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Does laser turbinectomy influence local allergic inflammation in the nose?*

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SUMMARY

The purpose of our study was to evaluate the effects of laser turbinectomy on local allergic inflammation by measuring the secretion of mediators (histamine, bradykinin, and TAME-esterase activity) in nasal lavage fluid after nasal provocation with different allergen concentrations. Our study included 15 patients, aged 15-35 years, who displayed perennial house-dust-mite rhinitis (positive prick test, RAST class >2, and positive nasal provocation with Dermatophagoides pteronyssinus (D.p.) extract) and hypertrophic inferior turbinates. Rhinomanometry (Rhino-test 441, Allergopharma, Germany) and nasal provocation with D.p. extract (Allergopharma, Germany) followed by lavage were performed in all patients. The procedure was repeated three and 12 months after Neodynium:YAG laser turbinectomy. Three and 12 months after laser turbinectomy, we found a significant improvement of nasal flow ($p < 0.01$ and $p < 0.05$, respectively) and resistance ($p < 0.1$ and $p < 0.01$, respectively) with a tendency towards airway blockage in the long-term follow-up, but no changes in mediator levels of nasal lavages after allergen provocation, suggesting that laser turbinectomy has no effects on local allergic inflammation.

Key words: lasers, turbinectomy, allergic inflammation, rhinitis

INTRODUCTION

Perennial rhinitis caused by house dust mite is a common otorhinolaryngological disease. Most patients with this disease are treated with antihistamines, decongestants, and topical corticosteroids. Some may respond to other non-surgical forms of therapy, including specific immunotherapy (Norman et al., 1984).

However, many cases are resistant to non-surgical treatment. We focus our attention on this type of refractory perennial rhinitis, which is caused by house dust mite and involves hypertrophic turbinates. A number of authors have confirmed the concept that partial resection of hypertrophic inferior turbinates can improve nasal airflow in patients who do not respond to non-surgical management of their obstructive rhinitis (Mittelman, 1982; Fukutake et al., 1986; Kirschner et al., 1988; Mladina et al., 1991; Saito, 1993).

Several authors have reported the successful use of lasers in the management of allergic hypertrophic rhinitis (Mittelman, 1982; Fukutake et al., 1986; Lenz, 1987; Saito, 1993; Kawamura et al., 1993). Fukutake et al. (1987) have used laser turbinectomy not only to decrease the size of the hypertrophic inferior turbinates, but also to inhibit the allergic reaction by causing scar tissue formation in the superficial submucosal layer of the turbinate.

The present study examines the possible influence of laser therapy on the local allergic reaction by measuring mediator levels in nasal lavage fluid after allergen provocation. *In vivo* measurement of mediator release in nasal secretion of allergic patients after antigen provocation permits the effect of laser therapy on the local allergic reaction, as mentioned by Fukutake et al. (1987), to be evaluated objectively, i.e. independently of the subjective parameters.

MATERIAL AND METHODS

Patients and study design

The study comprised 15 patients with perennial house-dust-mite rhinitis involving hypertrophic inferior turbinates. All patients (seven males and eight females, aged 15-35 years) were interviewed to obtain information on their past and present symptoms (nasal blockage, sneezing, and nasal discharge). They all had a positive skin prick test for *Dermatophagoides pteronyssinus* (D.p.), specific IgE antibodies (RAST >2 class), and positive nasal provocation with D.p. allergen extract. Patients with

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sinusitis, nasal polyps or severe septal deviation were excluded from our study.

All patients underwent rhinomanometric examination of the nasal cavity, nasal provocation with increasing dosages of D.p. allergen extract and nasal lavage.

All patients were re-examined on an out-patient basis, three and 12 months after the laser surgery. Patients received no anti-allergic treatment, especially not topical cortison sprays, within the 12-month post-operative period.

Histopathological changes were studied by resecting small nasal mucosa specimens of some patients before surgery as well as one month and three months thereafter. The specimens were examined microscopically after haematoxylin-eosin and Giemsa staining.

Rhinomanometry

Anterior rhinoscopy and clinical examination of the nasal cavity was followed by rhinomanometry with Rhinotest MP 441 (Allergopharma; Rheinbek, Germany). It measures the flow and pressure synchronously under physiological conditions. The selected flow at ΔP=150 Pa determines the resistance at low airway flow. The resistance is the quotient of the pressure and flow, and is given separately in Pa (cm^3/s) for the right and left side of the nose. These rhinomanometric parameters permit precise objectification of the momentary nasal patency.

