

Phototherapy for the Treatment of Allergic Rhinitis

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1. Introduction

Allergic rhinitis (AR) is one of the most common allergic diseases, affecting 20% of the adult population and up to 40% of children (Salib et al., 2003). It is associated with decreased learning, performance and productivity at work and school, as well as a reduced quality of life. The detrimental effects of AR on quality of life (QOL) include fatigue, irritability, memory deficits, excessive daytime somnolence, and depression. The annual economic impact of AR is calculated to be between \$ 6.3 billion and \$ 7.9 billion without counting its detrimental effects on QOL (Fineman, 2002). Current therapeutic options such as allergen avoidance, medication and immunotherapy are far from ideal. It is important to develop an effective modality to relieve the symptom except for targeting the complexity of underlying inflammatory mechanism of AR.

Phototherapy is the application of light to a pathological area to promote tissue regeneration, reduce inflammation and relieve pain. Several types of phototherapeutic devices are currently used for medical treatment using selected wavelengths and controlled dosage of irradiation. Significant suppression on the clinical symptoms of AR by the phototherapy treatment of ultraviolet (UV) and visible light was reported (Csoma, et al., 2004, 2006; Koreck, et al., 2005, 2007). Narrow-band red light phototherapy was found to markedly alleviate the clinical symptoms of AR (Neuman & Finkelstein, 1997). In addition to UV and visible light therapy, far infrared ray (FIR) therapy is also reported to have beneficial effects to patients with AR (Hu & Li, 2007). Photochemical effect is elicited using UV and visible light irradiation, whereas thermal effect is induced with FIR irradiation. Although different mechanisms are involved when light sources with different ranges of wavelengths are employed, phototherapy represents a noninvasive, alternative intervention for the treatment of AR.

This chapter is organized as follows. First, pathophysiology and traditional management of AR are briefly reviewed. Second, photobiology and phototherapy related to AR are summarized. Finally, the clinical outcomes of FIR therapy as well as red light acupoint stimulation on patients with AR are described.

2. Pathophysiology of allergic rhinitis

AR is defined as an abnormal inflammation of the membrane lining the nose, which is mediated by immunoglobulin E (IgE). The clinical symptoms of AR include sneezing,

itching of the nose, rhinorrhea and nasal congestion. Additionally, airway lining hypersensitivity, a loss of the sense of smell and an inability to taste may occur. It has become progressively clear that it is a common comorbid condition with asthma, allergic conjunctivitis, sinusitis, otitis media, nasal polyposis and respiratory infections (Berrettini, et al., 1999; Skoner, 2000). Nasal obstruction can often be seen with pale nasal mucosa, enlarged turbinates, clear nasal secretions, and pharyngeal cobble-stoning upon physical examination (Al Suleimani & Walker, 2007). The diagnosis of AR was based on definite symptoms of nasal itching, rhinorrhea, sneezing, nasal obstruction or mouth breathing, as well as positive reactions to blood tests to antigens, such as house dust mite, cockroach, molds, feathers, grass pollen, weed pollens, sage pollen, and local tree pollens, etc. Criteria for positive skin prick test responses were a wheel of 3 mm or greater diameter with erythema of at least 5 mm. Histamine control skin test was read at 10 minutes, allergen and negative control skin tests were read at 15 minutes. The score for each symptom is usually registered on a four-grade scale- absent, slight, moderate or severe (Linder, 1988) as shown in Table 1.

<p>Scoring of eye itching</p> <p>0: no eye itching</p> <p>1: rubbing eyes less than 5 episodes a day</p> <p>2: rubbing eyes 6-10 episodes a day</p> <p>3: rubbing eyes more than 10 episodes a day</p>	<p>Scoring of rhinorrhea</p> <p>0: no nasal blowing</p> <p>1: nasal blowing less than 5 episodes a day</p> <p>2: nasal blowing 6-10 episodes a day</p> <p>3: nasal blowing more than 10 episodes a day</p>
<p>Scoring of nasal itching</p> <p>0: no nasal itching</p> <p>1: rubbing nose less than 5 episodes a day</p> <p>2: rubbing nose 6-10 episodes a day</p> <p>3: rubbing nose more than 10 episodes a day</p>	<p>Scoring of smell impairment</p> <p>0: no smell impairment</p> <p>1: hyposmia with mild smell impairment</p> <p>2: hyposmia with moderate smell impairment</p> <p>3: anosmia</p>
<p>Scoring of nasal stuffiness</p> <p>0: no nasal stuffiness</p> <p>1: nasal stuffiness without mouth breathing</p> <p>2: nasal stuffiness with sporadic mouth breathing</p> <p>3: nasal stuffiness with predominant mouth breathing</p>	<p>Scoring of sneezing</p> <p>0: no sneezing</p> <p>1: sneezing less than 5 episodes a day</p> <p>2: sneezing 6-10 episodes a day</p> <p>3: sneezing more than 10 episodes a day</p>

Table 1. Scoring of symptoms for AR

Various mediators are associated to the pathophysiology of AR. For example, histamine plays a pivotal role in early allergic responses and also acts as stimulatory signal for cytokine production, expression of cell adhesion molecules and HLA class II antigens. Most of the effects of histamine in allergic disease are mediated through H1 receptors (Akdis & Blaser, 2003). Cysteinyl leukotrienes (CysLTs) increase nasal airway resistance and obstruction, and contribute to rhinorrhea via increased vascular permeability and mucus secretion (Okuda, et al., 1988). Prostaglandins cause congestion and rhinorrhea.

Neuropeptides induce vasodilation, thus causing congestion (Howarth, 1997). Cytokine secretion upregulates the expression of adhesion molecules on the vascular endothelial cells, thereby enhancing the activation and adhesion of inflammatory cells. An increase in interleukin-4 (IL-4), IL-5, and granulocyte-macrophage colony-stimulating factor (GM-CSF) is associated with a mucosal eosinophilia (Quraishi, et al., 2004).

