LIQUID NITROGEN CRYOTHERAPY IN MANAGEMENT OF ORAL LESIONS

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CERTIFICATE

This is to certify that **Dr.S.DURAIMURUGAN**, Post graduate student (2016-2019) in the Department of Oral & Maxillofacial Surgery (Branch III), Adhiparasakthi Dental College and Hospital, Melmaruvathur – 603319, has done this dissertation titled "**LIQUID NITROGEN CRYOTHERAPY IN MANAGEMENT OF ORAL LESIONS"** under our direct guidance and supervision in partial fulfilment of the regulations laid down by The Tamilnadu Dr. M.G.R Medical University, Chennai – 600032, for MDS., (Branch III) Oral & Maxillofacial Surgery degree examination .

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DECLARATION

TITLE OF THE DISSERTATION	Liquid Nitrogen Cryotherapy in Management of Oral Lesions
PLACE OF THE STUDY	Adhiparasakthi Dental College and Hospital,Melmaruvathur-603319.
DURATION OF THE COURSE	3 Years
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I hereby declare that no part of the dissertation will be utilized for gaining financial assistance or any promotion without obtaining prior permission of the Principal, Adhiparasakthi Dental college and Hospital, Melmaruvathur -603319. In addition, I declare that no part of this work will be published either in print or in electronic media without the guides knowledge who have been actively involved in dissertation. The author has the right to reserve for publish work solely with the permission of the principal, Adhiparasakthi Dental college and Hospital, Melmaruvathur-603319.

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INTRODUCTION

Cryotherapy is derived from the Greek word “kryos”, meaning frost hence cryosurgery is local destruction of tissue by freezing. Cryotherapy has long been noted as a good technique that, when used correctly, can reduce pain and swelling and destroy lesions with little scarring. Local application of low temperature was first used by Egyptians for pain relief, then during Franco-Prussian war for amputated limbs. Hippocrates recommended the use of cold to reduce swelling, hemorrhage and pain, while John Hunter in 1777 stated that “the local tissue response to freezing includes local tissue necrosis, vascular stasis and excellent healing.” James Arnott (1851) was the first to report and demonstrate this freezing therapy by using a mixture of salt and ice in malignant breast neoplasm. In 1899, White was the first person to use extremely cold refrigerants for medical conditions. He used liquefied air to treat warts and other dermatologic conditions.[1]

In 1908 A.W. Pusey used the term “Cryotherapy” to describe the treatment of skin lesions with very low temperatures. Currently Cryotherapy treatments invoved by lowering the body surface temperature without tissue destruction, whereas in cryosurgery diseased tissues are destroyed through freezing. The world's first cryogenic temperature chamber was set up in Japan, in 1978 by Yamauchi and his team.[1,2]

Contemporary cryogenics has been developed at the end of the 19th century , liquefaction of oxygen, nitrogen, carbon dioxide and hydrogen, and also the industrial production and storage of liquid coolants, enabled the development of cryobiology, used extremely at low temperature. Virtually all biological tissues subjected to a temperature of −20°C or below for a minute or more undergo cryogenic coagulation or necrosis.[3]

Principles of cryotherapy - Technique of cryotherapy stresses rapid cooling, slow thawing and repetition of the freezing process to maximize tissue destruction. The two methods recognized are a closed system with use of probes and nitrous oxide, or an open system with use of a liquid nitrogen spray or a cotton tip. Spray techniques are useful in widespread dermatological lesions, small skin cancers and intra-bony cavities after curettage to prevent recurrence. The nitrous oxide technique is useful for treatment of various benign and malignant lesions of the oral cavity where more predictable necrosis is necessary and depth of necrosis is also a factor. Current protocols suggest that for most benign mucosal lesions 1–2 minute freeze/thaw cycle using a cryoprobe is sufficient. Premalignant/malignant lesions are recommended to undergo three freeze/thaw for cycles for 2 mins. For smaller lesions, shorter freeze (20–30 seconds) are adequate. In cases where hyperplastic tissue exists, freezing of the mass and then

removing the bulk of tissue, followed by further freezing of the tissue base results in higher success rates.

Mechanism of Tissue damage by cryotherapy involves several mechanisms. It has been determined that most tissues freeze at -2.2ºC and that the temperature must fall below -20ºC for cell death to occur. The treatment of more aggressive cancers in the oral cavity may require repetitive freeze cycles at temperatures of at least -50ºC or more for tissue necrosis to occur. During the freeze cycle as the temperature drops, it is believed that extracellular water undergoes crystallization. In addition, membrane lipids harden take place at low temperatures decreasing cell resistance to shrinkage. Extracellular stores of water diminish, as the electrolyte concentration increases. In order to counteract this concentration gradient, intracellular water moves out of the cell, and this water becomes involved in the crystallization process. As intracellular ice formed, remains trapped within the cellular membrane. As a result of these processes, intracellular electrolytes reach toxic levels, which become lethal to the cell. During a slow thaw cycle, cells at the periphery of the cryolesion will take up excess electrolytes. To equalize this gradient, water enters the cell and lead to swelling and lysis. Further re-crystallization may contribute to cellular damage, however, this phenomenon may be avoided if cells are thawed rapidly.[2]

For the treatment of oral lesions, it is extremely easy to attack oral lesions repeatedly with the cryoprobe, with only little preliminary preparation of either patient or operative field. Tissues close to the probe freeze quickly, but ice is an efficient insulator, so advance freezing proceeds only slowly. As ice delays the spread of freezing, it reduces the chance of accidental damage to the underlying tissues. Because of the gradient of heat loss, neighbouring tissues are unharmed. In cryosurgery procedure , nothing is excised rather, the lesion is frozen and the resultant necrotic tissue is allowed to slough spontaneously. Tissue death results from a combination of direct cellular effects, such as formation of ice crystals, cellular dehydration, protein denaturation and disruption of cell membranes and from ischemic infarction resulting from failure of microcirculation. Vascular stasis enhances the direct lethal effect.[4,5]

Oral mucosa, being both warm and moist is ideally suited to this technical procedure. Initially, the use of cryotherapy was limited to the treatment of cancer of the lip and oral cavity. At present its applications in the head and neck region are broad and include treatment of various benign skin growths as well as malignant lesions. In fact, over 40 different dermatological conditions of the head and neck have been described as being amenable to cryotherapy. [4]

