DECLARATION OF ROGER LOPEZ

I, Roger Lopez, pursuant to 28 U.S.C. § 1746 and 37 C.F.R. § 1.68, hereby declare as follows:

1. I am a Translator for Morningside Translations.

2. I submit this declaration to certify the accuracy of the English translation of Kong et al., *Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis*, 19:5 J. Clinical Otorhinolaryngol 214 (Mar. 2005).

3. I am qualified to perform Chinese to English translations and certify the accuracy of Chinese to English translations.

4. My statements are based on personal knowledge and my review of Kong et al., *Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis*, 19:5 J. Clinical Otorhinolaryngol 214 (Mar. 2005) and its Chinese to English translation. If called as a witness about the facts contained in these statements, I could testify competently based on such personal knowledge and the investigation I have conducted.

5. Attached as **Exhibit A** is a true and accurate copy of Kong et al., *Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis*, 19:5 J. Clinical Otorhinolaryngol 214 (Mar. 2005).

6. Attached as **Exhibit B** is a true and accurate copy of an English translation of Kong et al., *Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis*, 19:5 J. Clinical Otorhinolaryngol 214 (Mar. 2005) (hereinafter, "Kong Translation"), which I prepared based on Exhibit A and my personal knowledge of the Chinese and English languages.

NEURENT 1074

7. Kong Translation is a true and accurate translation of Kong et al., *Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis*, 19:5 J. Clinical Otorhinolaryngol 214 (Mar. 2005) from Chinese to English.

8. All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true.

9. I have been warned and am aware that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001.

10. I understand that by submitting this declaration I may be asked to appear for a deposition asking me questions limited to the material in my declaration. With my signature below, I agree to make reasonable efforts to make myself available for such a deposition at a reasonable place and time.

* * *

I declare under the penalty of perjury that the foregoing is true and correct. Executed on December 7, 2023 in Missouri.

Roger Lopez

Roger Lopez

Exhibit A

J Clin Otorhinolaryngol (China), Mar 2005, Vol 19, No 5

等离子低温消融下鼻甲治疗常年性变应性鼻炎

孔勇刚[1] 盛建飞[1] 陶泽璋[1] 吴玉珍[1]

[摘要] **目的**:观察低温消融等离子体手术系统在治疗常年性变应性鼻炎中的作用。**方法**:鼻腔表面麻醉和下鼻甲黏膜下浸润麻醉后,应用鼻内镜对35例常年性变应性鼻炎患者的下鼻甲进行打孔消融治疗。**结果**:随访6个月以上,总有效率为94.3%(33/35),显效率为85.7%(30/35)。**结论**:等离子低温消融下鼻甲治疗常年性变应性鼻炎近期效果良好,操作简单,安全可靠,有较好的临床应用价值。

[关键词] 鼻炎,变应性,常年性;消融术

[中图分类号] R765.21 [文献标志码] A [文章编号] 1001-1781(2005)05-0214-02

Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis

KONG Yonggang SHENG Jianfei TAO Zezhang WU Yuzhen

(Department of Otolaryngology-Head and Neck Surgery, People's Hospital of Wuhan University, Wuhan, 430060, China)

Abstract **Objective**: To study the effect of radiofrequency ablation on perennial allergic rhinitis. **Method**: Thirty-five cases of perennial allergic rhinitis undergone the treatment in radiofrequency blation were study. **Result**: All patients were followed more than 6 months, total effective rate is 94.3%(33/35). Among the total, excellence is 85.7%(30/35). **Conclusion**: The radiofrequency ablation is a simple and safe instrument to treat perennial allergic rhinitis.