Laser surgery

Laser surgery was performed on an out-patient basis, and each patient was treated only once. The nasal mucosa was anaesthetized and decongested prior to surgery by inserting small pieces of 0.5% tetracaine/0.1% xylometazoline-soaked gauze for 15 min. After removal of the gauze, the epithelium and submucosa of the free margin of both inferior turbinates were irradiated with a Neodynium:YAG laser (MediLas 2, MBB) beam delivered through a highly flexible optical fibre with a diameter of 0.6 mm in continuous-wave mode by a contact procedure at a power of 10–20 W, a pulse duration of 0.5-1 s, and a total energy of 1,000 joules per turbinate.

Nasal allergen provocation

Nasal allergen provocation with subsequent lavage was performed according to the method of Naclerio et al. (1983). Briefly, four lavages (5 ml of 0.9% NaCl, at room temperature) were performed in each nostril to reduce possible resting mediator levels to a stable baseline. Then, a diluent provocation followed. Thereafter, increasing dosages of D.p. extract at 100, 1,000, and 10,000 BU (Allergopharma Germany) were applied to each nostril by a glass nebulizer (Deutsche Pharmacia; Freiburg, Germany), which delivers 0.1 ml per puff, followed 10 min later by a 5 ml lavage (0.9% NaCl, at room temperature) per nostril. The lavage fluid was immediately put on ice, centrifuged at 3,600*g* for 10 min at 4°C to remove cellular fragments and stored in adequate fractions at -70°C until analysis.

Histamine determination

Histamine is one of the most important preformed mediators of mast cells and basophils. It was assayed in the supernatants by an automated spectrofluorometric assay (Siraganian, 1974) with a sensitivity of 1 ng/ml and a precision of approximately 5%.

TAME-esterase activity

Enzymes that can hydrolize the synthetic substrate *N*-α-toluene-sulfonyl-L-arginine-methylester are designated as TAME-esterases. In principle, all serine proteinases (e.g. trypsin, kallikreins, mast-cell tryptase, and plasmin) come into question as potential TAME-esterases; however, Baumgarten et al. (1986) were able to show that 70% of TAME-esterase activity in nasal secretion after allergen provocation consists of plasma kallikrein-inhibitor complex, 25% of mast-cell tryptase, and 5% of tissue kallikrein. Other studies show that the TAME-esterase activity is a good measure for the kallikrein concentration (Beaven et al., 1971).

TAME-esterase activity was assayed according to the method of Imanari et al. (1976) based on the liberation of tritiated methanol from the synthetic substrate [^{3}H]-TAME. Assay sensitivity is defined as 1,500 cpm above background.

Determination of kinins

Kinins are biologically active end-products of the kallikrein-kinin system. Kinins comprise three oligopeptides – bradykinin, kallidin (Lys-bradykinin), and Met-Lys-bradykinin – with a biochemically identical nuclear structure, which likewise possess an identical, only qualitatively somewhat different, pharmacological effect. Bradykinin was assayed in nasal secretion according to the method of Proud et al. (1983), which was capable of detecting a minimum bradykinin dose of 20 pg/ml.

Statistical analysis

Wilcoxon's signed rank test for matched pairs was used for comparing the allergen-induced mediator release before and after laser therapy. Statistical significance was presumed to be achieved for values of $p < 0.05$.

RESULTS

Laser surgery improved the condition of all the patients by decreasing the nasal obstruction and, in some cases, by also reducing the watery nasal discharge and sneezing.

Both nasal passages showed a significant increase of airflow three months ($p < 0.01$) and 12 months ($p < 0.05$) after laser therapy (Figure 1) as well as a significant post-therapeutic decrease of resistance ($p < 0.01$; Figure 2). Repeated nasal lavages after provocation with increasing antigen dosages did not disclose any significant change in the mediators (TAME-esterase activity, kinin, and histamine; Figure 3).

Microscopical examination of specimens from the lower turbinates six weeks after laser surgery, revealed respiratory mucosa with largely regenerated epithelium and focal squamous metaplasia. The subepithelial stroma contained granulation tissue and a moderately dense, largely lymphocytic inflammatory infiltrate (Figure 4a). Three months after laser surgery, mucosal particles showed extensive cicatricial fibrosis of the stroma.

