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CRYOSURGERY – AN EXCELLENT METHOD FOR THE TREATMENT OF ORAL LEUKOPLAKIA

Dental Science

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ABSTRACT

Cryosurgery is a simple and definitive method to treat intraoral leukoplakia. A series of 50 patients, with oral leukoplakia (Histopathologically proven) on the lower lip, buccal mucosa, labia mucosa and tip of the tongue, were treated by direct application of nitrous oxide with a cryogen. Each lesion was exposed to two cycles composed of freezings of 60s and thawing of double of the freeing times. Lignocaine gel was used as transferring media. All lesions had disappeared completely 2-4 weeks after one or two treatment courses of cryosurgery. In all cases, neither scarring nor infection was noted during 3 months to 6 months of follow-up.

KEYWORDS

Cryosurgery, oral leukoplakia

INTRODUCTION

Oral leukoplakia is recognized as a precancerous lesion [4, 8, 9,11,] and carcinoma subsequently develops in 3.6% to 17.5% of patients[3,9,11]. Some of the most recalcitrant lesions in oral cavity are chronic white patches: despite attention to predisposing factors such as chronic irritation, vitamin B 12 deficiency or candidiasis, it is often extremely difficult to eradicate these lesion by conventional methods. Further treatment may include cryosurgery[4,7,10] or laser surgery[3,5]. Diffuse 'white' lesions in anatomically difficult sites such as the lip, commissure of mouth, palate and fauces can all be treated conveniently and satisfactorily by cryosurgery. Cryosurgery is a method of lesion destruction by rapid freezing in situ. The lesion is frozen and the resultant necrotic tissue is allowed to slough spontaneously. Healing of the oral mucosa after cryotherapy is relatively uncomplicated by infection or pain and the recurrence rate of leukoplakia lower than that for other methods of treatment.

MATERIALAND METHODS

The present study was conducted on the patients selected from the outpatient Department of Dentistry, PMCH, Patna. Fifty patients were included in the study without consideration of age , sex, and socioeconomic status. A thorough history consisting of chief complaint, history of present illness, past medical history, dental history, duration of lesion and habits like tobacco chewing, smoking, or both were noted. After recording the history, a thorough clinical examination and routine blood investigations as well as biopsy were done for every patient for establishing the diagnosis before undertaking the cryosurgery. All patients were advised to stop all deleterious oral habits before and after treatment. Informed written consent were obtained from all patients who underwent biopsy and cryosurgery procedures.

EXCLUSION CRITERIA:

1. Patients undergoing other forms of treatment.
2. Smaller size lesion suitable for excision.
3. Patients with biopsy proven squamous cell carcinoma or any malignant changes were not taken in the study.
4. Patients not willing for cryosurgery.
5. Cold entolerance.
6. Non co-operative patients.

MATERIAL USED:

A standard set of instruments were used to do biopsy for these lesions in addition to this Cryo apparatus was used to do the Cryosurgery procedure in these patients, which included Nitrous Oxide gas as well as three Cryoprobes designed for different purposes. {fig 1}

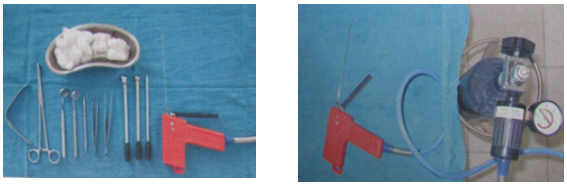


Fig1. Cryoapparatus : Cyoprobes And Nitrous Oxide Gas Unit

METHOD:

All patients after confirmed diagnosis were treated with cryosurgery, without anesthesia. The procedure carried out in the cryosurgery was as follows:

No analgesia was given in patients treated by cryosurgery. Nitrous oxide was used as the cryogen from a high pressure cryoprobe of the 'Cryo surgical unit' based on the freezing by gas expansion principle. The assistant retracted the region to be frozen and held it firmly. The lesion was kept moist for proper contact of the probe. The tip of the cryoprobe was made to contact the tissue by activating the cryoprobe. The indicator of pressure gauge was kept at 740lb/sq. inch range to ensure adequate supply of N2O. A white ice ball was formed on the contact site. Once the freezing started the probe got attached to the tissue with the formation of an ice ball which could not be separated until the thawing was carried out. Thawing was done by deactivating the cryogun.

A 60 second freezing cycle was given for each application & two such applications were made on each area with interval of 2 minutes for thawing.

