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Application of Endoscopic Sinus Surgery to primary atrophic rhinitis? A clinical trial*

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SUMMARY

The aetiology of primary atrophic rhinitis (AR) is still unclear. Based on the sinus infection theories, endoscopic sinus surgery (ESS) was applied to treat AR. ESS was performed on 14 patients following Stammberger's techniques along with middle turbinectomy. Patients were evaluated using clinical symptoms, radiological sinus images, saccharine time tests, bacterial cultures and mucosal ultrastructures, before and 2 years after ESS. Three patients had good recoveries, 6 had partial recoveries and another 5 had persistent disease. Good recovery patients showed clear nasal cavities and mucociliary transport system normalisation. Patients possess in meagre infectious signs or crusting extending to their nasopharynx had poor outcomes. Patients with evidence of obvious infections (cloudy sinus images, mucopus presence in the sinuses and positive culture for Klebsiella ozaenae) had good recoveries following ESS. Candidate selection is critical for the success of ESS treatment in AR. Although further clinical trials are required to prove this strategy.

Key words: atrophic rhinitis, endoscopic sinus surgery

INTRODUCTION

Primary atrophic rhinitis (AR) is a rare disorder of the nose. AR results in chronic nasal crustings, fetid odour and atrophy of the nasal mucosa. The exact aetiology remains unknown and controversial. The following theories hypothesise its pathogenesis: the endocrine theory, the deficiency theory, the developing theory, the reflex sympathetic dystrophy syndrome, the autoimmune imbalance theory, the infective theory and the sinus infection theory (Fouad et al., 1980, Hagrass et al., 1992, Pesti, 1949; Wachsberger, 1934, El-Barbary et al., 1970). The present treatment of AR is unsatisfactory. The beneficial results of various surgical operations such as implantation (Puchelle et al., 1981) and vestibuloplasty (Ghosh, 1987, Young, 1967) are often not sustained after reversal of these procedures (Pace-Balzan et al., 1991). The uncertain response of *Klebsiella ozaenae* to antibiotic treatment makes appropriate antibiotic selection difficult, although, systemic and topical aminoglycosides are reported to have a successful response (Dudley, 1987). Endoscopic sinus surgery (ESS) is used to treat chronic infectious diseases of the paranasal sinuses (Kennedy et al., 1985, Stammberger and Posawetz, 1990). El-Barbary et al. supported the belief that ozaenae is the result of a chronic purulent focus in the nasal cavity or accessory sinuses (El-Barbary et al., 1970). Eggston and Wolff considered that all cases of primary atrophic rhinitis are due to chronic infection (Hagrass et al., 1992). Our hypothesis relies on the infectious theory as the primary explanation for the pathogenesis of some AR patients. After ESS, outcomes were gauged using pre- and post-operative evaluations comparing clinical symptoms, signs and functional morphology of the mucosal epithelium. The application of ESS on carefully selected patients should prove beneficial.

PATIENTS AND METHODS

A total of 20 AR patients were enrolled in this study. Of these, 11 female and 3 male patients ranging in age from 16 to 32 years received ESS. The remaining 6 AR patients (AR controls) were treated with antibiotics for 2 to 6 weeks and local irrigation using normal saline solution. All of the patients had the following characteristics: anosmia, offensive odours, crusting and atrophic changes of their nasal mucosa. Preoperative profiles were administered to each patient which included the following: patient history (to exclude secondary AR), radiological image studies (Plain sinus film or CT scan), saccharine time tests (Stanley et al., 1984), bacterial cultures and recording of their

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symptoms and crustings. ESS was performed under local anaesthesia using the Stammberger technique for chronic sinusitis (Stammberger, 1986) in order to provide good ventilation and drainage for all of the paranasal sinuses. An additional middle turbinectomy was performed (Ssali, 1973). Systemic antibiotics were given for 2 to 6 weeks postoperatively. Once a week, the patients were treated in an outpatient clinic for their follow-ups. Normal saline nasal irrigations were administered twice daily following ESS. No long-term systemic antibiotics or periodic addition of topical antibiotics were administered along with the saline irrigation. Endoscopic findings were recorded and mucosal biopsies were taken at the time of the ESS and 2 years after for ultrastructural studies. Five nasal mucosa biopsies from patients who received rhinoplasty showing no evidence of rhinitis were used as the normal controls. All biopsies were prepared for electron microscopic comparison studies. The surface of the

Table 1. Localisations of crusting on the nasal cavity in the 14 AR patients. The severity of crusting was expressed arbitrarily as 0, none; +, scanty; ++, moderate; +++, severe. GR, good recovery; PR, partial recovery; PD, persistent disease. (n), case number.

