

Clinical evaluation of different treatment methods for oral submucous fibrosis. A 10-year experience with 150 cases

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Over a 10-year period (1982–1991), a total of 150 patients divided into two groups with varying degrees of oral submucous fibrosis (OSF) were treated by either medical or surgical therapies. Medical treatment involved (a) conservative oral administration of vitamin B-complex, buflomedial hydrochloride and topical triamcinolone acetonide 0.1%, or (b) conventional submucosal injections of a combination of dexamethasone and hyaluronidase, or (c) a combination of both (a) and (b). The surgical group was treated by the excision of fibrotic tissues and covering the defect with split-thickness skin, fresh human amnion, or buccal fat pad (BFP) grafts. Treatment was chosen according to the stage of clinical progression to gain maximal interincisal distance (ID). The cases were followed up by monthly examinations for at least two years, or when possible even longer. A combination of (a) and (b) medical treatment was satisfactory in cases of mild impairment (ID >20 mm) but in the long term it led to symptomatic relief only. Surgical therapy, on the other hand, when accepted by the patients, led to a significant improvement of trismus in cases of severe limitation (ID <20 mm). Following this strategy, an additional ID increase was observed in all patients. BFP grafting was particularly successful in diminishing scarring after two years as compared with the other two grafts. Together with a cessation of the betel quid chewing habit before and after therapy, these treatment regimens combined with daily mouth opening exercises were found to be necessary to manage OSF cases in early and advanced stages of progression.

Key words: betel quid chewing; interincisal distance; medical treatment; oral submucous fibrosis; surgical treatment

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Oral submucous fibrosis (OSF), a disease due to an insidious, chronic change in fibroelasticity, is characterized by a burning sensation in the oral cavity, blanching and stiffening of the oral mucosa and oropharynx, and trismus (1). The symptoms and signs depend on the progression of the lesions and on the number of affected sites. More than one oral site is involved in most cases. OSF has been reported to occur commonly in conjunction with other diseases, such as leukoplakia (1, 2) and lichen planus (3). In advanced lesion, the fibrosis extends from the subepithelial lamina propria through the entire submucosa to the muscle layer. Thick inextensible vertical fibrous bands appear in the cheeks, fau-

cial pillars, and encircle the lips. Narrowing of the oral aperture caused by circular fibrous bands in the lips is not only disfiguring, but also limits oral access, leading eventually to malnutrition and poor oral hygiene. It is considered to be a premalignant stage of oral cancer, affecting predominantly Indians and other Asians (1, 4). A high proportion of patients who develop oral cancer are betel quid chewers and sometimes habitual smokers and/or alcohol consumers. These findings are associated with an increased incidence of leukoplakia and squamous cell carcinoma (5). If untreated, the risk of malignant change in advanced cases of OSF is relatively high.

A wide range of treatments such as

medical management (6), surgical therapy (7–11), and physiotherapy (6) have been attempted in the past, with varying degrees of benefit, but none of them has proved to be a cure for this chronic fibrotic disease. In this article we present our experience in the management of early and advanced cases of OSF over the past 10 years, and propose an effective regimen for the treatment of this disease.

Material and methods

One hundred and fifty patients (145 men, 5 women) suffering from OSF diagnosed clinically and pathologically were treated at the Kaohsiung Medical

College Hospital, Taiwan, over a period of 10 years (1982–1991). The criteria for diagnosis of OSF were based on the blanched, slightly opaque and fibrous bands of the oral mucosa (12). The clinical diagnosis was confirmed by biopsy in every case. A detailed personal history, with special reference to smoking, alcohol drinking, and betel quid chewing habits was obtained from each patient. Routine blood and urine tests were made and radiographs were taken to exclude associated diseases. The distance between the incisal edges of upper and lower central incisors with the patient's mouth fully open was measured by using a special scale (Mitutoyo, Japan) (Fig. 1). Patients with temporomandibular joint problems and pericoronitis of the lower third molars were excluded from this study. Before treatment, cessation of the betel chewing habit and a full mouth periodontal scaling were requirements for all patients.