Over the decades, cryosurgery has been used in many clinical conditions of oro-facial region. Cryosurgery could be used to produce an extended, but reversible, nerve block in the management of intractable facial pain, neurogenic pain in the temporomandibular joint (TMJ) and in the treatment of localized intraoral tumors overlying bone.[6,7,8]The main advantages of cryosurgery include absence of bleeding, low incidence of secondary infection, minimal scarring and pain and low treatment cost.[9]

White lesion is a non specific term used to describe any abnormal area of oral mucosa that on clinical examination appears whiter than the normal tissue. It is usually slightly raised, roughened or of different texture from the adjacent normal mucosa (eg.frictional keratosis, leukoplakia, chronic hyperplastic candidiasis, Linea alba buccalis,). This normal colour of mucosa may turn into white due to increased thickness of the epithelium with increased production of keratin (hyperkeratosis) and production of abnormal keratin and imbibition of fluid by upper layers of mucosa. [10]

Red lesion refers to an area of reddened mucosa that may appear smooth and atrophic or exhibits a granular, velvety texture (eg. Erythroplakia, Median rhomboid Glossitis, Erythematous Candidiasis). These lesions may occur alone or in combination with white lesions. Healthy masticatory mucosa appears light pink in

colour, however, the lining mucosa (mucosa over the cheeks, vestibule, lips, floor of the mouth and ventral surface of the tongue) is reddish pink in colour.[10]

In our study we describe the use of cryosurgery in management of the oral lesions , followed by post operative healing and recurrence of the lesion.

AIM & OBJECTIVES

Evaluation of the efficacy of cryotherapy as a treatment modality for Oral lesions

OBJECTIVES

To evaluate the post-operative clinical outcome of oral lesions after treatment with cryotherapy, with respect to

- Post-operative wound healing.
- Recurrence of the lesion

REVIEW OF LITERATURE

Andrew A Gage(1965)[16], conducted a study on cryotherapy for oral cancers of the lip and oral cavity with modern apparatus utilizing liquid nitrogen in 5 patients. The reasons for the choice of therapy included resistance to radiotherapy, lesions in areas not amenable to excision without disabling bone sacrifice and severe heart disease which made the risk of operation prohibitive. Local or general anesthesia was used depending on patients overall condition. 1 patient died of arterial MI 4 Months post treatment and at autopsy no residual tumor was found in the treated area. In other patients the lesions completely healed and other was no sign of local recurrence. It was concluded that the use of cryotherapy was an effective way to destroy a lesion locally yet pressure structural continuity of the area. Cryotherapy requires more extensive trials and should be limited to carefully selected patients.

Poswillo DE (1971)[3] done A comparative study to evaluate the effect of electro surgery and cryosurgery in management of benign oral lesions . In this study, 6 mature macca irus monkeys were selected. Routine tissue resections were done in two monkeys and the wound was closed using sutures. In the remaining animals one side of the hyperplastic tissue of the mouth was treated by electro surgery where as other side by cryosurgery. The treated sites were observed 3 days, post-operatively and at weekly intervals until 5

weeks. At this time biopsy was done and histological examination was carried out, specifically to demonstrate the amounts of mature and immature college in the healing wounds. Results demonstrated that in the clean excised and sutured wounds mature college bundles were arranged in dermis parallel to epithelial surface. In the electrosurgery wound, histologically, both mature and immature collagen were present in approximately equal amounts. However, in the cryosurgery wounds, there were slightly more mature collagen formed but there arrangement was loose and irregular. The overall impression was again about the retarded repair, of both electro and cryosurgery treated case as compared to excised wound with rather less scar formation after cryosurgery than in either the excised or electro coagulated wounds. The author was concluded that the cryosurgery appears to have advantages over excision and electro surgery for small lesions and superficial lesions.

Sako et al(1972)[22] done study with Sixty patients with oral leukoplakia were treated by cryotherapy . The areas involved were buccal mucosa, hard palate, soft palate and the floor of mouth. The lesions ranged from discrete single lesions to involvement of multiple areas. A cryosurgical unit with probe tip diameter of 9.5mm was used. Liquid nitrogen was the cooling agent. For eradication of the lesions, 35 patients required 1 treatment, 14 required 2 treatments, 2 required 4 treatments and 2 required 5 treatments. Recurrence developed in 12 patients during the follow

up period ranging from 21/2 to 4 years.The authors have described several advantages of cryotherapy over excisional surgery. However, the major disadvantage appears to be the unavailability of the complete specimen for microscopic study. It has been suggested that 1 must lean towards overtreatment, to ensure adequate depth over the entire area. The incidence of malignant transformation of leukoplakia in 6.6% cases has led the authors to question cryotherapy as a routine treatment for leukoplakia.

Bekke JPH (1979)[14] used cryosurgery in 90 selected cases of intra oral benign and malignant lesions. This clinical study was carried out during a 6 year period to investigate the value of cryosurgery as supplemental or substitute therapy. Cryosurgery was used in the treatment of 22 cases of hemangioma, 5 cases of lymphangioma, 6 cases of inflammatory papillary hyperplasia, 24 cases of leukoplakia and 33 cases of malignant tumors of oral cavity. They had obtained good results in the treatment of small to moderate, superficially situated angiomas. Good results also obtained in oral leukoplakia without severe scare formation or impairment to function. Cryosurgery is also useful in symptomatic treatment of painful condition like inflammatory papillary hyperplasia of palate.

David Barnard, John Lloyd and James Evans (1981)[6] evaluated the use of cryoanalgesia to block peripheral branches of the trigeminal nerve in the management of patients with chronic facial

pain. 54 patients with chronic facial pain were treated by cryogenic blockade. The nerve was isolated and frozen with 2 one minute freeze-thaw cycles with a fine cryoprobe, and the wound was closed. The results showed that duration of pain relief exceeded the period of sensory loss in 67 % of patients with non-herpetic neuralgia (Tic doloureux 83 %;post surgicaly.

Tal H et al (1982)[23], Conducted a study in which, the effects of cryotherapy on widespread leukoplakia of the buccal and vestibular mucosa were observed clinically and studied histologically. The treated areas were clinically normal after the treatment for 2 month, and discomfort and inconvenience of treatment were minimal. The epithelium, which was orthokeratinized, with mild dysplasia, and which was almost entirely lacking in glycogen, reverted to the parakeratinized or non-keratinized form, with normal distribution of glycogen in the stratum spinosum.