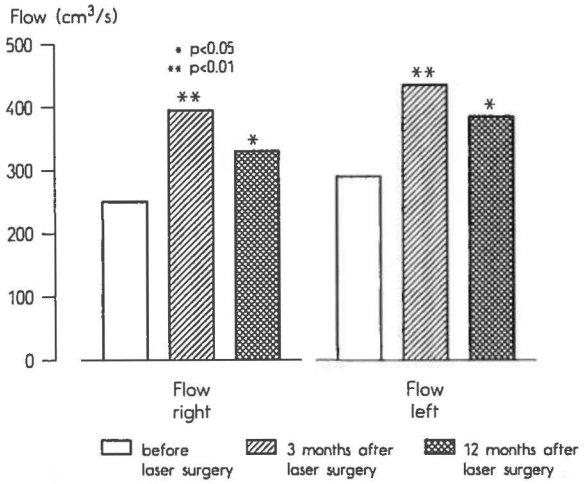

Figure 1. Mean flow values before, 3 months and 12 months after laser surgery.

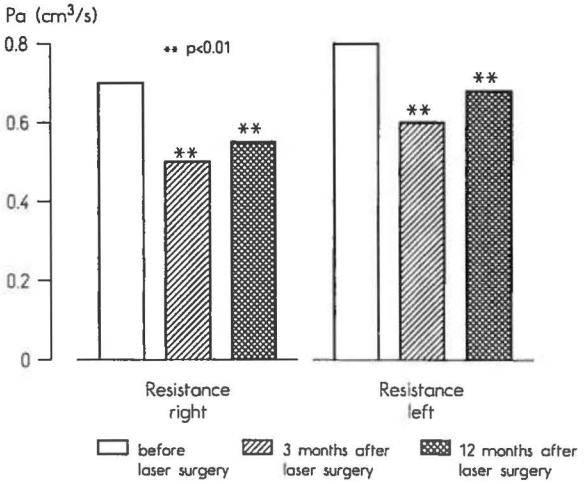

Figure 2. Mean resistance values before, 3 months and 12 months after laser surgery.

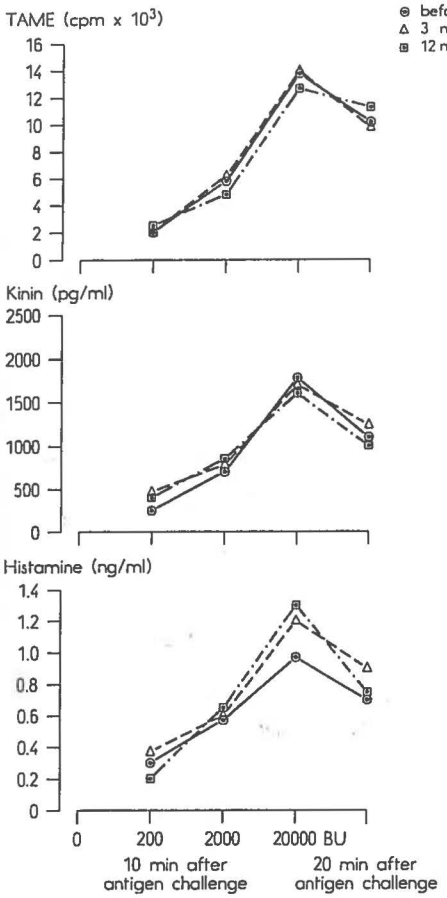

Figure 3. Mean mediator level in nasal lavage fluid before, 3 months and 12 months after laser surgery.