Key words Rhinitis, allergic, perennial; Radiofrequency

2003年3月～2004年4月,我科在鼻内镜下应用低温消融等离子体手术系统行下鼻甲打孔治疗常年性变应性鼻炎35例,取得较满意的疗效,现介绍如下。

1 资料与方法

1.1 临床资料

35例中,男15例,女20例;年龄16～50岁,平均34岁。病程6个月～10年。均有阵发性鼻痒、连续性打喷嚏、流清涕、鼻塞等症状,检查可见下鼻甲黏膜苍白水肿,鼻腔有清水样分泌物,符合变应性鼻炎诊断标准(1997年,海口)。全部患者均接受减充血剂、口服抗组胺药或外用类固醇皮质激素等系统治疗3个月以上,症状无明显改善。

1.2 手术方法

鼻腔1%丁卡因喷雾表面麻醉,双侧下鼻甲黏膜下1%利多卡因5ml浸润麻醉。选用4 mm外径0°鼻内镜(桐庐尖端天松牌)及ENTec等离子体手术系统(美国杰西公司)Hummingbird或ReFlex 45型射频电极,设定主机能量为6级,在打每个孔之前,将射频电极浸入生理盐水中,以确保消融组织时能形成等离子体薄层。打孔的位置选在下鼻甲下缘或内侧缘,根据下鼻甲的大小,将下鼻甲分为前后两部分或前中后三部分,每部分打1～2个孔。将射频电极插入下鼻甲,沿其长径方向在黏膜下推进至适当的深度(约1.5～2.0 cm);当打孔至所需深度后,射频电极保持不动,继续踩住切割踏板约10 s,继而停止激活射频电极,缓慢抽出电极。术后无需鼻腔填塞,进针处可适当覆盖明胶海绵,口服抗生素和鼻腔滴用减充血剂1周。

2 结果

全部病例均在10～15 min内完成手术,出血量约5～10 ml。术后第1天,手术部位开始有伪膜生成,下鼻甲肿胀,鼻腔通气欠佳,鼻腔有黏性分泌物。1周后清理鼻腔,伪膜不再生成,肿胀逐步减轻,分泌物减少,打喷嚏、流清水样涕症状改善,5例患者1周～1个月内针孔处少量结痂。术后1周、4周、3个月、6个月各随访1次,根据变应性鼻炎疗效评定标准(1997年,海口),6个月后显效30例,好转3例,效果不明显2例,总有效率为94.3%。未见手术并发症发生,无其他不适。

3 讨论

目前对于变应性鼻炎发病机制的研究已超出传统的特异型IgE介导的Ⅰ型变态反应范畴,集中到炎性递质、神经递质、细胞因子、内分泌水平,从而为变应性鼻炎新的治疗方法提供了理论依据[1]。

变应性鼻炎治疗的核心是在尽量避免与变应原接触的基础上,采用免疫治疗或抗组胺药物、肥大细胞稳定剂、类固醇激素联合式交替用药[1]。如疗效不满意可采用手术治疗,其主要原理是通过切除部分副交感神经纤维和下鼻甲微神经节及副交

[1]武汉大学人民医院耳鼻咽喉-头颈外科(武汉,430060)
通讯作者:孔勇刚(Email: kongyonggang@hotmail.com)

感丛致乙酰胆碱分泌和 P 物质释放减少，降低感觉神经敏感性从而降低血管通透性，减少腺体分泌。并使其对外界的物理、化学不良刺激敏感性降低，血管活性肽的分泌减少，抑制喷嚏反射，减少鼻涕，改善鼻腔通气，达到治疗常年性变应性鼻炎的目的[2]。山本一博对下鼻甲黏膜神经肽的分布研究发现，变应性鼻炎患者下鼻甲前方基底膜部有植物神经通过[3]，为变应性鼻炎下鼻甲手术治疗的依据之一。

低温消融的原理是利用双极射频所产生的能量，将射频电极与组织之间的电解液转换成等离子体的离子蒸汽层[4]。等离子体中的带电粒子使目标组织中的细胞以分子为单位逐渐解体，使鼻腔黏膜、黏膜下组织蛋白质凝固变性，腺体萎缩，血管封闭，从而减少肥大细胞脱颗粒过程（减少组胺的释放），破坏下鼻甲内胆碱能微神经节及来自该神经节后副交感神经纤维、鼻部无髓鞘性感觉神经纤维（SP 能神经）和来自翼管神经和筛前神经的副交感神经末梢，降低神经末梢的敏感性，减少腺体分泌量，改善鼻腔通气。由于这种效应局限于目标组织的表层，而且是在相对较低的温度下实现的，对周边组织的热损伤降至最小程度，可以达到既去除目标组织又引起组织收缩的双重效果。与激光、微波、切割器相比，此方法具有对下鼻甲损伤小，疼痛轻微，术后恢复快，术后基本无需护理等优点。