Postoperatively all the patients were prescribed similar analgesics (Paracetamol SOS) and no antibiotics were prescribed. Patients were advised hot saline gargles after 24 hours of the cryosurgery.

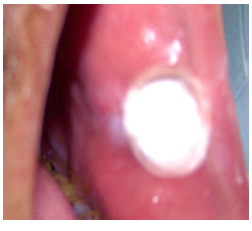


Fig.A

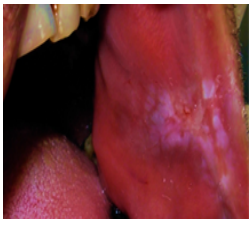


Fig.B

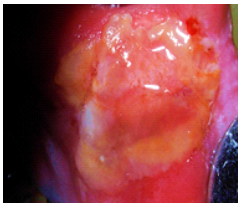


Fig.C

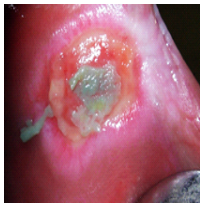


Fig. D

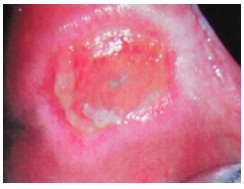


Fig.E

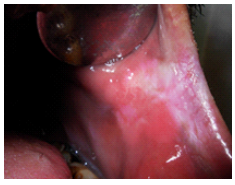


Fig.F

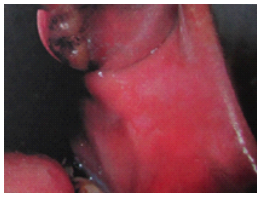


Fig.G

Fig. A: Leukoplakia involving left buccal mucosa and angle of mouth. B : Ice ball like appearance at lesion site. C: First post operative day. D: First post week. E: Second post operative week. F: Fourth post operative week. G: 3rd postoperative month

CLINICAL EVENTS FOLLOWING TREATMENT:

1. Within the first hour there is swelling & hyperemia (post operative pain may be marked at this stage, but ablates within half an hour or so).
2. Gross accumulation of extracellular fluid may lead to vesicle formation.
3. Within a day the epithelial surface breaks down to be covered by a grayish yellow coagulum.
4. Healing is by secondary intention, the surface being reepithialized by two to three weeks.
5. Throughout the healing period, the cryolesion appears inert, provoking very little surrounding inflammatory response.

EVALUATION CRITERIA:

Patients were followed immediate postoperatively, at 1st day, 1st week, 2nd week and 4th week, 2nd month, and 3rd month intervals by the following parameters: pain, swelling, slough, scarring and recurrence.

Pain evaluation was done postoperatively on a subjective basis analogous to a verbal rating method. The patients were questioned for the pain at standard intervals. Four categories of scoring were used i.e no pain to severe pain with score 0-10 (table-1)

Swelling evaluation was done subjectively which appeared after the procedure and was judged in a qualitative way by the observer and scored between 1-3 as per severity from mild to severe (table-1).

Slough is the mass of necrotic tissue found over the wound and its amount was scored between 0-3 with no slough to excessive slough.

Scarring was judged on the color of the oral mucosa, softness of the regional tissue & contracture by its presence or absence at treated site

.**Recurrence** was scored from 0-3 i.e no recurrence to recurrence at whole of operated site when the area subjected to the treatment again appeared as it was before (table-1).

Statistical Analysis was done using Statistical Package for Social Sciences (SPSS) Version 15.0 statistical Analysis Software.Standard error of mean was also calculated. $p < 0.05$ was considered statistically significant. Wilcoxon test was used to compare the different scores within groups. The values were represented in Number (%) and Mean±SD.

	Swelling	Slough	Recurrence	Pain
0	No	No	No	No
1	Mild	Little	Confined less then ½ of lesion	Mild pain Either tolerable or taken one analgesic tablet
2	Moderate	Moderate	Confined more then ½ of lesion but not whole.	
3	Severe	Excessive	Confined whole the operated lesion	
4				Moderate pain Definitive pain or needed more then one analgesic tablet
6				
7				
8				Severe pain Felt severe pain and either reported back or taken stronger or more then two analgesic.
9				
10				

Table. 1 : Evaluation Criteria With Score And Its Categorization.