The patients were divided into two groups of 75, one for medical and the other for surgical management. Ages ranged between 17 and 68 years. Within these two groups, patients were further subdivided into subgroups A, B, C, and D, E, F, irrespective of age and sex, according to their initial mouth opening as measured by the interincisal distance (ID). Subgroups A, B, and C each consisted of 25 patients with ID ranging from 20 mm to more than 35 mm (Table 1). Subgroups D, E, and F each consisted



Fig. 1. The interincisal distance with the patient's mouth fully open was routinely measured by using a special scale (Mitutoyo, Japan) before treatment.

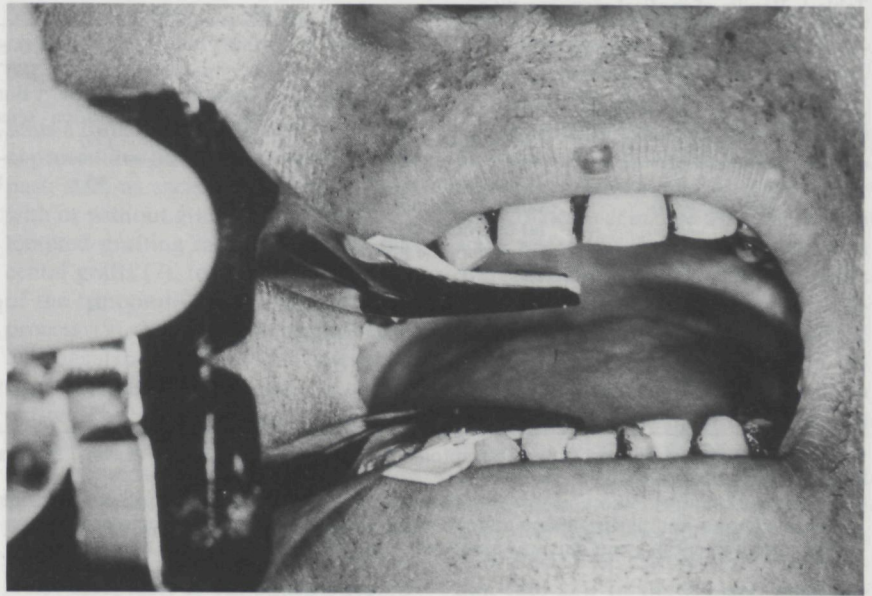


Fig. 2. Two weeks after surgery, patients were asked to perform forced mouth opening by a metal prop for a further 4 weeks.

of 25 patients whose ID was less than 20 mm (Table 2). Subgroup A patients were administered vitamin B-complex tablets orally in a dose of 200 mg twice a day, buflomedial hydrochloride as three tablets (450 mg) per day, and topical triamcinolone acetonide 0.1% on mucosal ulcers at bedtime. Subgroup B patients were given biweekly submucosal injections of a combination of dexamethasone (4 mg/ml) and two parts of hyaluronidase (200 u.s.p. unit/ml) diluted in 1.0 ml of 2% xylocaine by means of a gauge 27 dental needle, not more than 0.2 ml solution/per site, for a period of 20 weeks. Subgroup C patients received both the oral medication and submucosal injections as itemized above for subgroups A and B.

The second group of patients were treated surgically. A Sharplan (Israel) hand-held carbon dioxide (CO₂) laser, at a power setting of 20 watts in a continuous mode, was used under general anesthesia for the excision of circular fibrous bands in the lips. Then, linear incisions were made with a knife (No. 15) along each side of the buccal region, extending from the commissure of the mouth up to the retromolar area. The incisions were enough to expose the underlying muscles. Then a metal prop (Mysco, Japan) was placed into the patient's mouth to hold it in an open position at an ID of 30–35 mm. After access was gained, the gross fibrous tissues in the posterior third of the buccal area, pterygomandibular raphe, and faucial pillar were excised. To repair the re-

sultant defect, either (a) a split-thickness skin graft harvested from the patient's thigh for subgroup D, or (b) a single layer of fresh amnion obtained from clean vaginal deliveries of serologically normal women for subgroup E, was grafted over the wound. The graft was carefully contoured to the surgical site to prevent tenting over any depression in the defect. Then, a prefabricated resin stent of a round, curved shape with tissue conditioner, was molded to the defect after its initial setting. The prepared graft was wrapped around the compound stent smeared with a thin layer of Dermo-glue and sutured to adjacent buccal mucosa with cross stitches.

