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Topical inhalant steroid (budesonide, Pulmicort® nasal) therapy in intubation granuloma

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Abstract

Intubation granuloma of the larynx is an iatrogenic disease which is induced by endotracheal intubation. It has basically been managed by conservative medical treatment with observation. Surgical excision can be considered as a last resort due to the high recurrence rate which subjects the patients to repeated anaesthesia. The purpose of this study is to evaluate the therapeutic effect of topical steroid in intubation granuloma, comparing the results of conservative medical treatment with, or without, surgery (Group I, 14 patients) and inhalant therapy with topical budesonide (Group II, 20 patients).

In Group I, complete disappearance of granuloma occurred in six cases within a year (42.8 per cent) with conservative therapy only. Microlaryngeal surgery was performed on the eight cases of persisting granuloma after conservative therapy for a year, resulting in two cases of recurrence. In Group II, the granuloma disappeared completely in 85 per cent within six months and in 95 per cent within 12 months without any remarkable side-effects. We concluded that intubation granuloma of the larynx could be treated with topical inhalant steroid as the first choice of therapy rather than other medical treatment or surgical intervention.

Key words: Intubation, endotracheal; Granuloma; Drug therapy

Introduction

Intubation granuloma of the larynx is caused by trauma to the vocal process of the arytenoid cartilage from endotracheal intubation. Since the first report of intubation granuloma (Clausen, 1932), its incidence has gradually increased in line with the use of endotracheal general anaesthesia. It was reported that laryngeal granuloma occurred in 44 per cent of the patients who had prolonged intubation for longer than three days (Santos *et al.*, 1994). Usually the granulomatous lesion consists of a broad-based sessile mass presenting a more polypoid appearance between arytenoids. At a late stage the lesion may become pedunculated. The treatment for such traumatic granuloma in the early stages has been conservative therapy with observation including voice rest, and systemic administration of corticosteroid and antibiotics. Antacids have been used for hyperacidity. Generally, the granuloma has been known to disappear in 50 per cent (Schlorf and Duvall, 1969). Surgical intervention at an early stage has shown a high incidence of recurrence and subjected the patients to repeated general anaesthesia. Surgical removal is indicated when a mature pedunculated granuloma is present or the size of granuloma is large enough to threaten airway obstruction.

The inhalant topical steroid, budesonide, has been widely used in various countries since 1984. It has shown high local anti-inflammatory activity, rapid inactivation by means of metabolism in the liver and minimal systemic side-effects even with long-term medication. The purpose of this study is to evaluate the efficacy of topical steroid in intubation granuloma without any surgical intervention, comparing the results of conventional conservative medical treatment with, or without, surgery and inhalant therapy with topical budesonide (Pulmicort® nasal).

Materials and methods

Thirty-four patients were studied, comprising two groups according to treatment modalities. Group I subjects consisted of 14 patients with intubation granuloma who had been treated between January 1984 and October 1988 at the department of Otolaryngology – Head and Neck Surgery, Pusan National University Hospital, Pusan, Korea. Initially Group I subjects were given conservative medical treatment with observation. This included voice rest, antacids, anti-inflammatory agents, and oral corti-

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costeroids if the granuloma was diffusely large enough to produce severe hoarseness. They were followed up at two month intervals for one year. After a year, microlaryngeal surgery with, or without, the use of a laser was performed for the persisting or enlarged granuloma.

Group II subjects, consisting of 20 patients, were treated with inhalant topical steroid, budesonide (Pulmicort® nasal), from February 1990 to November 1993 at the same hospital. They were followed up and the lesion was recorded with telescopic videolaryngoscopy at one month intervals until complete disappearance of the granulomatous lesion. The follow-up was continued for two years at six months intervals after the disappearance of the lesion. A net amount of 50 micrograms of budesonide in the form of aerosol was administered in each application. The spray was inhaled through the oral cavity, four times daily, two sprays each time (gross daily dosage 400 mg). Inhalation treatment was continued until complete disappearance of the granuloma had been confirmed under telelaryngoscopic examination. After use of the spray, the patients were instructed to gargle with water or normal saline followed by swallowing a little of the gargle to remove the remaining aerosolized steroid from the mucosa of the oropharynx.