	Pre-operation			Post-operation		
	GR (3)	PR (6)	PD (5)	GR (3)	PR (6)	PD (5)
inferior turbinate	+	+++, ++	+++, ++	0	++, +	+++, ++
nasal septum	+++, ++	+++, ++	+++, ++	0	++, +	+++, ++
middle turbinate	+++, ++	++, +	++, +	0	+,0	+
nasopharynx	0	+, 0	+++, ++	0	+,0	+++, ++

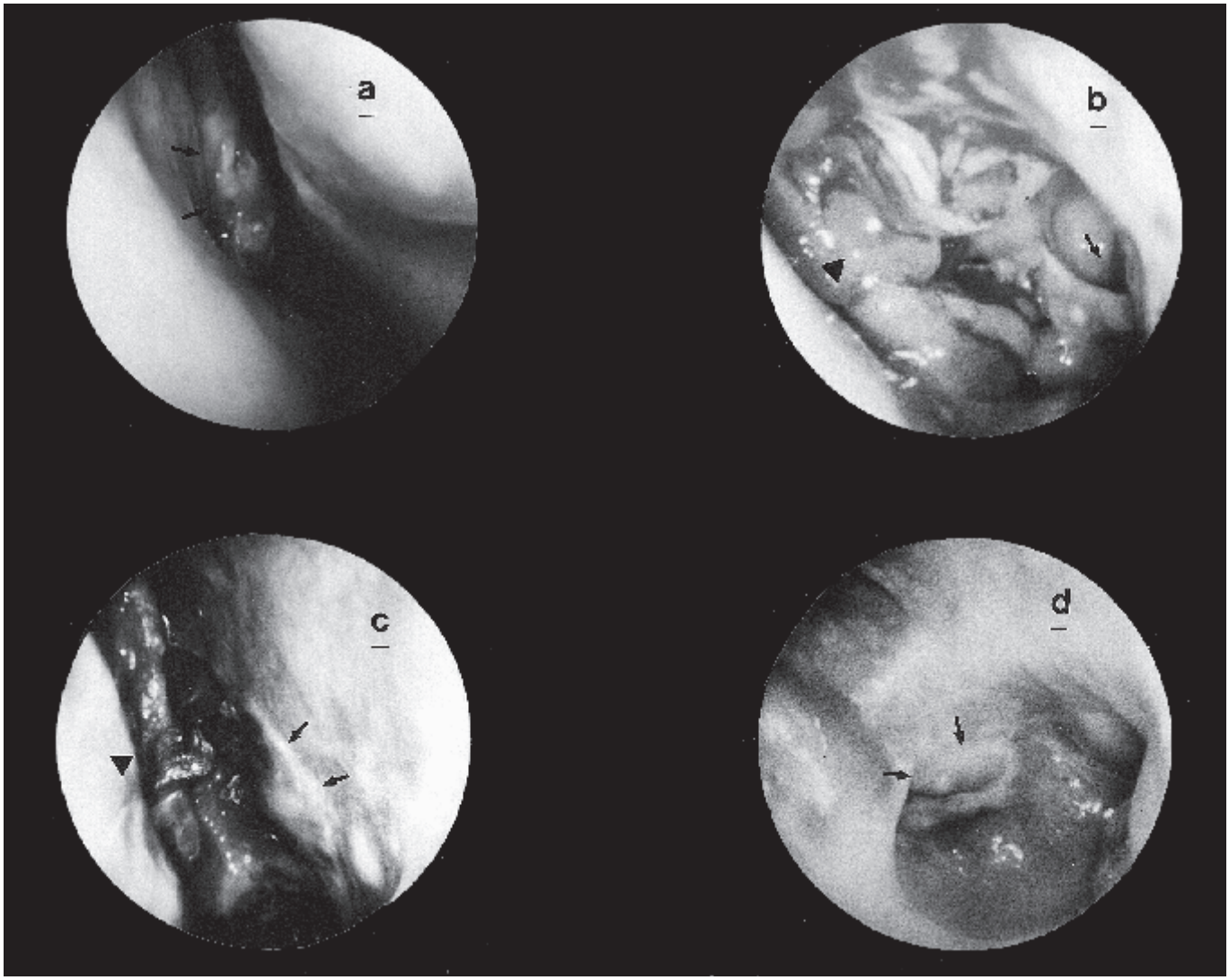

Figure 1. Endoscopic findings of AR patients. (Endoscope, Storz 30°).
a) major crustings on the middle turbinate (→).
b) polypoid ethmoid mucosa (▲) with thick mucopus (→) present in the antrum.
c) severe crustings on the inferior turbinate (→) and septum (▲).
d) crustings extended into the nasopharynx (→).

