

Original article

A clinical survey on compliance in the treatment of rhinitis using nasal steroids

Background: In the treatment of persistent rhinitis, the observed efficacy with intranasal steroids in clinical practice often falls short of that reported in clinical trials. We postulate that this could be due to patient non-compliance and thus designed this study to evaluate the impact of patient compliance on the efficacy of treatment in patients with persistent rhinitis.

Methods: Sixty-three consecutive adult patients with allergic and non-allergic rhinitis, treated with intranasal triamcinolone acetate, were included in the study. Compliance was determined both by direct questioning and by measuring the weight of medication consumed (WMC) after 30 days of therapy. Nasal symptom scores were used to determine treatment efficacy.

Results: Forty-nine patients (77.8%) reported a forgetfulness of using medication for a few times (1–5 times) during the treatment period. Less than 50% compliance was reported by one patient (1.6%) but detected in seven patients (11%) by WMC. There was a significant ($P < 0.001$) improvement in mean total symptom score before (7.45 ± 1.99) and after (3.59 ± 2.72) treatment in patients with WMC of at least 50%, but not when WMC was $< 50\%$ (8.43 ± 1.72 vs 6.29 ± 2.43 ; $P = 0.114$). With $> 50\%$ WMC, the positive predictive values for relief of each symptom were rhinorrhoea: 78%, nasal itch: 70%, nasal obstruction: 67% and sneezing: 65%.

Conclusion: Patients compliance has a significant impact on treatment efficacy with intranasal steroids. There is a discrepancy between reported and actual compliance. It is thus important to establish the actual compliance when evaluating patients who fail to respond to therapy.

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Allergic rhinitis, a common disease worldwide that affects 10–25% of the population, presents with nasal obstruction, rhinorrhea, sneezing and/or nasal itch (1). It is one of the top-10 reasons for consultation in primary care clinics (2). Hence, management of allergic rhinitis is routine, not only in specialized Allergy or Otolaryngology centres, but also in the primary care setting.

In Singapore, the prevalence of persistent rhinitis was reported at 10.8% in 1994 and 13.4% in 2002 (3, 4). In the tropics, the majority of allergic rhinitis is persistent in nature. The year-round warm and humid climate is conducive for the proliferation of dust mites and molds, two of the most common aeroallergens implicated in persistent allergic rhinitis (PAR). As patients with persistent allergic rhinitis are often symptomatic throughout the year and need long-term treatment, ensuring total compliance to treatment can be difficult.

The Allergic Rhinitis and Impact on Asthma (ARIA) Workshop report recommend intranasal corticosteroids as a highly effective first-line treatment for patients suffering from allergic and non-allergic rhinitis with

moderate to severe and/or persistent symptoms (1). However, the observed efficacy in clinical practice is often lower than that quoted in randomized controlled trials. This discrepancy could be partially because of differences in patient compliance. To test this hypothesis, we designed the first single blinded study to investigate the effect of patient compliance on the treatment efficacy of intranasal corticosteroids in clinical practice. Compliance was determined both by direct questioning and measuring the weight of medication consumed (WMC) after 30 days of therapy. Nasal symptom scores were used to determine treatment outcomes.

Methodology

Patients

Over 4 months, 66 newly diagnosed adult patients suffering from persistent rhinitis at the ENT outpatient clinic of the National University Hospital were included for this study. Persistent rhinitis was diagnosed if the patients had two or more of the following

symptoms: nasal obstruction, rhinorrhea, sneezing and/or nasal itch for more than 4 days a week and for more than 4 weeks a year (1, 5). The severity of their rhinitis was classified as 'moderate-severe' based on symptoms and quality of life parameters (1). Atopy was confirmed in 53 patients (84.1%) using radioallergosorbent test (RAST) with a panel of common local inhalant allergens (*Der-matophagoides pteronyssinus*, *D. farinae*, Bermuda grass, *Aspergillus fumigatus*, and cockroach), the remaining 10 patients (15.9%) were diagnosed as suffering from non-allergic rhinitis. Patients with concomitant sinusitis, nasal polyposis and septal deviation severe enough to cause persistent nasal obstruction and those treated with any other medications were excluded from the study.

