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Main Article

# Daily versus self-adjusted dosing of topical mometasone furoate nasal spray in patients with allergic rhinitis: randomised, controlled trial

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**Abstract**

Background: Many patients with allergic rhinitis are reluctant to use daily intranasal steroids for prolonged periods. A self-adjusted regimen which delivers reasonable control of allergic rhinitis may be more acceptable to such patients.

Objectives: To compare the efficacy of daily use of mometasone furoate nasal spray, versus a self-adjusted regimen, in patients with chronic allergic rhinitis, in terms of symptom control and nasal volume change.

Setting: Ambulatory visits in an office setting.

Patients and methods: Sixty patients with chronic allergic rhinitis were randomised: 30 were prescribed mometasone furoate nasal spray once daily for six weeks, while 30 were prescribed the same spray daily for one week, every alternate day for one week and then on a self-adjusted regimen for four weeks. Patients kept a symptom diary documenting sneezing, rhinorrhoea, nasal blockage and nasal itching. Acoustic rhinometry was used to measure the total nasal cavity volume at the first visit and at the end of the treatment period.

Results: The total nasal score on treatment days showed an improvement in both groups, compared with baseline measurements. There was no significant difference in total nasal scores between the two groups, except on days 10 ($p = 0.043$), 20 ($p = 0.008$), 23 ($p = 0.19$), 30 ($p = 0.008$) and 37 ($p = 0.000$), when the daily group's total nasal score was significantly lower than the self-adjusted group's total nasal score, and on day 8 ($p = 0.004$), when the self-adjusted group's total nasal score was significantly lower than the daily group's total nasal score. Total nasal cavity volume significantly increased in both groups ($p = 0.0001$), with no statistically significant difference between the groups.

Conclusions: Self-adjusted dosage of mometasone furoate nasal spray gives reasonable control of allergic rhinitis (albeit with some 'breakthrough' symptoms). Patients should learn how to control these symptoms with the least number of steroid doses.

**Key words: Allergic Rhinitis; Mometasone Furoate; Corticosteroids; Nasal Cavity**

## Introduction

Allergic rhinitis is not a life-threatening disease. However, if untreated or inadequately treated, it can substantially impair patients' overall quality of life by causing fatigue, headache, cognitive impairment and other problems.[1]

Systemic medications, taken either individually or in combination, can help to relieve the symptoms of allergic rhinitis. Antihistamines targeting $H_1$ receptors have a beneficial effect on sneezing and rhinorrhoea but little effect on nasal congestion. Sympathomimetics and leukotriene receptor antagonists are effective in reducing nasal congestion.[2]

A number of guidelines recommend daily intranasal steroids as first-line treatment for allergic rhinitis, as they improve all symptoms and have minimal side effects.[3] Intranasal steroid delivery enables adequate drug concentrations at receptor sites within the nasal mucosa, with little risk of adverse systemic effects. However, the various topical intranasal steroids vary in their pharmacokinetics, for example, regarding systemic absorption, potency, binding affinity, lipophilicity, distribution volume and half-life.[4]

More recent topical intranasal steroid formulations are safer because of their low bioavailability.[5] In spite of this, many patients are reluctant to use them on a daily basis for prolonged periods, due to

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concerns about prolonged steroid usage. In addition, the cost of such medication is sometimes an issue. Therefore, alternative topical steroid regimens should be explored, in order to improve patient compliance and reduce cost.[6] In cases of asthma, self-management by stable patients, with some medical guidance, has been found to be safe and less costly.[7] In cases of allergic rhinitis, a self-adjusted dosing regimen may be more acceptable to patients with this non-life-threatening disease.

Mometasone furoate improves the majority of nasal symptoms within two to five days of initiating therapy. A similar time for improvement has also been demonstrated in patients with nasal polyposis.[8–10] This drug has minimal systemic bioavailability following intranasal administration.[11]

We hypothesised that self-adjusted dosing of mometasone furoate nasal spray in patients with chronic allergic rhinitis would not compromise symptom control or objective improvement of nasal patency.

