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Comparison of intranasal medication delivery devices before and after functional endoscopic sinus surgery using Phacon sinus surgery models

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Abstract

Objective. Functional endoscopic sinus surgery for chronic rhinosinusitis improves sinus drainage and intranasal medication delivery. This study compares medication delivery with commonly used devices in normal and altered anatomy (post functional endoscopic sinus surgery) using sinus surgery models (Phacon).

Methods. Medication delivery was simulated via nasal drops, nasal spray and an irrigation device (Neilmed Sinus Rinse). Coverage was then calculated from endoscopic pictures taken at various anatomical sites in the normal nose and post functional endoscopic sinus surgery.

Results. In the normal nose, nasal spray did not penetrate the sphenoid sinus, and drops bypassed the vestibule anteriorly. Neilmed Sinus Rinse provided superior coverage at the sphenoid site following sphenoidectomy and the frontal site following Draf III. After ethmoidectomy, nasal drops overall provided less coverage than the other methods.

Conclusion. Neilmed Sinus Rinse generally provided the best distribution, followed by the nasal spray and then nasal drops. The type and extent of surgery also affects medication delivery.

Main Article

Christoforos Constantinou takes responsibility for the integrity of the content of the paper

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Introduction

Chronic rhinosinusitis comprises a spectrum of common conditions manifested by mucosal inflammation of the nasal cavity and paranasal sinuses.[1,2] Treatment often requires a combination of medical and surgical approaches.[3] Medical management usually involves delivering topical agents onto the inflamed mucosa, while avoiding systemic absorption and hence side effects.[4,5] In clinical practice, a variety of different topical delivery devices are used, including nasal drops, sprays, irrigation devices and nebulisers.[2,6] The factors determining optimal deposition of particles in the nasal cavity and the efficacy of individual devices for treating each condition remain controversial.[6,7]

In cases where medical therapy fails to provide an effective solution for chronic rhinosinusitis, surgery in the form of functional endoscopic sinus surgery (FESS) is usually preferred.[8] This constitutes a variety of surgical techniques that allow direct (endoscopic) visualisation and opening of the sinuses. The aim of surgery is to alleviate obstruction, remove infective or inflammatory burden, re-establish mucociliary clearance, and facilitate medication delivery.[9,10] At present, there is no consensus regarding the extent of surgery performed, which can range from limited FESS (uncinectomy, middle meatal antrostomy and anterior ethmoidectomy) to 'full house' FESS with Draf III procedure (opening of all sinuses and creation of a single common sinus cavity).

Functional endoscopic sinus surgery alters the anatomy of the nasal cavity, and different studies have been conducted to assess the delivery of medication post-operatively. These studies have used various methods to assess the effectiveness of delivery, ranging from subjective assessment utilising photography and video monitoring[11] to complex analysis using computational fluid dynamics.[12–14] These studies have involved live patients,[6] cadaveric models[5] and three-dimensional printed models of nasal cavities post FESS.[12–14]

Although these studies provide useful data on how different delivery techniques compare in a set scenario, they do not provide a comparison of how each method compares with different combinations of sinus surgery.

Objective

This study aimed to evaluate and compare drug delivery using different devices in non-operated and operated sinonasal cavities.

Table 1. Technique used for each delivery method

Delivery method	Technique
Nasal drops	2 drops into each nostril Head position simulated hanging back over edge of bed at 45° head tilt
Nasal spray	2 actuations aiming towards ipsilateral ear Head position – upright
Neilmed Sinus Rinse	2 × flushes with head bent forward & slightly tilted to ipsilateral side Head position – upright

Materials and methods

Ethical consideration

No human subjects or patient data were involved in the study and therefore no ethical approval was required.

Participants and settings

The experiments were conducted on Phacon® sinus surgery models (Phacon® sinus patient 'Meyer' – with skin).

Design and main outcome measures

Blue food colouring, which provides good contrast on endoscopic images, was placed into each drug delivery device (nasal drops, nasal spray and Neilmed© Sinus Rinse™), before being administered to the nose. A standardised technique was used for each device, as summarised in Table 1. Standardised endoscopic images were obtained to evaluate the distribution.