Study design

All patients were treated with pre-weighed bottles of intranasal triamcinolone acetonide (Nasacort® AQ, Aventis Pharmaceuticals, Bridgewater, NJ, USA) 220 mcg, administered as two puffs of 55 mcg in each nostril once daily. The attending physician demonstrated a six-step technique consisting of: clearing of the nose, shaking of the spray bottle, 30° forward neck flexion, correct axis of insertion, full depression of spray nozzle and alternating nostrils with each puff. Education on the safety profile and the importance of compliance to treatment was then given. They were instructed to return the used bottle at the follow-up visit 30 days later and were not aware that their compliance would be monitored. The use of other medications for rhinitis or allergy was discouraged.

Assessment and follow-up

The treatment efficacy was determined using nasal symptom scores. Nasal symptoms were assessed during the initial visit and 4 weeks after treatment using a four-point scale (0, no symptom; 1, mild: symptom clearly present but minimal awareness; 2, moderate: definite awareness of symptom which is bothersome but tolerable; 3, severe: symptom is hard to tolerate and causes interference with activities of daily life and sleep). Sum of the individual scores for nasal blockage, rhinorrhoea, sneezing and nasal itch derived the total symptom score.

During the follow-up visit, the nasal symptoms and six-step nasal spray administration technique were assessed and scored. One point was given for each correct step (a maximum of six points). The reported compliance by patients, reasons for non-compliance and usage of other medications were also determined. The returned bottles were weighed and the WMC was calculated.

Statistical analysis

All analysis was performed using SPSS 11.0 with statistical significance set at $P < 0.05$. The normality assumption of the change in total symptom score between pre and post-treatment was checked using the Kolmogorov-Smirnov one-sample test. When the normality and homogeneity assumptions were satisfied, a two-sample t -test was carried out to determine whether there was a significant difference in the change of total symptom score between those who complied (at least 50 or 75%) and those who did not comply to taking of the medication, otherwise the Mann-Whitney U -test was performed. A multiple regression was then carried out to account for age, gender and pre-treatment total score. 'Pre-' and 'Post-' comparison within each compliance group was assessed using the paired t -test or the equivalent non-parametric of Wilcoxon signed rank test. The following table defines the four categories of status in nasal symptoms between the pre- and post-treatment scores.

Pre-treatment status	Post-treatment status	Classification
No symptom	No symptom	No change
No symptom	Moderate	Worse
No symptom	Severe	Worse
Moderate	No symptom	Improve
Moderate	Moderate	No effect
Moderate	Severe	Worse
Severe	No symptom	Improve
Severe	Moderate	Improve
Severe	Severe	No effect

The association between improve/no change and worse/no effect with compliance was assessed using chi-square or Fisher's exact test with odds ratios presented where applicable. A logistic regression adjusting for age, gender and pre-treatment nasal symptom was performed. Comparisons between pre- and post-nasal symptom scores within the compliance group were determined using McNemar test.

Results

Sixty-three patients (95%), 49 male and 14 female, aged 15–68 years (mean 29 years) completed the study, and another three patients were lost at the follow-up visit. Thirteen (20.6%) of these patients had a history of rhinitis for a duration between 3 months and 1 year, and the remaining 50 (79.4%) patients had symptoms beyond 1 year. Nine patients had been treated previously with nasal steroids. Compliance to nasal spray as reported by patients and by WMC measurements are shown in Table 1.

Forty-nine patients (77.8%) reported forgetfulness of using medication for few times (1–5 times) during the treatment period. Less than 50% compliance was reported by one patient (1.6%) but detected in seven patients (11%) by WMC. There was no significant correlation between compliance and duration of rhinitis or previous treatment with nasal steroids. WMC was found to be more than 100% (105–130%) in 19 patients; this was mainly because of 'priming' of the spray prior to intranasal administration. Five patients complained of local irritation, sensation of post-nasal drip, sneezing or poor taste. There were no complaints of epistaxis, crusting or odors during the treatment.