Statistical analysis comparing two groups was performed using SPSS statistical software. Wilcoxon rank test was applied to age and initial symptomatology, and chi-square test to sex and incidence of bilateral lesions.

Results

In Group I, female patients (12/14, 85.7 per cent) and unilateral involvement (11/14, 78.5 per cent) were predominant in comparison with male patients and bilateral involvement, respectively. The ages ranged from 21 to 54 years with an average of 41 years. The most common symptoms were hoarseness developing within two months (13/14, 92.8 per cent) of endotracheal anaesthesia. Six cases (six out of 14, 42.8 per cent) showed complete disappearance of granuloma within 12 months of conservative therapy, three cases within six months and three cases within six to 12 months. After 12 months of conservative therapy, microlaryngeal surgery with, or without, laser was performed on the eight cases with persisting granuloma. Recurrence developed in two out of eight cases (25 per cent) after surgery, one of which disappeared in 2.5 years with conservative medical treatment and the other disappeared after re-surgery with an intralesional injection of dexamethasone (Table I).

In Group II, female (18/20, 90 per cent) and unilateral involvement (14/20, 70 per cent) were predominant as in Group I. The age distribution was 25-59 years with a mean of 37 years. The symptoms were hoarseness with sore throat and dyspnoea occasionally and developed mostly within two months (17/20, 85 per cent) of endotracheal general anaesthesia. There was no significant difference in terms of sex ($p = .70$), incidence of bilateral lesions ($p = .72$), age ($p = .19$) or initial symptomatology ($p = .37$) between the two groups. Most granulomas disappeared completely within six months (17/20, 85 per cent) of the start of inhalant topical steroid treatment; 95 per cent (19/20) disappeared within 12 months. The one persisting case of granuloma disappeared after 23 months. The only side-effect of inhalant topical budesonide was mild oral moniliasis which occurred in two cases (Table II, Figure 1).

Discussion

The precise incidence of laryngeal granuloma after intubation is unknown because the majority remain only transiently symptomatic and/or spontaneously regresses before the diagnosis is confirmed, although reported series quoted the occurrence rates ranging from 0.01 to 3.5 per cent (Balestrieri and Watson, 1982).

TABLE I
CHARACTERISTICS OF GROUP I PATIENTS

Case	Age/Sex	Site	Sx	Onset of Sx after intubation (months)	Disappearance of granuloma after conservative therapy (months)	Disappearance of granuloma after microlaryngeal surgery (months)
1	47/F	L	H	2	> 12	Disappeared
2	52/F	R	H	1	8	
3	41/M	B	H,D	1	> 12	Disappeared
4	54/F	L	H	1	4	
5	37/F	R	H,S	1	> 12	Recurred*
6	43/F	L	H	1	6	
7	23/F	R	H	3	> 12	Disappeared
8	21/F	B	H,D	1	> 12	Disappeared
9	44/F	L	H	1	10	
10	39/F	R	H	1	> 12	Disappeared
11	43/F	B	H	2	> 12	Recurred**
12	50/M	L	H,D	1	> 12	Disappeared
13	42/F	R	H	1	2	
14	38/F	L	H	1	12	

R: right; L: left; B: bilateral; H: hoarseness; S: sore throat; D: dyspnoea.
*: Disappeared after resurgery with intralesional dexamethasone injection.
**: Disappeared after 2.5 years with conservative therapy.

