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Videoendoscopic analysis of nasal steroid distribution*

Rainer Weber[1], Rainer Keerl[1], Roland Radziwill[2], Bernhard Schick[1], Daniel Jaspersen[3], Karen Dshambazov[4], Günter Mlynski[5], Wolfgang Draf[1]

[1] Department of Otorhinolaryngology, Head and Neck Surgery, Facial Plastic Surgery and Communication Disorders, Fulda Hospital, Academic Teaching Hospital of the University of Marburg, Germany
[2] Department of Pharmacy, Fulda Hospital
[3] Department of Gastroenterology, Fulda Hospital
[4] Department of Otorhinolaryngology, University of Plovdiv, Bulgaria
[5] Department of Otorhinolaryngology, University of Greifswald, Germany

SUMMARY

Topical corticosteroids are one of the main pillars in the treatment of nasal polyps. The exact topography of their intranasal deposition has not yet been adequately visualised. The intranasal distribution of a 1% sodium fluorescein solution applied with original Pulmicort Topinasal® (budesonide) metered pump bottles was analysed by videoendoscopy. The study group included eight healthy subjects and ten patients who had undergone endonasal sinus surgery. Videoendoscopy was performed in the study group within the first minute after application of the fluorescein solution. Additionally the deposition pattern of Pulmicort Topinasal® was analyzed using a nasal model. The examination showed that the majority of the substance is deposited on the anterior portion of the nasal septum and the head of the inferior turbinate. Only a small fraction actually reaches the middle meatus. The distribution is improved by application during the decongested phase of the nasal cycle, after use of vasoconstricting nasal drops and maintaining a spraying angle of 45° upwards. The development of new delivery techniques and systems could improve the efficacy of intranasally administered corticosteroids and reduce the complication rate.

Key words: intranasal distribution, topical steroids, budesonide, nasal polyps, videoendoscopy

INTRODUCTION

Several authors have investigated the intranasal deposition of nasal sprays and drops using radioisotopes (Hardy et al. 1985, Harris et al. 1988, Newman et al. 1987a, Newman et al. 1987b, Thorsson et al. 1993), measurements of particle concentration (Heyder et al. 1977) or nasal models (Hallworth et al. 1986, Mygind et al. 1978a). All studies showed that the majority of the administered drug remains in the anterior non-ciliated portion of the nose. But still, direct visualization of the distribution patterns is missing.

Topical corticosteroids have become established in the treatment of nasal polyps and are used either as sole treatment (Holopainen et al. 1982, Tos 1989), in preparation for surgery (Kennedy et al. 1988) or after polypectomy to accelerate healing (Weber et al. 1996a) and to prevent recurrence (Hartwig et al. 1988). Topical treatment can exclusively be effective if the drug actually reaches the seat of the disease. Topically applied corticosteroids only act where they come into contact with the mucosa. For treatment of nasal polyps, the corticosteroid must therefore reach the middle nasal meatus which is regarded as the key area in the development of chronic rhinosinusitis (Kennedy et al. 1985, Stammberger 1986). Moreover, for postoperative treatment or treatment of recurrences, deposition in the ethmoid cell system or the other paranasal sinuses would also be desirable.

The investigations performed to date do not provide sufficient information on whether this pattern of intranasal distribution is achieved using a metered-pump spray. We therefore conducted a videoendoscopic study to determine the exact distribution of topically administered budesonide for the treatment of nasal polyps.

MATERIAL AND METHODS

To investigate the intranasal distribution of budesonide (Pulmicort Topinasal®, Astra, Wedel, Germany) applied with original

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metered-pump bottles, the budesonide suspension was replaced by a 1% sodium fluorescein solution for better visualization inside the nose. As the variable to be investigated was the distribution pattern determined by videoendoscopy immediately after spraying, the physicochemical difference between a budesonide suspension and the fluorescein solution can be disregarded. The yellowish-green fluid is readily visible on the nasal mucosa. When a blue filter is used it is possible to detect even minimal traces of the greenish fluorescent dye so that artefact-free evaluation of the nasal deposition of the fluid sprayed in the nose is possible (Stammberger 1993). Documentation was obtained by videoendoscopy. The method has the advantage of permitting documentation and further image processing. For examination using a nose model the original budesonide suspension was used.