麻醉时，尽量不收缩鼻甲，每侧下鼻甲黏膜下浸润液体量为 5 ml，是为了让黏膜有一定的厚度，并在局部形成良好的导电层，打孔时易插入并易使离子刀保持在黏膜下，减少对黏膜的损伤。但同时也缩小了术野，增加了手术难度，故操作者要有一定的内镜手术基础。

参考文献

1 卜国铉. 鼻科学. 第 2 版. 上海：上海科学技术出版社，2000. 434－436.

2 Lin H C, Lin P W, Su C Y, et al. Radiofrequency for the treatment of allergic rhinitis refractory to medical therapy. Laryngoscope, 2003, 113: 673－678.

3 贵平，梁伟平，周水森. 变应性鼻炎的外科治疗. 国外医学耳鼻咽喉科学分册，2004，28(2)：95－98.

4 邓湖山，戴宪国，张志茂，等. 等离子低温消融治疗腺样体肥大. 华中医学杂志，2003，27(4)：211－212.

（收稿日期：2004-11-05）

微波在下鼻甲部分切除术中的应用

刘宗尚[1] 楚选云[1] 朱丽[2]

［关键词］ 微波；鼻炎，肥厚性；下鼻甲部分切除术
［中图分类号］ R454.1 ［文献标志码］ B ［文章编号］ 1001-1781(2005)05-0215-01

我科自 1997 年 9 月起对 1 500 例慢性肥厚性鼻炎患者行下鼻甲部分切除术后，应用微波处理创面，取得了很好的疗效。现报告如下。

1 资料与方法

1 500 例患者中，男 788 例，女 712 例；年龄 12～65 岁，平均 25 岁。

用 1%利多卡因注射液加入少许肾上腺素注射液（每 10 ml 1%利多卡因加入 0.1%肾上腺素 3 滴），局部麻醉生效后施行双侧下鼻甲部分切除术，术中切除下鼻甲后下端部分不超过 1/3。将鼻腔血性物质清除后，用微波烧灼下鼻甲创面，采取自创面后端向前端烧灼的方法（如果从前向后烧灼，有可能使靠后的创面发生遗漏），创面烧灼后局部留下黑色结痂，与未烧灼部分界限清楚。对侧下鼻甲创面用同样的方法处理。

2 结果

1 486 例术后未发生出血，伤口Ⅰ期愈合，术后 2 周复查，创面愈合时间与传统填塞方法相比无明显差异。14 例患者术后发生鼻腔渗血，当时将鼻腔内淤血清除干净，喷入 1%丁卡因及 1%麻黄素液对创面进行麻醉、止血，再次应用微波处理出血部位，8 例患者应用微波处理后同时将明胶海绵贴敷于创面上，外面再填入棉片支撑。14 例最终Ⅰ期愈合。

3 讨论

传统的鼻腔填塞方法给患者带来很大痛苦，表现为鼻腔填塞期间双侧鼻腔不能通气，头痛，牙痛，溢泪，患者一直用嘴呼吸，睡眠质量降低。应用微波烧灼创面后免去了鼻腔填塞，使患者术后即能用鼻呼吸，恢复了正常呼吸通道，提高了睡眠质量，避免了换药时抽纱条给患者带来的痛苦，减轻了患者的经济负担。

（收稿日期：2004-04-05）

[1] 南阳市第一人民医院耳鼻咽喉科（河南南阳，473010）
[2] 中国建筑第七工程局职工医院五官科
通讯作者：刘宗尚

Exhibit B

Low-temperature plasma ablation of inferior turbinate for the treatment of perennial allergic rhinitis

