on the fact that corticosteroids are a fast mechanism of action, but CysAc, even though more slowly than MFNS, has equally an effect on many symptoms that express the allergic inflammation. In particular, nasal discomfort and obstruction are the typical expression of type 2 inflammation as nasal airflow limitation and severity of nasal obstruction very well correlate (16). Moreover, olfaction impairment and snoring are closely linked to nasal inflammation (17, 18). These data confirm that 2-month CysAc treatment can control nasal inflammation as well as intranasal corticosteroids.

The intra-group analysis confirmed that MFNS was, as expected, effective in improving AR signs, symptoms, and nasal function (19). Interestingly, also CysAc significantly improved all the evaluated parameters. This finding depends on the dual mechanism of action of the medical device: the anti-inflammatory activity due to GlyAc and the anti-edema effect due to mannitol (20).

However, there are some limitations of this study: i) the open design, ii) the relatively limited number of treated patients, iii) the absence of inflammatory mediator assessment, and iv) the study was mono-center. Moreover, the two groups were not homogeneous for some parameters, even though it could occur in real-life studies. For these reasons, the findings should be considered preliminary; indeed, a continuation is ongoing.

## Conclusions

This preliminary study, conducted in clinical practice, evidenced that intranasal CysAC plus mannitol was able to significantly improve nasal endoscopic signs, perception of symptoms, and nasal function in patients with AR. In addition, there was no significant difference between nasal corticosteroid and GlyAC about the use of relievers, endoscopic signs of inflammation, and perception of nasal obstruction and discomfort. Therefore, GlyAc could be a reasonable therapeutic option to control allergic inflammation.

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**Conflict of interest:** Nobody of them, but VD employee of DMG, has conflicts of interest in this issue.

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