INTRANASAL ULTRAVIOLET PHOTOTHERAPY
IN THE TREATMENT OF ALLERGIC RHINITIS AND CHRONIC RHINOSINUSITIS
WITH NASAL POLYPS

Ph.D. Thesis

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1. INTRODUCTION

1.1. Allergic rhinitis and chronic rhinosinusitis with nasal polyps

The nasal airways and their closely-associated paranasal sinuses are an integral part of the respiratory tract. The nose protects the lungs by filtering and humidifying air prior to entry to the lungs. Dense collections of vascular sinusoids and distensible blood vessels termed capacitance vessels vary flow from one nasal passage to the other in a nasal cycle. Lateral or anterior serous glands generate secretions. The nose senses airborne volatile compounds via pattern recognition and olfactory receptors. Olfaction can be essential in avoiding exposure to toxins and pathogens in the air or food. The filtering function of the nose initiates immune sensitization to potential pathogens. These functions play an essential role in normal upper airway functioning.

Chronic upper airway inflammation can be roughly divided into two major clinical entities, rhinitis and rhinosinusitis. Both can be separated into the mild, moderate and severe subgroups, and for both anti-inflammatory medication is the first-line treatment. The allergic phenotype is the best characterized phenotype of rhinitis from a pathophysiologic point of view.

Allergic rhinitis is an allergen-induced, IgE-mediated inflammatory disease of the nasal mucosa. The development of the disease is characterized by an initial sensitization phase to a specific allergen. Later on, the encounter of the same allergen by sensitized individuals is followed by the activation of effector mechanism and specific immune response. Previously it was established that a shift toward T helper 2 (Th2) cells plays a role in the initiation and maintenance of the disease. Eosinophils, mast cells, and basophils are considered to be the mayor effector cells in hay fever. These cells release inflammatory mediators such as histamine, prostaglandins, cytokins, tryptase, leukotrienes and eosinophil cationic protein (ECP). These mediators are responsible for most of the pathological processes occurring in the nasal mucosa. Allergic Rhinitis and its Impact on Asthma, in cooperation with EPOS just published a statement about allergic rhinitis and chronic rhinosinusitis. It defines the diagnostic and therapeutic principles, analyses the risks and courses of accompanying diseases, and presents alternatives for the treatment of the disease.

Chronic rhinosinusitis (CRS) is classically divided into a phenotype with and without endoscopic or radiologic evidence of nasal polyps (CRSwNP and CRSsNP). (2) CRSwNP is a multifactorial disease. The majority of CRSwNP cases are the eosinophil-type, in which the eosinophils represent more than 60% of inflammatory cell population. The persistence of tissue eosinophilia is very important in the pathogenesis of CRSwNP. Thus apoptosis of eosinophils and T cells may represent a therapeutic target in nasal polyps. Chronic rhinosinusitis (CRS) describes a heterogeneous group of diseases of the nose and the paranasal sinuses that is characterized by two phenomena: inflammation and tissue
remodelling. According to the European position paper on rhinosinusitis and nasal polyps, CRS is defined by the presence of at least two of the following symptoms: nasal obstruction, nasal secretion and/or post-nasal drip (PND), headaches and/or facial pains, a reduction of smelling for more than 12 weeks during the last year while at least one of the first two mentioned symptoms should be observed. For the diagnosis or positive nasal endoscopic and/or CT findings are essential. The burden of the symptoms, the associated reduction of the quality of life and the influence of the disease on work productivity are often underestimated. The inflammatory conditions commonly divided into two phenotypes: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). Histologically, CRSsNP is characterized by fibrosis of the mucosa and the basal membrane while nasal polyposis is characterized by important edema with deposition of albumin and the development of pseudocysts.