Kong Yonggang[1], Sheng Jianfei[1], Tao Zezhang[1], Wu Yuzhen[1]

[Abstract] Objective: To observe the role of low-temperature ablation plasma surgery system in the treatment of perennial allergic rhinitis. **Method:** After surface anesthesia of the nasal cavity and submucosal infiltration anesthesia of the inferior turbinate, 35 patients with perennial allergic rhinitis were treated with endoscopic ablation of the inferior turbinate. **Results:** The patients were followed up with for more than 6 months, and the total effective rate was 94.3% (33/35), and the excellent rate was 85.75% (30/35). **Conclusion:** With a good short-term effect, low-temperature plasma ablation of the inferior turbinate in the treatment of perennial allergic rhinitis is simple in operation, and safe and reliable, and has high clinical application values.

[Keywords] Rhinitis, allergic, perennial; Ablation

[Chinese Library Classification No.]R765.21 **[Document Code]** A **[Article No.]** 1001-1781(2005)05-0214-02

Clinical observation on radiofrequency ablation treatment in perennial allergic rhinitis

KONG Yonggang SHENG Jianfei TAO Zezhang WU Yuzhen

(Department of Otolaryngology-Head and Neck Surgery, People's Hospital of Wuhan University, Wuhan, 430060, China)

Abstract Objective: To study the effect of radiofrequency ablation on perennial allergic rhinitis. **Method:**Thirty-five cases of perennial allergic rhinitis underwent the treatment in radiofrequency ablation were studied. **Result:**All patients were followed up for more than 6 months, the total effective rate was 94.3% (33/35). Among the total, and the excellence rate was 85.7% (30/35). **Conclusion:**The radiofrequency ablation is a simple and safe instrument to treat perennial allergic rhinitis.

Key words Rhinitis, allergic, perennial; Radiofrequency

From March 2003 to April 2004, low-temperature ablation plasma surgical system under nasal endoscopy was used in our department to treat 35 cases of perennial allergic rhinitis using inferior turbinate perforation and achieving satisfactory results. Now, the technique is reported as follows.

1 Data and Methods

1.1 Clinical data

Among the 35 patients, there were 15 males and 20 females aged from 16 to 50 years at an average age of 34 years. The course of the disease was 6 months to 10 years. All the patients had symptoms such as paroxysmal nasal itching, persistent sneezing, clear nasal discharge, and nasal congestion. Examination showed pale and swollen mucosa of the inferior turbinate, with clear, water-like secretion in the nasal cavity, which complied with the diagnostic criteria for allergic rhinitis (Haikou, 1997). All the patients received systemic treatments such as decongestants, oral antihistamines, or topical corticosteroids for more than 3 months, with no significant improvement in the symptoms.

1.2 Surgical methods

Surface anesthesia was carried out with 1% tetracaine spray in the nasal cavity, and infiltration anesthesia was carried out with 5 ml of 1% lidocaine under the bilateral inferior turbinate mucosa. One 0° nasal endoscope (TongluJianduanTiansong brand) with an outer diameter of 4 mm and a Hummingbird or ReFlex 45 RF electrode of ENTec plasma surgical system (Jesse Company, USA) was selected, the host energy was set to grade 6, and the RF electrode was immersed in the physiological saline before making each hole to ensure the formation of a plasma-thin layer during tissue ablation. The location for making the holes was selected at the lower or medial edge of the inferior turbinate. According to the size of the inferior turbinate, the inferior turbinate was divided into two parts, i.e., the anterior and posterior part, or three parts, i.e., the anterior, middle, and posterior part, with 1-2 holes made in each part. The RF electrode was inserted into the inferior turbinate and pushed along the longitudinal direction to an appropriate depth (approximately 1.5-2.0 cm) under the mucosa; after making the hole to the required depth, the RF electrode remained stationary, and the cutting pedal was pressed and held continually for about 10 seconds, then, the RF electrode was deactivated, and the electrode was slowly removed. After the surgery, nasal tamponade was not needed. The access site could be appropriately covered with gelatin sponge, and oral antibiotics and nasal drops of decongestant were given for one week.