3. Traditional management of allergic rhinitis

Effective allergen avoidance can lead to substantial relief of symptoms. However, patients are still not able to avoid their confirmed allergens such as mites or atmospheric pollens under many circumstances. Medication to manipulate the release of mediators is the next step in the management of AR. Table 2 summarizes the classes of pharmacological therapies for the treatment of AR. The two major classes of medication are oral H1 antihistamines and intranasal corticosteroids. According to the guidelines, oral antihistamines are the first-line therapy which relieve sneezing and rhinorrhea (Bousquet, et al., 2001; van Cauwenberge, et al., 2000; Dykewicz, et al., 1998). Topical administration can further minimize systemic adverse effects of antihistamines. H1 antihistamines are often combined with a decongestant to reach sufficient efficacy for nasal congestion (Quraishi, et al., 2004). The new generation of antihistamines acts as inverse agonists that stabilize the inactive conformation of the receptors and reverses constitutive activity of receptors (Oppenheimer & Casale, 2002). Intranasal corticosteroids are recommended as first-line treatment for moderate and severe AR, which are effective in relieving symptoms such as sneezing, rhinorrhea, itching and congestion (Weiner, et al., 1998). Corticosteroids target the inflammatory mechanisms; therefore the amount of oral corticosteroids for long-term treatment should be carefully adjusted to avoid adverse effects such as osteoporosis and growth inhibition in children (Wilson, et al., 1998).

Decongestants can reduce nasal obstruction and congestion by their vasoconstrictive action on α -adrenergic receptors. The application of intranasal decongestants may cause rhinitis medicamentosa. The adverse effects of oral decongestants include elevated blood pressure, tremor, tachycardia, loss of appetite, sleep disturbance. The long term use of decongestant is not recommended. (Quraishi, et al., 2004). Anticholinergics act as muscarinic receptor blocker which inhibits mucus secretion and subsequent rhinorrhea. Through inhibiting degranulation and neosynthesis of inflammatory mediators, mast cell stabilizers are shown to be effective in reducing symptoms of early inflammatory phase and are useful for preventive purposes (Al Suleimani & Walker, 2007). Leukotrienes inhibitors significantly reduce nasal blockade by inhibiting leukotriene synthesis or serving as antagonists for its receptors. Immunotherapy has the potential to provide a permanent cure for the disease. The proposed mechanisms for immunotherapy include suppression of IgE elevation, decrease in neutrophil and eosinophil activity, reduction in mast cell number, inhibition of T-lymphocyte proliferation (Jayasekera, et al., 2007; Pipet, et al., 2009). However, the technique is burdensome which requiring a lengthy series of injection and it may not be applicable to all patients (Naclerio, et al., 2002). Although most of the drugs are effective in treating certain symptoms of AR, they all have limitations due to their adverse effects. Due to the complex mechanisms involved in the AR, the ideal treatment for this disease has yet to be discovered.

Class	Route of administration	Mechanism of action	Symptom relief	Adverse effects
Antihistamines	Intranasal, oral	Antagonists or inverse agonists for histamine at the histamine receptor	Sneezing, rhinorrhea, itching	First-generation: sedation, impaired mental performance, dry mouth, dry eyes, urinary retention
Corticosteroids	Intranasal, oral	Bind to glucocorticoid receptors, affecting the production of various mediators	Sneezing, rhinorrhea, itching, congestion	Intranasal: nose irritation, bleeding Oral: long-term use may cause growth inhibition in children and osteoporosis
Decongestants	Intranasal, oral	Stimulate α -adrenergic receptors to induce vasoconstriction	Congestion	Intranasal: rhinitis medicamentosa Oral: elevated blood pressure, tremor, tachycardia, loss of appetite, sleep disturbance
Anticholinergics	Intranasal	Muscarinic receptor blockade	Rhinorrhea	Minimal
Mast cell stabilizers	Intranasal	Prevent mast cell degranulation and neosynthesis of inflammatory mediators	Sneezing, rhinorrhea, itching, congestion	Minimal
Leukotriene inhibitors	Oral	Leukotriene synthesis inhibitors, antagonists for the leukotriene receptors	Sneezing, rhinorrhea, congestion	Possibility of neuropsychiatric side effects
Immunotherapy	Subcutaneous injection	Suppress IgE elevation, neutrophil and eosinophil activity, mast cell number, T-lymphocyte proliferation	Early or late inflammatory phase responses	Unknown effects from the modification of immune system

Table 2. Current therapeutic agents in use for AR

4. Photobiology

Electromagnetic radiation comprises of radio, microwave, infrared (IR), visible light, UV, X-ray and gamma radiation. The phenomenon of light absorption to produce electronic excitation of atoms and molecules has long been accepted by photochemists and photobiologists. In phototherapy, wavelengths used include UV (100-400 nm), visible light (400-800 nm) and IR (800-10⁵ nm).

Photobiological reactions often involve the absorption of a specific wavelength of light by the functioning photoacceptor molecule. Photochemical effect is elicited using UV and visible light irradiation, whereas thermal effect is induced with FIR irradiation. Light in the ultraviolet range is absorbed by the protein part of the molecule and the visible and NIR wavelengths are absorbed by the metals. Further analysis of action spectra, it is suggested that the primary photoacceptor for the red-NIR wavelengths in mammalian cells is cytochrome *c* oxidase in terminal respiratory chain (Karu, et al., 2005, 2008). Flavoproteins such as NADH dehydrogenase in the beginning of the respiratory chain is believed to be the photoacceptor for the violet-to-blue spectral range (Karu, 2003). In addition, light induces a wave-like alternating electric field in a medium that is able to interact with polar structures and produce dipole transitions. These dipole transitions may lead to the primary actions at cellular and biochemical levels (Amat, et al., 2006).