In the first stage of the experiment, dye was delivered to an anatomically non-operated model using the technique shown in Table 1. Endoscopic images were obtained using the three-pass technique after each dye delivery at the vestibule, ethmoid and sphenoid areas, using a 0° rigid nasendoscope (Olympus®) and a digital signal processing unit. The endoscopic images were analysed using ImageJ® software to evaluate the distribution of liquid dye at various sinonasal sites. Examples of images obtained are shown in Figure 1.

In the second stage of the experiment, the model underwent different staged FESS operations by a single ENT surgeon with a subspecialty interest in rhinology. As in the first stage, dye was again delivered using the same technique, and images were obtained at the same sites with the addition of the frontal sinus. Each delivery (in both stages of the experiment) was repeated three times and the average percentage cover at each area was recorded. Examples of images obtained are shown in Figures 2–3.

Stages of operation included uncinectomy, middle meatal antrostomy, anterior ethmoidectomy, anterior/posterior ethmoidectomy, transnasal sphenoidotomy, transethmoidal sphenoidectomy and Draf III frontal sinus surgery.

All results were recorded and analysed in Microsoft Excel® spreadsheet software. The percentage area covered by each method was compared with each other method using the Mann–Whitney U test for each sinonasal site.

Results

In the non-operated nasal cavity, the sinus rinse spread to all sinuses; the nasal spray did not penetrate the sphenoid sinus and nasal drops bypassed the vestibule anteriorly. At the ethmoid site, nasal drops showed significantly lower coverage in comparison to both spray and Neilmed Sinus Rinse. The Neilmed Sinus Rinse showed significantly higher delivery to the sphenoid sinus in comparison to the other delivery methods. Kruskal–Wallis's test results suggested that these three modalities of delivery were statistically significantly different to each other. The summarised results are shown in Table 2.

After performing ethmoidectomies, there was distribution of dye into the ethmoid sinuses when using nasal drops in comparison to the non-operated nose. Delivery of the dye using nasal spray and sinus rinse was superior to that using nasal drops after ethmoid surgery, but the sinus rinse was only more superior than the spray when a complete ethmoidectomy had been performed. The results are summarised in Table 3.

Surgically connecting the ethmoid and sphenoid sites (transethmoidal sphenoidectomy) allowed distribution of the dye when using a spray. Neilmed Sinus Rinse was superior in delivering dye to the sphenoid cavity in comparison to both the spray and drops.

All three delivery methods were able to reach the frontal site following the Draf III operation. Comparisons showed significantly higher distribution with the Neilmed Sinus Rinse, followed by the nasal spray and finally the nasal drops. Comparisons between each delivery method and the statistical analysis results are shown in Table 4.