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TABLE II
CHARACTERISTICS OF GROUP II PATIENTS

Case	Age/Sex	Site	Sx	Onset of Sx after intubation (months)	Disappearance of granuloma after budesonide inhalation (months)	Side-effect
1	42/M	R	H,S	1	3	
2	29/F	R	H	2	1	*
3	43/F	B	H	1	6	
4	28/F	R	H,S	1	6	
5	53/F	R	H,S	2	5	
6	34/F	B	H,S	2	10	
7	40/F	R	H	1	2.5	
8	30/F	B	H,D	1	3.5	
9	25/F	B	H	4	3.5	
10	31/F	L	H	1	3	
11	30/F	R	H	1	12	
12	33/F	L	H	1	6	
13	38/M	L	H	3	3	*
14	47/F	L	H	2	3	
15	59/F	L	H	1	23	
16	28/F	L	H	1	2	
17	52/F	B	H,D	1	1	
18	23/F	B	H	1	1	
19	43/F	R	H	1	3	
20	33/F	R	H	4	4	

R: right; L: left; B: bilateral; H: hoarseness; S: sore throat; D: dyspnoea.
*: oral moniliasis.

A variety of specific aetiological factors has been reported (Ward *et al.*, 1980; Balestrieri and Watson, 1982; Kastanos *et al.*, 1983; Feder and Michell, 1984; Benjamin and Croxson, 1985). These include traumatic intubation and extubation, individual anatomical variation, the size, flexibility and positioning of the endotracheal tube, the duration of intubation, and the underlying medical condition of the patient. The pathogenesis and pathological findings have been understood as follows (Barton, 1953). At an early stage perichondritis occurs due to traumatic abrasion of the vocal process, exposing cartilage. Superimposed secondary infection then produces a so-called contact ulcer. The contact ulcer becomes a sessile granuloma as the denuded area is covered with granulation tissue. This is followed by the formation of an inflammatory polyp caused by proliferation of the central tissue and epithelialization of the periphery. These changes result in the conversion of a sessile mass into the pedunculated polyp of a pyogenic granuloma in the late stage of the disease.

The most common intralaryngeal site for intubation granuloma formation is the medial aspect of the vocal process of the arytenoid cartilage. The reasons why this area is easily damaged during intubation are its projection into the vocal cavity, the lack of elasticity where the perichondrium adheres closely to the cartilage and sparseness of connective tissue in the area.

Hoarseness is the most notable symptom. Other symptoms include the sensation of the presence of a foreign body, odynophagia, and in case of a large granuloma, cough and dyspnoea. The symptoms usually occur one to four months after endotracheal general anaesthesia. The diagnosis can be easily made from the history of the patient and direct visualization of the lesion using direct, indirect, telescopic or fibrescopic laryngoscopy. The condition needs to be differentiated from carcinoma, reflux laryngitis, or contact granuloma of the larynx.

Ideally, prevention of the condition is preferable rather than treatment for it. Avoidance of traumatic intubation by the use of muscle relaxants, the use of direct vision technique for placement of the endotracheal tube, the use of smaller and pliable tubes, the use of non-toxic lubricants and tube material, stabilization of the head and neck to minimize movement of the tube during the operation, avoidance of prolonged intubation, and extubation before recovery of laryngeal reflexes should be kept in mind to prevent subsequent granuloma formation (Elsamma *et al.*, 1971; Balestrieri and Watson, 1982).

The selection of treatment options should be based initially on the knowledge that the majority of these lesions will induce minimal symptoms and can resolve spontaneously. When the granuloma is comparatively small, sessile and does not provoke dyspnoea, the treatment is usually conservative with observation. It consists of voice rest, antacids, antibiotics with anti-inflammatory agent, and corticosteroid. Schlorf and Duvall (1969) reported the granuloma disappeared by medication and expectant therapy in 50 per cent of cases. The disappearance rate within 12 months using conservative therapy was 42.8 per cent (six out of 14) in this study. When the granuloma is refractory to conservative therapy or is producing progressive respiratory compromise, the mainstay of treatment has been surgical removal. If surgical excision is deemed necessary, postoperative prophylactic measures such as voice rest, cessation of smoking, antacids, corticosteroids, and antibiotics are again worthwhile to minimize the likelihood of recurrence. In this study the recurrence rate for granulomas requiring microlaryngeal surgery after one year of conservative treatment was 25