2 Results

The surgery for all the patients was completed within 10-15 minutes, and the blood loss was approximately 5-10 ml. On the first day after the surgery, there was pseudomembranous formation at the surgical site, swelling of the inferior turbinate, poor nasal ventilation, and sticky secretions in the nasal cavity. One week later, the nasal cavity was cleared, and pseudomembrane was no longer formed, the swelling was gradually relieved, the secretion was decreased, and the symptoms of sneezing and watery discharge were improved. In 5 patients, a small number of scabs were formed at the hole site within one week to one month. The patients were followed up with once every 1 week, 4 weeks, 3 months, and 6 months after the surgery. According to the evaluation criteria for the efficacy of allergic rhinitis (Haikou, 1997), 30 patients showed significant improvement, 3 patients showed improvement, and 2 patients showed no significant effect after 6 months. The total effective rate was 94.3%. No surgical complications or other discomfort were observed.

3 Discussions

Nowadays, studies on the pathogenesis of allergic rhinitis have gone beyond the conventional category of Type I allergic reactions mediated by specific IgE, focusing on the levels of inflammatory transmitters, neurotransmitters, cytokines, and endocrine systems and thus providing a theoretical basis for new treatments for allergic rhinitis.[1]

The core of treating allergic rhinitis is to use immunotherapy or a combination of antihistamines, mast cell stabilizers, and steroid hormones, alternately, while avoiding contact with allergens as much as possible.[1] If the therapeutic effect is not satisfactory, surgical treatment can be used. The main principle is to reduce acetylcholine secretion and substance P release by removing some parasympathetic nerve fibers, the inferior turbinate microganglia, and the

[1]Department of Otolaryngology-Head and Neck Surgery, People's Hospital of Wuhan University, Wuhan, 430060, China
Corresponding Author: Kong Yonggang (Email: kongyonggang@hotmail.com)

parasympathetic plexus, thereby reducing the sensory nerve sensitivity and the vascular permeability,reducing the glandular secretion, its sensitivity to external physical and chemical adverse stimuli, and the secretion of vasoactive peptides, inhibiting sneezing reflex, reducing nasal mucus, improving nasal ventilation, and achieving the objective of treating perennial allergic rhinitis.[2]Kazuhiro Yamamoto's study on the distribution of neuropeptides in the mucosa of the inferior turbinate showed that there are vegetative nerves passing through the anterior basal membrane of the inferior turbinate in patients with allergic rhinitis,[3] which is one of the bases for the surgical treatment of the inferior turbinate in allergic rhinitis.

The principle of low-temperature ablation is to use the energy generated by bipolar rf to convert the electrolyte between the rf electrode and the tissues into an ion vapor layer of the plasma.[4]The charged particles in the plasma cause the cells in the target tissues to gradually disintegrate on a molecular basis, causing protein coagulation and denaturation in the nasal mucosa and submucosal tissues, gland atrophy, and vascular closure, thereby reducing the degranulation process of mast cells (reducing the release of histamine), damaging the cholinergic microganglia and parasympathetic nerve fibers from the inferior turbinate, the unmyelinated sensory nerve fibers (SP energy nerves) and parasympathetic nerve endings from the pterygoid and anterior ethmoidal nerves in the nose, reducing the sensitivity of nerve endings, reducing gland secretion, and improving nasal ventilation. As this effect is limited to the surface layer of the target tissues and is achieved at relatively low temperatures, the thermal damage to the surrounding tissues is minimized, achieving a dual effect of both removing the target tissues and causing tissue shrinkage. Compared with lasers, microwaves, and shavers, this method has the advantages of minimal damage to the inferior turbinate, mild pain, fast postoperative recovery, and minimal postoperative care.