Increasing evidence suggests the heterogeneity in CRS manifestations may be explained by a variety of molecular and cellular pathways that result in the mucosal inflammation of CRS. The understanding of different pathophysiologic mechanisms in CRS allow the identification of disease variants as endotypes. Endotyping relies on immunohistologic biomarkers involved in disease pathophysiology and provides a more comprehensive approach to classify CRS variants. Approximately 80% to 85% of CRSwNP patients in the United States and Europe have shown a strong predilection for a skewed type 2 immune response, which is characterized by a high presence of eosinophils, mast cells, basophils, and T-helper 2 (Th2) cells, and comorbid associations with asthma and atopy. Released by type 2 innate lymphoid cells, Th2 cells, and mast cells, IL-5 is a common cytokine that coordinates the local influx, maturation, and survival of eosinophils. International guidelines recommend regular local nasal steroids (Ia evidency), short period systemic steroids (II), nasal lavage (Ib) and functional endoscopic sinus surgeries in combination for the treatment of chronic rhinosinusitis with nasal polyps. About 38% to 51% of CRS patients fail to respond to these recommended medical therapies. New treatment methods, which decrease eosinophil cell numbers and IL-5 levels are supposed to be of outstanding therapeutic importance in CRSwNP.

1.2. Genetic predisposing factors for Chronic rhinosinusitis with nasal polyps (CRSwNP)

Inflammation has been demonstrated to play a central role in the pathogenesis of CRSwNP, and TNFα is a key pro-inflammatory cytokine in these processes. In collaboration with the Department of Genetics genomic DNA were obtained from buccal swab samples in order to determine whether TNFA –308 G>A SNP has a role in a genetic predisposition to CRSwNP in the Hungarian population. The data suggest that not only the genetic predisposing factors but also the actual disease pathogenesis at the molecular level may differ in the various CRS subgroups. Szabo et al performed a case-control study for examining the frequency of 8.1AH carriers in subgroups of CRS and control. They found that the presence of the 8.1AH may be responsible for the development of severe CRSwNP ASA+ forms.
1.3. Effects of UV phototherapy

The therapeutic effect of UV light is generally attributed to its immunosuppressive and immunomodulative effect. It is used worldwide for the treatment of immunomediately inflammatory skin diseases like psoriasis or vitiligo. One of the most important mechanisms explaining the immunosuppressive effect of UV light is DNA damage inducing apoptosis in infiltrating T cells, the reduction in the number and function of Langerhans cells, and the induction of immunomodulatory cytokines such as IL-10. UV irradiation leads to the formation of photoproducts (cyclobutane-pyrimidine dimer, 6-4 photoproducts, Dewar isomers), which are the major triggers of UV-induced apoptosis. Inflammatory processes are very similar in the nose and in the skin; therefore rhinophototherapy is a promising, noninvasive treatment option for a number of inflammation-related pathological nasal conditions.

Hungarian inventors have experimented with the most efficient light composition to be applied in the nose in order to reduce allergic symptoms or even to treat various forms of nasal problems. Mixed ultraviolet light (Rhinolight®) is composed of more than 70% of visible light, 25% of UV-A light, less than 5% of UV-B. According to clinical studies it inhibits the antigen-induced histamine release from mast cells, and induces apoptosis in T-lymphocytes and eosinophil cells, thus reducing the number of eosinophil cells, ECP and IL-5.

During the initial research, photosensitizing drugs (psoralen) and phototherapy were combined (PUVA psoralen and ultraviolet A). Csoma et al proved that intranasal PUVA therapy significantly reduced the symptoms of patients suffering from allergic rhinitis. The UVB range mainly provides the immunosuppressive effect of UV light. Narrow-band UVB (NB-UVB: 305-315 nm wavelength) light sources are not only the most widely used in phototherapy, but it is also considered to be the gold standard for the treatment of inflammatory skin diseases as well.

Our previous publication revealed that mixed ultraviolet light/visible light (mUV/VIS) intranasal phototherapy was safe and effective in intermittent allergic rhinitis. UV phototherapy induced a dose-dependent increase of eosinophil and T-cell apoptosis.

In allergic rhinitis the first in vitro and in vivo studies assessing the applicability of UV phototherapy were conducted in Szeged, Hungary. UV-induced DNA damage response of respiratory epithelium was very similar to the response of the human epidermis, the nasal mucosa could efficiently repair UVB induced DNA damage.