The mean ($\pm$ SD) score for nasal spray administration technique was 4.98 ± 0.99 . Twenty-eight patients (44.4%)

Table 1. Number of patients with missed medication during the 30-day treatment period as reported by patients and calculated using WMC

Percentage of compliance	Reported by patients (%)	Calculated using WMC (%)
≥ 75	55 (87)	41 (65)
50–75	7 (11)	15 (24)
< 50	1 (2)	7 (11)

were able to fully demonstrate the six-step nasal spray technique at the follow-up visit. The errors in administration technique included: 30 patients (47.6%) did not clear their noses and nine (14.3%) did not shake the

bottle prior to nasal spray, five (7.9%) failed to maintain proper neck posture, four (6.3%) did not depress the medication fully, and three (4.8%) did not position the bottle correctly or alternate nostrils between applications.

The changes of individual nasal symptom status before and after therapy are given in Table 2. Furthermore, Table 3 shows the percentage of improvement for individual symptom according to compliance that was divided by 50 and 75% WMC. There were significant improvements of individual symptoms in both groups as divided by 75% WMC. With at least a 50% compliance, there were significant improvements for all nasal symptoms ($P < 0.001$, McNemar test), but no significant improvement for patients whose compliance were $< 50\%$ WMC. When comparing changes between the groups, a significant difference was only found for itch between WMC $\geq 50\%$ and WMC $< 50\%$ ($P = 0.017$, OR = 8.3, 95% CI 1.4–47.7), even after adjusting for age, gender and the respective nasal symptom baseline score.

There was a significant improvement in the mean total symptom score after treatment from 7.45 ± 1.99 to 3.59 ± 2.72 ($P < 0.001$) in patients with at least 50% WMC. However, no significant improvement was found (8.43 ± 1.72 to 6.29 ± 2.43 , $P = 0.114$) in patients with less than 50% WMC (Table 4). With compliance set at 75% WMC, both groups had significant improvement in the mean total symptoms score after treatment, indicating that a significant improvement is achieved only when patient's compliance is at least 50% WMC.

Table 2. Nasal symptom status change before and after treatment

Nasal Symptoms	WMC $\geq 75\%$		WMC $\geq 50\%$	
	Yes ($n = 41$)	No ($n = 22$)	Yes ($n = 56$)	No ($n = 7$)
Itch				
No change	11 (26.8)	2 (9.1)	12 (21.4)	1 (14.3)
Improve	20 (48.8)	12 (54.5)	31 (55.4)	1 (14.3)
No effect	10 (24.4)	6 (27.3)	12 (21.4)	4 (57.1)
Worse	0 (0.0)	2 (9.1)	1 (17.8)	1 (14.3)
Sneezing				
No change	3 (7.3)	0 (0.0)	3 (5.4)	0 (0.0)
Improve	26 (63.4)	11 (50.0)	35 (62.5)	2 (28.6)
No effect	12 (29.3)	9 (40.9)	17 (30.3)	4 (57.1)
Worse	0 (0.0)	2 (9.1)	1 (17.8)	1 (14.3)
Rhinorrhea				
No change	2 (4.9)	0 (0.0)	2 (3.6)	0 (0.0)
Improve	32 (78.1)	14 (63.6)	42 (75.0)	4 (57.1)
No effect	6 (14.6)	7 (31.8)	11 (19.6)	2 (28.6)
Worse	1 (2.4)	1 (4.6)	1 (17.8)	1 (14.3)
Nasal obstruction				
No change	2 (4.9)	0 (0.0)	2 (3.6)	0 (0.0)
Improve	26 (63.4)	13 (59.1)	36 (64.3)	3 (42.9)
No effect	13 (31.7)	9 (40.9)	18 (32.1)	4 (57.1)
Worse	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Values in this table are n (%).