specimen was analysed using a Hitachi-600 scanning electron microscope (SEM). The goblet and ciliated cells were counted and expressed as a percentage of the total number of epithelial cells counted. A minimum of 500 cells was counted by SEM (× 2000). The gland openings were counted in 15 visual fields by SEM (× 2000) (Fang, 1994). The average of 10 different counting sessions yielded the final score averages for each specimen. Student t-tests were used to compare the groups. All of the postoperative profiles were performed 2 years after ESS. The postoperative results were graded as follows: good recovery group, full resolution of nasal symptoms excluding anosmia and requiring no further irrigations; partial recovery group, improvement of nasal symptoms excluding anosmia and requiring continued nasal irrigations, persistent disease group, no improvement of the nasal symptoms.

RESULTS

After 2 years of postoperative follow-ups, anosmia persisted in all of the AR patients. Of the 14 ESS treated patients, 3 had good recovery, 6 had partial recovery and 5 had persistent disease. One patient from the persisted disease group initially had a good recovery in the l0th month following ESS. This symptom free period lasted for 5 months. However, his condition deteriorated and he came into the persistent disease group following an episode of severe rhinosinusitis. The 6 AR control patients showed no improvement in their clinical symptoms such as crustings and saccharine time tests. The severity and distributional patterns of the nasal crustings (before and after ESS) are described in Table 1. Patients having scanty crustings on their inferior turbinates and major crustings on their middle turbinates (Fig. 1) showed good recoveries. In contrast, patients having severe crustings on their inferior turbinates and/or nasopharyngeal areas (Fig. 1) showed poor improvements following ESS. Clinical findings from the endoscopy, radiological imaging, saccharine time tests and bacterial cultures for *Klebsiella ozaenae* are presented in Table 2. A synechia of the olfactory slit was found in all of the AR patients. The 3 good recovery patients preoperatively presented cloudy maxillary and ethmoid sinus images. Four of the 14 ESS treated patients who presented clear sinus images became persistent disease subjects. During ESS, 7 of the 14 cases possessed turbid, yellowish-green mucopus in their sinuses (Fig. 1). Eleven cases had antral mucosal thickening and the remaining 3 had grossly normal antrums. Eight ESS treated subjects had positive bacterial cultures for *Klebsiella ozaenae.* All 3 good recovery subjects had mucopurulent sinuses and positive cultures preoperatively.

All of the study patients had prolonged saccharine times (>30min) (Sakakura et al., 1983). The 3 good recovery subjects had improvements in their saccharine times following ESS. The partial recovery and persistent disease subjects remained at abnormal levels. Using SEM, squamous metaplasia, cilia degeneration and a significant increase in goblet cell population (Table 3) were identified and characterised the AR nasal epithelium (Fig. 2).

Table 2. The findings of radiological images, endoscopy, saccharine time test and bacteria culture of *Klebsiella ozaenae* in 14 AR patients. GR, good recovery; PR, partial recovery; PD, persistent disease. (n), case number. *, the patient had symptom free period for 5 months.

	Pre-operation			Post-operation		
	GR (3)	PR (6)	PD (5)	GR (3)	PR (6)	PD (5)
synechiae of olfactory slit	3	6	5 (1 *)	3	6	5 (1 *)
cloudiness of sinuses	3	6	1 *	0	6	1 *
thick mucopus	3	3	1 *	0	3	1 *
saccharine time > 30 min	3	6	5 (1 *)	0	6	5 (1 *)
Klebsiella ozaenae	3	2	3 (1*)	0	2	3 (1*)

Figure 2. The mucosa specimen from an AR patient taken during ESS. It shows a loss of cilia, squamous metaplasia and an increase in goblet cell number (→). (SEM×2.0K)

However, using transmission electron microscopy, normal cilia microstructure was noted (Fig. 3). Two years after ESS, the mucosa of good recovery subjects showed areas of cilia regeneration and a decrease in the number of goblet cells towards normal levels (Fig. 4).