In subgroup F patients, buccal fat pad (BFP) was mobilized through an intra-oral incision in the upper buccal sulcus 5.0 mm above the attached gingiva, 20 mm posteriorly from the maxillary second molar. With gentle traction, the pedicle fat was pulled over the wound and was lightly secured to the margins of the buccal defect with 3–0 glycolide and lactile-coated polyglactin sutures.

After surgery, patients were fed on a liquid diet through a fine-bore nasogastric tube for a week. Two weeks after surgery, patients were asked to perform daily mouth opening exercises and they attended our outpatient dental (OPD) clinic at a 4-week follow-up visit for forced mouth opening by a metal prop (Fig. 2). Follow-up sessions were repeated monthly for all six subgroups for at least two years, or even longer when possible. The improvement in mouth open-

Table 1. Results of medical management

Sub-group*	No. of patients (sex)	Initial maximal mouth opening (mm)**	Mode of treatment	Duration (weeks) of treatment	Improvement in symptoms†				The decrease of interincisal distance in the range of 3–5 mm after 2 years follow-up (%)
					Painful ulceration (%)	Burning sensation (%)	Blanching (%)	Trismus (%)	
A	25 (M: 22, F: 3)	>35	1) Oral administration of vitamin B-complex, buflomedial hydrochloride, and topical triamcinolone acetanide 0.1%	4	95	88	no	no	no
B	25 (M: 23, F: 2)	30~35	2) †Biweekly submucosal injections of dexamethasone and hyaluronidase	20	94	89	71	83	69
C	25 (M: 25, F: 0)	20~30	3) 1)+2)	20	96	91	81	86	66

* Each subgroup patient had suffered symptoms from 6 months to 15 years (mean 7.5 years) when they were examined.

** Interincisal distance (ID).

† Multiple submucosal injections for the blanched areas at a standard dosage of 0.2 ml per injection site. Diluting the combined drugs of dexamethasone and hyaluronidase into xylocaine with vasoconstrictor promotes retention of the steroid at the site of injection.

‡ The improvement in symptoms was measured at the end of the course of treatment.

Table 2. Results of surgical therapy

Subgroup*	No. of patients (sex)	Initial maximal mouth opening (mm)	Mode of treatment	Full mouth opening at operation (mm)	The decrease of interincisal distance in the range of 5–10 mm after 2 years follow-up (%)
D	25 (M: 25, F: 0)	<20	Surgical excision with split-thickness skin graft	30~35	50
E	25 (M: 25, F: 0)	<20	Surgical excision with fresh amnion graft	30~35	62
F	25 (M: 25, F: 0)	<20	Surgical excision with pedicled buccal fat pad graft	30~35	38

* Each subgroup patient had suffered symptoms from 2 years to 21 years (mean 12.5 years) when they were examined

ing was evaluated by measuring the ID before and after the full course of treatment.

Results

After a month of oral treatment with vitamin B-complex, peripheral vasodilator (i.e. buflomedial hydrochloride) and 0.1% topical triamcinolone acetanide, the symptoms of subgroup A patients were quickly relieved, although there was no improvement in their trismus. Most subgroup B patients (83%) given a course of 10 submucosal injections of hyaluronidase plus dexamethasone felt relaxation in the stiffness of their buccal mucosa. Subgroup C patients treated by both of the above modes of treatment had early and marked relief of symptoms. However, little difference was found in the improvement both in trismus (subgroup B: 83%, subgroup C: 86%) at the end of treatment course and in the decrease of ID within the range of 3–5 mm (subgroup B: 69%, subgroup C: 66%) during the two-year follow-up. No

patient developed infection at the injection sites in subgroups B or C.

Visual inspection of BFP graft revealed satisfactory healing within 2–3 weeks after the operation, yielding a good mucosal surface with minimum morbidity. In general, surgical treatments (subgroups D, E, and F) resulted in significant improvement of trismus in patients with severe limitation of mouth opening (ID of <20 mm). Increases in mouth opening were noted in all surgical treatment subgroups after 2 years of follow-up. Grafts and wounds contracted in all patients by varying amounts; most for fresh amnion grafts and least for BFP. During the following two years, the ID declined by 5–10 mm as compared to that at the end of surgery in 62%, 50%, and 38% of patients in subgroups E, D, and F respectively.