During anesthesia, the turbinate is not contracted as much as possible. The amount of liquid infiltration under the mucosa on each side of the inferior turbinate is 5 ml in order to make the mucosa have a certain thickness and form a good conductive layer locally. When punching, it is easy to insert and keep the plasma knife under the mucosa, reducing damage to the mucosa. But at the same time, the surgical field of view is also reduced, and the difficulty of surgery is increased, so the operators need to have a certain foundation in endoscopic surgery.

References

1. Bu Guoxuan. Nasal Science, 2nd Edition, Shanghai: Shanghai Scientific & Technical Publishers, 2000, 434-436.
2. Lin H C, Lin P W, Su C Y, et al. Radiofrequency for the treatment of allergic rhinitis refractory to medical therapy. Laryngoscope, 2003, 113:673-678.
3. Gui Ping, Liang Weiping, Zhou Shuisen. Surgical treatment of allergic rhinitis. Otolaryngology Foreign Medical Sciences, 2004, 28(2):95-98.
4. Deng Hushan, Dai Xianguo, Zhang Zhimao, et al. Low-temperature plasma ablation for the treatment of adenoid hypertrophy. Central China Medical Journal, 2003, 27(4):211-212.

(Received on: November 5, 2004)

Use of microwave in partial resection of inferior turbinate

Liu Zongshang[1], Chu Xuanyun[1], Zhu Li[2]

[Keywords] Microwave; Rhinitis, hypertrophic; Partial resection of inferior turbinate
[Chinese Library Classification No.] R454.1 **[Document Code]** B **[Article No.]** 1001-1781(2005)05-0215-01

Since September 1997, 1,500 patients with chronic hypertrophic rhinitis were treated with partial resection of the inferior turbinate in our department and received microwave treatment of the wound surface, with good results achieved. Now, a report is given as follows.

1 Data and Methods

In the 1,500 patients, there were 788 males and 712 females, aged at 12 - 65 years, with the mean age being 25 years.

A small amount of adrenaline injection was added into 1% lidocaine injection (3 drops of 0.1% adrenaline added into every 10 ml of 1% lidocaine), and bilateral partial turbinectomy was performed after the local anesthesia took effect. During the surgery, no more than 1/3 of the lower part of the inferior turbinate was removed. After removing the bloody substances from the nasal cavity, microwave was used to cauterize the wound of the inferior turbinate, using a method of cauterization from the back of the wound to the front (if cauterized from the front to the back, the wound at the back might be neglected). After cauterization of the wound, black scabs were left locally, and the boundary with the unburned part was clear. The wound of the contralateral inferior turbinate was treated using the same method.

2 Results

Among the patients, 1,486 did not experience postoperative bleeding, and the wounds had primary healing. There was no significant difference in the wound healing time at 2 weeks after the surgery compared to conventional tamponade methods.After the surgery, 14 patients experienced nasal bleeding. At that time, the congestion in the nasal cavity was cleared, and 1% tetracaine and 1% ephedrine solution were sprayed onto the wound for anesthesia and hemostasis. The bleeding site was then treated with microwave again, and after treatment with microwave, 8 of the patients had gelatin sponge applied to the wound, which was then supported by cotton pads. The 14 patients ultimately achieved primary healing.

3 Discussions

The conventional nasal tamponade method brings severe pain to patients, manifested as an inability to ventilate on both sides of the nasal cavity during nasal tamponade, headache, toothache, overflow of tears, persistent breathing through the mouth, and decreased sleep quality. The cauterization of the wound surface using microwave eliminates nasal tamponade, allowing patients to breathe through the nose immediately after surgery, restoring the normal breathing channels, improving the sleep quality, avoiding the pain caused by gauze changes, and reducing the patient's economic burden.

(Received on: April 5, 2004)

[1] Department of Otolaryngology, Nanyang First People's Hospital, Nanyang, Henan 473010 P.R. China
[2] Department of Five Organs, Staff Hospital, China Construction Seventh Engineering Bureau
Corresponding Author: Liu Zongshang