1.4. Efficacy of mixed ultraviolet light and visible light (mUV/VIS) therapy in persistent allergic rhinitis

Considering that phototherapy using combined wavelengths is successfully used in the treatment of severe atopic dermatitis and that allergic rhinitis and atopic dermatitis are characterized by several common pathogenic features, we sought to investigate whether
Phototherapy using mUV/VIS light may represent a therapeutic alternative in patients with persistent allergic rhinitis. Our results showed that by the end of the treatment phase, the morning scores for sneezing, rhinorrhea, nasal obstruction and the calculated total nasal score (TNS) and NIPF, and the evening scores for sneezing and NIPF demonstrated a significant improvement in the RL group relative to the placebo group. By the end of the 4-week follow-up, a significant improvement was seen in the morning and evening scores for nasal, the evening rhinorrhea score, and the TNS in the RL group. By the end of the follow-up, there was no significant difference between the morning and evening sneezing scores, both of which had improved significantly. The evening nasal obstruction proved to be the most resistant symptom. Although it improved considerably, it did not improve significantly as compared with the placebo group at any time examined.

1.5. Safety of ultraviolet (UV) phototherapy

The DNA-damaging effect of high-energy ultraviolet light irradiation is well known, and this effect may indicate the first step of carcinogenesis. The majority of literature data refer to the damage formed after UV irradiation of the skin. The mutagenic risk of DNA photodamage has stimulated interest to determine the wavelengths dependent distribution of different DNA photodamage types. (33) UV light is able to cause DNA damage by direct mechanisms (absorption of photons by the DNA) or by indirect mechanisms such as generation of reactive oxygen species. (34, 35) Cells possess repair mechanism in response to UV induced DNA damage. Although, skin diseases are successfully treated with phototherapy and data from the literature support that no significant increase in skin cancer risk is present in patients treated for decades with UVB light, no data were available regarding the effect of UV light on nasal mucosa.

Koreck et al detected the effect of the intranasal mUV/VIS phototherapy on DNA damage and repair mechanisms in vivo. In their studies, they processed the nasal mucosa samples of 26 allergic rhinitis patients in a double-blind experimental system using a Comet assay. Their results have shown that in the experimental study design they chose the UV/VIS phototherapy did not cause significant DNA damage. Nasal mucosa exposed to UV light possess the capacity to repair DNA damage which suggests that the multistep process of carcinogenesis has not been triggered.

Mitchell et al performed a safety study as well. In subjects exposed to broadband ultraviolet radiation, DNA damage frequencies were determined prior, immediately after treatment and at increasing times post-treatment. They observed significant levels of DNA damage immediately after treatment and efficient removal of the damage within a few days. No residual damage was observed several weeks after multiple UVB treatments. The data suggest that the UV-induced DNA damage response of respiratory epithelia is very similar to that of the human epidermis and that nasal mucosa is able to efficiently repair UVB induced DNA damage.
AIMS OF THE THESIS

2.1. To evaluate the efficacy and tolerability of intranasal mixed ultraviolet and visible light (mUV/VIS) phototherapy in nasal polyps

The aim of the study was to evaluate the capacity of mUV/VIS light in suppressing the clinical symptoms of patients with eosinophilic polyposis with a follow up of 12 months. Primary endpoints were the changes in total nasal score and nasal symptoms and the polyp size according to videoendoscopic images. Secondary endpoints were improvement in the ability of smelling, in the quality of life and the volume of nasal cavity measured by acoustic rhinometry. We aimed to specify the side effects and their severity, and rescue treatment, if needed.

2.2. To investigate the efficacy of postoperative intranasal mUV/VIS phototherapy in the prevention of recurrence of nasal polyps

The aim of this study was to evaluate in vivo the clinical effect of mixed UV light (Rhinolight®) on the recurrence of nasal polyps during a 12-week treatment period with a follow up of 12 months. Primary endpoints were the ratio of patients without recurrent nasal polyps in the two groups according to the videoendoscopic images and the changes in nasal symptom scores.