Discussion

Many of the patients at our OPD clinic complained either of hypersensitivity to spicy food and irritant substances or of

severe trismus. The former asked for symptomatic relief, the latter for improvements in mouth opening. A decline in ID at maximal mouth opening corresponds to the severity of the OSF lesions and a change in ID was a treatment criterion in our study. The improvements in subgroup A patients with maximal ID of >35 mm were restricted to symptoms other than ID changes.

MARTIN & KOOP (13) considered vitamin-B deficiency to be important in the etiology of degenerative changes in oral mucosa before malignant transformation. SIRSAT & KHANOLKAR (14) reported that the reaction caused by capsaicin in arousing a limited connective tissue response was enhanced by vitamin-B deficiency. Thus, administration of vitamin B-complex may relieve glossitis, inflammation of the tongue, and cheilosis in OSF patients. A peripheral vasodilator, such as buflomedial hydrochloride, affects the tissues in diffuse fibrosis to a noticeable degree by relief of the local ischemic effect. SHARMA *et al.* (15) observed that the OSF symptom-

atology included local ischemic effects secondary to local fibrous conditions, hyperkeratosis, and loss of suppleness. Therefore they recommended a peripheral vasodilator (a) to relieve the ischemic effect and (b) to aid nutritional and therapeutic substances in reaching the affected tissues. We thought this to be effective both in the earlier and advanced stages of OSF lesions. Additionally, steroid ointment was applied topically in cases with ulcers and painful oral mucosa. Its therapeutic effects were mainly anti-inflammatory and appeared to have a direct healing action (16). Steroids are well known to act as immunosuppressive agents for prevention or suppression of the fibroproductive inflammation found in OSF lesions, thus ameliorating this fibro-collagenous condition (7). Hyaluronidase degrades the hyaluronic acid matrix, actively promoting lysis of the fibrinous coagulum as well as activating specific plasmatic mechanisms (6, 7). Therefore, relief of trismus may be expected through softening and diminishing of fibrous tissue. Symptomatic relief of the burning sensation, feeling of stiffness, and disappearance of vesicles was also noted after five submucosal injections of a combination of steroids and enzyme. This could explain why our subgroup B patients showed more improvement than those in subgroup A.

There is a decade of experience with the dual mode of medical treatment given to subgroup C, leading to long-term relief of symptoms. BORLE & BORLE (16) stated that the mechanical insults due to insertion of injection needles and chemical irritation of injected fluids after a certain time aggravated fibrosis, trismus, dysphagia, and morbidity due to the progressive nature of the disease. We sought to improve this technique by (a) injecting not more than 0.2 ml solution at a time at a given site, (b) massaging the cheeks with the mouth closed, and (c) asking the patients to perform mouth opening exercises for 20 min after the submucosal injections in our OPD clinic.

OSF may be caused by many factors. According to CANNIFF *et al.* (9) the oral mucosa of OSF patients is genetically predisposed to chronic inflammatory changes upon betel quid chewing. It is usually initiated by chronic inflammation, and the progressive condition may be precipitated by poor oral hygiene and malnutrition due to severe trismus. For these reasons, surgical intervention is essential, especially for patients with an ID of <20 mm, to relieve trismus at least

for a period of time. Thus our choice of criteria for surgical treatment meets the patient's requirement.

To relieve severe trismus in OSF presents a difficult surgical problem. Several procedures have been proposed in the past, such as excision of fibrous bands with or without grafts. Materials for attempted grafting included skin or placental grafts (7), tongue flaps (8), splits of the temporalis tendon and coronoid process (9), lingual pedicle flaps (10), and nasolabial flaps (11). These grafts may certainly relieve trismus for a short period. The bilateral full-thickness nasolabial flaps technique was the only possible extraoral approach (11). Because this operation leaves external facial scars, it has not been recommended by oral surgeons. Disfigurement of the face is not acceptable to our patients according to the Chinese social culture.

Our patients had varying degrees of inability to open mouths irrespective of the stage of disease. The main clinical criterion adopted for grading OSF cases was the presence of palpable fibrous bands in the buccal mucosa. In 105 of our 150 cases, at least three fibrous bands were found encircling the lips, buccal mucosa, and faucial pillars. The constriction of the oral aperture is not only disfiguring but also limits access needed for surgery. To relieve this condition, the first task is frequently to excise the fibrous band around the lips by CO₂ laser. Then surgical access is gained. We preferred to use the CO₂ laser, rather than a scalpel or a technique involving multiple tiny incisions for surgical relief of the limited oral aperture, because the laser beam spontaneously sealed all blood vessels, allowing the surgeon perfect visibility and accuracy in excising the fibrous tissues (17). Furthermore, the laser excised wound heals with less contraction and scarring than wounds left by surgical excisions (18). With reference to use of the CO₂ laser for the surgical treatment of OSF, we considered it be practically impossible to excise all fibrous tissues in the oral cavity at one time.

