

Treatment of Chronic Rhinosinusitis with Pressure-Pulsed Corticosteroid Inhalation

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Abstract Chronic rhinosinusitis may cause olfactory dysfunction and affects quality of life in patients. In a prospective study we investigated the effect of topical application of corticosteroids through pressure-pulsed inhalation as treatment option of chronic rhinosinusitis with olfactory disorder. Patients with sinonasal olfactory disorder according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS) were allocated to the new nasal inhalation therapy or a systemic corticosteroid therapy, each receiving a corticosteroid course of 12 days. 18 patients received topical corticosteroid pressure-pulsed inhalation (AMSA, Schumacher, Dausenau) and 15 systemic corticosteroid. Olfactory function was measured before and after treatment using the Threshold Discrimination Identification score (TDI score) and visual analogue scales. Lund Mackay score (LMS) was measured before starting treatment. Olfactory function (OF) increased from 17.5 ± 6.4 to 21 ± 7.9 TDI points ($p < 0.0005$) after 2 months. OF decreased again to 19.5 ± 6.0 after 6 months ($p = 0.007$). OF increased from 17.0 ± 8.9 to 22.0 ± 9.5 points ($p = 0.002$) with systemic treatment after 2 months. In the follow-up period of 6 months, the mean TDI score dropped to 20.0 ± 9.2 points ($p = 0.01$). There was no correlation between LMS and TDI. Treatment of chronic rhinosinusitis with pressure-pulsed inhalation was demonstrated to be effective. Multicenter investigations with large participant numbers are needed.

Keywords Chronic rhinosinusitis · Pressure-pulsed corticosteroid inhalation · TDI · LMS · Systemic corticosteroid · Olfactory function

Introduction

Chronic rhinosinusitis and olfactory disorder (OD) is frequent in humans [1–3].

Due to mechanical obstruction and altered intranasal air flow, the transport of odour molecules to the olfactory epithelium is diminished [4]. As a consequence of inflammation, olfactory cells may also be restricted in function [5, 6]. According to the European Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS) chronic rhinosinusitis (CRS) is accompanied by polyp formation (CRSwNP) or without polyps (CRSsNP) [7]. In German-speaking countries, OD due to sinonasal aetiology is found in 72 % of the patients [8].

The best established therapy is systemic corticosteroid. The positive therapeutic effect of systemic corticosteroids in OD has been supported in several investigations [9–11].

However systemic corticosteroid treatment may cause various side effects, such as gastric ulceration, osteoporosis, diabetes, hypertension, Cushing's syndrome, depression and sleeping disorders, amongst others [12]. Furthermore, the patients concerns regarding systemic corticosteroids are not to be underestimated.

An alternative treatment option for OD is the application of a topical corticosteroid directly in the nose [13].

The therapeutic success of topical corticosteroids in the treatment of OD is not well documented in literature. Their benefit is controversial, yet there are investigations demonstrating a positive effect [14].

It is noticeable that in many of the investigations demonstrating a positive therapeutic effect, the topical

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corticosteroids were applied in the head-down-forward position. Due to the individuality of nasal anatomy, the manner of application potentially affects the delivery and distribution of topically applied corticosteroids [15] and consequently their effectiveness in the treatment of OD.

We therefore investigated the therapeutic effect of a special manner of topical corticosteroid application through pressure-pulsed inhalation.

The aim of this investigation was to evaluate the benefit of a topical corticosteroid treatment via pressure-pulsed inhalation in comparison to the benefit of the well established and efficient systemic corticosteroid treatment in patients suffering from chronic rhinosinusitis and olfactory loss.

Materials and Methods

33 patients with olfactory disorder and CRSsNP were included in a prospective, non-blinded study.

Ethical approval was obtained from our Institutional Review Board. All participants gave written informed consent.

The topical corticosteroid treatment consisted of a pressure-pulsed inhalation of 20 min for a total of 12 days, including 6 visits. At first visit (V0), the participants were instructed on how to use the device by a team member.

The AMSA[®] device (aérosoliseur manosonique automatique, Schumacher & Partner GmbH, Dausenau, Germany) is a “vibration aerosol atomizer” producing sonorous vibrations as well as inducible pressure impulses.