2.3. Development of a new device for phototherapy used under endoscopic supervision

To develop a new measurement method and a handler device, which permits easier, faster and safer therapy with the mUV/VIS equipment under endoscopic supervision.
3.1. Efficacy and tolerability of intranasal mUV/VIS phototherapy in nasal polyps

SUBJECTS

87 subjects with bilateral nasal polyposis (stage II-III) who regularly take local nasal steroid were included. They all previously underwent functional endoscopic sinus surgery, and obtained the histopathological diagnosis of eosinophil polyposis. The subjects were divided into two groups: in Group A, subjects received only local nasal steroid (mometasone furoate 2x200 μg per day) for the duration of the study. In Group B, local nasal steroid were administered (mometasone furoate 2x200 μg per day) to the subjects, combined with intranasal mUV/VIS phototherapy 3 times per week for 12 weeks. The used mUV/VIS device (Rhinolight Inc, Hungary) contained 5% ultraviolet B, 25% of ultraviolet A and 70% of visible light, with the spectrum between 280 and 650 nanometers. The dose of phototherapy was proportional to the measured surface of the polyps 6 J/cm² in the first two weeks, and then 9 J/cm².

METHODS

During the study, demographical data, nasal endoscopy images and clinical data were collected, nasal inspiratory peak flow, acoustic rhinometry, smell threshold test, and exhaled nasal nitrogene-oxide (NO) measurements were performed.

3.2. Efficacy of postoperative intranasal mUV/VIS phototherapy in the prevention of recurrence of nasal polyps

SUBJECTS

Thirty patients were enrolled from 16 to 65 years of age taking standard dose of intranasal steroid with bilateral recurrent nasal polyps. They were devided in two groups, in group A they received only intranasal steroid (mometason furoate, 2x100-100 μg) during the study. In group B they received combined UV light (6 J/cm²) 3 times per week for 12 weeks and intranasal steroid. They were not randomized, but selected in the two groups according to the history, atopy, the number of previous surgeries and the polyp size before present functional endoscopic surgery for the equal distribution. We started the 12 week treatment 2-4 weeks after functional endoscopic sinus surgery, depending on the recovery of the mucosa.

METHODS

During the study, demographical data, nasal endoscopy images and clinical data were collected. We recorded total nasal score, NOSE quality of life, smell threshold test, nasal inspiratory peak flow and acoustic rhinometry. The follow up interval was 12 months. For the
evaluation of short-term safety and tolerability we recorded side-effects, unwanted events and nasal endoscopic videoimages.

RESULTS

4.1. Efficacy and tolerability of intranasal mUV/VIS phototherapy in nasal polyps

76 of the 87 enrolled patients finished the study (average age 49, 61 ± 11, 23 years; female/male ratio 26/50). In Group A consisted of 24 patients (average age 49, 61 ± 11, 23 years; female/male ratio 10/14), and Group B consisted of 52 patients (average age 48, 19 ±11, 95 years; female/male ratio 16/36). Eleven subjects were excluded from the study: in Group A, 6 patients (2 systemic steroid use, 4 compliance problems) and in Group B, 5 patients (3 compliance problems, 2 intercurrent infections).

Nasal symptom score and total nasal symptom score

In the phototherapeutic Group B, significant improvement was observed in all of the nasal symptom scores and in the total nasal score both at the end of phototherapy and during follow-up (1 and 3 month) In Group A, no significant improvement was measured.

Nasal obstruction symptom evaluation

In Group B, significant improvement was found after phototherapy and at the two check-ups occasions during follow up, whereas in Group A, no significant change was observed.

Smell Threshold Test

In group B, the results of the smell threshold test showed a significant improvement after phototherapy, which was maintained even 3 months after phototherapy. In group A, no significant change was observed

Videoendoscopy

The videoendoscopic images showed significant improvements in polyp stage and grade on both nostrils of patients in Group B after phototherapy. No significant change was detected in patients belonging to Group A.