Richard K Gonglof (1983)[19] treated total 14 patients of oral lesions to study the effect of cryosurgical treatment on these lesions. The lesions ranged from papillary hyperplasia to superficially invasive squamous cell carcinoma. A CS-76 Cryosurgery System was used for the treatment. Lesions were frozen to a minimum temperature of - 2 0 C to - 40 C at the basal margin, depending on the histopathologic diagnosis of the lesion. Results showed that while lesions of papillary hyperplasia showed complete

regression and no recurrence, lesions of carcinomas showed regression initially but showed recurrence later. They concluded that when properly applied, cryosurgery is an effective, predictable, relatively self limiting, and conservative treatment method for all types of oral disease. Because of the necrosis and sloughing of the treatment area that must occur with proper therapy, delayed healing is an inherent problem with this surgical technique. Otherwise, it is free of complications such as pain, hemorrhage, infection, inadvertent damage to adjacent structures, or scar formation that are seen with other modes of therapy.

Whittaker DK (1984)[5] explained the mechanism of tissue destruction following cryosurgery. In his review the author has described the medical use of cold temperature & its application has been documented as early as 3500 BC. The first application of cryosurgery in and around the mouth appears to have been not complete , some trial on the treatment of cancer of lip and oral cavity. Studies indicate that the healing in case of cryosurgery is slower than following infusion but there is eventually less scar formation. Cryosurgery is a particularly suitable technique for the treatment of benign oral neoplasms like vascular or angiomatous lesions,lesions involving bone and for the treatment of poor risk patients.The mechanism of cell death involves formation of ice crystals, either intra or extracellularly. In the cryoprobed tissues variation in the size of ice crystal space (ICS) and their distribution

depends upon the proximity of the probe, the type of tissue and the blood supply. Ice crystal pattern in the epithelium and tissues at the periphery differ from that in the area of the probe. Some workers postulates that the initial freeze produces are increase in thermal conductivity which results in a more effective second freeze. The use of repeat freezes followed by a 5-30 mins thawing period has been considered more effective. Intracellular ice is more lethal than extracellular ice. Repeat freeze results in rather large intra cellular ice crystals and it is this increase in size, which appears to be more lethal following this technique. It is assumed that cryosurgery is a painless procedure because of immediate blockage of nerve transmission in the area. Although, cryosurgery caused ischemia in the localized tissue but the initial cause of cell death of the cryosurgery is due to the direct effects on ice crystals within the cell. Authors have concluded that repeat freezing caused large extracellular ice crystals and is more lethal. The effect of thawing on epithelium and muscles indicate osmotic damage rather than physical disruption.

Greg A Loitz(1986)[17] presented a case of erosive lichen planus of the tongue was treated successfully with cryosurgery. A 57-year-old white man had biopsy-proved erosive licen planus of the tongue. He complained of constant moderate pain in the tongue with intermittent exacerbations of severe pain. The ulcer was erythematous with a slightly raised margin, and measured 3 x 5 cm.

The remaining dorsal surface of the tongue appeared atrophic. Under general anesthesia, the entire lesion was frozen with a portable nitrous oxide cryosurgery unit and standard techniques. The patient did well after surgery, requiring only mild oral analgesics. Complete resolution of the symptoms was seen on day 6, and the lesion was healed with mild scarring by day 16.A biopsy performed 18 months after surgery showed moderate fibrosis with mild chronic inflammation. The patient was asymptomatic 20 months after treatment. The author concluded that extensive lingual erosive lichen planus can be successfully treated with cryosurgery.

Cryoneurotomy to the temporomandibular joint capsule and/or the great auricular nerve, for six consecutive patients with intractable neurogenic pain in the preauricular region, was done by **Goss AN**(1988)[7]. All patients had severe pain complicated by failed previous treatment, analgesic abuse or psychiatric problems. All patients had excellent pain relief for 1 year following cryoneurotomy but with recurrence in four patients. Repeated cryoneurotomy was performed but with decreasing effectiveness. In conclusion, the technique is a useful addition to the armamentarium of the oral and maxillofacial surgeon who works in association with a multidisciplinary pain clinic on patients with intractable facial pain.

Kardos TB, Ferguson MM(1991)[12] use portable carbon dioxide laser may provide an alternative form of treatment. The effectiveness and the healing response following use of the two techniques was compared by producing lesions on the lateral border of sheep tongues . The authors concluded that Cryosurgery produced more extensive lesions with a marked inflammatory reaction but no differences in the time course of healing were evident. Laser surgery was so as effective as cryosurgery in the removal of superficial tissues but caused less swelling and, therefore, may be advantageous in some clinical situations.

M.Anthony Pogrel(1993)[24] treated locally aggressive bone lesions by using a combination of enucleation and cryosurgery to devitalize the surrounding bone, thereby minimizing the need for segmental mandibular resection. Thirty seven patients with locally aggressive bone lesions like ameloblastoma , OKC, giant cell lesions etc. were treated with liquid nitrogen cryotherapy over a 7 year period. For osseous lesions, cryosurgery offers some unique advantages over other treatment modalities because it will kill cells within the bone but will leave the inorganic osseous framework untouched, so that it can remain as a matrix for new bone formation. Based on the results obtained in this study and those obtained by other investigators, liquid nitrogen helps in new bone formation by a phenomenon **'creeping substitution '**.

McCreary CE and McCartan BE(1999)[11] reviewed the clinical management of oral lichen planus. **T**here is an array of treatments, they are palliative rather than curative. Corticosteroids in various forms remains the main stay of treatment, but newer immunomodulatory agents have an increasing role. The authors have also described the use and advantages of surgical treatments like cryosurgery, CO2 lasers and conventional surgical excision. Cryosurgery appears to be more advantageous than lasers and excision due to its virtue of less scarring and better patient acceptance.

