



## Unique Journal of Medical and Dental Sciences

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Research Article

### CRYOSURGERY AS A TREATMENT MODALITY IN LEUKOPLAKIA - A PILOT STUDY

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Received: 04-06-2013; Revised: 30-06-2013; Accepted: 18-07-2013

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#### ABSTRACT

**Aims and objective:** The aim of this study was to evaluate the efficacy of cryosurgery using Liquid Nitrogen in the treatment of Oral Leukoplakia.

**Materials and methods:** Ten patients irrespective of age and sex presenting with homogenous leukoplakia visiting the OPD at the Oxford dental college were enrolled into the study. The cryogen is directly sprayed onto the lesion through an appropriate sized nozzle, which is chosen according to the size of the lesion.

**Results:** After 4 months 90% patients were showed normal mucosa without any recurrence. Only 1 patient showed persistent lesion.

**Conclusion:** Cryosurgery with liquid nitrogen gives satisfactory results with no intra or post operative bleeding, no surgical defects, minimal or no scarring, and no infection following treatment.

**Keywords:** Oral Leukoplakia, Cryosurgery, Liquid Nitrogen, Dysplasia, Conventional Surgery, Open Spray Technique.

#### INTRODUCTION

The term Leukoplakia originates from two Greek words Leuko=white, Plakia=patch. Oral leukoplakia is a white patch or plaque that cannot be characterized clinically or pathologically as any other disease. The term leukoplakia was first used by Schwimmer in 1877 to describe a white lesion of the tongue, which probably represented a syphilitic glossitis.<sup>1</sup> He proposed the term leukoplakia for a diffuse patch on the dorsum of the tongue. Since then it has evolved as a clinicopathologic concept over many years; sometime representing an innocent hyperkeratosis and sometimes dysplastic features<sup>1</sup>. Leukoplakia is the most common premalignant lesion of the oral mucosa. Dysplastic epithelium or frank invasive carcinoma is, in fact found only in 5% to 25% of biopsy samples of leukoplakia. The incidence of leukoplakia is increasing day by day due to increased deleterious oral habits among the people. The prevalence of leukoplakia in India varies from 0.2% to 4.9%<sup>2</sup>. Men are affected more frequently than women, and a vast majority of leukoplakia occurs in the age range of 35-45 years<sup>3</sup>. The disease is diagnosed more frequently now than in the past, probably because of an enhanced awareness on the part of

health professionals. Oral leukoplakia may affect any part of the mouth, but is usually seen on the buccal mucosa, tongue and gingiva. Research has shown that oral leukoplakias on the ventral surface of tongue, floor of mouth and soft palate are more likely to become precancerous/dysplastic. Some oral leukoplakias are not just white but may appear red, rough and warty. These too, have a higher chance of being precancerous/dysplastic<sup>4</sup>. The exact cause of oral leukoplakia is still unknown, although certain risk factors have been identified. More than 80% of patients with oral leukoplakia have a history of tobacco use and the condition is six times more common among smokers than non-smokers. Clinically, leukoplakia can be subdivided into a homogenous type (flat, thin, uniform white in colour) and a non-homogenous type<sup>5</sup>. The frequency of dysplastic or malignant alterations in oral leukoplakia has ranged from 15.6 to 39.2 percent in several studies<sup>1</sup>. There are various treatment modalities for oral leukoplakia. Treatment of oral leukoplakia depends on type and degree of dysplasia. In presence of moderate to severe epithelial dysplasia surgical treatment is recommended<sup>6</sup>. Treatment of oral leukoplakia includes surgical and non

surgical method. Habit cessation is an important factor in treatment. Non surgical treatment includes antioxidants, retinoids and photodynamic therapy. Surgical method includes wide excision of the lesion, carbon dioxide laser surgery and cryosurgery<sup>4</sup>.

Cryosurgery is a controlled and targeted destruction of diseased tissue by the application of cold temperature. It is a simple, cost effective, efficacious and esthetically acceptable modality for the treatment of various lesions like vascular lesions, benign tumors, acne, pigmented lesions, viral infections, inflammatory dermatoses, and infectious dermatoses, pre-malignant and malignant tumors<sup>7</sup>.

It has been used in Oral medicine for over 30 years. Several cryogens such as liquid nitrogen, nitrous oxide, carbon dioxide are available, but liquid nitrogen is the commonly used cryogen. Two techniques are there for the application of cryogen. Timed spot technique and Dipstic method. Timed spot technique again classified into two. Open spray technique and Confined-spray technique. The choice of method is based on the type of lesion. Open spray technique is used for large lesions or when light superficial freeze is desired. Confined-spray technique is preferred for round, small, discrete lesions or those close to vital structures<sup>7</sup>. The purpose of this study is to find out the efficacy of Cryosurgery in the treatment of oral leukoplakia.