Altogether 35 nasal cavities were examined. In 8 healthy subjects both sides were examined before and 15 minutes after application of decongestant nasal drops (0.1% xylometazoline, Otriven 0.1 %®, Zyma, Munich, Germany). Ten patients who had undergone endonasal paranasal sinus surgery 12 to 16 months previously were inspected also 15 minutes after decongestion with 0.1% xylometazoline. In one of these patients only one side of the nose was examined. The patients applied 1 spray of 50 µl sodium fluorescein in a seated position. The spray was applicated while the patient sniffed. The videoendoscopic analysis and documentation were performed within the first minute after application. Because we wanted to analyse which parts of the nose could maximally be reached by nasal sprays, patients with nasal polyps obstructing the middle nasal meatus were not included in this study.

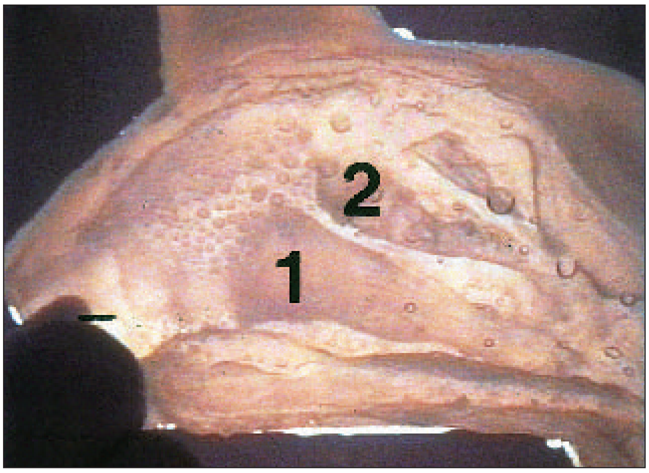

Figure 1: Application of budesonide into the nose model. Macroscopic view from medially on the lateral nasal wall.
1 = inferior turbinate, 2 = middle turbinate.

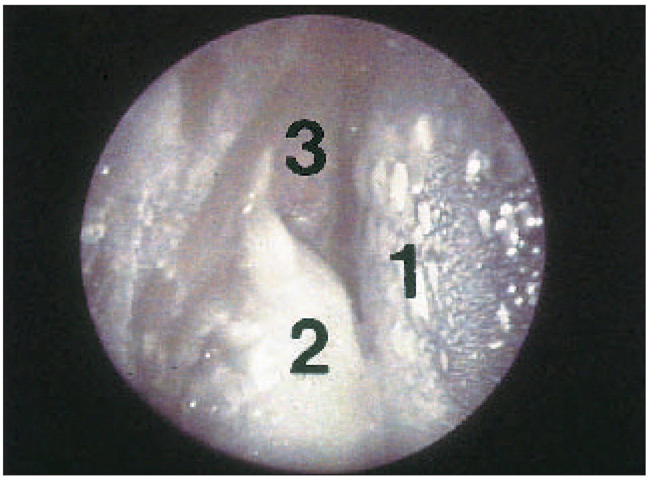

Figure 2: Endoscopic view into a right nasal cavity (nose model) during application of budesonide from a metered pump spray (Pulmicort Topinasal ®). The large majority of the white-coloured budesonide is deposited at the anterior part of the nasal septum and inferior turbinate in the case of mucosal congestion.
1 = nasal septum, 2 = inferior turbinate, 3 = middle turbinate.

The nose model was obtained by taking a cast from a cadaver with decongested nasal mucosa (Figures 1and 2). The nasal septum was built by a transparent glass plate to have an exact view of the structures on the lateral nasal wall. Congestion was simulated by enlarging the inferior turbinate, which is the main obstacle, with plastic modelling-material so that it reaches a size comparable to the congested phase of the nasal cycle. The spraying angle was 0° and 45° upwards from the nasal floor. During application of budesonide macroscopic and endoscopic examinations were performed simultaneously.

