

Septoplasty and Decongestant Improve Distribution of Nasal Spray^{*}

Jiaoping MI (米皎平)¹, Yunping FAN (樊韵平)^{1,2#}, Shaoyan FENG (冯韶燕)¹, Wentong XIA (夏文彤)¹,
Jingqing WANG (王静清)¹, Huabin LI (李华斌)^{2#}

¹Department of Otolaryngology-Head and Neck Surgery, the 5th Affiliated Hospital of Sun Yat-sen University, Zhuhai 519020, China

²Otorhinolaryngology Hospital, the 1st Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, China

© Huazhong University of Science and Technology and Springer-Verlag Berlin Heidelberg 2011

Summary: This study prospectively examined the intranasal distribution of nasal spray after nasal septal correction and decongestant administration. A cohort of 20 patients was assessed for the distribution of nasal spray before and after nasal septum surgery. Sprays were dyed and administered one puff per nostril when patients hold their head up in an upright position. Before and after decongestant administration, the intranasal distribution was semi-quantitatively determined by nasal endoscopy. The results showed that the dyed drug was preferentially sprayed onto the nasal vestibule, the head of the inferior turbinate, the anterior part of septum and nasal floor. As far as the anterior-inferior segment of the nasal cavity was concerned, the distribution was found to be influenced neither by the decongestant nor by the surgery ($P>0.05$). However, both the decongestant and surgery expanded the distribution to the anatomical structures in the superior and posterior nasal cavity such as olfactory fissure, middle turbinate head and middle nasal meatus. No distribution was observed in the sphenoidal recess, posterior septum, tail of inferior turbinate and nasopharynx. It was concluded that nasal septum surgery and decongestant administration significantly improves nasal spray distribution in the nasal cavity.

Key words: drug distribution; nasal spray; decongestant; surgery; nasal endoscopy

Nasal inflammatory disorders such as rhinitis and rhinosinusitis are common diseases and affect more than 30% population worldwide. Currently, topical nasal sprays including intranasal steroids and anti-histamine agents have been widely used in clinical practice to treat various types of nasal inflammation^[1]. Intranasal steroids are considered to be the treatment of choice for nasal inflammation by rhinologists. The efficacy of nasal steroid spray is affected by a range of factors including drug formulation, delivery device, deposition site, nasal structure and patients' compliance etc^[2]. It has been recognized that nasal anatomy and head position are the key factors in the deposition of topical nasal drugs and may determine the effectiveness of the local steroid or anti-histamine treatment^[3]. If anatomic abnormalities hinder the delivery of topic agents, the effectiveness of these topic drugs for nasal inflammatory disorders is logically expected to be low. Therefore, spraying the drugs to the exact inflammatory sites is critical for nasal inflammation treatment.

Nasal septum deviation and hypertrophy of the inferior turbinate are the most common conditions that pre-

vent nasal sprays from delivering into the exact inflammatory sites such as the middle turbinate and middle meatus. It has been demonstrated that the deposition of topical agents is decreased in the target area around the head of the middle turbinate in the presence of minor septal deviation, narrow nasal valve areas, or inferior turbinate hypertrophy^[3]. And a recent study demonstrated that the distribution of nasal drugs is significantly improved in the middle meatus after endoscopic sinus surgery^[4]. However, the influence of nasal septal deviation on the nasal spray distribution is unclear.

To address these problems, in this study, a cohort of patients with nasal disorders was enrolled to examine the nasal spray distribution by nasal endoscopy after nasal septum surgery, inferior turbinatoplasty and administration of nasal decongestants.

1 MATERIALS AND METHODS

1.1 Subjects

Twenty patients (14 males and 6 females, age: 20 to 58 years old) who would undergo surgical correction of nasal septum deviation with or without sinus surgery from October 2008 to March 2009 were prospectively enrolled in our study. All of them presented with nasal congestion caused by septal deviation. This study was approved by the Local Ethical Committee of the 5th Affiliated Hospital of Sun Yat-sen University. Written informed consents were obtained from all the patients.

Jiaoping MI, E-mail: siwen_mi@yahoo.com

[#]Corresponding authors, Yunping FAN, E-mail: zhcdc2003@sohu.com; Huabin LI, E-mail: allergyli@163.com

^{*}This study was supported by a grant from National Natural Science Foundation of China (No. 81070772), and Zhuhai Medical Scientific Research Fund (No. PC20081046).

