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Septal injection of botulinum neurotoxin A for idiopathic rhinitis: a pilot study☆,☆☆

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Abstract

Purpose: Botulinum neurotoxin A (BTA) is a promising therapeutic option in the treatment of idiopathic rhinitis (IR), a disease characterized by nasal obstruction and hydrous rhinorrhea. The conventional localization for the injection of BTA in IR is the nasal turbinates. In our own clinical experience, submucoperichondrial injection of BTA in the nasal septum is an alternative that is easy to perform for the therapist and also well tolerated by the patient.

Material and Methods: Five patients received an injection of in total 80 mouse units Dysport (Ipsen Pharma, Ettlingen, Germany) in the nasal septum. The unpleasantness of the nasal injection of BTA was measured on a visual analogue scale. Over the course of 14 days, nasal symptoms (rhinorrhea, nasal obstruction, urge to sneeze, nasal pruritus), the number of facial tissues used daily, and possible complications were evaluated.

Results: The unpleasantness of the injection of BTA into the nasal septum after local anesthesia was rated low (visual analogue scale, 0.76 on average). A good subjective symptom control was achieved in 3 patients concerning rhinorrhea and in all patients concerning nasal obstruction. The number of facial tissues used daily as a parameter for rhinorrhea was on average 21.0 before the injection of BTA, decreased in 4 patients over the course of time, and was on average 5.8 after 14 days. No patient reported any adverse effects after the injection of BTA.

Conclusions: This pilot study demonstrates that septal injection of BTA in patients with IR can achieve good symptom control and patient comfort and should be compared in further studies to the conventional turbinal injection technique.

1. Background and aims

Idiopathic rhinitis (IR) is an entity of unknown etiology, characterized by nasal obstruction and hydrous rhinorrhea. As a pathophysiological correlate of IR, neural, immunological, and mucosal dysfunctions are discussed; for therapy, corticosteroids, antihistaminergic, or anticholinergic drugs and capsaicin are recommended [1].

A new promising therapeutic option is botulinum neurotoxin A (BTA), which can effectively reduce the symptoms of IR with, if at all, marginal adverse effects [2-4]. BTA inhibits transmitter release from cholinergic nerve endings and is therefore used in the treatment of various functional disorders resulting from parasympathetic gland hyperactivity [5], like IR.

The localization for the injection of BTA in IR described by the literature is the nasal turbinates [2-4]. Recently, Rohrbach et al [6] reported that application of BTA with a sponge can also ameliorate symptoms in some patients.

In our own clinical experience, submucoperichondrial injection of BTA in the nasal septum is an alternative that is easy to perform for the therapist and also well tolerated by the patient. Its advantages are the good visual control of injection with the typical bleaching effect of the mucosa and the lower risk of intravascular systemic application of BTA.

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Therefore, we started this pilot study to evaluate symptom control and patient comfort after septal injection of BTA in patients with IR.

2. Methods

In a retrospective approach, we analyzed the medical records of all patients who were treated with BTA for IR in our department in the year 2009. The study was approved by the department's data protection official.

We chose to analyze in the year 2009 because since this time, the following data for IR patients receiving injections with BTA are systematically documented in the medical records of our department:

- nasal symptoms (rhinorrhea, nasal obstruction, urge to sneeze, nasal pruritus), quantified on a 5-point Likert scale (none, mild, moderate, severe, extreme),
- number of facial tissues used daily,
- tolerance of the nasal injection of BTA on a visual analogue scale with the 2 extremes: "not unpleasant" (0 mm) and "extremely unpleasant" (10 mm).

All patients were also encouraged to count the number of facial tissues used daily and were seen 14 days after the injection for a follow-up examination, wherein any complications after the injection of BTA and the nasal symptoms as described above were documented.

All patients had received 2 submucoperichondrial injections of 20 mouse units (MU) BTA, respectively, of Dysport (Ipsen Pharma, Ettlingen, Germany; concentration 200 MU/mL in saline solution) in the anterior nasal septum (region 2, 3) of both sides (ie, 80 MU in total). Before the injection, local anesthesia was applied for 5 minutes in the form of a cotton bud soaked in tetracaine (4%). For the injection, a 27-G hypodermic needle (Sterican; Braun, Melsungen, Germany) was used.

In all patients, IR had been diagnosed after an exhaustive exclusion of allergic, structural, infectious, or systemic causes for the nasal symptoms. All patients were of full age, did not have any contraindications for a therapy with BTA, and had given their written consent to treat their symptoms with BTA on off-label use.