RESULTS

Healthy subjects without previous nasal surgery:

In all patients the large majority of the solution was deposited in the anterior non-ciliated portion of the nose both before and after decongestion.

Only a minor amount was deposited at the head of the middle turbinate, the lateral wall of the nose at the agger nasi, the inferior surface of the middle turbinate and in the middle nasal meatus itself, in decreasing concentrations (Figure 3). The fractions deposited in these regions were larger after than before decongestion. Septal deviations influenced the deposition in the middle nasal meatus depending on their degree and location. Spurs in the posterior part did not have any influence. Slight deviations in the anterior or middle part increased deposition if the application was performed parallel to the deviation. Other-

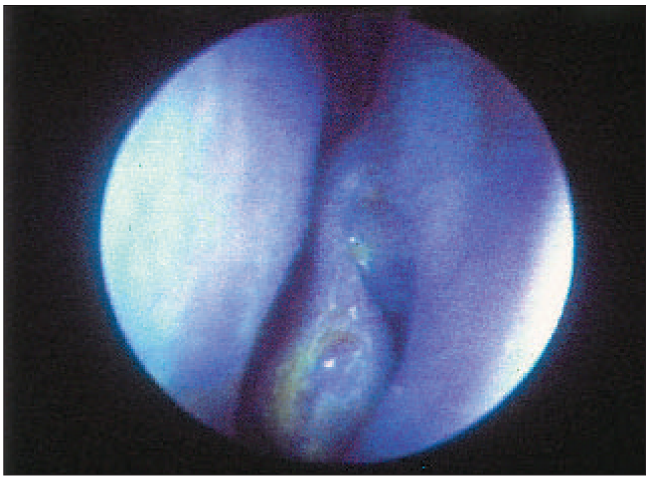

Figure 3: Endoscopic view into a left nasal cavity (30° wide angle optic, blue-light filter). Very small amount of fluorescein can be seen in the middle meatus.

wise deposition in the middle meatus was decreased. A pronounced deviation in the anterior part led to a marked reduction.

Patients with previous paranasal sinus surgery:
All patients had unobstructed nasal breathing and a straight nasal septum. In this group the majority of the solution was again deposited in the anterior non-ciliated portion of the nose. The fraction reaching the region of the middle nasal meatus or the operative cavity was slightly larger than in the patients without previous surgery. The solution was deposited at the head of the middle turbinate, at the entrance to the ethmoid sinus, on the lateral nasal wall at the agger nasi and on the inferior surface of the middle turbinate, in descending order (Figure 4). In the region of the paranasal sinuses themselves, deposition was most frequently found and was most marked in the anterior caudal region of the ethmoid sinuses with the entrance to the maxillary sinus (Figure 5). The posterior ethmoid region was reached considerably less often and deposition at the entrance to the sphenoid cavity or in the sphenoid cavity itself was only seen in individual cases (3 of 19). In patients with a particularly wide nasal cavity there was less deposition at the middle turbinate and in the paranasal sinuses.

In 9 of 35 nasal cavities (25.7%) small haemorrhages were seen under microscopic view, mainly in the region of the nasal septum and to a lesser extent at the head of the inferior nasal turbinate. Because the lesions were not seen before spraying they seemed to be caused by application of the spray.