The clinical symptoms included unilateral persistent or bilateral alternating stuffy nose, epistaxis, and rhinogenic headache. Some patients had complaint of paroxysmal sneeze, runny nose, and itching nose. Endoscopic inspection indicated septal deviation on the anterior or anterior-median segment of the nasal septum. Three of the patients were diagnosed with chronic rhinosinusitis on the basis of radiological finding (cloudy image by computerized tomography scanning), medical history and symptoms.

In terms of the anatomical relationship between the deviated nasal septum and the lateral wall of nasal cavity, and the nasal function, nasal septum deviation was classified into 3 degrees: degree I, in which the deviation fails to touch the inferior turbinate, therefore the nasal ventilation and sinus drainage aren't affected; the distance of the nasal septum to the midline is less than 0.3 cm; degree II, in which deviated septum touches the surface of the inferior turbinate, and contralateral turbinate presents compensatory hypertrophy, which affects the nasal ventilation and sinus drainage; the distance of the nasal septum to the midline is 0.3–0.6 cm, and the decongestant administration can improve the ventilation; degree III, in which deviated septum pushed the inferior turbinate; decongestants can not constrict the turbinate mucosa and improve the nasal ventilation; the distance of the nasal septum to the midline is greater than 0.6 cm. Of all the patients, there were 7 in degree I, 9 in degree II and 4 in degree III. The morphology of septal deviation consisted of type C (3 cases), type S (3 cases), spinous process (5 cases), ridge process (1 case) and irregular deviation (8 cases). According to the main position of deviation, 10 cases had upper deviation, 10 lower deviation, 12 anterior deviation and 8 posterior deviation.

1.2 Determination of Drug Distribution

Two nasal spray bottles for azelastine hydrochloride (MEDA Manu GmbH, Bad Homburg, Germany) were emptied and then refilled with 1 mg/mL methylene blue indicator and xylometazoline (0.1%, Wuhan Grand Pharmaceutical Group Co., China) separately. Nasal spraying was performed with the maneuver recommended by Benninger *et al*^[5]. All the patients hold head in a neutral upright position. The spray nozzle was inserted into the nostril. The drug was sprayed laterally away from the middle of the nose septum, and towards the outer canthus of the ipsilateral eye with gentle breathes through the nose in the course of spraying (one puff per nostril). Distribution of the sprays on nasal mucosa was observed under an endoscope (4.0 mm and 2.7 mm in diameters) without anesthesia. Methylene blue was cleaned by normal saline and cotton fleecy. Xylometazoline solution was used to spray twice per nostril at an interval of 5 min, and then the distribution of methylene blue was observed and recorded under the endoscope.

1.3 Evaluation Items

The distribution of the dyed spray on the nasal mucosa was recorded following the anatomic sites described below: the nasal vestibule, the anterior and middle and caudal tip of the inferior turbinate, the nasal septum, the

anterior tip and root of the middle turbinate, the middle meatus, the nasal floor and nasopharynx. The distribution area of the dyed spray was semi-quantitatively graded on a scale of 0–2: 0, no distribution; 1, the distribution area < 50%; 2, the distribution area > 50%. Scores from each patient were averaged by three observers. The distribution was evaluated one day before the operation and three months after the operation. Nasal conditions were observed before and 5 min after decongestant administration at each visit.

1.4 Statistical Analysis

The Mann-Whitney *U* test was conducted for statistical analysis with the aid of SPSS 11.0 statistic software for Windows. The experiment was a self-controlled and prospective study. Significant difference was considered when a *P* value was less than 0.05.

2 RESULTS

2.1 Intranasal Distribution of Nasal Spray before Nasal Septal Surgery

The dyed drug was found to be distributed mainly on the nasal vestibule, the anterior half of the nasal septum, the head of the inferior turbinate, and the anterior nasal floor before the decongestant administration (fig. 1, 2). The semi-quantitative scores are listed in table 1. As far as the anterior segment of the nasal cavity was concerned, decongestants failed to change the distribution of nasal spray significantly (table 2). And little distribution of the nasal spray was seen in the olfactory fissure, the head of the middle turbinate and the middle meatus. After administration of decongestants, as illustrated in table 1, the drug distribution was significantly improved in the olfactory fissure, the head of the middle turbinate and the middle meatus ($P < 0.05$ for all).

