Topical Corticosteroids Applied With a Squirt System Are More Effective Than a Nasal Spray for Steroid-Dependent Olfactory Impairment

Chih-Hung Shu, MD; Po-Lei Lee, PhD; An-Suey Shiao, MD; Kee-Tak Chen, MD; Ming-Ying Lan, MD

**Objectives/Hypothesis:** Oral corticosteroids may restore conductive olfactory dysfunction that has been defined as steroid-dependent olfactory loss, but the effect may be temporary. This study was designed to evaluate whether applying topical corticosteroids with a squirt system was more effective than using a nasal spray to maintain olfactory improvement following oral corticosteroids.

**Study Design:** Prospective randomized trial enrolling 32 patients.

**Methods:** Patients were enrolled if they had suffered from olfactory dysfunction for more than 3 months, and if their composite scores of odor threshold, discrimination, and identification scores in Sniffin’ Sticks olfactory tests increased by more than six points after 1 week of oral corticosteroid treatment. A total of 32 patients were enrolled and randomized into two groups. All patients were treated with topical corticosteroids for 2 months using either the spray or squirt system, respectively.

**Results:** Both measured and self-rated olfactory functions after 1 and 2 months of topical corticosteroid treatment were better in the squirt group than in the spray group. However, 2 months of topical corticosteroid treatment with the squirt system only partially maintained olfactory improvement.

**Conclusions:** The application of topical corticosteroids with a squirt system was more effective than with a spray in maintaining olfactory improvement with oral corticosteroid treatment. Nevertheless, it only partially maintained the improvement so that topical corticosteroid treatment using a squirt system needs to be combined with intervals of short-term oral corticosteroids to treat steroid-dependent olfactory loss while avoiding the side effects of long-term oral corticosteroid use.

**Key Words:** Olfactory function, smell, olfaction, olfactory dysfunction, Sniffin’ Sticks, corticosteroid, squirt.

**Level of Evidence:** 1b.

**INTRODUCTION**

Oral or topical corticosteroids are the most frequent medications prescribed for the treatment of olfactory dysfunction.1–4 The causes of olfactory dysfunction can be classified as conductive or sensorineural loss from the standpoint of treatment.5 Conductive olfactory dysfunction is caused by blockage of the olfactory cleft with polyps or swollen turbinates, with or without inflammatory change of olfactory neuroepithelium. Conductive olfactory loss that has been defined as steroid-dependent olfactory dysfunction can be restored with oral corticosteroid treatment.6–8 However, the effect of oral corticosteroids on conductive olfactory dysfunction is temporary.6,8 Long-term oral corticosteroid use is not advised due to the possible adverse effects. Oral corticosteroids should only be used for a short period of time and then usually shifted to topical corticosteroids in the treatment of olfactory impairment. However, using topical corticosteroids appears to have little or no positive effect on olfactory dysfunction.2,3 One of the reasons for this may be the inability of topical corticosteroids applied using the usual spray method to reach the olfactory cleft.9 Using a squirt system, the administered solution can reach the olfactory cleft in most subjects.9 The purpose of the study was to compare topical corticosteroids applied using a squirt system with a nasal spray for the maintenance of olfactory improvement with oral corticosteroids.