Table 3. The cilia cells, goblet cells and gland openings of the mucosa in normal and atrophic rhinitis subjects stated in mean±SED values. ( ) = case number; vf= visual fields; * = significantly different values compared to normal subjects ($p<0.01$).

	Normal	Pre-operative			Post-operative		
		GR (3)	PR (6)	PD (5)	GR (3)	PR (6)	PD (5)
cilia cells (%)	45.2±3.2	2.2±1.3*	3.5±2.1*	1.7±0.6*	39.7±2.1	14.1±1.9'	2.1±0.8*
goblet cells (%)	14.3±2.2	38.5±2.4*	35.9±1.8*	42.2±1.2*	18.7±1.6	37.5±2.6*	38.9±2.1*
gland openings (15 vf)	7.8±1.8	12.4±2.1	5.2±1.8	9.5±0.9	10.9±1.7	6.8±1.4	6.2±1.2

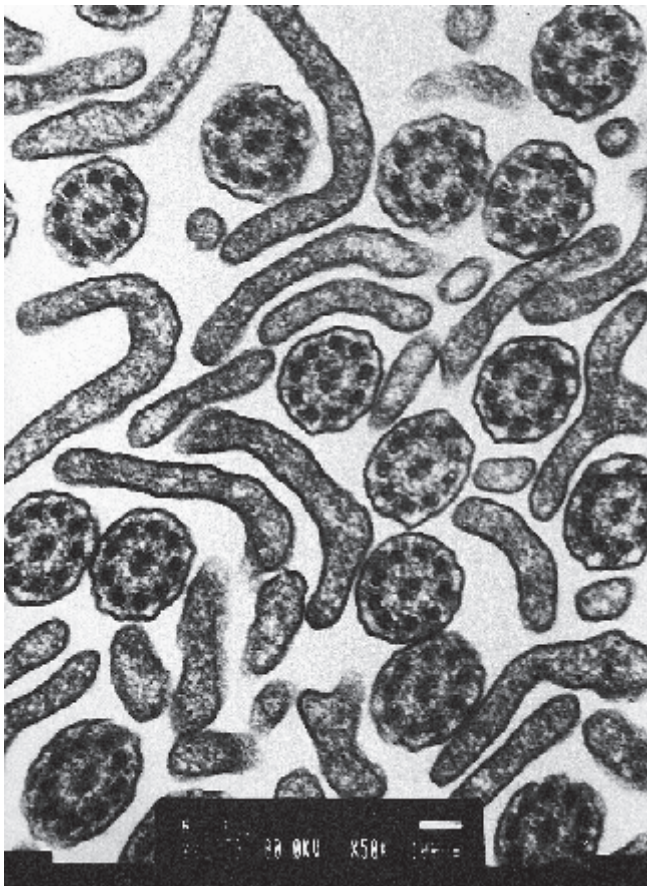

Figure 3. The mucosa specimen from an AR patient taken during ESS showing normal mucosal cilia microstructures. (TEM×50K)

Figure 4. The mucosa specimen from an AR patient who had a good recovery. This was taken 2 years following ESS. It shows cilia regeneration (▲) and normalisation of goblet cell number (→). (SEM×1.2K)

DISCUSSION

All AR subjects following ESS had persistent anosmia. Residual olfactory disorder is due to the permanent destruction of the olfactory mucosa or nasal stenosis (Borgstein et al., 1993). Synechiae of the olfactory slit in AR subjects during endoscopy may explain this result. Patients with severe to moderate crusting on their inferior turbinates and/or extending crusting to their nasopharynx had poor outcomes from ESS treatment. Possessing crustings in areas beyond the nasal cavity may indicate a more progressive stage of AR or show a greater systemic atrophic change resulting from an immunological disorder (Fouad et al., 1980). In contrast, those patients presenting scanty crustings on their inferior turbinates and major crustings on their middle turbinates had better outcomes from ESS treatment. Better outcomes were achieved from subjects having cloudy sinus images or conspicuous mucopus in the sinuses found by endoscopy during surgery when compared to subjects whose sinuses were clear. This suggests that preoperative radiological findings may help select suitable candidates for treatment using ESS while endoscopic findings may indicate their prognosis.