Table 3. Comparisons of improvement of individual nasal symptoms after treatment

Nasal symptoms (improvement/no change)	WMC $\geq 75\%$		P -value (between group)	WMC $\geq 50\%$		P -value (between group)
	Yes ($n = 41$)	No ($n = 22$)		Yes ($n = 56$)	No ($n = 7$)	
Itch	75.6%	63.6%	0.316	76.8%	28.6%	0.017*
P -value (within group)	<0.001	0.013		<0.001	1.0†	
Sneezing	70.7%	50.0%	0.103	67.9%	28.6%	0.089
P -value (within group)	<0.001	0.016		<0.001	1.0†	
Rhinorrhea	82.9%	63.6%	0.087	78.6%	57.1%	0.342
P -value (within group)	<0.001	<0.001		<0.001	0.25	
Nasal obstruction	68.3%	59.1%	0.465	67.9%	42.9%	0.226
P -value (within group)	<0.001	<0.001		<0.001	0.25	

* Those with at least 50% compliance more likely to improve in itch (OR = 8.3, 95% CI 1.4–47.7).

† $P = 1.0$: condition remains the same before and after treatment.

Table 4. Comparisons of improvement in mean ($\pm$ SD) of total symptom score after treatment

Total symptom score	WMC $\geq 75\%$		P -value (between group)	WMC $\geq 50\%$		P -value (between group)
	Yes ($n = 41$)	No ($n = 22$)		Yes ($n = 56$)	No ($n = 7$)	
Pre-treatment	7.17 (1.92)	8.27 (1.91)	0.693	7.45 (1.99)	8.43 (1.72)	0.168*
Post-treatment	3.39 (2.73)	4.82 (3.10)		3.59 (2.72)	6.29 (2.43)	
P -value (within group)	<0.001	0.001		<0.001	0.114	

* Adjusting for age, gender and pre-treatment total score, the change in score between those who comply compared with those who did not comply is statistically different ($P = 0.021$).

