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A study of intranasal distribution of azelastine hydrochloride aqueous nasal spray with different spray techniques

N.D. BATEMAN, A.D. WHYMARK, N.J. CLIFTON & T.J. WOOLFORD
Department of Otorhinolaryngology, Royal Hallamshire Hospital, Glossop Road, Sheffield, UK

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Topical aqueous nasal sprays are widely used in treating patients with a variety of nasal diseases. Previous studies have suggested that drug delivery to the ciliated mucosa is generally suboptimal. Little is known about the effects of nasal spray delivery technique on intranasal distribution and efficacy of topical nasal drugs. We assessed the intranasal distribution of a nasal spray with two commonly used techniques using azelastine hydrochloride labelled with fluorescein. After spraying, the nasal cavity was photographed endoscopically in two standardized positions, one showing the anterior portion in the region of the nasal valve and one the area of the middle meatus. The photographs were computer analysed to identify the proportion of coverage of fluorescein in each image field. The majority of drug was distributed anteriorly with poor coverage posterior to the nasal valve area. This was the case with both of the positions tested.

Keywords *nasal sprays* *nasal cavity* *drug administration*

Topical nasal drugs are an effective and widely used treatment modality for patients with rhinosinusitis. In the UK, these are most commonly delivered using an aqueous nasal spray. Studies using radioisotope distribution[1–4] and nasal models[5] have suggested that drug delivery with nasal sprays to the ciliated mucosa is generally suboptimal with most of the drug deposited in the anterior portion of the nose. Although colleagues in respiratory medicine have long realized the importance of good 'inhaler technique' in inhaled medications,[6] far less is known about the effects of nasal spray delivery technique on intranasal distribution and efficacy of topical nasal drugs.

Homer and Raine[7] studied the intranasal distribution of azelastine hydrochloride coloured with Methylene blue. They found no difference in intranasal distribution when the subject vigorously inhaled while spraying. The spray angulation was standardized for each patient. In a purely descriptive study, Weber *et al.*[8] used fluorescein labelled budesonide delivered by a metered pump spray. They suggested that using a spraying angle of 45 degrees maximized delivery.

Tsikoudas and Homer[9] used neurosurgical patties placed in the middle meatus to compare the delivery of Methylene blue-labelled aqueous spray and nasal drops to the region of the osteomeatal complex. Using a standardized technique of drug administration, they found no difference between drops and sprays.

Gani *et al.*[10] studied the effect of training patients with allergic rhinitis in nasal spray usage during the hay fever season and did not report any difference in their symptoms when compared to an untrained group. They did not report the exact nature of the training and whether any instruction regarding 'spray technique' was given. The rate of compliance was, however, significantly greater in the trained group. There is very little evidence in the literature concerning spray technique, intranasal distribution of drug and efficacy.

The aim of this study was to compare the intranasal distribution of azelastine hydrochloride (Rhinolast™) when administered with two different head positions, both commonly adopted by patients and both recommended by different drug companies.

Correspondence: Mr N.D. Bateman FRCS, Department of Otorhinolaryngology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK (e-mail: neilbateman@yahoo.co.uk).

Figure 1. Spray position 1.

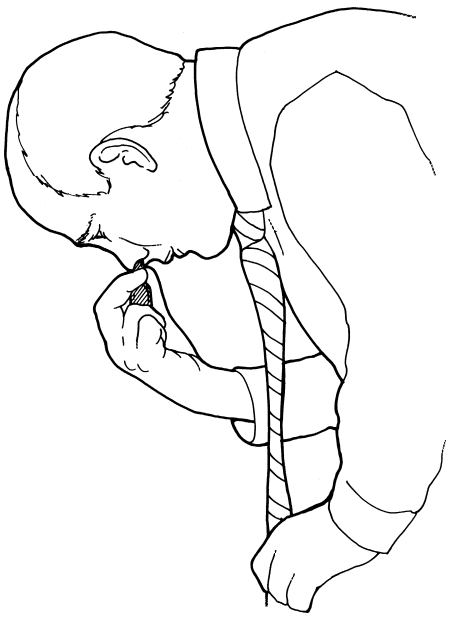

Figure 2. Spray position 2.