Klebsiella ozaenae is frequently isolated from AR patients. In this study, AR patients were associated with other bacterial infections, commonly, *Staphylococcus aureus, Bacteroides fragilis* and *Prevotella* species. Some authorities believe *Klebsiella ozaenae* isolation is a sinequanon of the diagnosis (Dudley, 1987). *In vitro*, *Klebsiella ozaenae* causes significant cilioinhibitory effects when bacteria-containing broth is placed on ciliated cells (Ferguson et al., 1990). *In vivo, Klebsiella ozaenae's* deleterious effects on cilia occurs when the protective mucous blanket is damaged or injured (Ferguson et al., 1990). This injury may be incited by opportunistic bacteria from the paranasal sinuses or other environmental factors. The injured area is colonised by *Klebsiella ozaenae* along with other opportunistic bacteria which proliferate in the stagnant mucus. An overgrowth of the bacteria and *Klebsiella ozaenae* results in dysfunction of the mucociliary clearance process. The combination of the bacterial proliferation and secretion drying results in crusting and foul odour that typifies AR. Preoperatively, all of the 3 good recovery subjects had positive bacterial cultures for *Klebsiella ozaenae.* Two years after ESS, they were negative implying two possibilities. The first is that ESS creates an aerobic environment that eradicates AR infectious origins including *Klebsiella ozaenae* and other anaerobic favouring bacteria such as *Staphylococcus aureus,* and *Bacteroides fragilis.* The second is that infection by *Klebsiella ozaenae* may prove to play a causative role in these AR subjects. Some reports have shown AR subjects responding well to ciprofloxacin (Nielsen et al., 1995; Borgstein et al., 1993). This evidence supports the infectious theories for a subpopulation of AR patients and lends credibility to the use of ESS in treating AR patients having infectious origins. In addition, the persistent disease patient, who had a 5 month symptom free period, relapsed ensuing severe rhinosinusitis. For this patient, infection may also play a significant role in the persistence of his AR. Based on these infectious factors, antibiotics, either topical or systemic, should be given to AR patients to achieve better results. However, no long term systemic antibiotics or periodic addition of topical antibiotics were administered along with the saline irrigation. This treatment method was utilised to diminish any confounding effects. This study demanded a comparison between pre- and post-operative groups which focused on the effect of local drainage and irrigation by endoscopy in AR patients. Thus, no long-term antibiotics were used to minimise changes. The middle turbinate is part of the ethmoid sinuses and may impede proper drainage from the ethmoid or frontal sinuses. The middle turbinate was recognised as a factor for possible failure of ESS in some chronic sinusitis patients (Stammberger, 1986).

Additionally, Ssali CL proposed a middle turbinectomy in treating AR patients (Ssali, 1973). Hence, application of ESS along with middle turbinectomy was attempted in the treatment of AR patients in this study. During inflammation, the epithelium showed an increase in goblet cell number while a decline in secreting cell number was observed as patients recovered from mucosal inflammation (Bienenstock and Befus, 1980; Tos, 1988; Fang, 1994). This correlates with our SEM findings of the nasal epithelium for good recovery subjects. Because normal cilia microstructure was noted in these AR patients, the delay in saccharine time tests (impaired mucociliary transport function) may result from cilia degeneration, a synchronised movement of cilia or mucus factors not related to the cilia itself (Puchelle et al., 1981; Sakakura et al., 1985; Majima et al., 1985). The mucosa from the good recovery patients showed regenerating ciliated epithelium and normal saccharine time tests coinciding with functional morphological changes. Thus, the impairment of the mucociliary transport system in AR patients may show improvement.

In summary, our results support the infectious theories for the pathogenesis of a subpopulation of AR patients. Hence, utilising ESS to eradicate the infectious origins from the sinuses seems to be a practical approach for treatment. The patients who presented little evidence of infection and crusting, extending into the nasopharynx may not benefit from ESS. Although the good recovery subjects were few, ESS treatment of AR proved to be a possible treatment strategy if patients are carefully selected prior to surgery. Thus, AR patients presenting evidence of obvious infection (cloudy sinus images, positive bacterial cultures for *Klebsiella ozaenae* and conspicuous response to antibiotics) should benefit from ESS. Further investigation needs to be undertaken, since these data are preliminary results that utilise a limited number of cases. AR is not a common nasal disease in Taiwan. Thus, sharing this novel treatment method with our otolaryngological colleagues will hopefully spark future clinical trials using this approach and shed new light on caring for these AR patients.

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