## Patients and methods

This study was performed in Qassim University King Fahd Specialist Hospital and Buraidah Central Hospital, in Buraidah, Kingdom of Saudi Arabia, from November 2007 to June 2008. Sixty patients with chronic allergic rhinitis of at least one year's duration were included. The diagnosis was made clinically; appropriate skin tests were also performed.

We excluded from the study patients with paranasal sinus disease, nasal polyps or a significantly deviated nasal septum. We also excluded: patients who had been treated with systemic steroids in the preceding 30 days; those who had used topical steroids, antihistamines, decongestants or cromolyn in the preceding two weeks; and those who had received immunotherapy in the preceding two years. In addition, we excluded pregnant and lactating women, and patients with concomitant bronchial asthma.

The institutional review board of Qassim University approved the study. Written, informed consent was obtained from each patient prior to study commencement.

Patients were randomised into two groups. One group (30 patients) was prescribed mometasone furoate nasal spray (as Nasonex®; Schering, Kenilworth, New Jersey, USA), to be taken as two puffs (100 μg each) in each nostril, once daily for six weeks. The second group (30 patients) was instructed to use the same preparation in the same dose, as follows: once daily in the first week; once on alternate days in the second week; and a self-adjusted regimen thereafter (for four weeks), as guided by the patient's symptoms. Patients were instructed that, when they decided to self-medicate, they should continue using the spray daily until their symptoms were controlled for at least two consecutive days.

All patients were instructed to use the spray when their nose was relatively dry (generally in the late afternoon), and to avoid its use when symptoms were at their worst. They were instructed to keep a symptom diary over the study period, to be completed in the morning. Sneezing, 'runny nose', 'stuffy nose' and itching were scored by patients on a scale of zero to three (where zero = no symptoms, one = mild symptoms; two = moderate symptoms and three = severe symptoms). The total nasal score comprised the sum of all four individual symptom scores. In addition, patients in the self-adjusted group recorded their spray use. No rescue medications (e.g. antihistamines) were permitted.

Acoustic rhinometry was used to measure the nasal volume at the first visit and at the end of the six-week study period. The total nasal cavity volume was calculated as the sum of the right and left nasal cavity volumes, measured 5 cm from the tip of the probe.

Statistical analysis was performed using the Statistical Package for the Social Sciences software. The signed rank Wilcoxon test was used to compare total nasal scores on each treatment day with the basal score for the same group. The Mann–Whitney U test was used to compare the two groups' total nasal scores. Paired and non-paired *t*-tests were used to compare total nasal volume within each group and between groups, respectively.

## Results

Fifty-eight patients completed the study (29 in each group) and were included in the data analysis. Descriptive statistics for each group are shown in Table I. Demographic data did not show any significant differences between the two groups. There was no statistically significant difference between the groups regarding basal total nasal score, taken as the average total nasal score over the two days before treatment.

Comparing total nasal scores on treatment days and between treatment groups, both groups showed improvement compared with basal scores. There

TABLE I

DESCRIPTIVE STATISTICS FOR SELF-ADJUSTED AND DAILY DOSAGE GROUPS

| Parameter | Self-adjusted grp | Daily grp |
|---|---|---|
| *Age* (y) | | |
| Mean | 37.3 | 35.7 |
| Range | 19–56 | 19–54 |
| *Sex* (*n*) | | |
| Male | 17 | 19 |
| Female | 12 | 10 |
| *Disease duration* (y) | | |
| Mean | 2.8 | 2.9 |
| Range | 1–7 | 1–7 |
| *Basal total nasal score* | | |
| Median | 6 | 6 |
| Distribution (*n* (%)) | | |
| −1–3* | 10 (34) | 9 (30) |
| −4–6† | 7 (27) | 8 (30) |
| −≥ 7‡ | 12 (40) | 12 (40) |
| *Basal total nasal cavity vol* ($cm^3$)** | 15.03 | 14.68 |