Chin-Jyh Yeh(2000)[15] conducted a study on the effectiveness of simple cryosurgery on 102 oral benign lesions on an outpatient basis. Among these lesions, based upon the histopathology reports, there were 36 mucoceles, 25 leukoplakias, 20 hemangiomas, 16 verrucous hyperplasia, 3 labial fibromas and 12 erosive lichen planus. Topical anesthetic, 4% xylocaine jelly, was applied on the lesion. Cotton swab was dipped into liquid nitrogen for 1–2 seconds and applying it on the lesion with pressure to form an ice-ball. Two consecutive freeze-thaw cycles were used. Results showed that 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. The lesion and overlying mucosa became necrotic and sloughed in 3–5 days. There was none or very

little scar formation and bleeding and infection did not occur. Pain in most patients, if present, was usually mild and easily controlled with non-narcotic pain medication. Healing was uneventful in all the patients and acceptance of the treatment procedure was excellent. Primary recurrence developed in 8 cases of leukoplakia (32%), 2 cases (5.6%) of mucocele, and 4 cases (25%) of verrucous hyperplasia. All were successfully treated by additional cryosurgery.

A.Darbandi, N.Amel Shahbaz(2004)[10] did a study on the effects of cryotherapy on physiological pigmentation of the oral mucosa in ten patients. The location and extent of every lesion was determined and local anaesthesia was obtained by supra periosteal injection. Depending on the size of the lesion a proper probe was selected and the pigmented area was frozen with nitrous oxide gas for 20-30 seconds. Due to the treatment method a white line caused by the necrosis of the mucosa appeared round the probe. In the second day after the treatment the lesions in all patientsshowed satisfactory appearance and 60% recovered by 7^{th} day after treatment. In all the patients the procedure was successful and the results were satisfactory. This study concluded that because of the smooth surface and presence of saliva, oral cavity is an ideal environment for cryotherapy and can be used as an effective method of treating oral pigmentations and other oral lesions.

Farah CS and Savage NW (2006)[2] in their review explained that Cryotherapy is the deliberate destruction of tissue by application of extreme cold. It is well received by patients due to relative lack of discomfort, absence of bleeding and minimal to no scarring after healing. It has many applications in oral medicine and oral pathology, and is extremely useful in patients for whom surgery is contra-indicated due to either age or medical history. The authors have also described the principles, mechanisms of action, and current applications of cryotherapy in the treatment of oral lesions.

I **Phillip J Ameerally and Graham B Clover**(2007)[4], emphasized on the, use, biology and clinical application of cryotherapy in maxillo facial region. The rate of heat exchange depends on several factors including water context, blood supply thermal conductively of the tissue, rate of freeze and temperature of the refrigerant. There are two principle methods of application, through closed probes or by spraying liquid nitrogen directly over the tissues. The contour of the cryolesion is approximately dome shaped down to a depth of 6mm and the lateral spread of the ice is approximately equal to the depth of freeze. The cell death occurs due to extra and intra cellular ice crystal formation. Ice crystal formation reduces extracellular water causing fluid shift and disrupts the cell membrane intracellular ice damages mitochondria and endoplasmic reticulum. The advantages of cryotherapy includes that it can be used in all age groups and even in those with poor oral health. Cryotherapy can be

used at sites like shoulder and anterior chest was which are prone to scarring. Patients on anti-coagulants can be treated safely. Authors have also described the application of cryotherapy in various cutaneous lesions like benign lesions, pre malignant lesions, Bowen's disease, solar keratosis, Actinicheilitis and skin cancers. Complication and side effects of cryotherapy include edema or blister formation with in 24-72 hours. There can also be hemorrhage and ulceration. Nerve conduction may be affected, pigmentary changes are most common long term complication of cryotherapy.

Manu Prasad et al (2009)[20] have discussed that out of other cryogens liquid nitrogen cryotherapy is more effective. Most tissue freezes at 2.2c and tissue death occurs at a temperature of 20c. The amount of mature collagen found in a cryosurgery is less than in scars produced by a knife or electrosurgery. However, due to lack of precision in this procedure, judgement of final volume of tissue necrosis is difficult. The authors have concluded that the initial results are promising and liquid nitrogen cryotherapy has certain advantages over other treatment modalities.

Chuan-Hang Yu et al(2009)[25], studied the effect of cotton-swab cryotherapy (CSC) technique on oral leukoplakia lesions, which is performed by directly applying liquid nitrogen to the lesion with a cotton swab. Two kinds of cotton swab with diameters of 4 and 7 mm were used for the therapy depending on the size of the lesion.

The site of the lesion was air-dried before treatment to prevent the cotton swab from sticking to the oral mucosa. The cotton swab was dipped in liquid nitrogen for at least 5 seconds and applied to the lesion with pressure for 20 seconds to form an ice ball and then allowed to thaw for another 20 seconds. Four consecutive freeze-thaw cycles were performed on the same area of the lesion. All 60 OL lesions showed complete regression without scar formation after an average of 6.3 (range, 1–17) cryotherapy treatments.

Sunita J (2010)[26] in her review the various aspects of cryotherapy has been discussed . The commonly used cryogens are liquid nitrogen, nitrous oxide, solidified CO2, Chlorodiflomehtane, dimethyl ether and proposed cryotherapy is used for the treatment of keratotic, hyperplastic, granulomatous, vascular, pigmented lesions salivary grand lesions. The major disadvantage of using liquid nitrogen is lack of control ones the temperature with in the cells and area of freezing. Also rapid evaporation of liquid nitrogen requires numerous applications on the lesion. Current protocol suggests that most begin mucosal lesions a 1-2 min Freeze /thaw cycle using lesionsare recommended to undergo thrice 2 min freeze / thaw cycles. Cryotherapy does not convey cold to the tissues because cold is not transferable, in contrast, the tissue looses heat because they warm the cold agent. The author has also described the effects of clod therapy in cases of inflammation, trauma and post-surgery.

It can be concluded that cryotherapy is an effective treatment method for intraoral surgeries.

Leonardo tonietto et al(2011)[27] did a study on keratocystic odontogenic tumors (KOT's) of the jaws by following a technique of lesion enucleation without capsule disruption combined with liquid nitrogen cryotherapy. Eight patients were induced in the study. After enucleation, liquid nitrogen was applied twice for 1 minute, with 5 minute intervals between applications to allow defrosting between applications. No patients had any pathological fracture during follow up period .One patient had loss of sensation in the left lower lip region but gradually returned to normal within 12 months. In the conclusion, liquid nitrogen which has cell necrotising properties and preserves inorganic structures, in contrast to carnoy solution, which destroys osteogenic and osteoconductive properties. Thus, cryotherapy technique in KOT's preserves the bone framework and results in better repair.