50% of subgroup D patients had a relapse of decreased ID in the range of 5–10 mm after 2 years of follow-up (Table 2). We attribute this to the thin split-thickness epidermal grafts used for covering deep buccal defects. These grafts displayed pronounced contraction, and full-thickness dermal grafts, which are known to contract little, would have been preferable for the larger mucosal wounds. Therefore the

choice of appropriate skin graft thickness for cases of severe trismus is essential in the determination of postoperative mouth opening.

The value of amniotic membranes as dressings for partial-thickness burns has been demonstrated by DINO *et al.* and COLOCHO *et al.* (19, 20). There is no acute rejection (21), and its application over partial-thickness defects provides for pain relief and even for re-epithelialization. In about 62% of subgroup E patients (Table 2) for whom deep defects were covered by fresh amnion grafts, the ID two years after surgical treatment decreased by 5–10 mm. Therefore, fresh amnion grafts would not appear to be effective in a single layer over deep buccal defects.

BFP has been used in oral reconstruction (22, 23). In the present study, we used BFP as a pedicled graft in subgroup F patients suffering from advanced OSF lesions. Our results confirmed previous clinical findings that epithelialization did indeed take place. Convenient and reliable pedicled BFP grafts were used in the reconstruction of intraoral defects up to 4.0 cm in diameter in the ipsilateral side of the posterior third of the buccal defect. Subgroup F patients treated with pedicled BFP had the least percentage (38%) decrease in mouth opening among our three reconstruction subgroups. Technically, the surgical procedure is easy and the donor site is in close proximity to the posterior third of the buccal defect. Thus we consider this as the quickest and most efficient form of therapy for OSF patients with severe trismus to ensure long-term improvement in mouth opening.

GUPTÁ & SHARMA (7) reported that their 14 patients with severe OSF lesions did not respond to conservative treatment. They were all treated surgically using fresh human placenta (1 cm²) as grafts. After 2 weeks, this was followed by biweekly submucosal injections of dexamethasone for a further 4 weeks, which led to definite relief of symptoms. Our clinical studies do not seem to substantiate these findings. Additional follow-up is needed after surgical therapy. We concluded that this proposed method may be useful in giving patients suffering from trismus improved long-term prospects after surgery.

Betel quid chewing is rooted deeply in Chinese culture, especially among lesser educated men and blue collar workers (24). Therefore, follow-up of betel chewers suffering from OSF on a regular basis often presents an insur-

mountable problem. Frequently, after some improvements in symptoms from an incomplete course of treatment a sufferer will not return to our OPD clinic. Such cases were excluded from the present study. Chronic irritation caused by betel nut has been thought to be the local factor inducing the pathologic change of the oral mucosa (25). Our advice to patients before treatment and participation in our follow-up study was to give up betel quid chewing altogether. Our advice was accepted by all. The patients in this study found it easier to give up betel quid chewing than to stop alcohol drinking or tobacco smoking. Patients suffering from this incurable, chronic fibroelastic scarring disease need to be fully informed. It is essential at the onset of treatment to avoid raising expectations. Many patients with a history of years of betel quid chewing come to our OPD clinic and expect within a short period of time a complete cure, which at present is not possible. Treatment needs to be coupled with cessation of betel quid chewing and daily mouth exercises in order to manage properly both early and advanced stages of OSF.