Early hypothesis of the mechanism of primary action upon visible light irradiation can be divided into two categories: (1) singlet oxygen hypothesis based on the singlet oxygen generation from the endogenous molecules possessing the properties of photosensitizers, such as porphyrins and flavoproteins, upon irradiation (Vladimirov, et al., 2004), and (2) the oxidation-reduction hypothesis based on the excitation in chromophores of cytochrome-oxidase complex such as Cu_A, Cu_B or heme *a*(*a*₃), thereby enhancing the electron transfer rate (Lubart, et al., 2005). Later, the nitric oxide (NO) hypothesis was proposed suggesting that the activity of cytochrome *c* oxidase can be regulated by NO, here light irradiation can reverse the partial inhibition by NO (Karu, et al., 2005). Superoxide anion hypothesis was also suggested because of increased production of superoxide anion by irradiation, possibly through promoting the mitochondrial respiratory chain (Karu, 2003). The transient local heating hypothesis suggested that the irradiation energy may lead to a local transient increase in the temperature of absorbing chromophores, which may cause structural changes and trigger biochemical activity (Hallen, et al., 1993). The primary reactions upon light irradiation mainly occur in the mitochondria, which may lead to the secondary reactions occurring in the nucleus and cytoplasm. The secondary reactions involves cellular signaling cascade including increased intracellular ATP level, activation of transcription factors such as Nuclear factor-kappa B (NF-κB) and AP-1, activation of NADPH oxidase, change of the cellular redox potential to more oxidized direction (increased ROS production), manipulation of Ca²⁺ concentration, alteration of mitochondrial transmembrane potential (ΔΨ_m), regulation of inducible nitric oxide synthase (iNOS) activity and intracellular pH, and increased DNA/RNA synthesis (Karu, 2003). Other phenomena such as suppression of inflammatory cytokines, up-regulation of growth factor production, modification of extracellular matrix components, inhibition of apoptosis, stimulation of mast cell degranulation, and up-regulation of heat shock protein are also observed (Lin, et al., 2010).

IR are invisible electromagnetic waves which are subdivided into three categories: near-infrared (NIR) (0.8-1.5 μm), middle-infrared (1.5-5.6 μm) and far-infrared (FIR) (5.6-1000

µm). Different photobiological mechanisms are involved when FIR radiation is employed in phototherapy. The main principles of FIR are radiation, deep penetration and absorption of resonance. At molecular level, FIR exerts rotational and vibrational effects that are biologically beneficial. FIR therapy is often used as alternative physical therapy to decrease joint stiffness, relieve muscle spasms, assist soft tissue injury repair, lead to pain relief, and help to resolve inflammatory infiltrated edema. FIR therapy can improve blood flow and survival of the arteriovenous fistula in hemodialysis patients (Lin, et al., 2007). Furthermore, FIR stimulation on acupoints at Qihai, Kuan yuan and Chung chi decreases both stress and fatigue levels as well as stimulates autonomic nervous system activity in hemodialysis patients (Su, et al., 2009). IR radiation is believed to transfer energy that is perceived as heat by thermoreceptors in the surrounding skin (Inoué & Kabaya, 1989). The abdominal skin temperature steadily increased to a plateau between 38 and 39°C when the top FIR radiator was 20 cm above the rats (Yu, et al., 2006). The expression of HSP70 participates in cytoprotection and may be induced by hyperthermia, infection, UV radiation, NO, etc. However, an *in vitro* study demonstrated that FIR radiation inhibited the proliferation of cancer cells by the low expression level of heat shock protein 70A (Ishibashi, et al., 2008). In addition to the thermal effect, the non-thermal biological effects of FIR therapy led to enhance the extensibility of collagen tissue, stimulate the secretion of transforming growth factor-β1, and increase microcirculation via L-arginine/NO pathway (Toyokawa, et al., 2003; Yu, et al., 2006). Repeated FIR therapy could upregulate the expression of endothelial NO synthase (eNOS) (Akasaki, et al., 2006). FIR therapy was found to exert an anti-inflammatory effect via the induction of heme oxygenase-1 in endothelial cells via stimulating NF-E2-related factor (Nrf2) dependent promoter activity. TNF-α-induced expression of E-selectin, vascular cell adhesion molecule-1 (VCAM-1), and intercellular cell adhesion molecule-1 (ICAM-1) were suppressed (Lin, et al., 2008). A study on the mechanism of action demonstrated that FIR radiation activated p38 and extracellular signal-regulated kinase (ERK), but not Akt or c-Jun N-terminal protein kinases (JNK), and significantly promoted angiogenesis by increasing tube formation and the migration of endothelial cells (Rau, et al., 2010). Based on the above studies, the mechanism of action by FIR therapy can be both thermal and non-thermal effects.

5. Phototherapy in allergic rhinitis

Phototherapy is an effective treatment modality in inflammatory and immune mediated diseases. It has been successfully used in dermatology practice for several decades. The XeCl UV-B laser irradiation and mixed irradiation with UV-A (25%), UV-B (5%) and visible light (70%) (mUV/VIS) resulted in a dose-dependent inhibition of the allergen-induced wheal formation on the skin (Cosma, et al., 2004; Koreck, et al., 2004). Development of new phototherapeutic devices made it possible to treat the inflammatory disease of the nasal mucosa. Intranasal UV-B phototherapy with medium-dose 308 nm XeCl excimer significantly suppressed the nasal symptoms of patients with severe hay fever (Cosma, et al., 2004). Rhinophototherapy consist of using mUV/VIS resulted in a significant improvement of clinical symptoms for sneezing, rhinorrhea, nasal itching, and total nasal score (Koreck, et al., 2005). The number of eosinophils and the level of eosinophil cationic protein and IL-5 were also reduced. Statistically significant differences were found in the average results of the

Rhinoconjunctivitis Quality of Life Questionnaire (Cingi, et al., 2009). Another prospective, randomized, single-blind study showed that total nasal scores decreased in both mUV/VIS and low-intensity visible light (mUV/VIS without UV) treated groups (Cingi, et al., 2010). But the decrease was highly significant in the mUV/VIS treated group when compared with the low-intensity visible light treated group. However, the impact of endonasal phototherapy on the number of Langerhans cells in the nasal mucosa was limited (Brehmer & Schön, 2010). DNA damage was significantly higher in nasal cytology samples collected immediately after the last treatment (Koreck, et al., 2007). The DNA damage induced by intranasal UV phototherapy was efficiently repaired two months after ending therapy. One of the possible mechanisms that explain the immunosuppressive effect of mUV/VIS is the induction of apoptosis of T cells and eosinophils after UV damage, thus, leading to the inhibition of synthesis and release of pro-inflammatory mediators (Kemény & Koreck, 2007). The side effect of phototherapy is dryness of nasal mucosa, which can be overcome with emollients. Another disadvantage of UV-B treatment is the risk of carcinogenesis. Therefore, it is important to develop phototherapeutic devices using wavelengths other than UV (Morita, et al., 2008).