Sidebottom AJ, Carey EC and Madahar AK (2011)[8], 17 done a retrospective study for 5 years patients who had severe pain of temporomandibular joint that had failed to respond to all forms of conventional conservative treatment, were treated by cryotherapy. Patients were given preliminary diagnostic injections of intra-articular bupivacaine to relieve the pain. Patients were treated under general anaesthesia. A preauricular incision was made and the area

dissected until the capsule was reached. Using a cryoprobe, three freeze-thaw cycles of 90 seconds duration were applied in each case in an inverted L fashion to the posterior and lateral portion of the capsule. The patients were followed up routinely at 6 weeks and up to one year. Results suggested that Cryoanalgesia provides short-term relief of intractable neurogenic pain in the TMJ, with some chance of long-term relief. The authors have concluded that Cryoanalgesia can be a useful adjunct to the management of intractable pain localised to the TMJ.

Hung-Pin Lin et al (2011)[28] conducted a study to evaluate the efficacy of cryogun to treat 60 oral leukoplakia lesions in 54 patients, with an aim to access whether oral leukoplakia lesions treated by the cryogun cryotherapy needed significantly fewer treatments to achieve complete regression than those treated by the cotton-swab cryotherapy. Fifty-four patients (48 men and 6 women; mean age, 54 _ 11 years; range, 33–80 years) with a total of 60 oral leukoplakia lesions were recruited. All lesions were biopsied for conformation and treated with cryogen cryotherapy.The lesion was air-dried and sprayed with liquid nitrogen for 7 to 10 seconds onto the lesional surface to form an ice ball or field that extended 2 to 3 mm beyond the visible pathologic border of the lesion. The frozen field was then allowed to thaw for at least 20 seconds. Four or 5 consecutive freeze–thaw cycles were performed on the same lesion. All 60 oral leukoplakia lesions showed complete regression, with

little or no scar formation after an average of cryogun cryotherapy treatments.

Ashok Bansal et al (2012)[1], described the applications of cryosurgery in treatment of oro-facial lesions. Earlier authors have documented that low temperatures could be used to destroy cancerous growths. All biological tissues subjected to temperatures of -20c or below for a minute or more undergo cryogenic congelation or necrosis. Oral lesions being both warm and moist are ideally suited to this technical procedure. In cryosurgery, the lesion is not excised rather, the lesion is frozen and the resultant necrotic tissue is allowed to slough spontaneously. Healing is usually excellent and the mucosa largely returns to normal by 6 days after treatment. There are various distinct mechanisms of tissue damage depending on apparatus used, type of tissue, distance from cryoprobe, rate and degree of cooling. An understanding of these mechanisms enables one to vary technique according to nature, site, size and depth of lesion. The factors associated with tissue destruction have been explained as direct & indirect effect.The direct effects being ice crystal formation, cellular dehydration & electrolyte disruption, thermal shock, inhibition of enzymes, protein changes and effects of thawing. In direct effects are vascular effects & immunologic effects. The available apparatus for cryotherpy can be classified as open system & closed system. Cryosurgery can be useful and effective treatment for various oro-facial lesions. Like

vascular malformation, hyperkeratosis and leukoplakia, granulomatous and hyperplastic conditions, mucus cysts, polyps and lichen planus. Other applications of cryosurgery can be in cases of intractable facial pain, TMJ pain, oral cancers and herpetic or aphthus ulcers. Contraindications for cryosurgery are cold intolerance, cold urticaria, cryoglobulinemia, agammaglobulinemia, Raynaud's and collagen diseases, patients undergoing hemodialysis or immune suppressive therapy patients with platelet alterations or with multiple myeloma. The authors have concluded that cryosurgery is a very safe easy to perform & inexpensive and atraumatic for treating various oral lesions in an out-patient clinic.

Ravi Narula and Bhavna Malik (2012)[9],studied in 34 patients which includes (lichen planus, mucocele, leukoplakia, pyogenic granuloma) .He used freeze thaw cycles each of one and a half minute freeze and 3 minute thaw at overlapping sites for all the cases of leukoplakia. Epulis fissuratum required double freeze thaw cycles each of 2 minutes freeze and four minutes thaw. All the lesions of mucocele were treated in single session and each lesion required double freeze-thaw cycle of one minute freeze and two-minutes thaw. All cases of ranula required only a single session. Two cases of lichen planus and one case of mucocele showed recurrence. Two cases of lichen planus and one case of mucocele showed recurrence. All cases showed normal healing between second to fourth week postoperatively after last cryo-application

except one case of epulis fissuratum showed reduction in size but incomplete healing. The results of treatment of various lesions managed by cryosurgery support the clinical contention that cryosurgery has earned a place on the armamentarium of maxillofacial surgery.

Daveinthiran Thanabalan(2012)[30] has described a time spot freeze technique for lesions upto size of 2 cms in diameter. This method utilizes a small spray gun holding liquid nitrogen. The spray gun is positioned at a distance of 1 to 1.5 cm from the skin and aimed at the center of lesion. After the initial ice ball formation the spray is kept on for atleast 30 seconds to allow adequate freezing of the lesion. The applications of cryosurgery in various oral lesions like hyperkeratotic and oral leukoplakia, lymphangioma, hemangiomas, accelerations, hyperplastic condition, oral cancers and oral lichen planus have also been described. The author have further described the advantages, disadvantages and complications of cryosurgery and concluded that it is an effective treatment option for variety of lesion of head and neck region.

Syed Nayeema and Subha M(2013)[13], in their review described cryotherapy as a novel treatment modality in oral lesions. The physical principle behind cryotherapy is based on Joule Thompson expansion which enables substances to undergo a drop is temperature when moved from a high pressure to a lower pressure

area. The biophysical changes in the tissue due to cooling is vasoconstriction, however, when the temperature is reduced and maintained low for more than 15 minutes it causes cold induced vasodilation. The cycle keeps repeating continuously and is known as hunting response. The tissue death occurs either due to direct response to cold, like ice crystal formation, thermal shock, cellular dehydration or by indirect effects like, ischemic neurosis and immunological effects. The factors influencing cryotherapy are, type of apparatus, coolant used, temperature achieved, duration, number of cycles, volume of tissue and type of tissue. Cryotherapy has various applications in lesions of oral mucosa like, vascular malformations, leukoplakia, hyperplastic lesions, mucous clyster, facial pain, TMJ pain and oral cancers. The authors have concluded cryotherapy is advantageous over surgery and is well accepted in plates, right from infants to elderly.