In spite of use of decongestant or not, little drug distribution was found in the sphenoethmoidal recess, the posterior septum, the tail of the inferior turbinate and nasopharynx before the septal surgery (fig. 1 and 2). Septal deviation and hypertrophy of the inferior turbinate was found to prevent the intranasal distribution of the methylene blue nasal spray. As illustrated in table 1, the superior deviation was shown to affect the distribution of methylene on the olfactory cleft and the ostiomeatal complex, and the inferior deviation would influence the distribution on the inferior meatus, the inferior turbinate and the posterior nasal cavity. The distance between the nasal septum and the inferior turbinate was found to directly affect the sprayed drugs to reach the ostiomeatal complex.

2.2 Intranasal Distribution of Nasal Spray after Surgery

The dyed blue nasal spray was mainly distributed in the nasal vestibule, the anterior portion of the nasal septum, the anterior half portion of the inferior turbinate and the nasal floor after surgery in the absence of decongestants (fig. 1). As far as the anterior segment of the nasal cavity was concerned, the spray distribution after decongestant administration was not significantly different from that before the decongestant use (table 2).

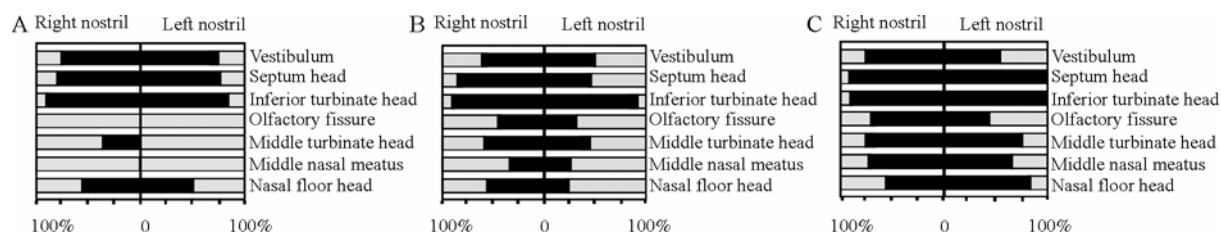


Fig. 1 The influence of the septal deviation on the distribution of nasal sprays

The intranasal distribution of methylene blue was shown in 3 patients before surgery. The presence or absence of dye was indicated by a bar on the X-axis. The gray dotted bar showed the absence of dye. The black showed the presence of dye. The anatomical sites were on the Y-axis. A: Significant nasal septum deviation to the left, and a narrow valve area; B: Nasal septum with moderate left-side deviation, right inferior turbinate hypertrophy and septal turbinate hypertrophy that affect the distribution of methylene blue in the olfactory cleft; C: Mild deviation of the top of the nasal septum to the left and a large valve area

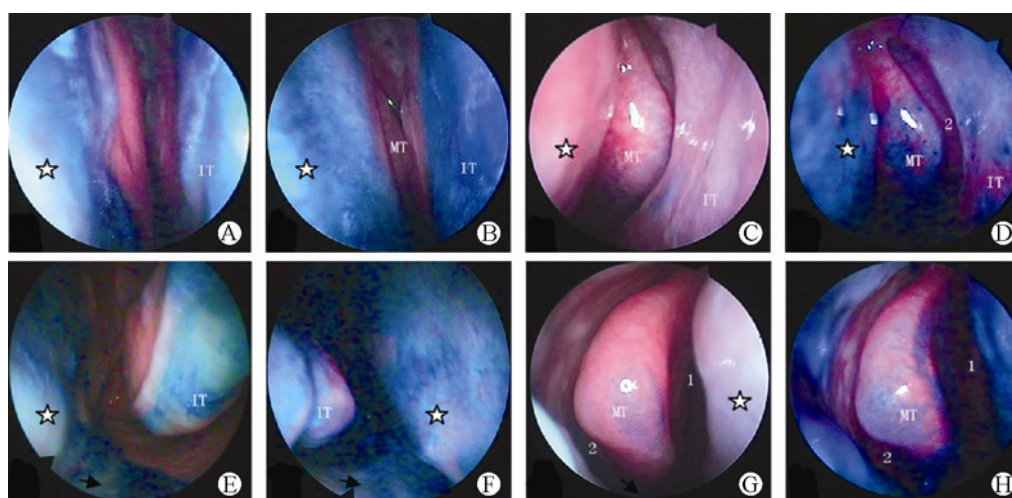


Fig. 2 Endoscopic views of dyed sprays in the nasal cavity after different interventions