Nasal inspiratory peak flow

In Group A, no significant improvement was found. In Group B, a significant increase was measured between the screening visit and the 3 month follow-up.

Acoustic rhinometry

In group B, a tendency of improvement was measured, but this was not significant. In group A, no improvement could be identified.
Exhaled nasal NO

Neither of the groups showed significant changes in the expiratory nasal NO level.

4.2. Efficacy of postoperative intranasal mUV/VIS phototherapy in the prevention of recurrence of nasal polyps

From the 30 enrolled patients 15 finished the study (15 months), eight in Group B (female/male ratio 1/7) and seven in Group A (female/male ratio 2/5).

We observed significant improvement in NOSE Quality of life (p=0,009) and in total nasal score (p=0,008) in Group B at six months follow up.

In Group B 4 of eight patients had recurrent polyps 6 months after finishing mUV/VIS phototherapy. In Group A: all of 7 patients had recurrent polyps. This difference was significant between the two groups (p=0,0289).

4.3 Development of a new handler and measurement device, and the armrest

The base device emitting cold light has been equipped with a target light. Prior to the application of the therapeutic light, this made the area to be treated well-visible. The target light was blue and fell into the visible light range. It fitted to the basic Rhinolight IV. device

Measurement of polyps

The nasal polyp surface area to be treated was separately measured by means of a special measurement instrument in both halves of the nasal cavity in the following main zones: superior ethmoid sinus, medial wall of the ethmoid sinus, lateral wall of the ethmoid sinus, sphenoid recess. Under endoscopic supervision we measured the size of the polyps with the special instrument, an optical extension designed for the study by Ferencz Ignácz from the Department of Optics and Quantum Electronics University of Szeged to measure precisely the extension of the polyps.

Handler device

We developed in cooperation with the Department of Optics and Quantum Electronics a handler device, which has a curved ending to reach even the narrowest parts of the nasal cavity. This handler device is capable of transmitting the light (both the target and the therapeutic) in a targeted manner onto the polyp’s surface. It can be connected to the flexible light guide of the base device. The device is made of fiber optic quartz bunch transmitting the UV spectrum, located in a stainless steel tube. The end of the handler device is bent. It is compatible with cleaning, disinfection and sterilization procedures generally applied in clinical circumstances.
The armrest:

It is of outstanding importance to stay fixed as possible during phototherapy, because the operator uses both hands at the same time, in the same nostril. Designing the armrest the first aspect was the long duration of treatment, sometimes 30-40 minutes, so both the patient and the operator has to stay in a well controlled head and arm position. The phototherapy was done in sitting position, so it was very important not to move more than 2-3 mms.

DISCUSSION

5.1. Efficacy and tolerability of mUV/VIS in nasal polyps

CRSwNP is a chronic disease, which has a major impact on quality of life and daily activity. The prevalence of CRSwNP in the population is 1-4%, often present with concomitant allergic rhinitis, asthma and other pulmonary diseases like cystic fibrosis, primary ciliary dyskinesia or aspirin intolerance. CRSwNP can be clinically characterized by oedoma formations extending into the nasal cavity causing nasal obstruction, rhinorrhea, reduction/loss of the sense of smell, and/or facial/headache. In the pathogenesis, terminally differentiated eosinophils migrate and accumulate in the tissues where they release various cytokines and chemokines, such as IL-5, IL-3, GM-CSF, or RANTES. These factors can further enhance the inflammatory process by contributing to stromal fibrosis, epithelial damage, increased oedema and increased extracellular matrix protein production. Thus, eosinophils potentially damaged cells and their prolonged survival are the key factors in the pathogenesis. Apoptotic cell death is determining in the regulation of eosinophil’s removal. Delayed apoptosis has been reported as an important mechanism for tissue eosinophilia in several diseases, including nasal polyps. IL-5 is one of the principle cytokines which promotes eosinophil maturation, activation and survival. CD4+ T cells are considered to be the main source of IL-5, but other cell types including mast cells and eosinophils also release this cytokine. Regarding to the role of surface epithelial cells in the process of nasal polyp formation, is not neglectable since they have a capacity to produce eotaxins, GM-CSF and RANTES activating eosinophils, and SCF attracting mast cells, respectively. In addition, the proliferation capacity of surface epithelial cells is related to recurrence rate of polyp similarly to degree of eosinophil density. These facts make the surface epithelials cells considerably targeted by rhinophototherapy.