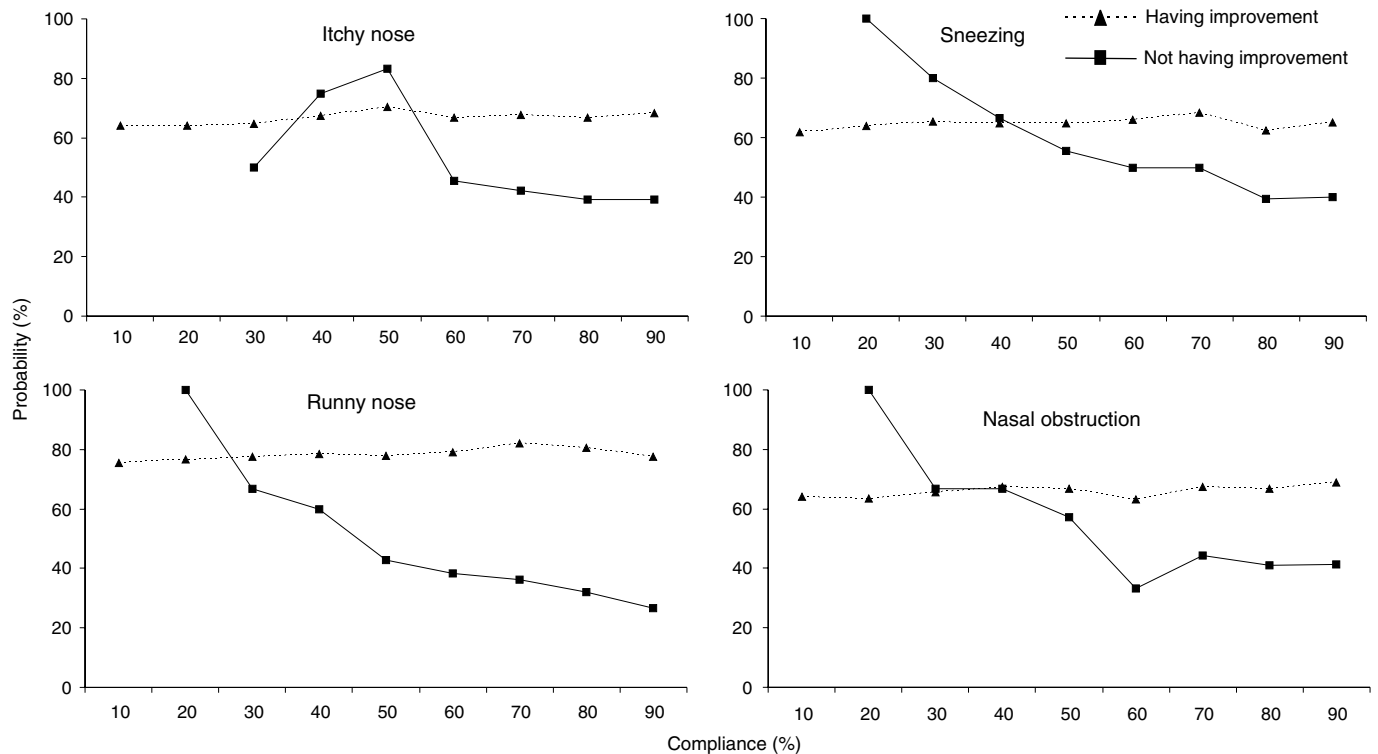


Figure 1. Logistic regression of patient compliance and individual symptom improvement.

There were no significant differences between the change of the mean total symptom score after treatment between compliance groups set at 50 or 75% WMC. However, after adjusting for age, gender and pre-treatment total symptom score, there was a statistical significance ($P = 0.021$) in the changes of the mean total symptom score at the 50% WMC cut-off compliance.

The positive predictive values for relief of each symptom (with at least 50% WMC) were: itch, 70%; sneeze, 65%; running nose, 78%; and blocked nose, 67%. An inverse relationship was found between compliance and therapy failure (Fig. 1).

Discussion

Intranasal corticosteroids are strong anti-inflammatory agents, and have been proven highly effective as first-line treatment for patients suffering from allergic and non-allergic rhinitis with moderate to severe and/or persistent symptoms (1). However, the effect of patient compliance, long thought to be critical for optimizing treatment outcome, has not been well studied in the clinical setting. In reviewed literature, most efficacy studies were based on clinical trials, where patients voluntarily participated in the study and were closely monitored by follow-up visits and daily diaries.

This study demonstrated a substantial number (11%) of patients who failed to achieve at least 50% of

treatment dose, which in turn contributed directly to unsatisfactory treatment outcome. This was despite the fact that the study period was immediately upon commencement of therapy and that rigorous patient education was instituted by the attending physician. Given the chronic nature of the disease, the compliance is expected to decrease with time. Data of this study may partially explain the reason for the unexpected low use of nasal glucocorticosteroid sprays (3%) in clinical practice and the poor control of the disease in the general community (4).

This study highlights the inaccuracy of reported compliance by patients. It is not practical to routinely calculate the weight of medication consumed in the clinic; however, this is invaluable in ruling out non-compliance in those who have failed therapy. Despite the easy once-daily dosing schedule and the low prevalence of side effects, a large portion of non-compliant patients simply 'forgot' to use their medication as recommended.

While morbidity associated with PAR may not be as dramatic or well publicized as those caused by other chronic diseases such as hypertension and diabetes, the sheer prevalence of allergic rhinitis has tremendous impact social economically. An estimated \$1.2 billion is spent annually on treating PAR and its associated complications such as chronic sinusitis, nasal polyposis and obstructive sleep apnea in the United States alone (6), and this was despite the fact that only approximately 13% of allergic rhinitis patients sought treatment.

It is only through continued education by the physician that the patient can be convinced of the important benefits of continued treatment in this often trivialized disease. Patient education is often neglected in clinical practice and its effect should not be underestimated. Training on the use of nasal sprays and education on rhinitis increases compliance and can be enforced at several levels through the nursing practitioner and pharmacist (7). The creation of specialist educators where clinical load is high can also be considered, such adjunct education has been demonstrated to be effective in increasing compliance with other aspects of rhinitis treatment, such as environment control measures in mite-sensitized rhinitis patients (8).

In conclusion, our study shows that education and monitoring of patient compliance are critical elements in the treatment of persistent rhinitis using intranasal corticosteroids. It is important to establish the actual compliance especially when evaluating patients who failed to respond to therapy.

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