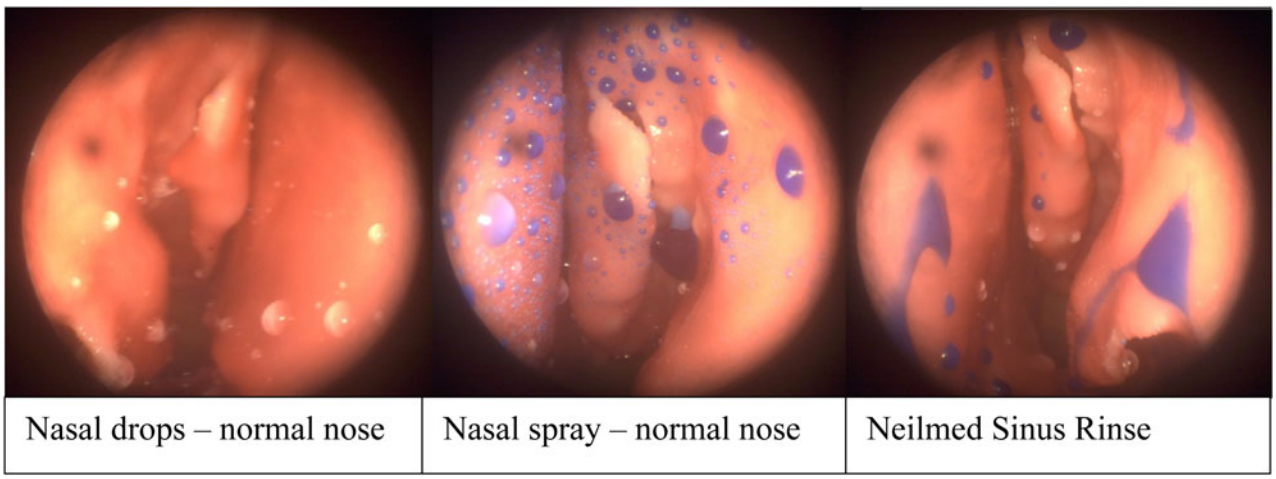

Figure 1. Views at the vestibule site.

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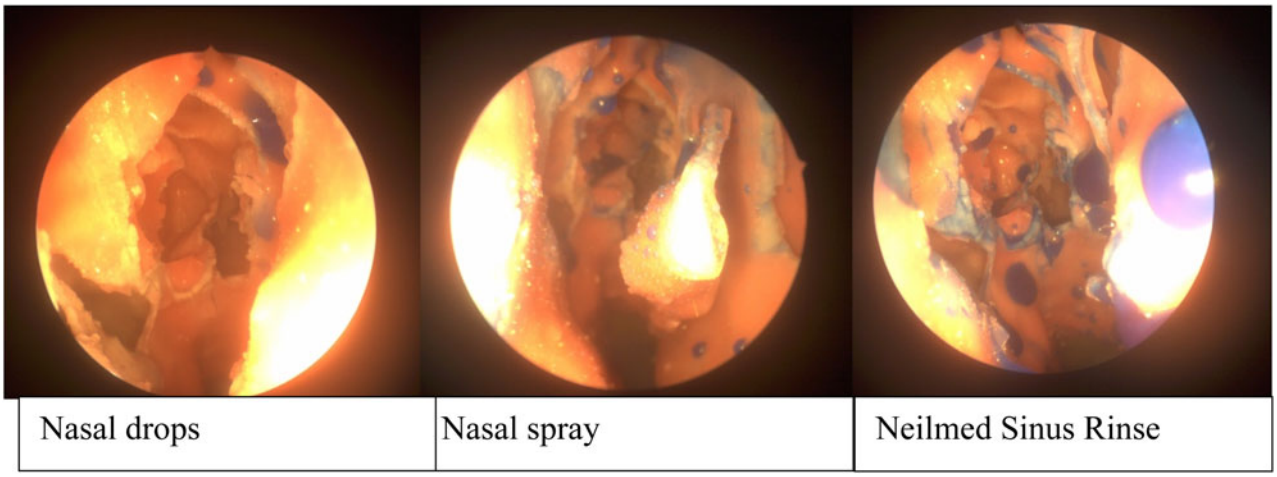

Figure 2. Views at the ethmoid site.