Very few papers report the application of the light in the other wavelengths in addition to UV light for the management of AR despite that over 2500 papers have been published regarding low level light therapy as a therapeutic modality to speed up tissue repair as well as related biochemical, cellular, histological and functional effects. NIR irradiation suppressed contact hypersensitivity reaction in rats via systemic immunomodulatory effect (Kandolf-Sekulovic, et al., 2003). A double-blind randomized study showed that 70% improvement of clinical symptoms on AR after intranasal illumination at 660 nm (Neuman & Finkelstein, 1997). Thus, light in red or NIR wavelengths with different mechanism of action from UV and visible light may be an ideal candidate for the intervention of AR after systematic study.

5.1 Far infrared irradiation in allergic rhinitis

FIR therapy, a non-invasive and convenient therapeutic modality, can improve blood flow and inflammatory status through both its thermal and non-thermal effects. By applying FIR therapy to the nasal region in the patients with AR, our study demonstrated that FIR therapy could improve significantly for the clinical symptoms of eye itching, nasal itching, nasal stuffiness, rhinorrhea and sneezing during period of therapy (Hu & Li, 2007).

Thirty-one patients with perennial AR enrolled in the study completed the FIR therapy. All patients had daily symptoms despite antihistamines and local steroid spray treatments. Patients with severe deviation of the nasal septum causing bilateral nasal obstruction and suffering from sinusitis were excluded from the study. A FIR emitter was used for FIR therapy in this study. The wavelength of the light generated from the electrified ceramic plates of this emitter was in the range between 5 and 12 μm with a peak at 8.2 μm . The radiator was positioned via facing patient's nasal region at a distance of 30 cm. The therapeutic time was 40 minutes everyday for 7 days. All the FIR therapies were performed in the morning between 9 am and noon. During the course of the study, the patients did not receive any other anti-allergic management. The effects of FIR on the clinical symptoms were analyzed by the paired sample t-test.

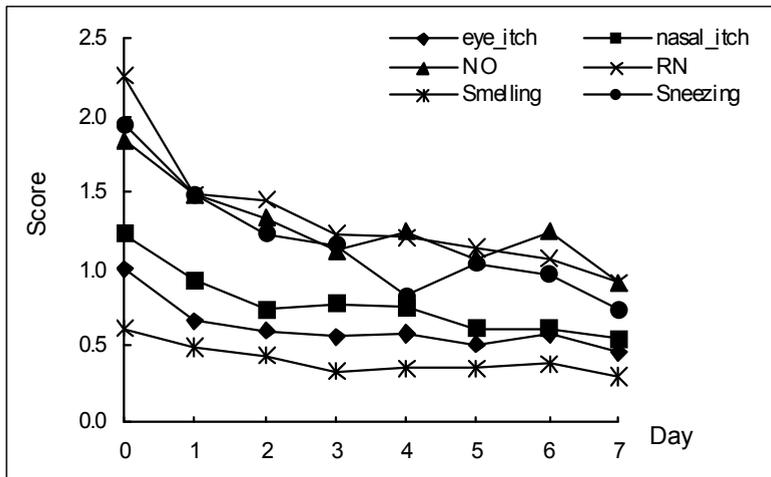


Fig. 1. Mean values of daily scores for six symptoms of AR. The score is given on a scale from 0 = no symptom to 3 = severe symptom. The symptom scores decreased over the period of FIR treatment. Pre-treatment (Day 0); during treatment (Day 1-7).

Mean values of daily registrations for eye itching, nasal itching, nasal stuffiness, rhinorrhea, smell impairment and sneezing after FIR therapy are given in Figure 1. All the symptom scores were reduced by more than 50% by the end of the FIR therapy. The most severe symptom of the pre-treat patients was rhinorrhea, which the mean value of the symptom score was 2.26, followed by sneezing and nasal stuffiness with scores of 1.94 and 1.84, respectively. The least severe symptom of the pre-treat patients was smell impairment with a mean score of 0.61. After the one-week treatment period, significant improvements were observed in all the symptoms of AR patients. The improved clinical symptoms were usually seen 1 day after the start of therapy, and thereafter the improvement was continuous. However, the smell impairment did not reveal significant improvement until after the 7th therapy. This was probably because the pre-treatment score of smell impairment was only 0.61 and not much room for improvement of the score or FIR was not very effective on improving olfactory disorder.

Our study demonstrated the improving effect of FIR therapy on the clinical symptoms of AR. Most of the clinical symptoms improved quickly and significantly. The patients tolerated the treatment well, and no severe adverse effect was observed during FIR treatment.

5.2 Red light acupoint stimulation in allergic rhinitis

Acupuncture involves the stimulation of acupoints that are located at a lines of meridians that correspond to the flow of energy through the body. Traditional treatment for AR by acupuncture may include needling and moxibustion. Modern acupuncture has evolved other methods of stimulating acupoints including the use of an electrical current, by applying pressure to the acupoint (acupressure) or using a low intensity laser or light emitting diodes (LEDs). Evidence suggests that acupuncture is a useful complementary or

alternative treatment option for AR in both adults and children (Xue, et al., 2002; Ng, et al., 2004). Points of the ear are sensitive acupuncture treatment sites for a range of clinical conditions. Ear-acupressure is commonly used as a non-invasive alternative stimulation method by using small seeds or metal pellets on ear acupoints. A review based on 92 research papers searched from 21 electronic English and Chinese databases concluded that ear-acupressure was more effective than herbal medicine, as effective as body acupuncture or antihistamine for short-term effect. But it was more effective than anti-histamine for long-term effect. However, the benefit of ear-acupressure for systematic relief of AR is unknown due to the poor quality of included studies (Zhang, et al., 2010).