The atomizer (volume of up to 12 ml) is a handheld device furnished with a binary nose adapter and produces from of a fluid composed of prednisolone, panthenol and sodium chloride an aerosol with particle size of 1 to 3 micron, emitted at a flow rate of 4 to 15 millilitres per minute. It is attached to the device by two tubes, one conveying sonorous vibration, the other transporting the pressure impulses.

The close-fitting binary nose part is positioned in the nostrils. When asked, the patient has to swallow. Once the soft palate encloses the nasal pharynx producing an enclosed system (nasal cavity, paranasal sinuses, Eustachian tube, middle ear), the device’s compressed air buffer is automatically released into this system with a short pressure impulse of about 30 (10–40) mb. The sonorous vibration phase ensures the diffusion of the aerosol and its contact with the mucosa.

During six sessions, a total prednisolone dosage of 25 mg was applied.

The systemic corticosteroid treatment consisted of prednisolone tablets administered for 12 days (starting with 80 mg daily, decreasing to 10 mg).

Follow-Up Treatment

After completion of initial intervention, all participants received treatment with topical mometasone furoate nasal spray (Nasonex[®]) for 2 months, followed by a treatment-free period of 4 months.

Two sprays of mometasone were applied in a reclined head position twice daily, resulting in a daily dosage of 200 µg.

Patients

Inclusion criteria were OD of sinonasal aetiology according to EP3OS with typical symptoms as nasal blockage, postnasal drip, headache and age between 18 and 70 years. All patients underwent CT or MRI no longer than 6 months before entering the study. None of the patients showed signs of chronic rhinosinusitis with nasal polyps in CT or MRI. Computed tomography records of the patients were evaluated according to the Lund-Mackay grading system [16]. This staging system is recommended for outcome research by the TASK Force on Rhinosinusitis [17]. None of the patients showed a score more than four, which has been proposed as minimum for patients undergoing surgery [18].

Exclusion criteria were pregnancy, existence of a malignant tumour, radiotherapy, chemotherapy, presence of severe colitis ulcerosa, severe diverticulitis, presence of a disease for which large dosages of corticosteroids are contraindicated (e.g. diabetes mellitus), topical or systemic corticosteroid therapy during the last month, existence of nasal polyps, sinus or nose surgery during the last 6 months and laryngectomy.

A total of 33 outpatients presenting with the primary complaint of chronic rhinosinusitis and olfactory dysfunction, recruited continuously from July 2009 until November 2010, were eligible for the study. 18 patients received topical corticosteroid pressure-pulsed inhalation and 15 systemic corticosteroid.

Outcome Measures

The primary outcome measure was the change in olfactory function (OF) before, 2 months after and 6 months after treatment.

OF was measured by one trained assessor using the standardized TDI score, a tripartite test measuring olfactory threshold, discrimination and identification applying the “Sniffin’ Sticks test kit” (*n*-butanol odour threshold, odour discrimination, and odour identification) [19–21].

In general, a score of 15 points and less indicates functional anosmia, a score up to 30 points hyposmia, and a score of above 30 points normosmia.

Secondary outcome measures were the patients' subjective estimation of OF (sOF).

The subjectively estimated measures were determined using a visual analogue scale (VAS) ranging from 0 points (no sOF) to 10 points (perfect sOF).

A detailed history including questions concerning the aetiology of OD, the time period of symptoms, general diseases, previous surgery and medication was taken before starting treatment. On every visit, a detailed physical examination including nasal endoscopy was performed by an ENT specialist.

Statistical Analysis

Statistical analysis was performed using IBM SPSS 18.0 (Chicago, USA) for Microsoft Windows. The sample size was calculated applying the "n query" program.

For numeric data according to a Gaussian distribution, *t*-tests for dependent and independent samples were applied. For numeric data not of Gaussian distribution, the Mann–Whitney-*U* test for independent samples was employed for comparison of several groups. For categorical data, the Chi square test was used. Correlations were assessed by means of bivariate linear regression analysis according to Pearson.

A difference was considered to be statistically significant at a *p* value of 0.05.

Results

9 females (50 %) and 9 males (50 %), aged 24 to 70 years (54.4 ± 13.4 years), with chronic rhinosinusitis and OD received corticosteroid inhalation treatment with AMSA.

7 female (46.7 %) and 8 male patients (53.3 %) aged 42 to 70 years (55.73 ± 9.1 years) with same symptoms and Lund-Mackay score not more than 4 received systemic corticosteroids.