References

1. PINDBORG JJ, SIRSAT SM. Oral submucous fibrosis. *Oral Surg Oral Med Oral Pathol* 1966; **22**: 764-79.
2. WARNAKULASURIYA KAAS. Clinical and pathological criteria for diagnosis of oral submucous fibrosis. Proceeding of The 1st Asia-Pacific Workshop for Oral Mucosal Lesions. 1992; Nagoya, Japan.
3. PINDBORG JJ, MEHTA FS, DAFTARY DK. Occurrence of epithelial atypia in 51 Indian villagers with oral submucous fibrosis. *Br J Cancer* 1970; **24**: 253-7.
4. AXÉLL T. The professional role of the dentist under the aspects of precancer and cancer diagnosis and management. *Int Dent J* 1993; **43**: 609-11.
5. SEEDAT HA, VAN WYK CW. Betel chewing and dietary habits of chewers without and with submucous fibrosis and with concomitant oral cancer. *SA Med J* 1988; **74**: 572-5.
6. KAKAR PK, PURI RK, VENKATACHALAM VP. Oral submucous fibrosis-treatment with hyalase. *J Laryngol Otol* 1985; **99**: 57-9.
7. GUPTA D, SHARMA SC. Oral submucous fibrosis - a new treatment regimen. *J Oral Maxillofac Surg* 1988; **46**: 830-3.
8. TEPAN MG, SAIGAL GS, TILAK SB. Use of tongue flap in submucous palatal fibrosis. *J Laryngol Otol* 1986; **100**: 455-60.
9. CANNIFF JP, HARVEY W, HARRIS M. Oral submucous fibrosis: its pathogenesis and management. *Br Dent J* 1986; **160**: 429-34.
10. GOLHAR SU, MAHORE MN, NARKHEDE S. Oral submucous fibrosis. *Dent Dialogue* 1987; **12**: 44-6.
11. KAVARANA NM, BHATHENA HM. Surgery for severe trismus in submucous fibrosis. *Br J Plast Surg* 1987; **40**: 407-9.
12. WORLD HEALTH ORGANIZATION. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. Eds. KRAMER IRH, PINDBORG JJ, SARDO INFIRRI J. Copenhagen: Munksgaard, 1980; 1-26.
13. MARTIN H, KOOP EC. Precancerous mouth lesions of avitaminosis B: their aetiology, response to therapy and relationship to intraoral cancer. *Am J Surg* 1942; **57**: 195.
14. SIRSAT SM, KHANOLKAR VR. Submucous fibrosis of the palate in diet-preconditioned Wistar rats. Induction by local painting of capsaicin - an optical and electron microscopic study. *Arch Pathol* 1960; **70**: 171-9.
15. SHARMA JK, GUPTA AK, MUKHIJA RD, NIGAM P. Clinical experience with the use of peripheral vasodilator in oral disorders. *Int J Oral Maxillofac Surg* 1987; **16**: 695-9.
16. BORLE RM, BORLE SR. Management of oral submucous fibrosis: A conservative approach. *J Oral Maxillofac Surg* 1991; **49**: 788-91.
17. FRAME JW. Carbon dioxide laser surgery for benign oral lesions. *Br Dent J* 1985; **158**: 125-8.
18. STRONG MS, JAKO GJ, POLANYI T, WALLACE RA. Laser surgery in the aerodigestive tract. *Am J Surg* 1973; **126**: 529-33.
19. DINO BR, EUFEMIO GG, DEVILLA MS. Human amnion: the establishment of an amnion bank and its practical applications in surgery. *J Phil Med Assoc* 1965; **41**: 890-8.
20. COLOCHO G, GRAHAM WP, GREENE AE, MATHESON DW, LYNCH D. Human amniotic membrane as a physiologic wound dressing. *Arch Surg* 1974; **109**: 370-3.
21. AKLE CA, ADINOLFI M, WELSH KI, LEIBOWITZ S, MCCOLL I. Immunogenicity of human amniotic epithelial cells after transplantation into volunteers. *Lancet* 1981; **ii**: 1003-5.
22. SAMMAN N, CHEUNG LK, TIDEMAN H. The buccal fat pad in oral reconstruction. *Int J Oral Maxillofac Surg* 1993; **22**: 2-6.
23. TIDEMAN H, BOSANQUET A, SCOTT J. Use of the buccal fat pad as a pedicled graft. *J Oral Maxillofac Surg* 1986; **44**: 435-40.
24. KO YC, CHIANG TA, CHANG SJ, HSIEH SF. Prevalence of betel quid chewing habit in Taiwan and related sociodemographic factors. *J Oral Pathol Med* 1992; **21**: 261-4.
25. SHIAU YY, KWAN HW. Submucous fibrosis in Taiwan. *Oral Surg Oral Med Oral Pathol* 1979; **47**: 453-7.

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