Allergic symptoms are largely dependent on oxygen radical formation, which were found to be suppressed after red light illumination. Shangyingxiang Xue is an acupoint at the upper end of nasolabial fold. Acupuncture to Shangyingxiang Xue helps to relieve symptoms of AR, rhinorrhea with turbid discharge, stuffy nose, and headache. Here, we evaluated the clinical effects of phototherapy using red light to Shangyingxiang Xue on patients with AR (Hu & Yan, 2009).

Sixty-one AR patients who met the inclusion criteria were enrolled in this study. Patients were divided randomly into the treating group and control group. All patients filled out the informed consent form before treatment and recorded their symptom scores everyday in a diary before and during treatment. Thirty-one patients in the treating group received phototherapy with LEDs consisted of two wavelengths, 660 and 850 nm, to bilateral Shangyingxiang Xue. Phototherapy was performed once a day for 7 days. The duration of each treatment was 10 minutes. Thirty patients in the control group received antihistamine (Zyrtec, 10 mg) once a day for 7 days. A symptom score of 0 to 3 was assigned for each of the following rhinitis symptoms: eye itching, nasal itching, nasal obstruction, rhinorrhea, smell impairment, sneezing and size of inferior turbinate. The scores of pre- and post-therapy in both groups were collected after the course of treatments and analyzed by using the paired sample t-test.

Thirty-one patients enrolled in the study completed the red light phototherapy. Mean values of daily registrations for eye itching, nasal itching, nasal stuffiness, rhinorrhea, smell impairment and sneezing are given in Figure 2. Most of the symptoms were quickly and significantly improved. The most severe symptom of the pre-treat patients was rhinorrhea, which the mean value of the symptom score was 2.0, followed by sneezing and nasal stuffiness with scores of 1.84 and 1.55, respectively. The least severe symptom of the pre-treat patients was smell impairment with a mean score of 0.71. After the one-week treatment period, significant improvements were observed in all the symptoms of AR patients. The improved clinical symptoms were usually seen 1 to 2 days after the start of therapy, and thereafter the improvement was continuous. However, the smell impairment did not reveal significant improvement until after the third treatment. This was probably because the pre-treatment score was lower than the others that there was not much room for improvement or phototherapy to acupoint was not so effective on improving olfactory disorder.

Comparing the clinical effects of phototherapy and antihistamine control groups with repeated measures analysis, no difference was observed except the size of inferior turbinate. To sum up, phototherapy to Shangyingxiang Xue could relieve the symptoms. Its low cost and low side effect suggest that phototherapy to Shangyingxiang Xue is an attractive alternative to conventional treatment for AR patients.

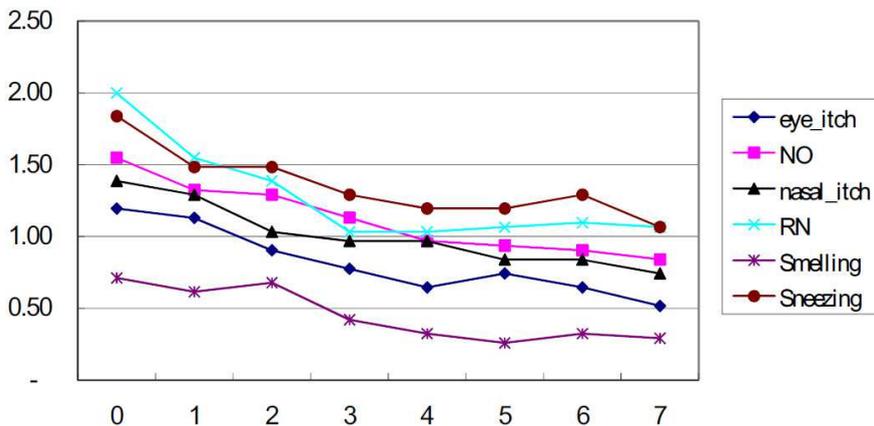


Fig. 2. Mean values of daily scores for symptoms of experimental group by using red light phototherapy. The symptom scores decreased over the period of red light treatment. Pre-treatment (Day 0); during treatment (Day 1-7).

6. Conclusion

Although new medication and topical applications are used with good results in the management of AR, there are cases in which complete resolution of symptoms cannot be obtained. Moreover, the use of drugs is not suitable for pregnant and breast-feeding women. Phototherapy is a safe and promising therapeutic modality for AR. Accumulating evidence supports that phototherapy suppresses the effector phase and results in significant improvement of clinical symptoms of AR. By applying FIR therapy to the nasal region in the patients with AR, our study demonstrated that FIR therapy could improve the clinical symptoms of eye itching, nasal itching, nasal stuffiness, rhinorrhea and sneezing significantly during period of therapy. Employing phototherapy to bilateral Shangyingxiang Xue (an acupoint at the upper end of nasolabial fold) at 660 and 850 nm, symptom scores of AR had all significantly decreased in the treating group. In addition to UV and visible light, phototherapy with FIR and red light irradiation can improve the symptoms of AR and may serve as a novel modality in the treatment of AR.