RESULTS

Parameter	No	Mild/ Little	Moderate	Severe/ Excessive
Pain	28 (56%)	21 (42%)	1 (2%)	0
Swelling	0	17 (34%)	25 (50.0%)	8 (16%)
Slough	8 (16%)	24 (48%)	13 (26%)	5 (10%)

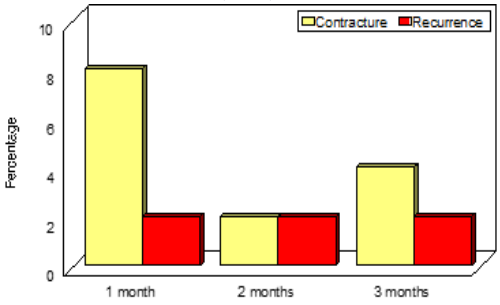
Table.2 : Basleline evaluation (n=50) on 1st day

Parameter	No	Mild/ Little	Moderate	Severe/ Excessive
Pain	49 (98%)	1 (2%)	0	0
Swelling	16 (32%)	33 (66%)	1 (2%)	0
Slough	3 (6%)	18 (36%)	17 (34%)	12 (24%)

Table .3 :Basleline evaluation (n=50) on 1st week

Parameter	No	Mild/ Little	Moderate	Severe/ Excessive
Pain	50 (100%)	0	0	0
Swelling	49 (98%)	1 (2%)	0	0
Slough	43 (86%)	7 (14%)	0	0

Table.4 : Basleline evaluation (n=50) on 2nd week



Graph.1 : Contracture And Recurrence Post Operatively

At day first from baseline, no pain was seen in 28 (56%) subjects, whereas in 21 (42%) mild pain was seen. One case (2%) of moderate pain was also seen. Mild swelling was seen in 17 (34%), moderate in 25 (50%) and severe in 8 (16%) subjects. Slough ranged from nil in 8 (16%) to excessive in 5 (10%) subjects. In 13 (26%) subjects moderate slough was seen while in 24 (48%) it was of mild category. At first week follow up, no pain was seen in 49 (98%) subjects and in the remaining 1 (2%) it was of mild category. There were 16 (32%) subjects with no swelling while in remaining 23 (66%), the swelling was mild and in the remaining 1 (2%) it was moderate. No slough was seen in 3 (6%) subjects while in 18 (36%), little slough was seen, in 17 (34%) it was moderate while in 12 (24%) it was excessive. At second week follow up, all the patients had no pain, only 1 (2%) patient had mild swelling while little slough was seen in 7 (14%) patients. It was seen that contracture was evident in 4 (8%) at 4 week, however at 2 months, in 3 patient it was resolved and only 1 (2%) had contracture but at final interval (3 months), another patient developed contracture, thus making the total to 2 (4%). Recurrence was seen in 1 (2%) patient only at 1st month itself. No further case of recurrence was reported in subsequent follow ups (graph-1).

DISCUSSION

Cryosurgery is a successful mode of therapy for the conditions which have traditionally presented problems in the management such as leukoplakia, vascular malformation and certain extensive surface lesions like Lichen planus. In addition to this, cryosurgery has emerged as a simple method of treatment.

The principle behind the cryosurgical treatment is the removal and destruction of pathological tissues by freezing for the ultimate benefit of patients.

It is concluded that within its limitations, cryosurgery is an effective, simple, predictable, relatively self limiting and safe method for almost all types of oral lesions. Most tissues freeze at -2.2°C, and tissue death occurs at a temperature of -20°C. The effectiveness of cryosurgical treatment stems from the formation of extracellular and intracellular ice crystals. A rapid build-up of toxic electrolyte concentrations, alteration in pH, protein denaturation and disruption of cell membranes subsequently occur. The vascular status of the cryolesion is also regarded as the factor responsible for the completion of cell destruction in the frozen area. As it causes necrosis and sloughing as part of treatment, delayed healing is an inherent problem with this surgical technique. Otherwise, it is free from complications such as pain, haemorrhage, infection, inadverent damage to adjacent structures, or scar formation that are seen with knife excision on electrosurgery.

The present study was done to evaluate the role of cryosurgery in 50 leukoplakia patients. The efficacy of the treatment was considered in the light of post-operative signs and symptoms, patient acceptance, healing process and recurrence of the lesions after providing identical condition of healing as far as practicable.