Patients and methods

Ethical approval was obtained from the South Sheffield Research Ethics Committee before commencement of the study. Five healthy volunteers were recruited.

Subjects were excluded from the study if they gave a history of current intranasal disease, were taking intranasal medication, were smokers or had abnormalities of intranasal anatomy on nasendoscopy. Septal deviation was judged to be significant if it precluded easy visualization of the middle turbinate using a 25° nasal endoscope.

Two head positions were studied; they were:

1. Head neutral (i.e. 0–10° to the vertical plane), spray at 30° to plane of face (Fig. 1).
2. Head forward (i.e. 60–90° to the vertical plane), spray at 90° to plane of face (Fig. 2).

Volunteers were studied endoscopically on two occasions, 1 week apart. On each occasion, one spray technique was studied.

The spray used was azelastine hydrochloride, 20 ml, dyed with 2 ml of 2% fluorescein. This delivers 0.14 ml of drug via an aqueous spray.

The subjects were instructed to:

1. Blow their nose.
2. Prime the spray.
3. Adopt the selected position.
4. Gently block the contralateral nostril.
5. Introduce the spray into the nostril.
6. Administer two sprays.

Immediately after this, the subject was asked to adopt a head neutral position and the nasal cavity was examined using a 2.7-mm, 25° endoscope. Two intranasal images were recorded digitally. The two intranasal views were as follows:

1. At 10° to the horizontal plane, in the sagittal plane introduced to a depth of 2 cm from the inferior margin of the nostril (showing the anterior end of the inferior turbinate and adjacent nasal septum) (Fig. 3).
2. At 30° to the horizontal plane, in the sagittal plane to a depth of 4 cm from the inferior margin of the nostril (showing the anterior end of the middle turbinate and adjacent nasal septum) (Fig. 4).

The procedure was then repeated for the other nasal cavity.

The photographs were then computer analysed. This process divided the picture into pixels and identified those that

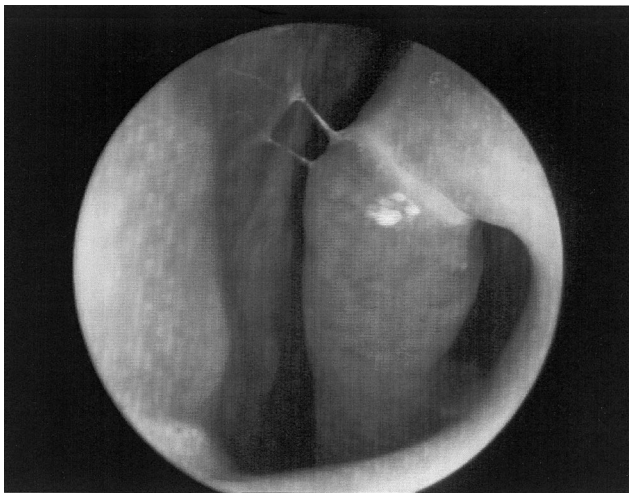

Figure 3. The anterior endoscopic view.

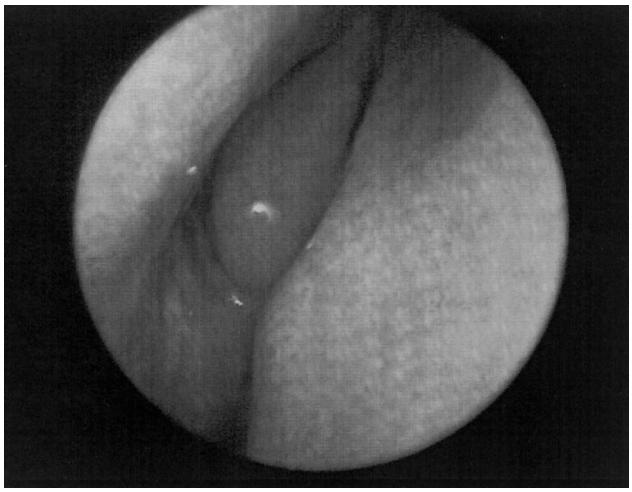

Figure 4. The posterior endoscopic view.