A: Intranasal drug distribution before the operation without use of decongestion. With the nasal septum having severe deviation to the left side, the methylene blue was distributed in the nasal septum and the anterior turbinate. There was no methylene blue distribution in the olfactory cleft, the middle turbinate and the middle meatus. B: Intranasal drug distribution after the decongestant administration. The methylene blue could not reach the olfactory cleft, the middle turbinate and the middle meatus due to the deviation of the nasal septum and the severe inferior turbinate shrinkage. C: A significant relief of nasal obstruction 3 months after surgery. The nasal cavity was found widened as compared with the pre-operation. There was a little deposition in the middle turbinate. D: Intranasal drug distribution after nasal septal surgery and decongestant administration. The distribution of nasal spray in the sites aforementioned was highly increased. E: Methylene blue distributed in the inferior turbinate head, the nasal floor and the anterior nasal septum; F and G: The intranasal methylene blue distribution in the olfactory cleft, the middle turbinate, the middle meatus before and after the decongestant used. ☆ stands for the location of nasal septum, MT for middle turbinate, IT for inferior turbinate, 1 for olfactory cleft, 2 for middle meatus and the arrow for the nasal floor.

Table 1 The intranasal distribution ratio of methylene blue before surgery without decongestant administration

Sites	Left (n/%)			Right (n/%)		
	0	1	2	0	1	2
Vestibulum	2 (10.00)	12 (60.00)	6 (30.00)	2 (10.00)	16 (80.00)	2 (10.00)
Septum head	0 (0.00)	7 (35.00)	13 (65.00)	0 (0.00)	5 (25.00)	15 (75.00)
IT head	0 (0.00)	2 (10.00)	18 (90.00)	0 (0.00)	3 (15.00)	17 (85.00)
Olfactory fissure	14 (70.00)	5 (25.00)	1 (5.00)	15 (75.00)	4 (20.00)	1 (5.00)
MT head	14 (70.00)	5 (25.00)	1 (5.00)	14 (70.00)	4 (20.00)	2 (10.00)
Middle meatus	15 (75.00)	4 (20.00)	1 (5.00)	13 (65.00)	5 (25.00)	2 (10.00)
Nasal floor head	0 (0.00)	14 (70.00)	6 (30.00)	0 (0.00)	16 (80.00)	4 (20.00)

The distributions were significantly improved in olfactory fissure, the head of middle turbinate, and the middle meatus after surgery in the absence of decongestant use when compared with those before surgery ($P < 0.05$ for all, fig. 1 and 2). After decongestant administration, the dis-

tributions of nasal spray were expanded significantly after surgery compared with those before surgery [P values (left and right sides, respectively): the olfactory fissure, 0.026, 0.005; the middle turbinate head, 0.030, 0.011; the middle meatus, 0.038, 0.004, respectively].

Table 2 The comparison among the intranasal distributions of dyed spray after different interventions