Aarti Garg et al (2014)[21] treated a mucocle case in a 6 year old male patient, with a painless swelling in the floor of mouth using cryoprobe. After local anesthesia was administered the lesion was directly exposed to 4 rounds of freeze and thaw cycles using a cryoprobe, attached to the liquid nitrogen equipment. Each cycle lasted 5 to 10 seconds and moved from the center of the lesion to the borders until the lesion appeared white and frozen, resembling and ice ball. No recurrence at the 1st, 3rd and 6th months follow up was reported. The authors have further discussed that the main

disadvantage of this technique is the lack of specimen to be examined microscopically to confirm diagnosis. A biopsy prior to cryotherapy may compromise the final result for clinically diagnosable lesion such as mucocele. Other disadvantages include unpredictable degree of swelling and lack of precision electron depth and area of freezing. The authors have concluded that liquid nitrogen cryosurgery is a useful and effective therapeutic alternative for treating mucocele in children

A series of 5 cases were treated by **Karla Myra Rezende et al** (2014)[29], to demonstrate the clinical efficiency of cryosurgery as an alternative to invasive surgical treatments of the most common oral lesions in children. The cases were randomly selected and consisted of mucocels, Ranula, Verruca Valgaris, Molescum Coatagiosum and pyogenic granuloma. Liquid nitrogen was used as a cryo-agent in all the cases four quick freeze and thow cycles were used. Post-operative period was uneventful in all the cases. Healing occurred with out any pain, bleeding, discomfort, infection and with minimum or scar formation. The author suggest that whenever cryosurgery is possible, it should be the first option to treat a wide variety of skin and oral mucous disorders instead of other surgical techniques. It was concluded that cryosurgery is an effective and painless treatment method of oral lesions in children.

Hsin-Ming Chen, Shih-Jung Cheng, Hung-Pin Lin, Chuan-Hang Yu, Yang-Che Wu, **Chun-pin Chiang(2015)**[18] did a study to determine the effectiveness of cryogun cryotherapy for Oral Leukoplakia and adjacent melanotic lesions. In this study cryogun cryotherapy was used to treat 72 oral leukoplakia and adjacent smoking induced melanosis (OLM) lesions on the buccal mucosa. Complete regression was achieved in all 72 OLM lesions after a mean of 3.3±1.3 cryogun cryotherapy treatments. We found that OLM lesions in patients without smoking habit, with the greatest diameter <2.8 cm, with epithelial dysplasia, or with surface keratin thickness ≤ 50 μm needed significantly fewer number of cryogun cryotherapy treatment to achieve complete regression than those OLM lesions in patients with smoking habit with greater diameter ≥ 2.8 cm, without epithelial dysplasia or with a surface keratin thickness of > 50μm respectively. The study concluded that cryogun cryotherapy is a good and effective treatment modality for oral leukoplakia.

MATERIALS AND METHODS

Source of data

This study was undertaken up for the outpatient who reported to Adhiparasakthi Dental College & Hospital . Patients were included in the study were those affected with oral lesions, either benign or premalignant lesions. 15 patients who were randomly selected from the outpatient, to evaluate the effectiveness of cryosurgical method of treating oral lesions with liquid nitrogen after obtaining ethical clearance.

Method of collection of data

This study was conducted in the Department of Oral and Maxillofacial surgery, Adhiparasakthi Dental College & Hospital with a sample size of 15 lesions.

• Informed/written consent was taken from the subjects/care takers.

• Routine, pre-surgical Haematologic investigations were done.

Inclusion criteria:

- Patients who diagnosed with benign or premalignant oral lesion
- Lesion size more than 1cm
- Patient willing for cryotherapy
- Patients under ASA I / ASA II category

Exclusion criteria:

- Patients diagnosed with oral malignant lesions.
- Patients not willing for cryotherapy.
- Medically compromised patients

STUDY DESIGN:

SAMPLE SIZE:-A sample size of 15 oral lesions.

- All the subjects, selected on the basis of inclusion criteria were treated with cryogun spray cryotherapy, using liquid nitrogen . Clinical photographs of the lesions were taken prior to cryotherapy and the procedure is performred

Materials:

Liquid nitrogen is a liquefied atmospheric gas produced industrially in large quantities by performing fractional distillation of liquid air. It is colorless pure liquid at a very low temperature (-196°C). It is stored and transported in cryocan or liquid nitrogen low volume container available in wide range of capacities.

Armamentarium used:

1. Mouth mirror
2. Straight probe
3. Tweezer
4. Stainless steel bowl
5. Cheek retractor
6. Gauze
7. Cryospray
8. Liquid nitrogen
9. Cryocan for storage of liquid nitrogen
10. Local Anasthesia