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8. References

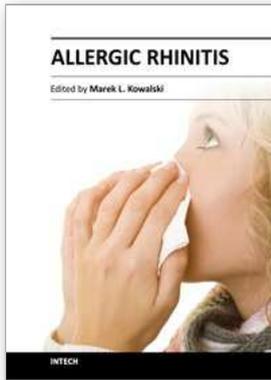
Akasaki, Y., Miyata, M., Eto, H., Shirasawa, T., Hamada, N., Ikeda, Y., Biro, S., Otsuji, Y. & Tei, C. (2006). Repeated Thermal Therapy Up-Regulates Endothelial Nitric Oxide

- Synthase and Augments Angiogenesis in a Mouse Model of Hindlimb Ischemia. *Circulation Journal*, Vol.70, No.4, pp. 463-470
- Akdis, C.A. & Blaser, L. (2003). Histamine in the Immune Regulation of Allergic Inflammation. *The Journal of Allergy and Clinical Immunology*, Vol.112, No.1, pp. 15-22
- Al Suleimani, Y.M. & Walker, M.J. (2007). Allergic rhinitis and its pharmacology. *Pharmacology and Therapeutics*, Vol.114, No.3, pp. 233-260
- Amat, A., Rigau, J., Waynant, R.W., Ilev, I.K. & Anders, J.J. (2006). The Electric Field Induced by Light can Explain Cellular Responses to Electromagnetic Energy: A Hypothesis of Mechanism. *Journal of Photochemistry and Photobiology B : Biology*, Vol.82, No.2, pp. 152-160
- Berrettini, S., Carabelli, A., Sellari-Franceschini, S., Bruschini, L., Abruzzese, A., Quartieri, F., Sconosciuto, F. (1999). Perennial Allergic Rhinitis and Chronic Sinusitis: Correlation with Rhinologic Risk Factors. *Allergy*, Vol.54, No.3, pp. 242-248
- Bousquet, J., van Cauwenberge, P. & Khaltaev, N. (2001). Allergic Rhinitis and Its Impact on Asthma. *The Journal of Allergy and Clinical Immunology*, Vol.108, Suppl.5, pp. S147-S334
- Brehmer, D. & Schön, M.P. (2011). Endonasal Phototherapy Significantly Alleviates Symptoms of Allergic Rhinitis, But Has A Limited Impact on the Nasal Mucosa Immune Cells. *European Archives of Oto-Rhino-Laryngology*, Vol.268, No.3, pp. 393-399
- Cingi, C., Cakli, H., Yaz, A., Songu, M. & Bal, C. (2010). Phototherapy for Allergic Rhinitis: A Prospective, Randomized, Single-Blind, Placebo-Controlled Study. *Therapeutic Advances in Respiratory Disease*, Vol.4, No.4, pp. 209-213
- Cingi, C., Yaz, A., Cakli, H., Ozudogru, E., Kecik, C. & Bal, C. (2009). The Effects of Phototherapy on Quality of Life in Allergic Rhinitis Cases. *European Archives of Otorhinolaryngology*, Vol.266, No.12, pp. 1903-1908
- Csoma Z., Koreck, A., Ignacz, F., Bor, Z., Szabo, G., Bodai, L., Dobozy, A. & Kemény, L. (2006). PUVA Treatment of the Nasal Cavity Improves the Clinical Symptoms of Allergic Rhinitis and Inhibits the Immediate-type Hypersensitivity Reaction in the Skin. *Journal of Photochemistry and Photobiology B : Biology*, Vol.83, No.1, pp.21-26
- Csoma, Z., Ignacz, F., Bor, Z., Szabo, G., Bodai, L., Dobozy, A. & Kemény, L. (2004). Intranasal Irradiation with the Xenon Chloride Ultraviolet B Laser Improves Allergic Rhinitis. *Journal of Photochemistry and Photobiology B : Biology*, Vol.75, No.3, pp.137-144
- Dykewicz, M.S., Fineman, S., Skoner, D.P., Nicklas, R., Lee, R., Blessing-Moore, J., Li, J.T., Bernstein, I.L., Berger, W., Spector, S. & Schuller, D. (1998). Diagnosis and Management of Rhinitis: Complete Guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. *Annals of Allergy, Asthma and Immunology*, Vol.81, No.5, pp. 478-518
- Fineman, S.M. (2002). The Burden of Allergic Rhinitis : beyond Dollars and Cents. *Annals of Allergy, Asthma and Immunology*, Vol. 88, No.4, pp. S2-S7
- Hallen, S., Oliveberg, M. & Brzezinski, P. (1993). Light-induced Structural Changes in Cytochrome c Oxidase. Measurements of Electrogenic Events and Absorbance Changes. *FEBS Letters*, Vol.318, No.2, pp. 134-138