Sites	With and without decongestant				Pre- and post-operation			
	Pre-ope		Post-ope		Undec		Dec	
	Z	P	Z	P	Z	P	Z	P
Vestibulum								
Left	-0.284	0.820	-1.090	0.369	-1.090	0.369	-0.247	0.841
Right	-1.002	0.478	-0.311	0.820	-0.334	0.820	-0.277	0.841
Septum head								
Left	-1.408	0.429	-1.309	0.289	-0.637	0.602	-0.374	0.799
Right	-0.374	0.799	-0.350	0.799	-0.350	0.799	-0.374	0.799
IT head								
Left	-0.472	0.799	-0.472	0.799	-0.472	0.799	-0.472	0.799
Right	-0.411	0.799	-0.472	0.799	-0.472	0.799	-0.411	0.799
Olfactory fissure								
Left	-2.773	0.001	-3.299	0.002	-2.268	0.040	-2.429	0.026
Right	-2.555	0.023	-3.711	0.001	-2.405	0.033	-3.201	0.005
MT head								
Left	-3.376	0.001	-3.255	0.003	-3.431	0.001	-2.458	0.030
Right	-3.468	0.001	-4.032	0.000	-2.727	0.011	-3.058	0.011
Middle meatus								
Left	-3.135	0.004	-3.319	0.002	-3.385	0.001	-2.401	0.038
Right	-2.702	0.011	-3.619	0.001	-2.605	0.014	-3.365	0.004
Nasal floor head								
Left	-0.655	0.602	-0.374	0.799	-0.350	0.799	-1.363	0.289
Right	-0.721	0.602	-0.322	0.799	-1.049	0.429	-0.655	0.602

Pre-ope: Pre-operation; Post-ope: Post operation; Dec: Decongestant; Undec: Undecongestant; IT: Inferior turbinate; MT: middle turbinate

3 DISCUSSION

In the present study, our results demonstrated that septal surgery for deviation is beneficial for the distribution of nasal spray. Intranasal steroids have been commonly used for the treatment of nasal disorders due to their high efficacy, convenience and few adverse effects. For the treatment of chronic rhinitis and rhinosinusitis, nasal steroids were recommended as the first choice and gained the evidence-based recommendation of A level in EPOS guideline (2007)^[1]. For this reason, we hypothesized that if the nasal spray was able to deliver directly to the inflammatory area by expanding the delivery approach, the best therapeutic effectiveness would be achieved. However, the distribution of intranasal agents is affected by many factors, such as abnormal nasal anatomy, delivery device and spray maneuver. That the nasal spray distribution can be improved by correcting the abnormal anatomic structure has not yet been well established.

Our findings that septal correction expanded the approach of nasal spray to the middle meatus and improved nasal spray distribution in this study therefore provided reliable evidence that septal deviation is a critical factor that can affect clinical efficacy of nasal sprays. In a recent study, Tsikoudas *et al* demonstrated that functional endoscopic sinus surgery can improve the distribution of nasal spray into the middle meatus^[4]. However, they didn't take into account the effect of septal deviation on nasal spray distribution. In our study, we examined the distribution of nasal spray by endoscopic inspection in a cohort of patients with nasal septal deviation and chronic rhinitis, and we found the improvement of distribution after expanding the approach by some

interventions, such as surgical correction of anatomical abnormalities and administration of decongestant. These results suggested that expanding the approach of drug delivery can improve the clinical efficacy of nasal steroid or anti-histamine spray.

Our observation thus highlighted the importance of nasal septoplasty in expanding the distribution of nasal spray. In this study, distribution was improved to the middle-posterior portion of the nasal cavity which nasal spray usually can't reach. Meanwhile, our observation also indicated that decongestants, if added after the surgical correction of anatomical abnormalities, is able to further improve the distribution of nasal spray.

Nasal spray and nasal drop are the two common delivery methods and the distribution of aqueous spray currently has taken the place of nasal drop^[6]. A recent study has shown that nasal spray was more widely distributed in the nasal cavity than nasal drop did^[7]. However, no difference in the delivery of nasal drugs to the middle meatus between the nasal drop and aqueous spray was found in two other researches^[8, 9]. Some scholars compared four different topical delivery systems (spray bottle, atomizer, nebulizer, and bulb syringe) and found there was no statistical difference in the efficacy of drug delivery between the atomizer and spray bottle. The bulb syringe was superior to the atomizer and spray bottle in the ethmoidal region^[9]. It is known that the nasal cavity consists of left and right halves, and the volume of each half is approximately 7.5 mL. And the total surface area of the nasal cavity is around 150 cm²^[10]. The proportion of the ciliated epithelium that nasal spray reaches is able to be readily assessed by observing the proportion of nasal spray transported by mucociliary flow^[11]. Berridge *et al* introduced a technique which utilizes positron emission tomography (PET) to measure the radioactivity

of administered isotopes^[12]. And Wormald *et al* reported that they used saline-contained radioactive Tc99 to evaluate the drug distribution in the nasal cavity and paranasal sinuses^[13]. However, these studies exclusively focused on the drug distribution in the nasal cavity, and little is known about the influence of the anatomical abnormalities on the drug distribution. The results of our study added to the academic data because we here observed not only the drug distribution in the nasal cavity with anatomical abnormalities, but also the drug distribution in the nasal cavity after surgical correction.