Fig 4.1 Cryocan

Fig 4.2 Cryospray

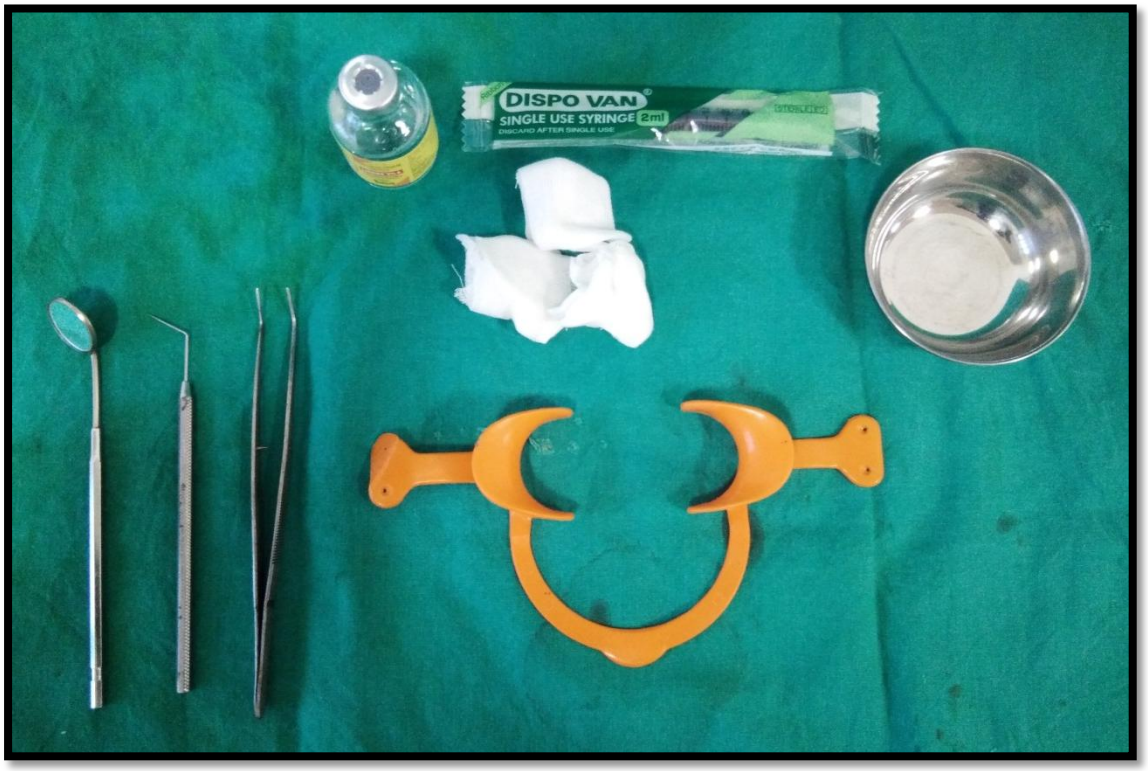


Fig 4.3 Armamentarium

METHOD OF STUDY:

There are two methods of Cryotherapy:

1. Open method: In this method the cryogen is directly applied to the lesion by cotton swabs or cryogun spray.

2. Closed method: In this method the cryogen is applied to the lesion by the use of Cryo-probes.

In the present study, the open method used for treat the lesions via, direct application of liquid nitrogen with cryogun spray. Intra oral lesions like premalignant leukoplakia patches, lichen planus, irritational growths and mucoceles were selected. Local anaesthetic infiltration was given around the lesion. The method of application should start from the centre to the periphery. Lesions is too large to be frozen by single spray it is managed by multiple overlapping applications of liquid nitrogen.

Freezing time was 30-50 seconds for mucoceles, erosive lichen planus and 60-70 seconds for fibromas, leukoplakia . Thawing proceeds spontaneously for 30-60 seconds. After the ice ball produced during freezing was completely thawed, the next freezing was performed. High speed suction is necessary during treatment to control visual obstruction of the vapour fog. Secondary treatment was performed after 1 -2 weeks if any residual lesion remained. Liquid nitrogen being a highly volatile substance and has

to be used instantly from the time of dispensing it. Post operatively the patients were prescribed analgesics. The patients were examined on the 3rd day, 1st week, 2nd week and 1 month post operatively.

STUDY PARAMETERS INCLUDED:

Wound Healing:

Pre-operatively, the size of the lesions was measured in anteroposterior and superoinferior dimensions with a vernier caliper. Similarly, the dimensions were measured at 1st, 2nd and 3rd post-treatment.

1) Post-operative pain was assessed and scored on the day of surgery, 3rd day and 1 week after surgery as:

0- No pain

1- Slight pain

2- Mild pain

3- Severe pain

4- Very severe pain

5- Extremely severe pain

2) Presence of post-operative **swelling** was evaluated on 3rd and 1 week surgery:

0- No swelling

1- Slight swelling

2- Mild swelling

3- Severe swelling

4- Very severe swelling

5- Extremely severe swelling

3) Presence of **sloughing** was noted at the end of 1 week as:

Present

Absent

4) Presence of **granulation tissue** was noted at the end of 2 weeks as:

2-Good-(entire wound)

1-Fair-(nearly entire wound)

0-Poor - (inadequate)

5) Epithelization was noted at the end of the month as:

2-Good – (entire wound)

1-Fair- (nearly entire wound)

0-Poor-(inadequate)

Recurrence :

Recurrence of the lesion was evaluated clinically at the 2 month post op. The results of the study should be evaluated statistically, with the help of CHI SQ TEST and N par TEST.

CASE 1

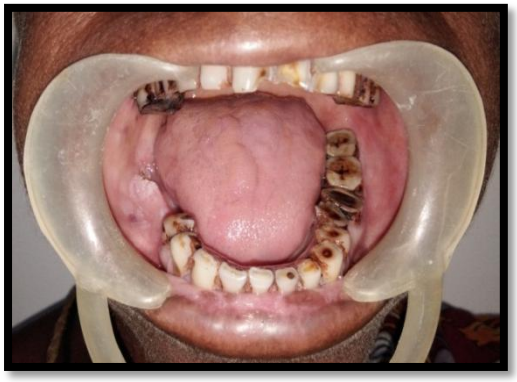
Pre operative mucocele seen in the ventral tongue region

Intra operative

1st week post operative showing sloughing

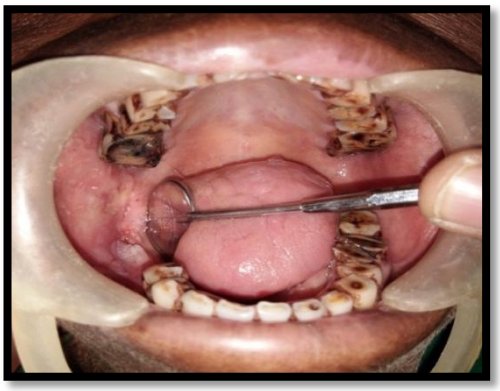
1st month post operative showing complete