During the initial research, photosensitizing drugs (psoralen) and phototherapy were combined (PUVA psoralen and ultraviolet A). Csoma et al proved that intranasal PUVA therapy significantly reduced the symptoms of patients suffering from allergic rhinitis. Our research group showed that in CRS, both the number of eosinophils and the level of IL-5 decreased after intranasal PUVA phototherapy, accompanied by a decreasing trend of the level of ECP, a cytotoxic mediator which participates in tissue damage. We proved that intranasal PUVA phototherapy had an anti-inflammatory effect in nasal polyposis without Samter’s triad (asthma, aspirin sensitivity and nasal polyps).
As mUV/VIS light showed the induction of apoptosis in eosinophils in vitro and phototherapy released the clinical symptoms in patients with CRSwNP, the aim of the study was to evaluate the capacity of mUV/VIS light in suppressing the clinical symptoms of patients with eosinophilic polyposis and to compare the efficacy of a treatment based only on the regular use of intranasal steroids with a unique combination therapy of mUV/VIS phototherapy and intranasal steroids in vivo. During the 12-week treatment period, the subjects received the total dosage of phototherapy in lower energy prolated over time. This kind of treatment protocol fits in the safety research methods. The treatment was delivered under endoscopic visualization, in a targeted, highly controlled way, to affect only the pathological mucosa and to save the normal mucosa from direct ultraviolet light strain. In the control group, intranasal steroid therapy, the gold standard basic therapy in nasal polyposis was applied. Due to medical-ethical reasons, the placebo controlled study design was not preferred.

Different subjective and objective methods were used to assess the efficacy of phototherapy. A major problem in the nasal area is that objective measures of nasal resistance do not correlate with subjective sense of obstruction. The nasal valve region primarily determines nasal resistance, whereas the sensation of nasal obstruction may be related to congestion in other areas, like the ethmoid region.

The quality of life of patients with CRSwNP is determined by the nasal congestion, discharge, headache and lose of the sense of smell. Subjects scored these symptoms on a visual analog scale during the study. The results were compared to endoscopic findings during visits. All of this data showed significant improvement in the group that received phototherapy.

The disturbance of olfaction has an effect on everyday life, because it is closely involved in the regulation of visceral function and emotional expression. The olfactory receptor area is localized to a small region of the cribriform plate, adjacent to nasal septum and superior turbinate. Phototherapy induced shrinking of the nasal polyps cause airflow increase into this superior nasal area, improving the olfaction of the patient. The results showed significant increase in the smell threshold in the phototherapy group.

The Lund Mackay scoring system of the nasal endoscopic findings is the only system regarding mucosal thickening. As polyposis is present, nasal endoscopy scoring is very useful in treatment evaluation, despite the discrepancy between objective and subjective findings. We performed endoscopy as an objective measurement to evaluate the efficacy of phototherapy. Significant improvement in the stage and grade of the polyps in the phototherapy group was observed, and these findings were present in the 3-month follow up.

Several authors studied acoustic rhinometry (ARM) and nasal inspiratory peak flow (NIPF) in CRSwNP. Proimos et al found both methods promising for objective evaluation and monitoring of nasal obstruction in CRS. NIPF correlated strongly with nasal obstruction visual analog scale (VAS), ARM correlated moderately with VAS scaling. According to Spronsen et al subjective nasal obstruction correlates better with objective functional measurements of nasal airflow resistance, like NIPF, than with measurements of nasal cavity width, like ARM, despite the fact that they are used in many studies as an outcome of treatment effects. Nathan et al found 5 to 10% of reproducibility by acoustic rhinometry in
allergic rhinitis. The main basis for poor repeatability can arise from technical factors (nosepiece fits) and both the nasal cycle and diurnal variations in nasal airway caliber. In the present study, a significant improvement was observed in NIPF one month after the end of phototherapy, and a tendency of improvement at the end of phototherapy. In ARM, the results showed moderate, non-significant improvement at the end of phototherapy.