Both treatments were comparable with regard to the participants' age and gender distribution. None of the patients had nasal polyposis or polyps closing the olfactory cleft. None of the patients had a Lund-Mackay score more than 4.

Primary Outcome Measure

Change in OF According to TDI Score

(1) Inhalation-treatment ($n = 18$):

After initial intervention, OF increased from 17.5 ± 6.4 to 21.0 ± 7.9 TDI points ($p < 0.0005$).

During the follow-up period, OF decreased again to 19.5 ± 8.9 after 6 months ($p = 0.007$).

(2) Systemic-treatment ($n = 15$):

OF increased from a mean TDI score of 17.0 ± 8.9 to 22.0 ± 9.5 points ($p = 0.002$) after 2 months. None of the subtests of the TDI score changed significantly, either.

After 6 months of follow-up period, the mean TDI score dropped to 20.0 ± 9.2 points ($p = 0.012$).

There was no significant difference between both groups in TDI score before ($p = 0.89$), after 2 months ($p = 0.74$) and after 6 months of follow-up ($p = 0.67$).

Secondary Outcome Measures

Subjectively Estimated Olfactory Function (sOF) Assessed by VAS

(1) Inhalation-treatment ($n = 18$):

After intervention, sOF increased significantly from a mean score of 2.0 ± 1.5 to 3.5 ± 2.2 ($p < 0.0005$). During the follow-up period, sOF decreased significantly to 3.0 ± 1.8 ($p < 0.0005$) after 6 months.

(2) Systemic-treatment ($n = 15$):

sOF increased from a mean score of 1.7 ± 1.63 to 3.4 ± 2.5 ($p = 0.003$) after 2 months and after a total of 6 months it decreased to 3.3 ± 2.3 ($p = 0.002$).

There was no significant difference in VAS between inhalation-treatment and systemic-treatment after 2 months ($p = 0.81$) and after 6 months ($p = 0.89$).

Side Effects/Adverse Events

After inhalation, the reported side effects were as follows: dry nasal mucosa ($n = 2$), sore throat ($n = 1$) and headache ($n = 2$).

After systemic corticosteroid treatment, the mentioned side effects were: costiveness ($n = 1$), lassitude ($n = 1$), sleeping disorder ($n = 2$), dry mouth ($n = 1$) and parosmia ($n = 2$).

Discussion

Chronic rhinosinusitis is one of the main causes of olfactory dysfunction [22]. However most studies about this topic investigate the correlation of nasal polyps and smell loss. In current literature there are no studies to the topic CRSsNP and olfactory disorder. The evaluation of the olfactory cleft in patients with CRSsNP combined with the Lund-Mackay grading system [16] and CT/MRI findings have not been analyzed before. Many studies show that OD affects quality of life in patients [23], therefore, clinical efficacy of therapeutic strategies in chronic

rhinosinusitis and olfactory loss should be highlighted and discussed.

In this investigation, we examined for the first time the effect of a special and innovative manner of topical corticosteroid application through pressure-pulsed inhalation on OF in patients with chronic rhinosinusitis without polyps over a period of 6 months.

The fact that corticosteroid pressure-pulsed inhalation is more effective than corticosteroid nasal spray [14] may be due to the manner of application. Due to the pressure with which the corticosteroid is applied obstructive lesions in the nasal cavity may be overcome; similar to the head-down-forward position [24].

Apart from that, it may be a dose-related phenomenon. During 12 days of inhalation, a total dosage of 25 mg was applied, while throughout 2 months of corticosteroid nasal spray in general only about 12 mg are administered. Consequently, this innovative manner of topical corticosteroid application applies a greater dosage during a shorter period of time and therefore provides higher concentrations than a common corticosteroid nasal spray.

After administration of systemic corticosteroids, patients experienced a continuous increase of sOF after 2 months, too.

Although OF measured by TDI score decreased after 6 months, patients experienced a subjective improvement in OF until the end of follow-up investigation.

This shows that patients who treated and given hope for improvement of their OF, experience subjective amelioration, but more investigations are needed to find out more about the precise pathophysiological relationship between chronic rhinosinusitis and OD.

Conclusion

Sinonasal olfactory disorder due to chronic rhinosinusitis with its typical symptoms can be treated with pressure-pulsed inhalation and show similar results as a systemic corticosteroid treatment. Therefore multicenter investigations are needed to strengthen these results, including a control group.

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