Nasal septal deviation is a very common abnormality and a large proportion of patients with rhinitis and rhinosinusitis also present with comorbid septal deviation. It is unknown whether the nasal deviation will prevent the distribution of nasal spray in these occasions. In this study, we found that the majority of drug was distributed in the nasal vestibule, the head of nasal septum, and the anterior segment of the inferior turbinate nasal floor. Only a small proportion of the drug could reach the head of the middle turbinate, the middle meatus and the olfactory cleft. The intranasal drug distribution was affected by the degree of nasal septum deviation and the inferior turbinate hypertrophy. The narrowed space between the nasal septum and inferior turbinate directly prevented the drug from reaching the ostiomeatal complex. After the septoplasty, we found the intranasal drug distribution was expanded more widely. The drug distribution into the middle meatus was further increased significantly after the decongestant was used. Our finding thus suggested that septoplasty, as well as decongestant use, is able to facilitate the delivery of nasal spray.

In summary, we found that the distribution of nasal spray was significantly expanded to the nasal cavity and the middle meatus after septoplasty. For patients with severe rhinitis and nasal septum deviation, surgical correction should be preferentially recommended in order to facilitate the ensuing nasal spray administration, which hopefully contributes to the improvement of the clinical efficacy of topic agents.

REFERENCES

- 1 Fokkens W, Lund V, Mullol J, *et al*. European position paper on rhinosinusitis and nasal polyps 2007. *Rhinol Suppl*, 2007,45(20):1-136
- 2 Harvey RJ, Schlosser RJ. Local drug delivery. *Otolaryngol Clin North Am*, 2009,42(5):829-845
- 3 Merkus P, Ebbens FA, Muller B, *et al*. Influence of anatomy and head position on intranasal drug deposition. *Eur Arch Otorhinolaryngol*, 2006,263(9):827-832
- 4 Tsikoudas A, Barnes ML, White PS. The effect of functional endoscopic sinus surgery on nasal spray distribution to the middle meatus in patients with rhinosinusitis. *Am J Rhinol Allergy*, 2009,23(5):546-548
- 5 Benninger MS, Hadley JA, Osguthorpe JD, *et al*. Techniques of intranasal steroid use. *Otolaryngol Head Neck Surg*, 2004,130(1):5-24
- 6 Hardy JG, Lee SW, Wilson CG. Intranasal drug delivery by spray and drops. *J Pharm Pharmacol*, 1985,37(5):294-297
- 7 Scheibe M, Bethge C, Martin W, *et al*. Intranasal administration of drugs. *Arch Otolaryngol Head Neck Surg*, 2008,134(6):643-646
- 8 Sanan JD, Laube BL, Lin TC, *et al*. Validity of *in vitro* tests on aqueous spray pumps as surrogates for nasal deposition. *Pharm Res*, 2002,19(1):1-6
- 9 Timothy R, Harlan R, Gilbert E, *et al*. Comparison of topical medication delivery systems after sinus surgery. *Laryngoscope*, 2004,114(2):201-204
- 10 Proctor DF. Nasal mucous transport and our ambient air. *Laryngoscope*, 1983,93(1):58-62
- 11 Newman SP, Moren PF, Clarke SW. The nasal distribution of metered dose inhalers. *J Laryngol Otol*, 1987,101(2):127-132
- 12 Berridge MS, Heald DL, Muswick GJ, *et al*. Biodistribution and kinetics of nasal carbon-11-triamcinolone acetate. *J Nucl Med*, 1998, 39(11):1972-1977
- 13 Wormald PJ, Cain T, Oates L, *et al*. A comparative study of three methods of nasal irrigation. *Laryngoscope*, 2004,114(12):2224-2227

(Received Sep. 28, 2010)

Copyright of Journal of Huazhong University of Science & Technology, Medical Sciences is the property of Springer Science & Business Media B.V. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.