Corresponding allergic rhinitis severity: *mild; †moderate; ‡severe. **Normal = 0–5 $cm^3$. Grp = dosage group; y = years; vol = volume

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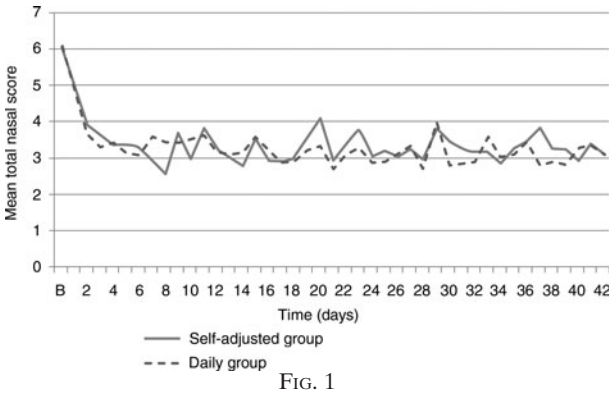


FIG. 1

Mean total nasal scores in self-adjusted and daily dosing groups over the six-week study period.

was no statistically significant difference between the two groups' total nasal scores, except on days 8 ($p = 0.004$), 10 ($p = 0.043$), 20 ($p = 0.008$), 23 ($p = 0.19$), 30 ($p = 0.008$) and 37 ($p = 0.000$). On day 8, the self-adjusted dosage group's total nasal score was lower than the daily dosage group's total nasal score. On the remaining above-mentioned days, the daily dosage group's total nasal score was significantly lower than the self-adjusted dosage group's total nasal score (Figure 1).

The total nasal cavity volume measured at the end of the study showed significant improvement compared with volumes measured at the beginning of the study ($p = 0.0001$). The mean change in this parameter was 16.4 per cent in the self-adjusted dosage group and 13.4 per cent in the daily dosage group; this difference was not statistically significant (Figure 2).

The median number of doses administered in the self-adjusted dosage group was 22 (range: 16–30). There was no correlation between the total number of doses and the basal total nasal score ($r = 0.36$); however, there was some correlation with the average total nasal score in the first week of treatment ($r = 0.52$).

## Discussion

Topical steroids have an anti-inflammatory effect on nasal mucosa, via an influence on Langerhans' cells and eosinophils. The numbers of epithelial and mast cells are also reduced. The number of T-lymphocytes only decreases following high doses of topical corticosteroid therapy or long-term treatment. However, T-lymphocyte function is influenced, as shown by reductions in concentration of interleukins 4 and 5.[12] This reduces the influx of eosinophils and other inflammatory cells, resulting in diminished symptomatology.

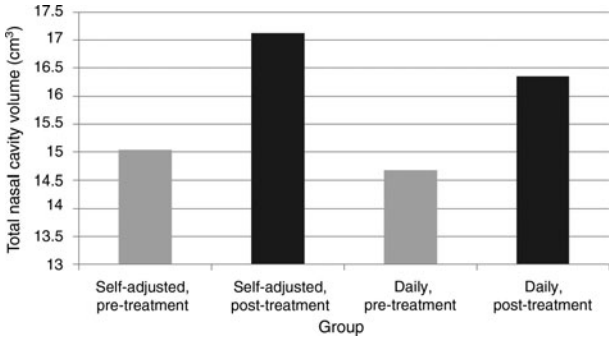


FIG. 2

Total nasal cavity volume in self-adjusted and daily dosing groups, before and after treatment.

Mometasone furoate has very low bioavailability. This is probably because of its inherently low aqueous solubility, which allows only a small fraction of the drug to cross the nasal mucosa and enter the bloodstream, and also because a large amount of the administered drug is swallowed and undergoes extensive first-pass metabolism.[13]

Patients with allergic rhinitis should be considered as effective partners in decision-making about their disease. They can be responsible, with the physician, for controlling the symptoms of this non-life-threatening disease. Under- or overtreatment should be avoided, and the cost of treatment should be reduced if at all possible. Several variables determine the need for treatment, e.g. the degree of nasal blockage, the amount of nasal discharge, the severity and frequency of sneezing, and the presence of itching. Tolerance of minor symptoms also differs from patient to patient. Therefore, the patients themselves are best placed to determine their need for treatment, and to adjust their topical steroid use accordingly.