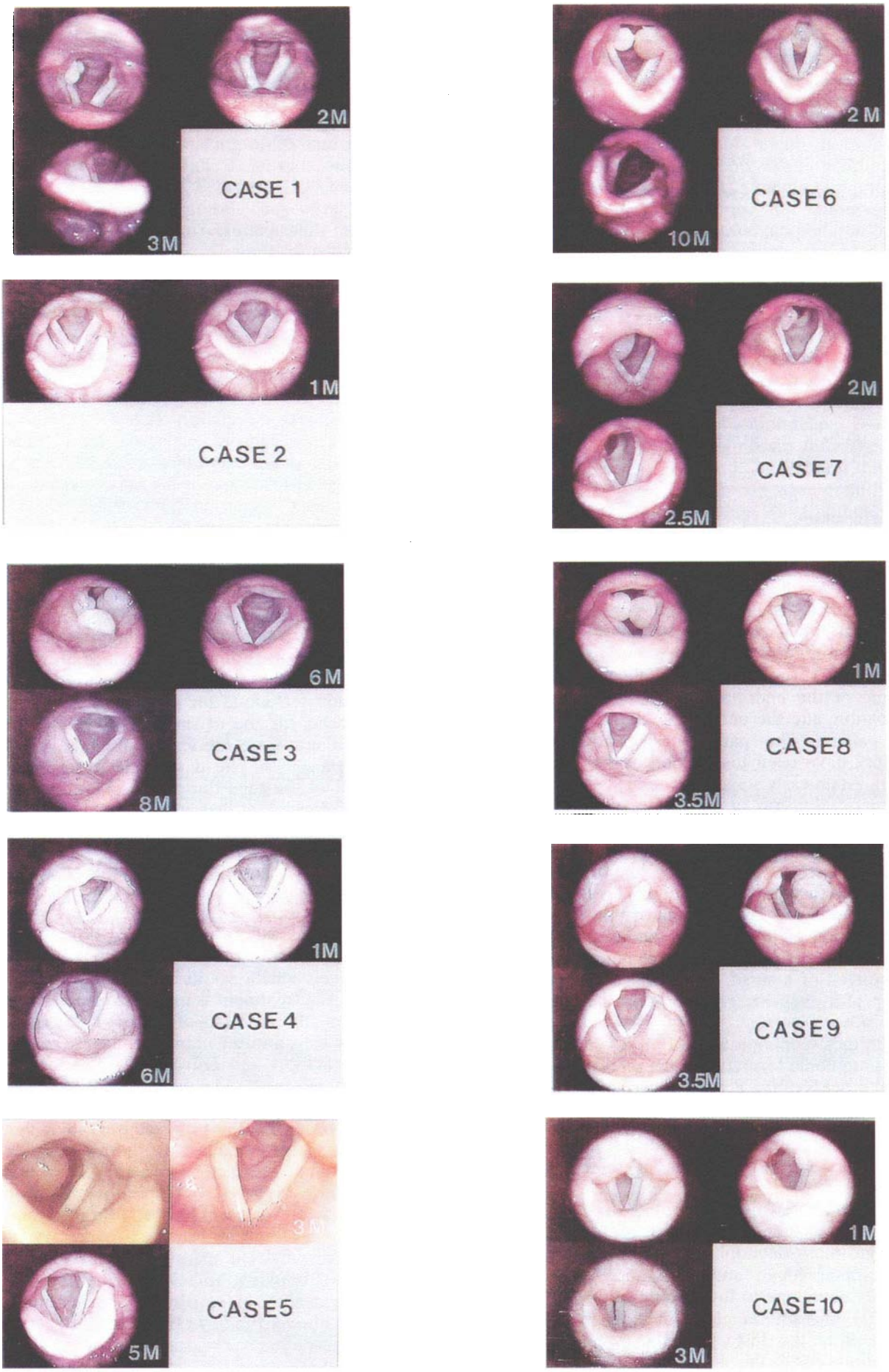

FIG. 1
A series of telelaryngoscopic photographs in 20 patients.