**MATERIALS AND METHODS**

**Patients**

This study was performed in accordance with the Declaration of Helsinki on Biomedical Research involving human subjects and was approved by the institutional review board of Taipei Veterans General Hospital (201005004IC). Patients were required to be older than 18 years and to have had a history of olfactory dysfunction continuously for more than 3 months. At initial presentation, a detailed history of olfactory dysfunction was established with the use of a questionnaire that included...
duration of disease, possible etiology, related nasal symptoms, and medical and surgical diseases. All patients underwent nasal endoscopic examinations with an emphasis on the condition of the middle meatus and olfactory cleft. The patients self-rated their olfactory function using a 0 to 10 visual analogue scale (VAS), 0 indicating total loss of smell and 10 indicating extremely sensitive smell. Olfactory function was measured using a Sniffin’ Sticks test battery, specifically n-butanol threshold, odor discrimination, and odor identification tasks. A summation of the results determined the odor threshold, discrimination, and identification (TDI) score. Patients with a TDI score of <30 were prescribed oral prednisolone at a dosage of 0.5 mg/kg/day in the morning for 7 days. If their TDI score increased by 6 or more after 1 week of taking oral corticosteroids, the patients were enrolled in the study. Exclusion criteria included if the patients’ olfactory cleft region could not be seen by intranasal endoscopic examination because of profound nasal septum deviation, or if patients needed to take oral prednisolone continuously for treatment of other diseases. Thirty-two patients were enrolled and randomized into the spray group and squirt group. One patient in the spray group was lost to follow-up in the first month, thus 15 patients in the spray group and 16 patients in the squirt group were investigated. Two patients in each group withdrew from the study due to a poor response to the treatment in the second month. If the patients had nasal polyposis, the polyps were graded as 0, no polyposis; 1, polyps in the middle meatus; 2, polyps beyond the middle meatus and above the lower edge of the inferior turbinate, and 3, polyps beyond the lower edge of the inferior turbinate.

**Study Design**

The patients in the squirt group learned to squirt 0.2 mL of blue food coloring into their nose by themselves using a syringe mounted with an 18-gauge intravenous indwelling cannula (Introcan; Certo, B. Braun, Germany) with the head tilted up by about 30°. The distribution of the blue food coloring in the insertion of the middle turbinate or the olfactory cleft was confirmed in all patients by intranasal endoscopic examination. The patients then started treatment by squirting 0.2 mL triamcinolone acetonide (Nasacort; sanofi-aventis, Paris, France), or two sprays of Nasacort in the squirt and spray groups, respectively, into each nostril once a day for 2 months. The spray delivered 0.1 mL per spray, thus two sprays of Nasacort administered into the nasal cavity was equal to 0.2 mL of Nasacort. The scheduled dose was therefore equal in both groups. The spray group sprayed Nasacort according to the manufacturer’s instructions, which included bending the head forward, closing the other nostril with a finger, sniffing gently when spraying, and holding their breath for several seconds after spraying. In addition, the patients were instructed to direct the nozzle toward the olfactory cleft. TDI scores in the Sniffin’ Sticks tests were evaluated at the first and second month after nasal topical corticosteroid treatment.

**Statistical Analysis**

Post hoc power analysis was performed to analyze the primary measures in the study (i.e., the TDI and self-rated olfactory scores). Using an α error of .05, the statistical power to identify the differences in TDI scores between the spray and squirt groups after 1 and 2 months of topical corticosteroid treatment were 77% and 86%, respectively. The statistical power to identify the differences in self-rated scores between the two groups after 1 and 2 months of topical corticosteroid treatment were 66% and 69%, respectively. Differences in age, TDI scores, and self-rated olfaction between the spray and squirt groups were analyzed using the Mann-Whitney U test. The distribution of sex, polyp size, and frequencies of accompanying nasal diseases were analyzed using the χ² test. A P value of <.05 was regarded as statistically significant.

**RESULTS**

There were no significant differences between the spray and squirt groups in age, sex ratio, polyp size, frequencies of accompanying nasal diseases, measured olfactory function, and self-rated olfactory function before nasal corticosteroid treatment (Table I). In the spray and squirt groups, the mean TDI scores were 12.7 (95% confidence interval [CI], 10.6–14.9) and 12.6 (95% CI, 10.3–14.8), respectively, before treatment, increasing to 28.2 (95% CI, 24.9–31.5) and 28.9 (95% CI, 26.4–31.4) after 1 week of oral corticosteroid treatment. The TDI values then decreased to 14.3 (95% CI, 10.6–17.9) and 22.4 (95% CI, 17.7–27.2) after 1 month of topical corticosteroid treatment, and to 11.1 (95% CI, 9.2–12.9) and 20.1 (95% CI, 14.5–25.6) after 2 months of topical corticosteroid treatment (Fig. 1). The differences in TDI scores at the first and second month between the spray and squirt groups were significant (Mann-Whitney U test, P = .015 and P = .011) (Fig. 1). The change of mean self-rated olfactory function scores by the 0 to 10 VAS correlated well with that of TDI scores (Figs. 1 and 2). The mean self-rated olfactory function scores in the spray and squirt groups were 1.3 (95% CI, 0.2–2.3) and 1.6 (95% CI, 0.6–2.6), respectively, before treatment, increasing to 5.9 (95% CI, 4.9–7.0) and 5.6 (95% CI, 4.9–6.4) after 1 week of oral corticosteroid treatment. The