In this study, we found that self-adjusted use of mometasone furoate nasal spray resulted in reasonable symptom control (albeit with some 'breakthrough' symptoms), compared with a strict daily dosing regimen. After one week of daily mometasone use, most patients' symptoms were under control. By the end of the second week, patients were able to effectively determine their dosage needs. We acknowledge that daily mometasone spray use may be unavoidable in patients with severe symptoms. In this subgroup, the addition of other pharmacotherapy (e.g. antihistamines and leukotriene antagonists) may also be needed.

It is only after using the topical spray for at least two weeks that it becomes evident which patients require it daily. The basal total nasal score cannot predict the need for daily or intermittent use.

Kirtsreesakul *et al.* studied patients with persistent allergic rhinitis, and found a self-adjusted dosing regimen of intranasal triamcinolone acetonide to be efficacious.[14] Patients with mild, intermittent symptoms were instructed to use the medication once daily only when symptoms occurred. Patients with symptoms which lasted more than one day and/or which interrupted daily activities or sleep were instructed to continue their morning daily dose until they had been symptom-free for 24 hours, before stopping usage. All nasal symptom scores and peak expiratory flow measurements showed significant improvements.

The intermittent use of topical steroids has been trialled in other allergic diseases. Veien *et al.* studied the efficacy of intermittent use of

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mometasone furoate fatty cream for treatment of chronic hand eczema.[15] Mometasone furoate was used daily until the condition was controlled. Thereafter, it was used either every alternate day or twice weekly. Disease control rates were 83 and 68 per cent, respectively.

In allergic rhinitis, control of symptoms by self-adjusted dosing can be enhanced if the patient is instructed to use the spray only when the nose is relatively dry. Patients should avoid using the spray when symptoms are at their worst. In this way, the spray is more likely to be distributed evenly across the nasal mucosa, rather than being washed away by excess mucus (due to rhinorrhoea and sneezing). In this way, the maximum benefit is derived from each puff, and the total number of puffs required is reduced to a minimum.

Other studies have evaluated nasal mucosal status using the modified endoscopic score of Lund and Kennedy.[16] This scoring system takes account of the presence of nasal polyps and septal deviations. However, patients with these two conditions were excluded from our study.

We used acoustic rhinometry for objective evaluation of nasal airway and mucosal status. This technique is easy to use and is not effort-dependent; however, it is not suitable for home monitoring. In our study, patients' total nasal volume improved with both regimens, with no statistically significant difference between the two groups. We acknowledge the limitations of acoustic rhinometry in conditions such as allergic rhinitis. Multiple or daily measurements with other devices may have given a more accurate indication of the nasal airway.

- **Many patients with allergic rhinitis are reluctant to use daily intranasal steroids for prolonged periods**
- **Use of a self-adjusted dosage of mometasone furoate nasal spray gives reasonable control of allergic rhinitis**
- **Some 'breakthrough' symptoms do occur with the self-adjusted regime; patients should learn to control these with the least number of steroid doses, without losing confidence in their spray**

Our study found that an alternative topical steroid dosing regimen was effective in patients with allergic rhinitis. Decreasing the number of doses in a large proportion of patients has a great impact on the cost-effectiveness of treating this common disease.[17] However, patients should expect some breakthrough symptoms if they choose a self-adjusted regimen.

## Conclusion

Self-adjusted use of mometasone furoate nasal spray gives reasonable control of allergic rhinitis. Some breakthrough symptoms should be expected; patients should learn how to control such symptoms with the least number of steroid doses, without losing confidence in their spray.

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