Patients who had taken corticosteroids, anticholinergic, or any other drugs with a potential influence on nasal symptoms in the last 2 months before the nasal injection of BTA were not included in this study.

3. Results

Five patients met the strict criteria described above to be included into this study. The unpleasantness of the injection of BTA into the nasal septum after local anesthesia was rated as 0.76 on average on a visual analogue scale (minimum, 0.0; maximum, 2.2).

Before the injection of BTA, 2 patients described their rhinorrhea as extreme, 2 patients as strong, and 1 patient as moderate. Fourteen days after the injection, rhinorrhea had decreased in 3 patients (Fig. 1A).

Nasal obstruction was rated as extreme and severe by 1 patient each, respectively, whereas 3 patients reported no obstruction before the injection of BTA. After 14 days, the nasal obstruction was reduced in both affected patients (Fig. 1B).

The urge to sneeze was described as extreme and severe by 1 patient each, respectively (in both cases ameliorated after the injection of BTA), whereas the other 3 patients had no urge to sneeze (Fig. 1C).

Three patients complained about nasal pruritus before the injection of BTA (in 1 case rated as extreme, in 2 as severe), a symptom ameliorated in 2 cases after 14 days (Fig. 1D).

The total nasal symptom score calculated by addition of the 4 categories (rhinorrhea, nasal obstruction, nasal pruritus,

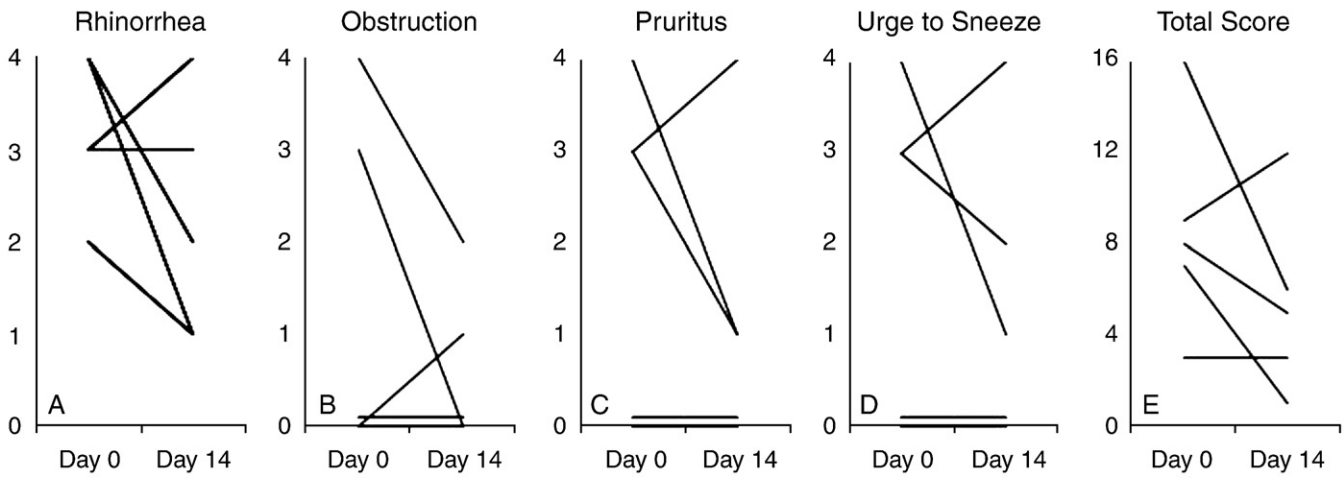

Fig. 1. Nasal symptoms before (day 0) and 14 days after the injection of BTA into the nasal septum, rated on a Likert scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme). A total score was calculated by addition of the symptom scores for rhinorrhea, nasal obstruction, nasal pruritus, and urge to sneeze.

urge to sneeze) was reduced in 3 patients, and raised and stayed equal in 1 case each, respectively (Fig. 1E).

The number of facial tissue used daily as a parameter for rhinorrhea ("tissue score") was on average 21.0 (minimum, 10; maximum, 30) before the injection of BTA. The course of time is shown in Fig. 2: after 14 days, the patients used on average 5.8 facial tissues (minimum, 2; maximum, 10). Use of facial tissues decreased in 4 patients after the injection of BTA and remained constant in 1 case.