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**TABLE I. Clinical Data of the Patients Before Nasal Corticosteroid Treatment.**

<table>
<thead>
<tr>
<th>No.</th>
<th>Spray Group</th>
<th>Squirt Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>52.5 ± 13.6</td>
<td>45.5 ± 14.6</td>
</tr>
<tr>
<td>Male/female</td>
<td>6/9</td>
<td>7/9</td>
</tr>
<tr>
<td>Accompanying nasal diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>CRS without polyposis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>CRS with polyposis</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Polyp size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In middle meatus</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Beyond middle meatus</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>TDI before treatment</td>
<td>12.7 ± 3.9</td>
<td>12.6 ± 4.3</td>
</tr>
<tr>
<td>TDI after 1 week of oral steroid treatment</td>
<td>28.2 ± 5.9</td>
<td>28.9 ± 4.7</td>
</tr>
<tr>
<td>Self-rating olfaction before treatment</td>
<td>1.3 ± 1.9</td>
<td>1.6 ± 1.9</td>
</tr>
<tr>
<td>Self-rating olfaction after 1 week of oral steroid treatment</td>
<td>5.9 ± 1.9</td>
<td>5.6 ± 1.4</td>
</tr>
</tbody>
</table>

*By visual analogue scale, 0 indicating complete loss of olfaction, 10 indicating extremely sensitive olfaction. CRS = chronic rhinosinusitis; TDI = composite score of olfactory threshold, discrimination, and identification scores in Sniffin’ Sticks.
scores then decreased to 2.0 (95% CI, 0.6–3.4) and 4.5 (95% CI, 2.9–6.1) after 1 month of topical corticosteroid treatment, and further decreased to 0.9 (95% CI, 0.3–1.6) and 3.2 (95% CI, 1.5–5.0) after 2 months of topical corticosteroid treatment (Fig. 2). There were significant differences in self-rated olfactory function at the first and second month between the two groups (Mann-Whitney U test, \( P = 0.019 \) and \( P = 0.038 \)) (Fig. 2).

**DISCUSSION**

The results revealed that administration of topical corticosteroids using the squirt method was more effective than the usual spray method in terms of maintaining olfactory improvement following oral corticosteroids. One of the reasons may be that a nasal spray is relatively ineffective in applying a drug onto the olfactory epithelium.\(^2\) A nasal spray distributes the solution mainly on the anterior portion of the nasal septum and head of the inferior turbinate, with only a small amount reaching the inferior surface of the middle turbinate or the middle meatus.\(^15\) Furthermore, the amount of nasal spray reaching the middle meatus varies profoundly. Homer et al. used a surgical patty placed in the middle meatus to absorb radio-labeled aqueous nasal spray, and found that the measured amount of nasal spray that reached the middle meatus ranged from 0.3% to 39.5% of the spray.\(^15\) The insertion of the middle turbinate and olfactory cleft, on which the olfactory neuroepithelium lies, are even more difficult to access by nasal spray because the middle turbinate intercepts most of the nasal spray.\(^9\) Deposition of solution on the insertion of the middle turbinate or olfactory cleft was detected in only two of the 15 participants using the nasal spray method, in contrast to 11 of the 15 participants using a squirt system.\(^9\) In the current study, all of the patients in the squirt group were able to squirt solution onto the insertion of the middle turbinate or olfactory cleft, and this may be the main reason why the application of topical corticosteroids using the squirt method was more effective than using the spray method for the maintenance of olfactory improvement.