## MATERIALS AND METHODS

### Study procedure

Total 10 patients irrespective of age and sex presenting with homogenous leukoplakia visiting the OPD at the Oxford dental college were enrolled into the study. Age, gender, smoker status, location, size and microscopic evaluation of oral leukoplakia were recorded. Incisional biopsy of the oral leukoplakia was performed in all patients before the treatment with cryosurgery. The whole study process and its experimental nature were described to the patients before and written consent was taken before the treatment.

The cryogen is directly sprayed onto the lesion through an appropriate sized nozzle, which is chosen according to the size of the lesion. The nozzle is held 1cm away from the surface and the cryogen is sprayed in the centre of the lesion until ice ball forms that completely encompasses the lesion and the desired margin is reached. For adequate treatment, the lateral spread of freeze should extend at least 2mm beyond the margin. The spraying is continued for an adequate duration after which lesion is allowed to thaw to complete one freeze thaw cycle. For larger lesions (>2cm in size) different parts of the lesion are treated separately with overlapping margins. The patient will be examined after half an hour and 2 hours, 10<sup>th</sup> day for the clinical changes. If any remaining lesion is there, cryosurgery will be repeated after 2 weeks. Patient will be recalled after 1, 2 and 4 months for evaluation of the status.

### Statistical analysis

Descriptive Study was done and distribution of patients according to age, gender, associated habits, size of lesion, histopathology report, no. of cycles of cryosurgery, follow ups were calculated. SPSS 13 windows program was used for the statistical analysis.

## RESULTS

Clinical and microscopic findings of ten patients with oral leukoplakia treated with cryosurgery are summarized in table 1. The mean age of patients was  $48 \pm 13.20$  years and 7 patients were male. This indicates study group comprised of more number of males than females. 3 patients had lesion of size 1 x 1.5 cm and 7 patients had lesion of size 2 x 2 cm. This suggests study group included more number of patients who had wide lesions. Only 1 patient had hyperkeratosis with mild dysplastic changes. Study group contained more number of patients who completely quit their habit. Correlation between no. of cycles for cryosurgery and 1 month, 4 month follow up were given in table 2.

**Table 1: Distribution of patients according to clinical and histological findings**

	No. of Patients	% of Patients
<u>AGE</u>		
<50 years	6	60%
>50 years	4	40%
<u>GENDER</u>		
Male	7	70%
Female	3	30%
<u>HABIT</u>		
SMOKING TOBACCO	5	50%
SMOKELESS TOBACCO	5	50%
<u>SIZE OF THE LESION</u>		
1×1.5cm	3	30%
2×2cm	7	70%
<u>HISTOPATHOLOGY</u>		
Hyperkeratosis with mild dysplasia	1	10%
Hyperkeratosis without dysplasia	9	90%
<u>STATUS OF HABIT</u>		
Persistent, no reduction in habit	2	20%
Persistent, reduction in habit	1	10%
Quit the habit	7	70%

**Table 2: correlation between no. of cycles for cryosurgery and 1 month, 4 month follow up**

No. of cycles of cryosurgery given	No. of patients	follow up after 1month of cryosurgery		4 month follow up	
		Complete regression	Partial regression	Recurrence	Persistent
<b>1 cycle</b>	3 (30%)	2 (20%)	1 (10%)	0	1 (10%)
<b>2 cycles</b>	4 (40%)	4 (40%)	0	0	0
<b>3 cycles</b>	2 (20%)	2 (20%)	0	0	0
<b>4 cycles</b>	1 (10%)	1 (10%)	0	0	0
<b>Total</b>	10 (100%)	9 (90%)	1 (10%)	0	1 (10%)

Hyperemia and edema of the treated area occurred immediately after cryosurgery. Local swelling and bullous formation were evident during the following 2 to 3 days. Subsequently, superficial necrosis occurred, and the lesion was covered with a thin layer of a yellowish pseudo membrane. Epithelialization of each treated area was complete after 10-14 days, depending on the location and area of the lesion. After 1 month complete regression of lesion in 9 patients and only 1 patient showed partial regression in the lesion. At the follow up of 4 months, 9 (90%) patients showed normal mucosa with no recurrence. 1 (10%) patient showed persistent lesion which may be due to his smoking habit which was continued after treatment.