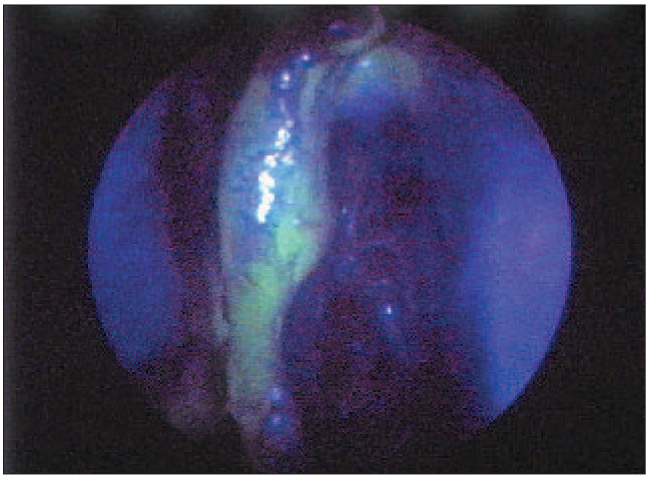

Figure 4: Deposition of fluorescein after complete ethmoidectomy (Endoscopic view, left side, 30° wide angle optic, blue-light filter).

Nose model (Figures 1 and 2):
The results of the in vivo investigations could be confirmed. Most of the solution was deposited in the anterior part of the nose and didn`t reach the middle nasal meatus. The inferior turbinate was the main obstacle and could be by-passed at least partly if the mucosa was decongested or if the spraying angle was 45° upwards from the nasal floor. In this position a greater amount reached the deeper parts of the nose and the middle nasal meatus compared with a spraying angle of 0°. Using an angle of approximately 60° which was taken spontaneously by some patients led to a decrease in deposition in the deeper parts of the nose.

DISCUSSION

Topical corticosteroids can only reduce the size of nasal polyps if they come into contact with the polyps mucosa. The local side-effects reported include nasal dryness and crusting, epistaxis, ulceration of nasal mucosa or septal perforation (Mabry 1992).

Previous investigations on the intranasal deposition of nasal sprays didn’t show the exact topographic deposition patterns (Hardy et al. 1985, Harris et al. 1988, Heyder et al. 1977, Newman et al. 1987a, Newman et al. 1987b, Thorsson et al. 1993). It remained unclear whether the deposition is on the nasal septum, the turbinates, the lateral nasal wall or the middle nasal meatus.

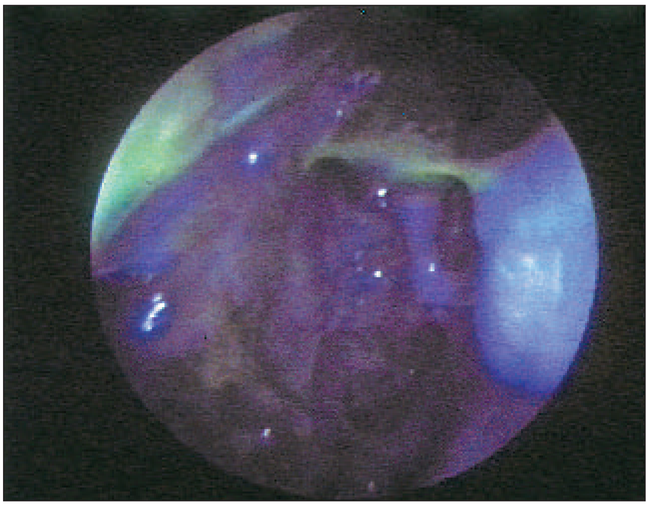

Figure 5: Endoscopic view (30° wide angle optic, blue-light filter) into a right nasal cavity after complete pansinusoperation. Only minor deposition at the anterior remnant of the middle turbinate and the anterior caudal region of the ethmoid cavity near the entrance to the maxillary sinus. No deposition in the depth of the ethmoid.

Figure 6: Nasal polyp after topical application of budesonide. Endoscopic view (30° wide angle optic) into a left nasal cavity. The polyp has withdrawn into the middle meatus and does not respond to further topical treatment because the drug could not reach the polyp in a sufficient amount.

Using videoendoscopy we could confirm that by far the greatest amount of the substance is deposited in the anterior non-ciliated part of the nose on the nasal septum and the head of the inferior turbinate. In addition, we clearly visualized that in normal subjects only a small portion reached the head of the middle turbinate, the lateral wall of the nose at the agger nasi, the inferior surface of the middle turbinate and in the middle nasal meatus itself, in decreasing concentrations. After endonasal sinus surgery the fraction reaching the region of the middle nasal meatus or the operative cavity was slightly larger than in the patients without previous surgery. Nevertheless the deposition in the sinuses itself was small and inconsistent.