Pain : Since cryosurgery is a painless procedure which was confirmed by many authors like **Emmings FGet al(1967)**[4]treated several patients of oral hemangiomas, hyperkeratosis & leukoplakia which were painless after treatment. Similar finding was found in our study, pain was absent in more than half of the cases but mild pain was present in remaining cases and on 1st postoperative day, and it was absent, on 1st and 2nd week postoperatively, which were confirmed by the **Poswillo DE& Leopard PJ (1974)**[5]**, Poswillo DE(1975)**[6] who treated hemangioma, lichen planus, hyperkeratosis and leukoplakia and found same result except in few cases they found mild pain postoperatively. This study is having same result as of **Yeh CJ (2000)**[2] in which cryosurgically treated 92 patients with benign oral lesions without any pain but if pain present, was usually mild and easily controlled with non-narcotic pain medication and resolve within hours or next day.

Swelling : Swelling in this study was present (81.25%) where swelling was moderate to severe. At first follow up i.e. 1st week, in almost all the cases the swelling was from nil to mild category. At second follow up (2 weeks) on comparing the data statistically, it was seen that there was a significant fall in swelling at 2 weeks as compared to baseline (1 day).On comparing the change between 1 week to 2 weeks follow up interval, it was seen that fall in swelling took place and was significant statistically ($p<0.001$) but no statistically significant difference ($p=0.395$) among groups could be seen. Similar finding was found by **Emmings FG et al (1967)**[4], **Poswillo DE & Leopard PJ(1975)**[5]in their study in which who have treated several patients of oral hemangiomas, hyperkeratosis, leukoplakia and lichen planus found same result except in few cases they found mild to moderate swelling postoperatively which resolve within 5-7 days. **Yeh CJ (2000)**[2]treated several benign oral lesions in which hyperemia and edema of the treated area began to appear immediately after treatment. Bullous formation appeared in 10 cases within 30 minutes after treatment. Swelling increased for 1-2 days and remained for 2-3 days and later subsided.

Slough the soft slimy mass over the wound was the product of devitalized tissue, inflammatory exudates and phagocytes. **Fred G.Emmings et al (1967)**[4]in his study found thatslough begins in 3-4 days to 1st week and vanishes in 10-12 days as well as **Tal H et al (1992)**[7]also found that slough was formed fully in 1 week & removed in 2-4 week, in our study at first follow up 18 (36%) little slough was seen, in 17 (34%) it was moderate while in 12 (24%) it was excessive and later at second follow up (2 weeks), little slough was seen in only 7 patients thus this study match the above mentioned result as well.

Contracture (Scar) Formation. Poswillo DE (1975)[5] reported that healing after freezing takes place mainly by complete epithelial regeneration of oral tissues with least amount of collagen tissue similar result was proved in present study also. Result of scar formation in this cryosurgical study found that pathologically changed mucous membranes could be completely eliminated in most of the cases without severe scar formation which is similar in the previous clinical studies of **Bekke JP,Baart JA(1979)**[8]**, Tal Het al (1992)**[7]and **M. Toida, J.L Ishimaru, N. Hobo.(1993)**[9]In the **Recurrence** parameter this cryosurgical study upon regular follow up at 1, 2,3 months interval and found tohad the lowest value of 2% only which is also justified in previous studies by **Tal Het al (1992)**[7]**, M. Toida et al (1993)**[9]**&Jain RK et al (1995)**[10]it was concluded that various oral benign lesion upon treatment with different modalities among them cryosurgery have less value in recurrence index. As well as by **Yeh CJ (2000)**[2]who had treatedseveral cases of recurrence oral benign lesion with cryosurgery and all were having successful result thereafter with no recurrence. So, this proved that recurrence rate after cryosurgery is almost negligible.

The overall outcome of the study was that cryosurgery has been used to successfully treat leukoplakia patient.

The treatment has certain advantages over surgery. No local anesthesia is required during treatment. Because of the painlessness and the ease of application, infants and nervous patients can be treated easily and secondary infection and hemorrhage are rare. Recurrences are less frequent after cryosurgery.

CONCLUSION

Nitrous oxide cryosurgery is a safe, simple, painless and bloodless treatment, with a very low incidence of secondary infection, a relative lack of post operative scarring and pain. However, cryosurgery is not widely used. This study was done to popularize and describe efficacy of nitrous oxide cryosurgical treatment of oral benign lesions offering very satisfactory results. Advantages were its high degree of surgical convenience, haemostasis and anaesthetic action. It can be repeated on any number of occasions with no permanent side effects. It can be easily used in elderly, debilitated patients and advanced, unoperable lesions with a high risk of bleeding. It is concluded that cryosurgery holds good for the treatment of leukoplakia with the added advantage of low rate of recurrence, minimum scarring and pain and without any side effect.

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