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Main Article

Amphotericin B nasal spray has no effect on nasal polyps

A Helbling, A Baumann*, C Hänni†, M Caversaccio*

Abstract

Nasal polyps and chronic rhinosinusitis are the products of an inflammatory process. Recently, fungal involvement has been thought to stimulate the development of polyps, and administration of antifungal agents was therefore considered a potential treatment. Several studies have been published indicating amphotericin B as an effective treatment for nasal polyps and chronic rhinosinusitis. The aim of our investigation was to evaluate the efficacy of intranasal applied amphotericin B on the growth of nasal polyps in a three-month, prospective, open trial. Our results show that nasal amphotericin B spray is not effective for nasal polyps and may even cause deterioration.

Key words: Nasal Polyps; Amphotericin B; Antifungal Agents

Introduction

Nasal polyps and chronic rhinosinusitis are inflammatory diseases; however, their aetiology is not clear. Recently, fungi-mediated processes have been hypothesized to stimulate the development of polyps, and antifungal agents have therefore been considered in the treatment of nasal polyps and chronic rhinosinusitis.[1,2] Ricchetti *et al.* suggested a favourable effect of topical amphotericin B (AMB) treatment, based on an endoscopic scoring system;[3] however, concomitant intranasal or oral corticosteroid therapy was continued. The aim of our investigation was to evaluate the efficacy of intranasal applied AMB on the growth of nasal polyps, without concomitant therapy, in a three-month, prospective, open trial.

Materials and methods

In 2003, we investigated 21 consecutive patients (10 men, 11 women; mean age 49 years; range 22 to 72 years) with nasal polyps of stage II to III according to the classification of Malm.[4] Fourteen patients (67 per cent) had stage II polyps and seven (33 per cent) had stage III nasal polyps. Computed tomography (CT) scans were available for 14/21 (67 per cent) patients before receiving topical treatment and for 5/21 (23 per cent) patients after receiving topical treatment. Histology of polyp biopsies from all study participants showed a light to moderate eosinophilia in all specimens. Skin prick tests using commercial allergen extracts, including 16 mould species (Allergopharma®, Reinbek, Reinbek, Germany), were performed according to the recommendation of the European Academy of Allergy and Clinical Immunology (EAACI).[5] Eight patients were aspirin-sensitive and three were sensitized to house-dust mites. None had a positive skin test reactivity to any mould extracts tested. Asthma had been documented in 12 subjects (57 per cent).

Patients were enrolled if: no topical or systemic corticosteroid treatment had been used for at least the previous three weeks; no sinus surgery had been performed for at least the previous six months; and informed consent could be obtained. Amphotericin B 1 per cent nasal sprays were manufactured by the pharmacy of the University Hospital of Bern (10 ml AMB suspension in 100 ml distilled water), with one puff delivering 0.1 ml of AMB 1 per cent. Patients were instructed to keep the spray in a refrigerator and to rinse the nose with saline water (2 per cent) prior to taking AMB three times a day (one puff in each nostril). The primary study end-point was the endoscopic photo-documented course of the nasal polyps, combined with the results of a short questionnaire used to score subjective symptoms.[6]

Informed consent was obtained from every study participant. The study was classified as exempt by the local institutional review board because AMB was already used in the ENT department to treat nasal polyps.

The Wilcoxon matched pairs signed ranks test was used for statistical analysis of the subjective symptom and endoscopic scores.

Results

The endoscopic findings after three months of AMB treatment are shown in Table I. In the majority of

From the Division of Allergology, Department of Rheumatology and Clinical Immunology/Allergology, the *Department of ENT and Head and Neck Surgery, and the †Department of Oncology, Institute of Pharmacy, University Hospital (Inselspital), Bern, Switzerland.
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TABLE I

ENDOSCOPIC FINDINGS FOR NASAL POLYPS BEFORE AND AFTER AMB TREATMENT*

Endoscopic findings	Number of patients (%)		Polyp stage†	
			Before AMB	3 months after AMB
Improvement	3 (14%)	2	II	I
		1	III	II
Unchanged	16 (76%)	10	II	II
		6	III	III
Deterioration	2 (10%)	2	II	III

*Topical amphotericin B (AMB) (1%) for 3 months in 21 patients. †According to Malm.[4]

patients, the intranasal appearance of polyps was unchanged. Subjective symptom scores (measured according to the method of Radenne *et al.*)[6] indicated an improvement in seven patients (33 per cent); however, an objective endoscopic improvement was only present in 3/3 patients, and findings were unchanged in 6/18 ($p > 0.05$; Table I). The endoscopic and CT findings of a representative case are illustrated in Figures 1 and 2. Two (10 per cent) of the 21 patients showed an objective deterioration. Not included in the study were two participants who discontinued AMB after one month; one experienced nausea and the other complained of nasal mucosal inconvenience.

Discussion

Although our study was open and no controls were included (so an observer bias cannot be excluded), our findings are in line with those recently published by Weschta *et al.*[7] Antifungal treatment using intranasal AMB 1 per cent resulted in a small subjective effect but showed no statistically significant impact on the growth of nasal polyps based on endoscopic criteria.

Recently, Ponikau *et al.* found an improvement in endoscopic scores and a relative reduction of mucosal thickening on CT scans in patients treated with AMB.[8] Although these results were statistically significant, on closer examination, some study parameters were marginal. This may be explained by the low number of subjects enrolled in the study. On the other hand, the results were controversial and inconclusive, allowing a positive statement in favour of AMB. For example, a reduction (from baseline) of inflammatory mucosal thickening was seen in as many of the placebo-treated patients as the AMB-treated patients. On the contrary, half of the AMB-treated patients experienced an increase in mucosal thickening after six months of AMB treatment, an outcome which rather supports our findings.