No patients reported any adverse effects after the injection of BTA, such as epistaxis, dry eyes or dry nasal mucosa, allergic reactions, or muscular palsies.

4. Discussion

Kim et al [2] were the first authors to describe BTA injections for IR in 1998. The effectiveness of BTA in the therapy of IR was confirmed in studies conducted by Özcan et al [3] and Sapci et al [4]. All authors used a technique of injection of BTA into the inferior and middle nasal conchae.

In the present study, we describe an injection technique into the nasal septum. From our experience, this technique is easier to perform because the nasal septum can usually be visualized without any difficulty by anterior rhinoscopy or nasal endoscopy. In addition, the septal injection after local anesthesia is well tolerated by the patients, with the unpleasantness of the procedure rated as 0.76 on average on a visual analogue scale. By reason of the submucoperichondrial approach, there is a lower risk of intravascular injections and of systemic adverse effects of BTA.

No complications of intranasal injection of BTA were found in this study, which matches the available literature [2-4]. Therefore, there is yet no clue that septal injection of BTA should not be as safe a as turbinal injection.

The "tissue score" as a parameter for rhinorrhea decreased in 4 of the 5 patients and on average from 21.0 before to 5.8 after the injection of BTA. The subjective severeness of rhinorrhea rated on a Likert scale decreased in 3 of the 5 patients. Therefore, hydrous rhinorrhea as the main symptom of IR can be effectively treated by septal and not only turbinal injection of BTA. This is pathophysiologically comprehensible because the mucosa of the anterior nasal septum contains more serous glands than the mucosa of the inferior concha [7].

Because the effect of BTA is dose dependent and an individual dose has to be found in the treatment of different patients [5], it can be expected that the degree of the reduction of nasal symptoms by septal injection of BTA is probably higher in follow-up treatments. In the present study, the same dose (80 MU Dysport) was used for all patients.

The promising results of this small pilot study advocate the conduction of studies with larger patient numbers to analyze septal injection of BTA for IR; however, this study has its restrictions. First, there was no control group. In following studies, septal injection of BTA must be compared with a placebo injection and/or the turbinal injection technique to evaluate its effectiveness. No standardized documented data for longer follow-up times than 14 days were available from the medical records of our patients, so we cannot compare with the literature if the effect of septal injection of BTA is longer or shorter than the turbinal technique. Dose-dependently, the effect of intraturbinal injected BTA lasts for 4 to 8 weeks [2,3]; most of our patients reported that the symptom reduction lasted for some months. It can be speculated that because of less abundant blood flow, the clearance of BTA in the nasal septum is slower than in the nasal conchae. Lastly, there were only subjective data collected in this study (nasal symptom scores, tissue score, visual analogue scale); however, it is virtually not possible to obtain mainly objective data to evaluate IR. Theoretically, it would be possible to collect nasal discharge and measure nasal

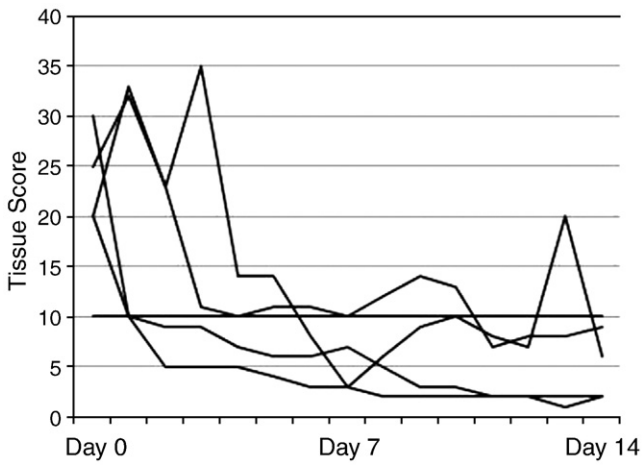

Fig. 2. Number of facial tissues used daily ("tissue score") as a parameter for rhinorrhea before (day 0) and over the course of time after the injection of BTA into the nasal septum.

patency by rhinomanometry, rhinoresistometry, acoustic rhinometry [8], or long-term rhinoflowmetry [9]; but other symptoms of IR, such as nasal pruritus, cannot be objectified. Therefore, the existing studies analyzing the effectiveness of turbinally injected BTA in IR exclusively use subjective instruments.

Despite the above problems, this is, to the best knowledge of the authors, the first report in the literature about effective symptom reduction by septal injection of BTA for IR; in our opinion, this septal injection technique is worth being evaluated and compared in further studies.

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