## DISCUSSION

There are different treatments for leukoplakia, which have shown different results. In order to determine treatment for leukoplakia, a biopsy is necessary to obtain a definitive histological diagnosis. If the lesion is found to be non-cancerous, treatment involves removing the contributing factors, such as removing the source of irritation. In the presence of moderate or severe epithelial dysplasia, surgical treatment is usually recommended. Leukoplakia's located on the floor of the mouth, soft palate, and tongue are considered lesions of high-risk for malignant transformation, while, in other areas, such as the gingiva, hard palate and buccal mucosa are considered to represent a low risk of malignancy.<sup>8</sup> However, when the decision regards leukoplakia presenting low to moderate malignancy risk, one should consider other factors such as location and size. Surgical treatment of leukoplakia can be done through conventional surgery, laser surgery, electrosurgery, or cryosurgery. Conventional surgery is more frequently used, but may cause scars and a loss of tissue and there is a high time of work in relation to the cryosurgery. Moreover, recurrence has been reported in 10% to 35% of the cases.<sup>8</sup>

Cryosurgery is the deliberate destruction of tissue by application of extreme cold and has been used in oral medicine and pathology for over 30 years. Reports of tissue destruction by freezing date back to the British physician, Arnott in 1851. Initially, its use was limited to the treatment of cancer of the lip and oral cavity. At present, cryosurgery has a wide application in the treatment of both benign and malignant lesions in the head and neck region. In fact, over 40 different dermatological conditions of the head and neck have been described as being amenable to cryosurgery.<sup>9</sup>

The mechanisms for cell destruction after cryosurgery are complex involving a combination of direct and indirect effects. Direct effects consist of ice crystals that form in

extracellular and intracellular fluid, cellular dehydration, toxic intracellular electrolyte concentration, inhibition of enzymes, protein damage, thawing effects that cause the cell to vacuolate, swell, and rupture and thermal shock injury to cells. Indirect effects include vascular changes.<sup>10</sup>

The early complications include pain and vesicle formation. Exposure of bone occurs where freezing has been applied to thin mucoperiosteal surfaces such as the attached gingiva, the mucosa over the lingual aspect of the mandible, and the hard palate, where freezing has been too harsh. Although healing may be delayed for many weeks in such cases, the devitalized exposed bone remains uninfected and pain-free, until sequestration and/or resorption have occurred, and the area is covered by mucosa. In such sites, therefore, if the nature of the lesion permits, the tendency is to freeze for less than one minute, and to repeat treatment later if necessary. Scarring and fibrosis are minimal following cryosurgery, compared with both excision and suture or diathermy excision. On the facial skin, freezing for longer than 20-30 seconds produces superficial necrosis in the usual way, and healing is attended by a slightly depressed, thin epidermis with reduction in pigmentation and absence of skin appendages.<sup>11</sup>

Cryosurgery is well accepted by patients due to a relative lack of discomfort, absence of bleeding, and minimal to no scarring. Apparently, postoperative healing does not cause tissue retraction particularly in the alveolar ridge, which is beneficial to prosthetic rehabilitation. Cryosurgery is a relatively painless procedure. This is due to the immediate blockage to neural transmission in the area. Within one minute of the thaw cycle, earliest signs of nerve damage are apparent. This is due to a combination of the freezing episode itself, as well as ischemic changes resulting in energy deprivation. The neuron itself is devitalized by freezing, but the axon sheath is resistant to freezing and remains intact. This allows growth of a new neuron and regeneration is apparent in one week. Normal function can be expected to return within 1-2 months.<sup>9</sup>

This study found that smaller leukoplakia lesions needed significantly fewer treatments to achieve complete remission (CR) than did larger lesions. Pogrel et al showed that soft tissues at the center of the ice ball produced by liquid nitrogen ultimately undergo necrosis, while those at the margin of the ice ball usually do not reach sufficiently low temperatures to induce effective tissue necrosis. In this study, we successfully treated 10 leukoplakia lesions with the cryosurgery. Some patients received more than one cycles of treatment. Out of 10 patients 3 patients have received 1 cycle of treatment, 4 patients have received 2 cycles of treatment, 2 patients have