Exhaled nitric oxide (NO) measurement is a simple and non-invasive method for monitoring airway inflammation. The major part of nitric oxide is produced by the ciliary epithelia cells in the paranasal sinuses. Its level may be low even in the presence of normal activity if the sinus ostia are blocked because of nasal polyps. Successful treatment results in higher nasal NO (nNO) by opening the maxillary sinus ostium. An increase in inflammation could also show a rise in concentrations, therefore, a nasal endoscopy is needed to distinguish between these possibilities. Jeong et al found lower nNO in CRSwNP, than in CRSwNP combined with allergic rhinitis (AR). The healthy control group’s nNO levels were the highest. They found a significant inverse relation between nNO and severity of nasal obstruction. We performed nNO level measurement with an electrochemical analyzer in 30 subjects: a non-significant difference was found, phototherapy group nNO level increased, however, in INS group, it decreased.

5.2. Efficacy of mUV/VIS in the prevention of recurrence of nasal polyps

In our previous study we proved, that mUV/VIS phototherapy reduced the symptoms of patient with CRSwNP. During phototherapy mUV/VIS targeted directly the surface of the polyps. In this study we wanted to examine the efficacy of mUV/VIS on the mucosa. There is no international literature or guideline regarding the use of mUV/VIS phototherapy after functional endoscopic surgery. Our study was the first to evaluate the efficacy and tolerability of postoperative phototherapy.

Regarding the high recurrence rate of CRSwNP several observations were made. Batra et al’s cross sectional study’s objective was to construct the clinical profile of patients with chronic rhinosinusitis (CRS) with/without polyposis undergoing revision sinus surgery and to evaluate the relationship of polyposis, asthma, acetylsalicylic acid (aspirin) (ASA) sensitivity, inhalant allergies, and previous sinus surgery on disease severity. 225 patients data were analysed. They found that patients with CRS with polyposis had a statistically significant increase in presence of asthma, inhalant allergy and ASA sensitivity. The number of previous surgeries had a statistically significant correlation with endoscopy and CT scores. The group of recalcitrant CRS patient undergoing revision sinus surgery has a high prevalence of polyposis, asthma, inhalant allergy, ASA sensitivity, and elevated disease. The polyp phenotype signifies statistically higher prevalence of associated comorbidities and greater objective disease severity. The presence of asthma, inhalant allergy, and ASA sensitivity also predicts statistically higher disease burden.

McMains et al reported objective and subjective outcomes after revision sinus surgery (RESS) for chronic rhinosinusitis (CRS). They performed a retrospective analysis of prospectively
collected data in 125 patients requiring revision functional endoscopic sinus surgery after failing both maximum medical therapy and prior sinus surgery for CRS. Computed tomography (CT) scans were graded as per Lund-MacKay and patient symptom scores were recorded using the Sinonasal Outcome Test 20 (SNOT-20) instrument. Individual rhinosinusitis symptoms were evaluated on a visual analog scale (0-10) before and after surgery, with a minimum 2-year follow-up. They found that patients with asthma and polyposis had higher CT scores. At 12-month follow-up, each individual symptom score decreased significantly. Overall, 10 patients failed RESS and required additional surgical intervention, all of them had nasal polyposis.

Wynn et al. aim was to provide reference information for recurrence rates and need for revision surgery in patients with severe nasal polyposis. One hundred and eighteen records were reviewed. Fifty percent of patients had asthma, and 79% had documented allergy. All patients required extensive bilateral nasal polypectomy, complete anterior and posterior ethmoidectomy, and maxillary sinusotomy, 85% also had frontal or sphenoid sinusotomy. Follow-up ranged from 12 to 168 months. 60% developed recurrent polyposis, from which 47% were advised to undergo revision surgery, and 27% underwent surgery. History of previous sinus surgery or asthma predicted higher recurrence and revision surgery. History of allergy also predicted recurrence and need for revision. In their study, patients with asthma are at higher risk of recurrence.