The total daily dose of AMB in our study was 3 mg. Although this amount was lower than that used in Weschta's study, the dose was designed to be well above the minimal inhibition concentrations of the most frequently identified moulds within the nose and paranasal sinuses.[3,9] Amphotericin B has been shown to have cytotoxic effects on nasal polyp

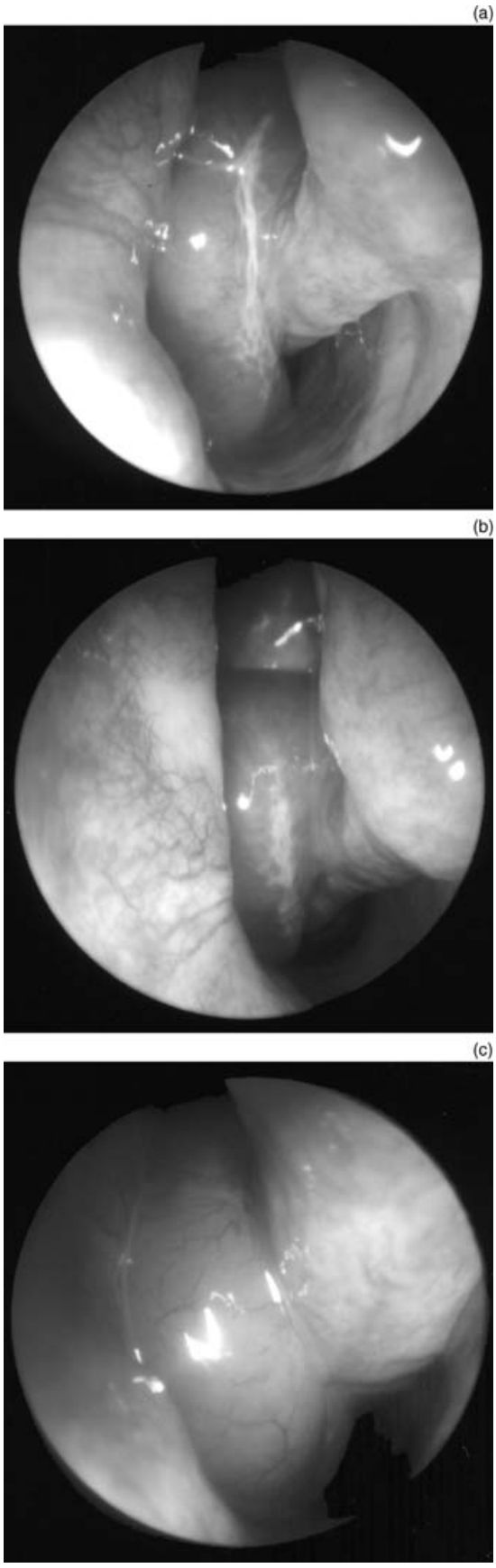

FIG. 1

Persistence of nasal polyps after 3 months of amphotericin B (AMB) treatment. Endoscopic view (a) before treatment; (b) after 1 month of AMB; (c) after 3 months of AMB.

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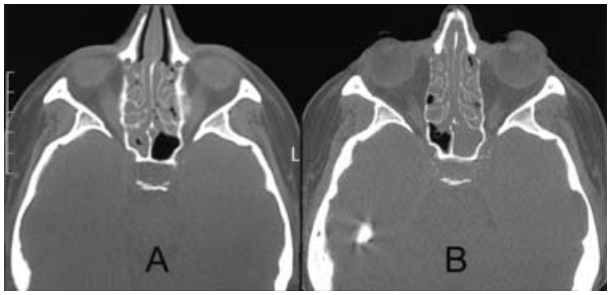

FIG. 2
Computed tomography scans of the paranasal sinuses (a) before and (b) 3 months after amphotericin B treatment.

epithelial cells and on fungal cell membranes.[9,10] However, since this effect of reduced nasal polyp growth is not regularly detected, either clinically or objectively, by various methods, other factors (such as concomitant use of nasal or systemic corticosteroids) may have an influence. In those in whom AMB was considered effective, cytotoxicity should be taken into consideration.[7,10]

Whether the hypothesis of fungi-mediated polyp growth (implying a role for antifungal treatment) is correct has not been shown.[1,8] Fungal spores and mould elements are ubiquitous aerogenic particles and are found in healthy subjects as well as in patients with chronic rhinosinusitis and nasal polyps.[1,11,12] The theory that fungi play a causal role in the development of chronic rhinosinusitis needs more evidence; thus, the postulate that AMB may attenuate the antigen production needed to initiate nasal inflammation seems doubtful.[8]

Conclusion

Nasal AMB 1 per cent spray is not effective for the treatment of nasal polyps and may even cause deterioration. Thus, the indication for nasal AMB treatment in patients with nasal polyps or chronic rhinosinusitis is questionable.

- **Fungal involvement has been postulated as an aetiological mechanism in polypoid rhinosinusitis**
- **This study investigated the effect of topical amphotericin B in 21 patients with nasal polyposis**
- **Nasal amphotericin B did not have a beneficial effect on nasal polyps, based on symptom score and endoscopic appearance**

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Address for correspondence:
Dr Marco Caversaccio,
Department of ENT and Head and Neck Surgery,
University Hospital (Inselspital),
CH-3010 Bern, Switzerland.

Fax: +41 31 632 49 00
E-mail: marco.caversaccio@insel.ch

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