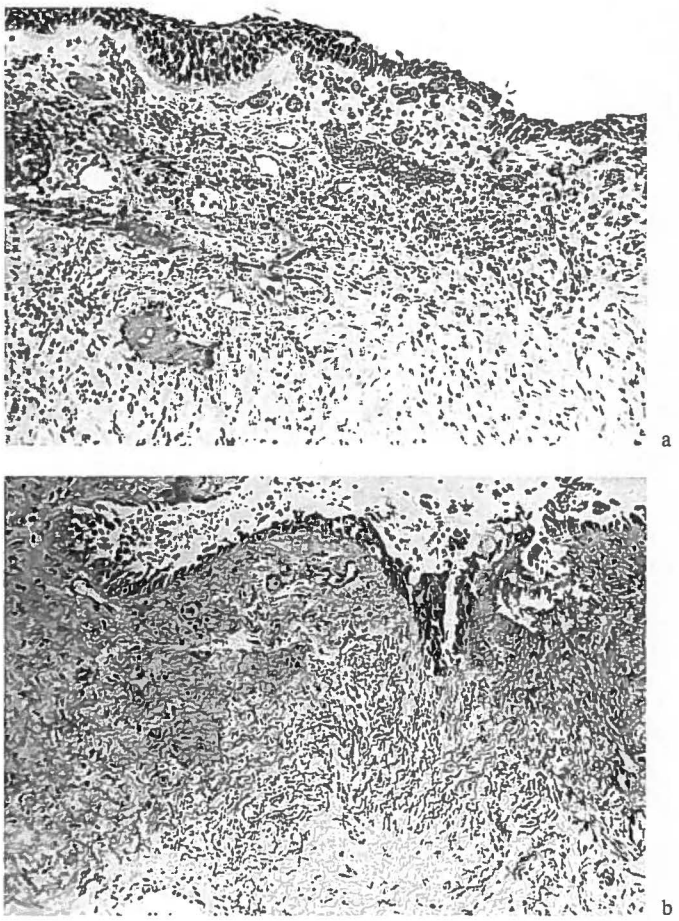

Figure 4. Histological picture of a biopsy from the lower turbinate of a patient with perennial house-dust-mite rhinitis, 6 weeks (a) and 3 months (b) after Nd:YAG laser turbinectomy (haematoxylin and eosin staining; ×40).

High-magnification views revealed goblet cells in the epithelium with squamous metaplasia in some places. Inflammatory infiltrates could scarcely be found in the stroma; granulation tissue had completely disappeared and been replaced by scar tissue (Figure 4b).

DISCUSSION

Several authors have reported the successful use of lasers in the management of allergic or hypertrophic rhinitis (Mittelman, 1982; Saito, 1983; Fukutake et al., 1987; Lenz, 1987; Mladina et al., 1991; Kawamura et al., 1993). Fukutake et al. (1987) specu-

late that laser turbinectomy could inhibit the allergic reaction by causing scar tissue formation in the turbinate.

The authors of all previous studies have examined the effect of laser turbinectomy by evaluating more or less subjective parameters. The improvement of related symptoms in patients with perennial allergic rhinitis after turbinectomy is largely attributed to the elimination of the nasal breathing obstruction and not to an influence on the allergic reaction.

In our study we have aimed to demonstrate the effect (or the absence of any effect) of laser turbinectomy on the local allergic inflammation in the nose by measuring the mediator levels after nasal challenge, before and after laser treatment. *In vivo* measurements of mediator release in nasal secretions of allergic patients after antigen provocation permit objective evaluation of the effects of laser turbinectomy on allergic nasal inflammation. Nasal allergen challenge, which reproduces the symptoms of rhinitis in inducing pruritus, sneezing and nasal blockade, is associated with the local release of histamine, PGD_2, LTC_4, LTB_4, and tryptase, as identified by analysis of sequential nasal lavage (Freeland et al., 1989). These findings are consistent with mast-cell degranulation. In addition, the kinins kallidin and bradykinin have been identified in nasal lavage fluid following nasal allergen challenge parallel with symptom generation. Kallidin and bradykinin are vaso-active peptides formed as cleavage products from low- and high-molecular-weight kininogens by kallikreins (Baumgarten et al., 1986). As mast-cell tryptase possesses kallikrein-like activity, the local generation of kinins within the nose following nasal allergen challenge may be linked to mast-cell degranulation. TAME-esterase activity in nasal secretion measures mainly a plasma kallikrein-α2-macroglobulin complex together with mast-cell tryptase (Baumgarten et al., 1985).

Our results following laser therapy show no significant change in mediator levels from the nasal lavage after allergen provocation. Although, histologically, scar tissue forms in the turbinate tissue after laser application, our results indicate that neither scarry alterations nor tissue loss after laser turbinectomy are able to influence the local allergic inflammation. It is thus clear that laser turbinectomy cannot be the treatment of choice for allergic rhinitis without obstructive components.

The patients in our collective, who had perennial rhinitis and were thus exposed to consistent allergen contact (*Dermatophagoides pteronyssinus*), exhibited hypertrophy of the nasal turbinates due to the chronicity of their condition. Three months after laser turbinectomy, all patients displayed a significant reduction of resistance and significant improvement of nasal airflow. Compared to conventional turbinectomy, laser turbinectomy offers numerous advantages (out-patient procedure, topical anaesthesia, no nasal packing, less bleeding, et cetera). In accordance with the literature, our results show a tendency towards blockade of the airway in the long-term follow-up (after one year). We ascribe this in part to the lasting contact of the patients with the allergen and the resultant allergic inflammation of the nasal mucosa.

We nevertheless recommend that patients suffering from perennial allergic rhinitis with turbinate hypertrophy initially undergo laser-surgical treatment of the obstruction in the sense of turbinectomy with subsequent conservative anti-allergic measures that lead to a reduction of the allergic reaction. These consist primarily in allergen avoidance, drug therapy and immunotherapy.

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