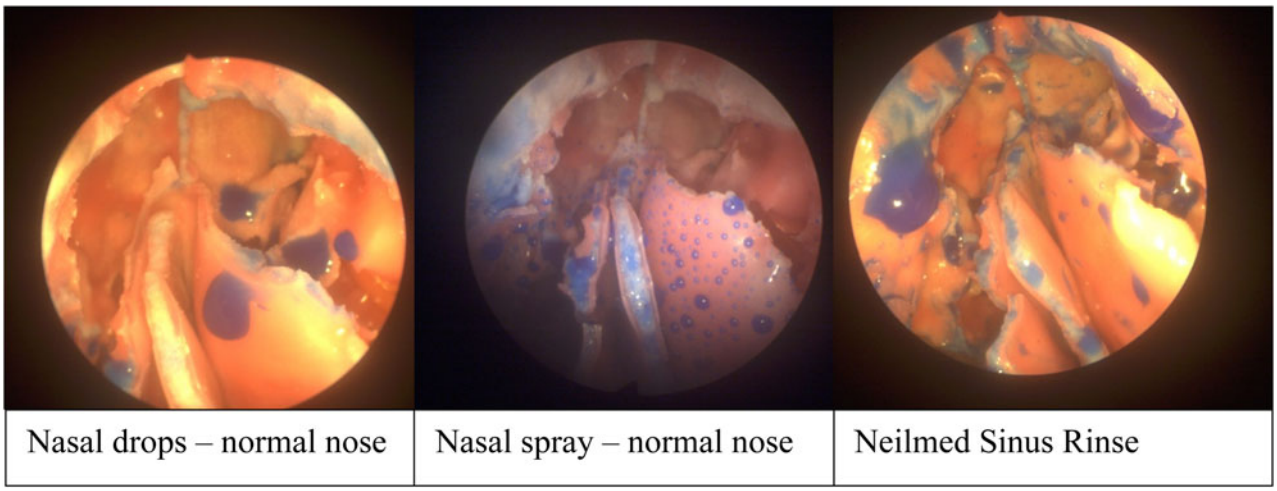

Figure 3. Views at the frontal sinus (Draf III procedure).

Table 2. Average percentage coverage at different sites in the non-operated nasal cavity

	Imaging site		
Delivery method	Vestibule site	Ethmoid site	Sphenoid site
Nasal drops (% coverage)	0	0.93	10.15
Nasal spray (% coverage)	7.53	7.29	0
Neilmed Sinus Rinse (% coverage)	6.65	4.27	3.69
Kruskal–Wallis test (*p*-value)	0.0034	0.032	0.0011

Table 3. Average percentage coverage at different sites in the operated nasal cavity

	Imaging or operative site						
Delivery method	Left vestibule	Anterior ethmoidectomy	Transnasal sphenoidotomy	Right vestibule	Complete ethmoidectomy	Transethmoidal sphenoidectomy	Frontal Draf III
Nasal drops	1.61	2.368	2.25	2.03	3.05	2.94	7.6
Nasal spray	5.37	11.6	0	4.34	6.36	1.42	13.5
Neilmed Sinus Rinse	10.2	10.1	13.5	11.9	14.4	32.0	30.2

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Table 4. Comparison of delivery methods at each operated site

Operative site	Method	% Coverage	Kruskal–Wallis test (*p*-value)	Mann–Whitney U test (*p*-value)
Anterior ethmoidectomy	Drops	2.368	0.018	Spray had significantly greater coverage than drops (0.023)
	Spray	11.6		Sinus rinse had significantly greater coverage than drops (0.003)
	Neilmed Sinus Rinse	10.1		Sinus rinse coverage not significantly different to that of spray (0.12)
Complete ethmoidectomy	Drops	3.05	0.001	Spray had significantly greater coverage than drops (0.006)
	Spray	6.36		Sinus rinse had significantly greater coverage than drops (0.003)
	Neilmed Sinus Rinse	14.4		Sinus rinse had significantly greater coverage than spray (0.006)
Transnasal sphenoidotomy	Drops	2.25	0.002	Drops coverage not significantly different to that of spray (0.116)
	Spray	0		Sinus rinse had significantly greater coverage than drops (0.003)
	Neilmed Sinus Rinse	13.5		Sinus rinse had significantly greater coverage than spray (0.001)
Transethmoidal sphenoidectomy	Drops	2.94	0.003	Drops coverage not significantly different to that of spray (0.47)
	Spray	1.42		Sinus rinse had significantly greater coverage than drops (0.003)
	Neilmed Sinus Rinse	32.0		Sinus rinse had significantly greater coverage than spray (0.003)
Frontal Draf III	Drops	7.6	0.001	Spray had significantly greater coverage than drops (0.03)
	Spray	13.5		Sinus rinse had significantly greater coverage than drops (0.003)
	Neilmed Sinus Rinse	30.2		Sinus rinse had significantly greater coverage than spray (0.003)