received 3 cycles of treatment and only 1 patient received 4 cycles of treatment. Patients recalled after 1, 2 and 4 months for check up. 1 month after treatment complete regression of lesion seen in 90% of patients. After 4 months 90% patients showed normal mucosa without any recurrence. Only 1 patient who was not ready to quit the habit showed partially persistent lesion. Clinical healing was determined when the leukoplakia could no longer be seen in the primary location. In the present study out of 10 patients 9 patients showed complete regression of lesion by the end of 2<sup>nd</sup> and 4<sup>th</sup> month. Out of the 3 patients who received only one cycle of treatment, 1 patient showed partial regression. This indicates that multiple cycles of cryosurgery is necessary for effective treatment of large lesions. Healed mucosal tissue could be observed with a normal clinical appearance. Loss of tissue, postoperative pain, haemorrhage, infection, or scarring did not occur in all cases. However cryosurgery is also having its own limitation and advantages which we noticed in our study. As we didn't use local anesthesia with cryosurgery some patients was telling mild burning sensation and mild pain during cryosurgery which will stop immediately after stoppage of spraying liquid nitrogen to the lesion. It can be better explained as mild discomfort than pain or burning sensation when liquid nitrogen is sprayed continuously on the lesion for longer duration to achieve sufficient depth into the lesion. Patients having cervical abrasion, attrition and dentinal hypersensitivity cannot tolerate cryosurgery using spray technique as it increases dentinal hypersensitivity which has forced us to take necessary treatment for hypersensitivity before starting cryosurgery in that patients. Eventhough we didn't use antibiotics and analgesics, after cryosurgery no patients complained of pain or infection after cryosurgery. Healing after cryosurgery was uneventful. Treatment duration is more when compared to conventional surgery as patient has to undergo many cycles of cryosurgery depending on the type of lesion, but longer duration of treatment can be justified because of many other advantages of cryosurgery over conventional surgery.

From this study it could be derived that cryosurgery is a highly effective treatment modality for oral leukoplakia lesions. The present study results are in accordance with the majority of the studies reviewed concerning the treatment of Oral Leukoplakia with cryosurgery<sup>8,12,13</sup>

### CONCLUSION

Cryosurgical treatment has certain advantages over conventional surgery and these include bloodless treatment, very low incidence of secondary infection and a relative lack of scarring and pain. Hence cryosurgery which is not much used in dentistry has got a key role when used properly in treatment of oral leukoplakia which is resistant to all other conventional treatments. Cryosurgery represents a sound alternative to surgical excision, given that the destruction of the pathologically changed tissue is possible and subsequently allows the mucosa to return to normal clinical appearance with no formation of scars.

From this study we could derive that cryosurgery using liquid nitrogen is very effective for the treatment of oral leukoplakia when it is used appropriately with 1 or 2 applications (cycles). Larger and deep seated lesions require multiple applications.

Liquid nitrogen cryosurgery is very safe, inexpensive and easy performing technique for use in outpatient basis for treatment of various oral lesions particularly oral leukoplakia. The patients who have the fear of knife and needle will be more comfortable with this modality of treatment. Although the follow up period in the study is very short the results obtained are promising. Hence it is advocated that further studies should be carried out with larger sample size and longer follow ups to confirm the efficacy of cryosurgery.

### REFERENCES

1. Neville BW, Day TA. Oral cancer and precancerous lesions. *CA cancer J clinic.*2002;52:195-215
2. Waal IVD, Schepman KP. Oral leukoplakia: a clinicopathological Review. *Oral oncology.*1997; 33(NO.5):291-301
3. Keluskar V, Kale A. An epidermological study for evaluation of oral precancerous lesions, conditions and oral cancer among Belgaum population with tobacco habits. *Biosci. Biotech. Res. Comm.*2010;3:50-54
4. Mathew AL, Pai KM. The prevalence of oral mucosal lesions in patients visiting a dental school in Southern India. *Indian J Dent Res.*2008;19:99-103
5. Waal IVD. Potentially malignant disorders of the oral and oropharyngeal mucosa; terminology, classification, and present concepts of management. *Oral oncology.*2009;45:317-323
6. Ribeiro AS, Salles PR. A review of the nonsurgical treatment of oral leukoplakia. *International Journal of Dentistry.*2010.1:10
7. Sharma VK, Khandpur S. Guidelines for cryotherapy. *Indian J Dermatol Venereol Leprol.*2009; 75: 90-100
8. Ribeiro AS, Nogueira MH. The use of Cryosurgery in treatment of the Gingival Leukoplakia: Report of a case series. *International Journal of Oral and Maxillofacial Pathology.* 2012;3(1):28-33
9. Borges HOL, Munhoz EA. Clinical use of Cryotherapy to treat oral inflammatory hyperplasia. *Int. Journal of Clinical Dental Science.*2011;2(1)50-54
10. Sagtani A, Sybil D. Cryotherapy of intra-oral lesions using dipsticks. *Journal of Nepal Dental Association.*2011;12:29-32
11. Lin HP, Chen HM. Cryogun cryotherapy for Oral Leukoplakia. *Head Neck,* 2012;34(9)1306-1311
12. Yeh CJ. Simple Cryosurgical treatment for oral lesions. *International Journal of Oral & Maxillofacial Surgery.*2000;29:212-216
13. Yu CH, Chen HM. Cotton-swab cryotherapy for Oral Leukoplakia *Head Neck,* 2009;31: 983-988

Source of support: Nil, Conflict of interest: None Declared