- Howarth P.H. (1997). Mediators of Nasal Blockage in Allergic Rhinitis. *Allergy*, Vol.52, Suppl.40, pp.12-18
- Hu, K.-H. & Li, W.-T. (2007). Clinical Effects of Far-Infrared Therapy in Patients with Allergic Rhinitis, *Proceedings of the 29th Annual International Conference of the IEEE EMBS*, pp.1479-1482, Lyon, France, August 23-26, 2007.
- Hu, K.-H. & Yan, D.-N. (2009). Clinical Effects of Phototherapy to Shangyingxiang Xue on 31 Patients with Allergic Rhinitis, *Journal of Changchun University of Traditional Chinese Medicine*, Vol.25, No.4, pp 266-267
- Inoué, S. & Kabaya, M. (1989). Biological Activities Caused by Far-Infrared Radiation. *International Journal of Biometeorology*, Vol.33, No.3, pp. 15-150
- Ishibashi, J., Yamashita, K., Ishikawa, T., Hosokawa, H., Sumida, K., Nagayama, M. & Kitamura, S. (2008). The Effects Inhibiting the Proliferation of Cancer Cells by Far-Infrared Radiation (FIR) Are Controlled by the Basal Expression Level of Heat Shock Protein (HSP) 70A. *Medical Oncology*, Vol.25, No.2, pp. 229-237
- Jayasekera, N.P., Toma, T.P., Williams, A. & Rajakulasingam, K. (2007). Mechanisms of Immunotherapy in Allergic Rhinitis. *Biomedicine and Pharmacotherapy*, Vol.61, No.1, pp. 29-33
- Kandolf-Sekulovic, L., Kataranovski, M. & Pavlovic, M.D. (2003). Immunomodulatory Effects of Low-Intensity Near-Infrared Laser Irradiation on Contact Hypersensitivity Reaction. *Photodermatology, Photoimmunology and Photomedicine*, Vol.19, No.4, p.203-212
- Karu, T.I. (2003). Low Power Laser Therapy, In: *Biomedical Photonics Handbook*, T. Vo-Dinh, (Ed.), 48-1-25, CRC Press, ISBN 978-084-9311-16-1, Boca Raton, FL, USA
- Karu, T.I., Pyatibrat, L.V. & Afanasyeva, N.I. (2005). Cellular Effects of Low Power Laser Therapy can Be Mediated by Nitric Oxide. *Lasers in Surgery and Medicine*, Vol.36, No.4, pp. 307-314
- Karu, T.I., Pyatibrat, L.V., Kolyakov, S.F. & Afanasyeva, N.I. (2005). Absorption Measurements of a Cell Monolayer Relevant to Phototherapy: Reduction of Cytochrome c Oxidase under Near IR Radiation. *Journal of Photochemistry and Photobiology B : Biology*, Vol.81, No.2, pp. 98-106
- Karu, T.I., Pyatibrat, L.V., Kolyakov, S.F. & Afanasyeva, N.I. (2008). Absorption Measurements of Cell Monolayers Relevant to Mechanisms of Laser Phototherapy: Reduction or Oxidation of Cytochrome c Oxidase under Laser Radiation at 632.8 nm. *Photomedicine and Laser Surgery*, Vol.26, No.6, pp. 593-599
- Kemény, L. & Koreck, A. (2007). Ultraviolet Light Phototherapy for Allergic Rhinitis. *Journal of Photochemistry and Photobiology B : Biology*, Vol.87, No.1, pp.58-65
- Koreck, A., Csoma, Z., Boros-Gyevi, M., Ignacz, F., Bodai, L., Dobozy, A., Kemeny, L. (2004). Inhibition of Immediate Type Hypersensitivity Reaction by Combined Irradiation with Ultraviolet and Visible Light. *Journal of Photochemistry and Photobiology B : Biology*, Vol.77, No.1-3, pp.93-96
- Koreck, A., Szechenyi, A., Morocz, M., Cimpean, A., Bella, Zs., Garaczi, E., Raica, M., Olariu, T.R., Rasko, I. & Kemény, L. (2007). Effects of Intranasal Phototherapy on Nasal Mucosa in Patients with Allergic Rhinitis. *Journal of Photochemistry and Photobiology B : Biology*, Vol.89, No.2-3, pp.163-169
- Koreck, A.I., Csoma, Z., Bodai, L., Ignacz, F., Kenderessy, A.S., Kadocsa, E., Szabo, G., Bor, Z., Erdei, A., Szony, B., Homey, B., Dobozy, A. & Kemény, L. (2005).

- Rhinophototherapy : A New Therapeutic Tool for the Management of Allergic Rhinitis. *The Journal of Allergy and Clinical Immunology*, Vol.115, No.3, pp. 541-547
- Koreck, A.L., Csoma, Z., Bodai, L., Ignacz, F., Kenderessy, A.S., Kadocsa, E., Szabo, G., Bor, Z., Erdei, A., Szony, B., Homey, B., Dobozy, A. & Kemeny, L. (2005). Rhinophototherapy: A New Therapeutic Tool for the Management of Allergic Rhinitis. *The Journal of Allergy and Clinical Immunology*, Vol.115, No.3, pp. 541-547
- Lin, C.C., Chang, C.F., Lai, M.Y., Chen, T.W., Lee, P.C., Yang, W.C. (2007). Far-Infrared Therapy: A Novel Treatment to Improve Access Blood Flow and Unassisted Patency of Arteriovenous Fistula in Hemodialysis Patients. *Journal of the American Society of Nephrology*, Vol.18, No.3, pp. 985-992
- Lin, C.C., Liu, X.M., Peyton, K., Wang, H., Yang, W.C., Lin, S.J. & Durante, W. (2008). Far Infrared Therapy Inhibits Vascular Endothelial Inflammation via the Induction of Heme Oxygenase-1. *Arteriosclerosis, Thrombosis, and Vascular Biology*, Vol.28, No.4, pp. 739-745
- Lin, F., Josephs, S.F., Alexandrescu, D.T., Ramos, F., Bogin, V., Gammill, V., Dasanu, C.A., De Necochea-Campion, R., Patel, A.N., Carrier, E. & Koos, D.R. (2010). Lasers, Stem Cells, and COPD. *Journal of Translational Medicine*, Vol.8, No.16, pp. 1-10
- Linder, A. (1988) Symptom Scores as Measures of the Severity of Rhinitis. *Clinical and Experimental Allergy*, 1988, Vol.18, No.1, pp. 29-37
- Lubart, R., Eichler, M., Lavi, R., Friedman, H. & Shainberg, A. (2005). Low-energy Laser Irradiation Promotes Cellular Redox Activity. *Photomedicine and Laser Surgery*, Vol.23, No.1, pp. 3-9
- Morita, A., Weiss, M. & Maeda, A. (2008) Recent Developments in Phototherapy: Treatment Methods and Devices. *Recent Patents on Inflammation and Allergy Drug Discovery*, Vol.2, No.2, pp. 105-108
- Naclerio, R., Rosenwasser, L. & Ohkubot, K. (2002). Allergic Rhinitis: Current and Future Treatments. *Clinical and Experimental Allergy Reviews*, Vol.2, No.4, pp. 137-147
- Neuman, I. & Finkelstein, Y. (1997). Narrow-band Red Light Phototherapy in Perennial Allergic Rhinitis and Nasal Polyposis. *Annals of Allergy, Asthma and Immunology*, Vol.78, No.4, pp.399-406
- Ng, D.K., Chow, P.Y., Ming, S.P., Hong, S.H., Lau, S., Tse, D., Kwong, W.K., Wong, M.F., Wong, W.H., Fu, Y.M., Kwok, K.L., Li, H. & Ho, J.C. (2004) A Double-Blind, Randomized, Placebo-Controlled Trial of Acupuncture for The Treatment of Childhood Persistent Allergic Rhinitis. *Pediatrics*, Vol.114, No.5, pp.1242-1247
- Okuda, M., Watase, T., Mezawa, A. & Liu, C.M. (1988). The Role of Leukotriene D4 in Allergic Rhinitis. *Annals of Allergy*, Vol.60, No.6, pp.537-540
- Oppenheimer, J.J. & Casale, T.B. (2002). Next Generation Antihistamines: Therapeutic Rationale, Accomplishments and Advances. *Expert Opinion on Investigational Drugs*, Vol.11, No.6, pp. 807-8174
- Pipet, A., Botturi, K., Pinot, D., Vervloet, D. & Magnan, A. (2009). Allergen-specific immunotherapy in allergic rhinitis and asthma. Mechanisms and proof of efficacy. *Respiratory Medicine*, Vol.103, No.6, pp. 800-812
- Quraishi, S.A., Davies, M.J. & Craig, T.J. (2004). Inflammatory Responses in Allergic Rhinitis : Traditional Approaches and Novel Treatment Strategies, *The Journal of the American Osteopathic Association*, Vol.104, Suppl.5, pp.S7-S15