Discussion

The treatment of chronic rhinosinusitis often requires a combination of approaches that include the delivery of topical agents to the inflamed mucosa. Optimising intranasal distribution and the retention of topical treatment is essential in the management of these patients, including those who have undergone FESS.[14] Common topical delivery devices used in clinical practice include nasal drops, nasal sprays and irrigation devices, and their efficacy has been compared in the past in set scenarios using various methods.[6,7]

Our results demonstrated that surgically manipulating the nasal cavity appeared to improve coverage at most sites. This was especially true for nasal drops, which showed a significant increase in percentage coverage at the ethmoid sites after ethmoidectomy. This serves as a proof-of-concept for FESS facilitating medication delivery in chronic rhinosinusitis, and is in line with the findings of other studies to date.[12]

Our data also provided some insight in regard to how different degrees of FESS can play a role in optimising medication delivery. We found a significant increase in the delivery of nasal spray at the sphenoid sinus after transethmoidal sphenoidotomy when compared to a stand-alone procedure.

The final comparison cycle investigated how each delivery method compared to each other method at each stage of FESS performed. Our results demonstrated that the Neilmed Sinus Rinse device generally provided the best distribution of dye after surgery. This was true for most sites, including the frontal site, sphenoid site (both after stand-alone and transethmoidal sphenoidotomy) and ethmoid site (except for anterior ethmoidectomy only, in which there was no significant difference between the spray and the sinus rinse).

The next best delivery method appeared to be the nasal spray, which showed significantly increased coverage when compared to drops at the frontal and ethmoid sites. No significant difference was found between the spray and the drops at the rest of the sites.

- Altered paranasal sinus anatomy after surgery affects intranasal distribution of medication, but factors affecting optimal distribution and efficacy of delivery devices remain controversial
- This study compared medication distribution in the normal nasal cavity and after different stages of functional endoscopic sinus surgery
- The sinus rinse device provided the best overall medication delivery throughout the paranasal sinuses
- In the normal nose, nasal spray provided better medication distribution in the anterior paranasal sinuses compared to drops that better penetrated the sphenoid sinus
- Transethmoidal sphenoidectomy enabled medication delivery using a nasal spray to the sphenoid sinus
- Following frontal sinus surgery (Draf III), all three devices could deliver medication in the frontal sinus

There are some limitations to our study concerning the evaluation of different drug delivery techniques following FESS. Although the Phacon sinus models simulate sinonasal anatomy, they do not replicate the properties of human

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mucosa and the physiological response to intranasal medication. Furthermore, they do not replicate common anatomical variations such as septal deviations, nor do they simulate mucosal infection or inflammation. Functional endoscopic sinus surgery alters the anatomy and physiology of the paranasal sinuses, and this is likely to influence mucociliary function, microbial ecology and wound healing in the sinonasal cavities.[15] Antrostomy size and particle diameter are also factors that affect topical drug delivery distribution in the paranasal sinuses and osteomeatal complex.[12,13] In addition, the sinus model does not recreate nasal airflow, which is a factor affecting intranasal drug delivery in clinical studies.[13,14,16,17]

Our study results indicate that an irrigation device, such as the Neilmed Sinus Rinse kit, provides the best delivery of dye in both the non-operated and operated nasal cavity. In our clinical practice, this is the preferred method of drug delivery following FESS, and is usually followed by the use of nasal spray for maintenance treatment.

Conclusion

Our results suggest that surgically manipulating the ethmoid sinuses allows better distribution of dye in the ethmoid cavity via nasal drops. Additionally, a transethmoidal sphenoidectomy allows dye to enter the sphenoid cavity using a nasal spray. Finally, an irrigation device, such as Neilmed Sinus Rinse kit, appears to provide the best distribution of medication at most sinonasal sites following surgery. Further studies are required to evaluate the concentration of medication delivered to the sinuses following surgical manipulation of the sinus anatomy.

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Competing interests. None declared

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