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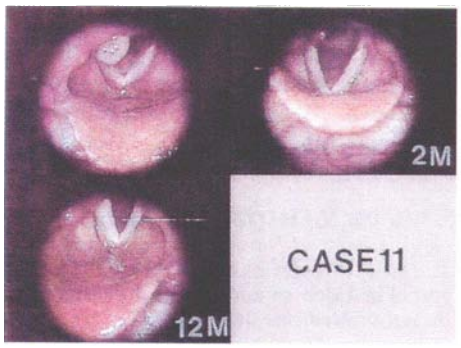

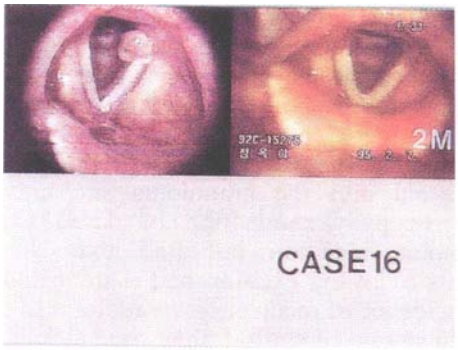

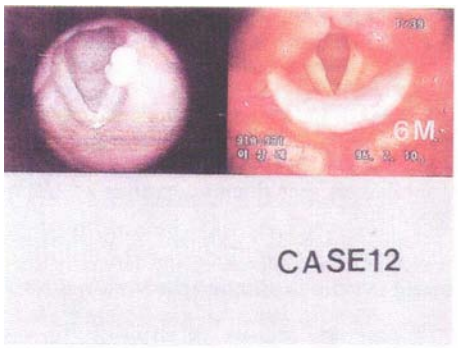

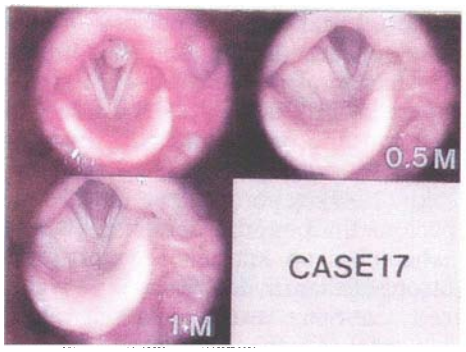

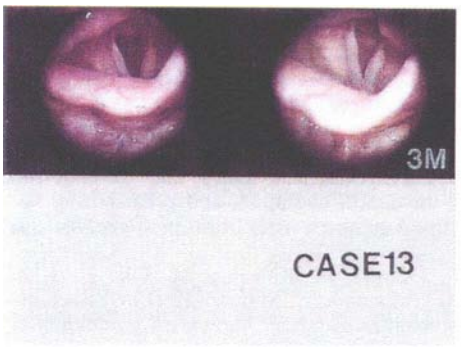

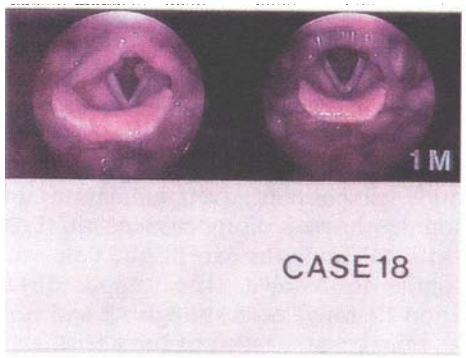

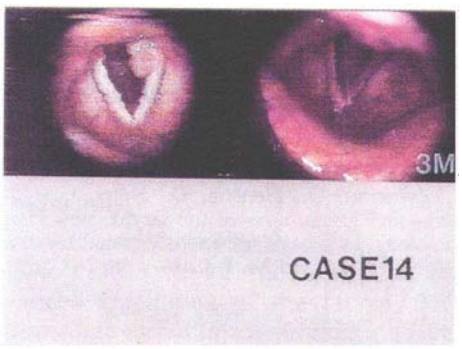

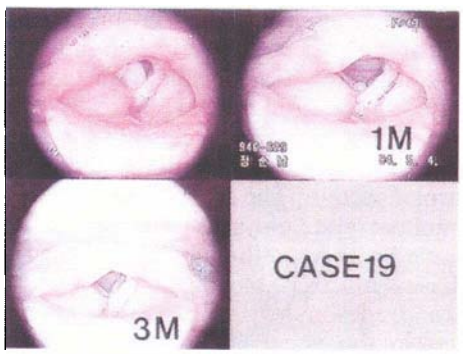

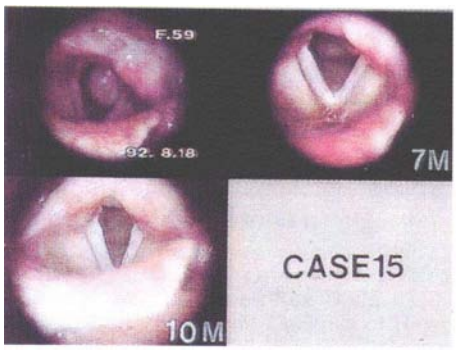

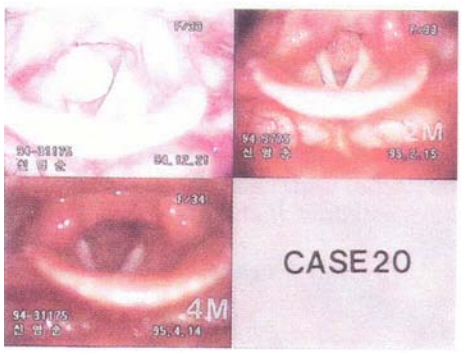

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per cent (two out of eight). Some granulomas that were highly refractory to medical treatment and repeated surgery have even been treated successfully with low-dose radiotherapy (Harari *et al.*, 1991).

Iwamura *et al.* (1983) reported satisfactory results after surgical removal from repeated local injections of steroid into the granuloma site under direct laryngoscopy. Examination of cured cases after incomplete excision indicated that the healing process following excision had a great influence on the incidence of recurrence. In addition to the direct local injection of steroid, they tried steroid delivery by other routes of administration, i.e. oral intake or nebulization. Local injection performed under direct laryngoscopy caused pain and discomfort to the patient, whilst oral administration of steroid had a high chance of producing systemic side-effects. The delivered concentration using a laryngeal nebulizer was too low producing only temporary effects. Kawasaki (1989) reported that inhalation therapy with beclomethasone dipropionate (BDP, Becotide®), which has an anti-inflammatory effect 5,000 times stronger than hydrocortisone (Mygind, 1979), produced gratifying results in seven of nine cases (77.8 per cent) of intubation granuloma.