had been coloured yellow with the fluorescein. We were therefore able to calculate for each image the proportional coverage of yellow in the field. This was performed by an assessor blind to the subject identification and spray technique.

Results

The results are presented in Tables 1 and 2. The results were statistically analysed using a Student's *t*-test. Table 1 shows the results for the anterior and posterior images for each head position. These results were combined to give a proportionate coverage for both the images added together, i.e. the proportion of all the photographed mucosa for each head position. These results are presented in Table 2.

These results demonstrate that in both positions there is more deposition of spray anteriorly than posteriorly. This is only statistically significant ($P = 0.008$) in position 2 (head facing down, spray pointing up). There is no statistically significant difference between the two head positions in terms of distribution anteriorly ($P = 0.058$) or posteriorly ($P = 0.14$). For the combined results, position 2 gives slightly greater coverage although there is no statistically significant difference between the two.

Table 1. The percentage mucosal coverage of the anterior and posterior endoscopic images

		Anterior view		Posterior view	
Subject	L/R	Position 1	Position 2	Position 1	Position 2
1	L	14.3	26	7.6	9.9
	R	24.3	13.3	15.1	13.2
2	L	3.5	40	8.8	8.3
	R	18.3	30.1	10.3	11
3	L	17.3	24.4	8.7	12.4
	R	39	17.4	20.2	9.7
4	L	9.6	40.7	13.1	20.6
	R	44.2	57.3	25.3	17
5	L	17.3	23.1	20.2	10.9
	R	8.6	17.7	17.7	13
Mean values		19.7	29	14.8	12.6

Table 2. The mean combined coverage for both images

	Anterior view	Posterior view	Combined coverage
Position 1	19.7	14.8	17.2
Position 2	29	12.6	12.8

All figures are percentages.

Discussion

Although nasal sprays are effective in the management of rhinitis, this study and previous work suggest that a very small proportion of the ciliated mucosa of the nose receives a dose of spray at initial delivery. Very little of the mucosa in the posterior nasal cavity appears to have any drug deposited on it at the initial spray. Effective treatment may be facilitated by mucociliary transport of the spray or via a systemic mechanism. However, given that the systemic absorption of nasal sprays is limited, it seems reasonable to assume that the efficacy of nasal sprays could be improved by increasing the distribution topically, although no studies have addressed this directly. This may be of particular importance in people with deficiencies in mucociliary transport.

It was our observation that although the 'head down–spray up' position (technique 2) may give marginally superior coverage to the area of the nasal valve area, the 'head up–spray slightly up' position deposited spray high on the septum anteriorly. It is unclear whether this would have an effect on spray efficacy, especially if mucociliary transport mechanisms have a role to play in drug distribution. Further studies are underway to observe the change in distribution with time.

This study confirms the findings of others, which suggest that the distribution of spray is poor to the posterior aspect of the nasal cavity.[1–5] This would seem to be the case with both of the positions we tested.

Although the use of fluorescein to demonstrate intranasal drug distribution has been used in a descriptive study,[8] we believe that the use of computer analysis to quantify the degree of coverage is a novel and useful technique in the assessment of intranasal drug distribution.

Conclusions

Both spray techniques studied resulted in limited distribution of azelastine hydrochloride to the nasal mucosa. Both positions delivered more of the drug anteriorly and there was no difference between the two techniques. We have found the use

of fluorescein-labelled spray to be a useful technique to quantify the degree of intranasal drug distribution.

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