As no investigations were done several minutes after application, analysis of the mucociliary transport was not included. It's well known that mucociliary transport is directed from the middle nasal meatus to the nasopharynx.

Using the conventional spraying technique, the small fraction of substance reaching the middle meatus can only be increased slightly if there is unobstructed nasal breathing and a decongested inferior nasal turbinate. A spraying angle of 45° upwards from the nasal floor enhances the deposition in the middle nasal meatus too.

Large nasal polyps in the nasal cavity are easily reached. Polyps which have become smaller as a result of treatment, or polyps which are small to begin, are only reached by a small fraction of the drug. This appears to provide a plausible explanation for the failure of these polyps to respond to continued treatment and for the differences in efficacy between different patients with different flow conditions (Weber et al. 1996b). It has been shown that nasal polyps which visibly obstructed the passage of air before treatment with budesonide begin by shrinking rapidly but then fail to show any further reduction in size. The polyp has, so to speak, withdrawn from the line of fire and cannot be reached by a sufficient amount of the initially effective budesonide (Figure 6).

Our results seem to indicate that the local side-effects of mucosal damage of the anterior nasal portion (haemorrhage, erosion, crusting) are caused by the effect of spraying. Trauma of the nasal mucosa may be referred to direct mechanical contact of the too far inserted nozzle or just due to the impact of the spray itself. Long-term studies on the effect of topical corticosteroids have shown that atrophy does not occur (Mygind et al. 1978b). This supports the above hypothesis that the local side-effects are caused by the act of application itself and not by the action of the drug.

The implications of our investigations for endonasal topical corticosteroid therapy of nasal polyps are as follows:

1. Nasal breathing must be unobstructed before application. As prolonged use of decongestant nasal drops is unacceptable, application should be synchronised with the nasal cycle. As only one side of the nose is normally decongested, the patient must administer the drug to each side separately when that side is decongested. Breathing in deeply through the nose while spraying appears to have a positive effect. The spray should not be directed towards the nasal septum but should be administered paraseptally in an anterior-posterior direction, 45° upwards from the nasal floor.
2. Marked septal deviation with obstructed access to the middle nasal turbinate will only produce side-effects and should be regarded as a contraindication.
3. More effective treatment and decreased side-effects could be achieved by use of different delivery techniques and systems, e.g. by spraying the corticosteroid directly into the middle meatus. The ENT surgeon could apply the drug directly to the polyps and the paranasal sinuses under direct vision. It is likely that a significant number of patients with nasal polyps who were regarded as non-responders to local corticosteroid therapy will respond to this direct treatment. Surgery, with its attendant risks and considerable costs, might then be avoided.

CONCLUSION

Videoendoscopic analysis of the intranasal distribution of budesonide shows that the majority of the substance remains on the anterior portion of the nasal septum and the head of the inferior nasal turbinate. This may explain the good to excellent effectiveness in allergic rhinitis patients. Only a small fraction reaches the middle nasal turbinate, which is the crucial region in regard to the treatment of chronic sinusitis and nasal polyps. The deposition and effectiveness of the topical corticosteroids could be increased by the development of new delivery techniques and systems, by application during the decongested phase of the nasal cycle, and prior administration of vasoconstricting nasal drops. Direct intranasal application to the target site would reduce the local side-effects which are caused at least in part by mechanical traumatisation as a result of the currently used delivery technique.

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Privat dozent Dr. Rainer Weber
Department of Otorhinolaryngology,
Head and Neck Surgery, Facial Plastic Surgery and
Communication Disorders
(Director: Prof. Dr. W. Draf) , Fulda Hospital,
Academic Teaching Hospital of the University of Marburg
Pacelliallee 4, D-36043 Fulda, Germany
Phone: +49-661-846001
Fax: +49-661-846002