The degree of congestion in the inferior turbinate is an important factor for the ability of the nasal spray to reach the middle meatus, and congestion of the inferior turbinate significantly decreases the ability of the spray to reach the middle meatus.\(^16\) Our patients did not use nasal decongestants before applying topical corticosteroids with either the spray or squirt method to increase the compliance of the patients. The olfactory function improved greatly following oral corticosteroids in our patients, indicating that patients had inflammatory sinonasal diseases. Congestion of the inferior turbinate is common in inflammatory sinonasal diseases and may be another factor hindering the nasal spray from reaching the olfactory cleft. However, this was avoided in the squirt method because the needle bypassed the inferior turbinate into the upper part of nasal cavity.

Our results revealed that almost all patients in the spray group returned to an anosmic condition after 1 month of treatment (Fig. 1). Topical corticosteroids alone or following oral corticosteroids does not appear to be effective on olfactory dysfunction.\(^2,3\) Nevertheless, Stener et al. reported that adjacent application of topical corticosteroids enables maintaining improvement of olfactory function following oral corticosteroids.\(^17\) In that report, the patients enrolled had limited olfactory improvement after treatment with oral corticosteroids, with TDI scores increasing from 15.5 ± 0.8 to 18.7 ± 0.9.\(^17\) Inflammation seemed to be a minor factor in these patients, and might have been completely restored with the initial oral corticosteroids; therefore, the olfactory function did not decrease when shifted to topical corticosteroid use. In contrast, the patients enrolled in the

![Fig. 1. Odor threshold, discrimination, and identification (TDI) scores before and after 1 week of oral corticosteroid treatment, and after 1 and 2 months of nasal corticosteroid treatment. The mean TDI scores in the squirt group at 1 and 2 months were 22.4 (95% confidence interval [CI], 17.7–27.2) and 20.1 (95% CI, 14.5–25.6), respectively, and were significantly higher than the values of 14.3 (95% CI, 10.6–17.9) and 11.1 (95% CI, 9.2–12.9) in the spray group.](image1)

![Fig. 2. Self-rated olfaction before and after 1 week of oral corticosteroid treatment, and after 1 and 2 months of nasal corticosteroid treatment. The self-rated olfaction scores in the squirt group at 1 and 2 months were 4.5 (95% confidence interval [CI], 2.9–6.1) and 3.2 (95% CI, 1.5–5.0), respectively, and were significantly better than the values of 2.0 (95% CI, 0.6–3.4) and 0.9 (95% CI, 0.3–1.6) in the spray group.](image2)
study had profound olfactory improvement with treatment with oral corticosteroids, indicating inflammatory or conductive factors were the major pathophysiologic mechanisms for the olfactory impairment that had been defined as steroid-dependent olfactory impairment.\textsuperscript{7,8} Topical corticosteroid application with a spray or squirt system does not seem to be as effective as oral corticosteroids in treating such extensive inflammatory or conductive olfactory impairment.

Almost all of the patients were anosmic at the initial presentation, and their olfaction improved dramatically to nearly normal levels with oral corticosteroid treatment (Table I). Therefore, the patients would have little difficulty in self-rating their olfaction with such extreme changes in olfactory function. Afterward, the patients were able to self-rate their olfaction reliably based on the olfaction recovered with oral corticosteroid treatment. Therefore, self-rated olfaction correlates well with measured olfaction in such conditions (Figs. 1 and 2), and may be used as a tool to evaluate the effect of treatment for olfactory dysfunction.

Because application of topical corticosteroids with a squirt system for 2 months partially maintained the olfactory improvement with oral corticosteroids, topical corticosteroid application with a squirt system needs intervals of short-term oral corticosteroids to keep the olfactory function normal. However, it should be highlighted that such treatment should be confined to steroid-dependent olfactory impairment, that is to say, the olfactory loss can be restored to nearly normal with oral corticosteroids. Under such conditions, the olfactory function can remain in relatively good condition while avoiding the complications of long-term oral corticosteroid use.

**CONCLUSION**

Nasal corticosteroids applied with a squirt system was more effective than nasal spray for maintaining olfactory function improved with oral corticosteroid treatment. However, the application of topical corticosteroids using a squirt system only partially maintained the olfactory improvement following oral corticosteroids, and it needs to be combined with intervals of short-term oral corticosteroids to treat steroid-dependent olfactory loss while avoiding the side effects of long-term oral corticosteroid use.

**BIBLIOGRAPHY**