- Rau, C.S., Yang, J.C., Jeng, S.F., Chen, Y.C., Lin, C.J., Wu, C.J., Lu, T.H. & Hsieh, C.H. (2011). Far-Infrared Radiation Promotes Angiogenesis in Human Microvascular Endothelial Cells via Extracellular Signal-Regulated Kinase Activation. *Photochemistry and Photobiology*, Vol. 87, No. 2, pp. 441-446
- Salib, R.J., Drake-Lee, A. & Howarth, P.H. (2003). Allergic Rhinitis : Past, Present and the Future. *Clinical Otolaryngology*, Vol.28, No.4, pp. 201-303
- Skoner, D.P. (2000). Complications of Allergic Rhinitis. *The Journal of Allergy and Clinical Immunology*, Vol.105, No.6, pp. S605-S609
- Su, L.H., Wu, K.D., Lee, L.S., Wang, H. & Liu, C.F. (2009). Effects of Far Infrared Acupoint Stimulation on Autonomic Activity and Quality of Life in Hemodialysis Patients. *The American Journal of Chinese Medicine*, Vol.37, No.2, pp. 215-226
- Toyokawa, H., Matsui, Y., Uhara, J., Tsuchiya, H., Teshima, S., Nakanishi, H., Kwon, A.H., Azuma, Y., Nagaoka, T., Ogawa, T. & Kamiyama, Y. (2003). Promotive Effects of Far-Infrared Ray on Full-Thickness Skin Wound Healing in Rats. *Experimental Biology and Medicine (Maywood)*, Vol.228, No.6, pp. 724-729
- van Cauwenberge, P., Bachert, C., Passalacqua, G. Bousquet, J., Canonica, G.W., Durham, S.R., Fokkens, W.J., Howarth, P.H., Lund, V., Malling, H.J., Mygind, N., Passali, D., Scadding, G.K. & Wang, D.Y. (2000). Consensus Statement on the Treatment of Allergic Rhinitis. European Academy of Allergology and Clinical Immunology. *Allergy*, Vol.55, No.2, pp. 116-134
- Vladimirov, Y.A., Osipov, A.N. & Klebanov, G.I. (2004). Photobiological Principles of Therapeutic Applications of Laser Radiation. *Biochemistry (Mosc)*, Vol.69, No.1, pp. 81-90
- Weiner, J. M., Abramson, M.J. & Puy, R.M. (1998). Intranasal Corticosteroids versus Oral H₁ Receptor Antagonists in Allergic Rhinitis, Systemic Review of Randomized Controlled Trials. *British Medical Journal*, Vol.317, No.7173, pp. 1624-1629
- Wilson, A.M., Sims, E.J., McFarlane, L.C. & Lipworth, B.J. (1998). Effects of Intranasal Corticosteroids on Adrenal, Bone, and Blood Markers of Systemic Activity in Allergic Rhinitis. *The Journal of Allergy and Clinical Immunology*, Vol.102, No.4, pp. 598-604
- Xue, C.C., English, R., Zhang, J.J., Da Costa, C. & Li, C.G. (2002). Effect of Acupuncture in the Treatment of Seasonal Allergic Rhinitis: A Randomized Controlled Clinical Trial. *The American Journal of Chinese Medicine*, Vol.30, No.1, pp. 1-11
- Yu, S.Y., Chiu, J.H., Yang, S.D., Hsu, Y.C., Lui, W.Y. & Wu, C.W. (2006). Biological Effect of Far-Infrared Therapy on Increasing Skin Microcirculation in Rats. *Photodermatology, Photoimmunology and Photomedicine*, Vol.22, No.2, pp.78-86
- Zhang, C.S., Yang, A.W., Zhang, A.L., Fu, W.B., Thien, F.U., Lewith, G., Xue, C.C. (2010). Ear-acupressure for Allergic Rhinitis: A Systematic Review. *Clinical Otolaryngology*, Vol.35, No.1, pp. 6-12



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Allergic rhinitis, while troublesome for a patient, may be also a challenge for the physician. That is why physicians must still learn more on the pathophysiology, clinical spectrum and novel diagnostic and therapeutic approaches to the disease. The chapters of this volume address a variety of important topics related to allergic rhinitis. They begin with a description of innovative translational approaches allowing for unification of animal and human models. Contributing authors provide up-to-date reviews of clinical aspects of allergic rhinitis in children, its association with bronchial asthma and other co-morbid conditions. They also discuss the impact of allergic rhinitis on sleep and sports. Together with articles on diagnostic approaches as well as novel treatments, the book offers a comprehensive and stimulating review of the topic. May this book find a wide readership among allergists and other physicians interested in allergic disease, and also among pediatricians, general practitioners and other specialists who increasingly have to deal with this seemingly benign, but sometimes extremely troublesome, disease.

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