Budesonide (Pulmicort® nasal) topical inhalant steroid has been used mainly in nasal polyposis, in allergic and in vasomotor rhinitis. It has shown local anti-inflammatory activity stronger than both BDP (two times) and triamcinolone acetonide (three times). It undergoes rapid inactivation through metabolism in the liver (Johansson *et al.*, 1982). In our study all patients given inhalations of topical budesonide showed disappearance of their granuloma within 12 months except one case which took 23 months to resolve. The supposed failure of inhalation therapy, even though we did not experience it, may be as a result of the use of an aqueous solution and an air-pump action inhaler instead of the aerosolized delivery used in this trial. Difficulty might also be expected with the granuloma accompanying a 'kissing' ulcer of the other vocal fold due to voice abuse, and where there is pre-existing underlying gastro-oesophageal reflux as may be the case in an intubation granuloma developing after Caesarean section. The topical inhalant budesonide has minimal systemic side-effects even with long-term medication, although there may be oral moniliasis, mucosal bleeding or even hoarseness due to budesonide itself causing inflammatory changes in the vocal folds. These side-effects can be prevented by rinsing the mouth with water or normal saline solution after inhalation and by regular, close observation of the larynx. In this trial the only experienced side-effect was mild oral moniliasis in two cases, which was treated easily with oral gargling using normal saline.

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