DeConde et al performed a prospective multicenter cohort study of patients undergoing ESS for medically recalcitrant CRSwNP. The objective was to evaluate the prevalence of nasal polyt recurrence up to 18 months after endoscopic sinus surgery (ESS) with congruent continuing medical management. All patients received baseline nasal endoscopy quantified using Lund-Kennedy grading. All patients included for final analysis provided at least 6 months of postoperative endoscopy examinations. 363 CRSwNP patients were enrolled. Surgery plus postoperative medical management significantly improved endoscopy total scores at 6 months. The recurrence of nasal polyposis 6 months after ESS was 35% and 40% after 18 months. They targeted on the fact both surgical and medical management strategies are warranted to improve upon the observed prevalence of recurrence.

Veloso-Teles et al investigations objective was to evaluate ESS efficacy in CRSwNP treatment and to establish prognostic factors for disease recurrence. They tried to find independent variables that can predict surgical outcomes in patients with CRSwNP.

Eighty-five patients with CRSwNP submitted to ESS, and a minimum follow-up of 9 months were selected. Patient demographics, occupational organic exposure (e.g., cotton, fuel gas, wood dust) and inorganic dust exposure (e.g., bleach, metals, cement), comorbidities, previous nasal surgeries, pre- and postoperative symptoms, ear, nose and throat examination findings, computed tomography results, and medical and surgical treatment information were collected from medical records. All rhinologic symptoms improved after surgery, in a statistically significant way, with the best recovery rate for nasal obstruction and the worst for hyposmia. Disease recurrence occurred in 31% of the patient, but only 7% required surgical
reintervention. Their analysis identified occupational dust exposure and non-immunoglobulin E mediated asthma as independent predictive variables in CRSwNP recurrence.

International guidelines recommend conservative treatment after surgery in case of chronic rhinosinusitis with nasal polyps, to reduce the number of recurrences. Our previous studies proved the positive effect of mUV/VIS phototherapy in CRSwNP. The aim of this study was to answer the question, whether mUV/VIS phototherapy can reduce the rate of recurrence in nasal polyps after surgery. Our thought was that irradiating the mucosa locally, in predilective areas as soon as possible after endoscopic sinus surgery might have an additive role in the treatment of this chronic disease. Our results showed, that it might have a supportive role in the treatment of recurrent CRSwNP cases.

6. NEW RESULTS

6.1. Efficacy of intranasal mUV/VIS phototherapy in nasal polyps

Our data show that mixed ultraviolet/visible light phototherapy led to improvement in chronic rhinosinusitis with nasal polyps. Nasal symptoms, sense of smell and nasal obstruction improved even 3 months after the end of phototherapy, which is an outstanding importance in this chronic disease. The improvement could be observed even after 6 months. Mixed ultraviolet and visible light (UV/VIS) phototherapy was well tolerated. No severe side-effects were found. Few patients reported mild dryness of the nasal mucosa, which disappeared in a few days with the use of ColdastopTM nasal drops. No systemic rescue treatment was necessary.

6.2. Efficacy of postoperative intranasal mUV/VIS phototherapy in the prevention of recurrence of nasal polyps

Mixed UV/VIS therapy significantly reduced the recurrence of nasal polyps, and a significant improvement in Total Nasal Score (TNS: nasal discharge, sneezing, smell ability, nasal obstruction), and Nasal Obstruction Score Evaluation (NOSE) was observed. Rhinophototherapy with standard nasal steroid may have a supportive role in the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP).

6.3. Development of a new handler-device and armrest for phototherapy

We have developed and successfully used the armrest and handler device and the new measurement method. It made the treatment of the patients easier and preciser under endoscopic supervision.
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