CASE 2

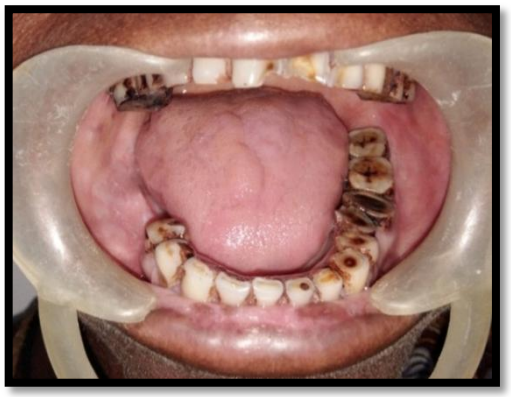


Pre operative Leukoplakia , seen in 48 region

Intra operative



1st week post operative

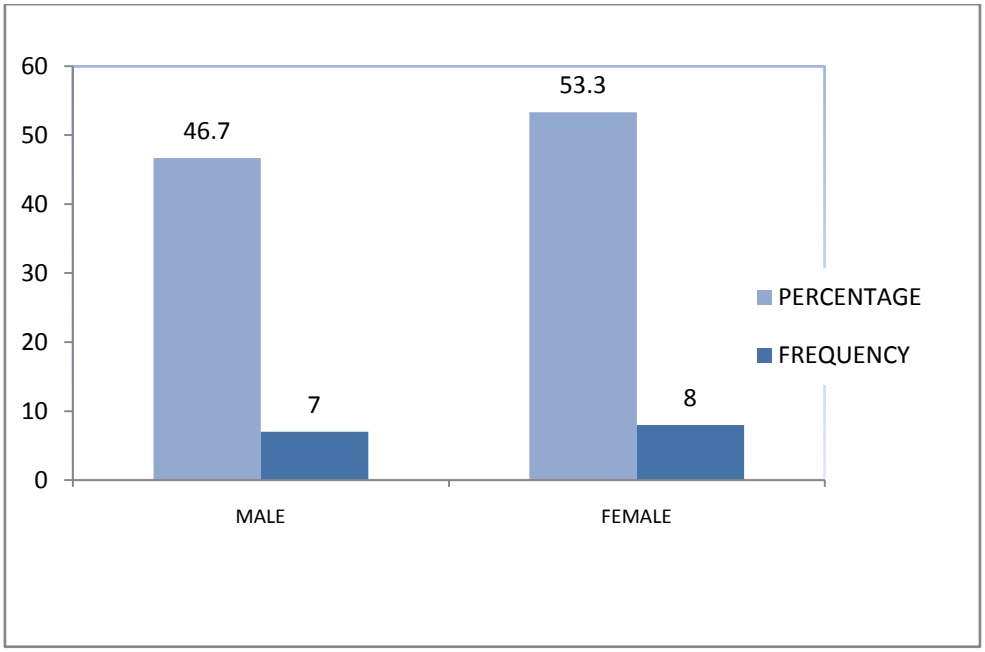


1st month post operative

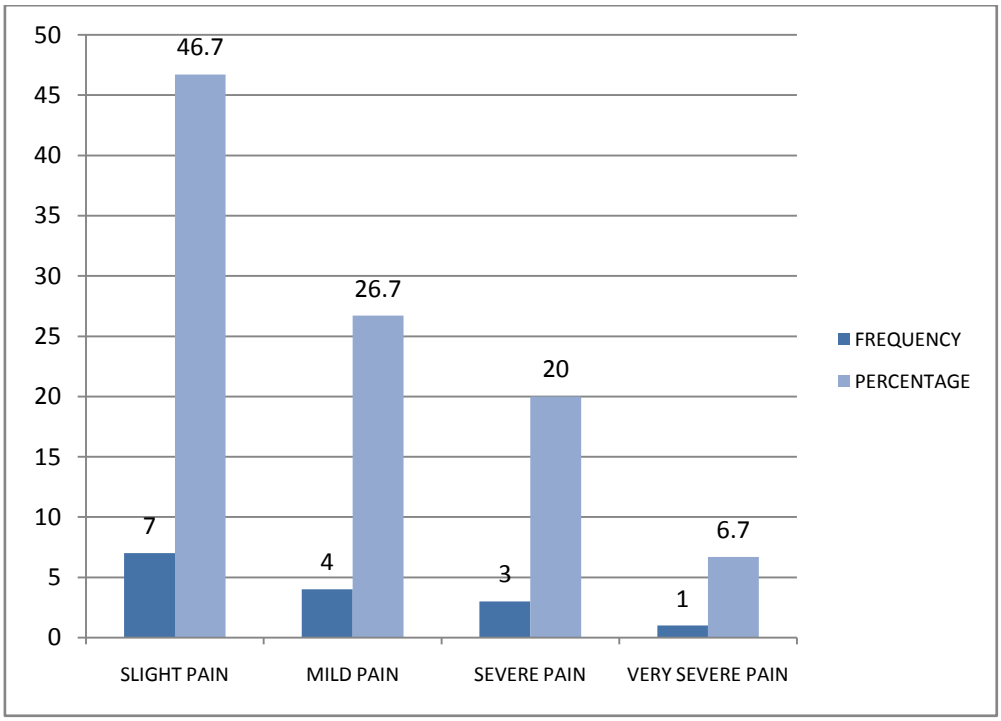
RESULTS

The present studywas conducted to evaluate the efficacy of cryotherapy as treatment modality for oral lesion, to evaluate the post operative clinical outcome of oral lesion after treatment with cryotherapy with respect to post- operative wound healing and recurrence of the lesion in the department of Oral and Maxillofacial Surgery, at Adhiparasakthi dental college and hospital. 15 patients who was affected with oral lesion either benign or pre-malignant lesion of size more than 1cm ,were randomly selected from out-patient to evaluate the effectiveness of the cryosurgery method of treating oral lesion with liquid nitrogen after obtaining ethical clearance. The age of patients ranged between 22yrs-52yrs with 46.7% of male and 53.3% of female. The overall mean age of the study population 33.6. In this study the open method was used to treat the lesion by direct application of liquid nitrogen with cryogun spray, all subjects selected on the basis of inclusion criteria. Among 15 patients, there were 5 mucocele lesions, 2 traumatic fibroma, 1 leukoplakia, 2 erythroplakia, 3 lichen planus, 2 Apthous ulcers were seen. The site of occurrence of the lesion varied in different subjects the lesions were present on the buccal mucosa, floor of the tongue, upper vestibule, lower vestibule. Post-treatment follow up was done at 3rd day, 1st week and 1st month and 2nd The results were evaluated statically with the help of Descriptive statistics and NPar tests: chi-square test, kolmogorov-smirnov test.

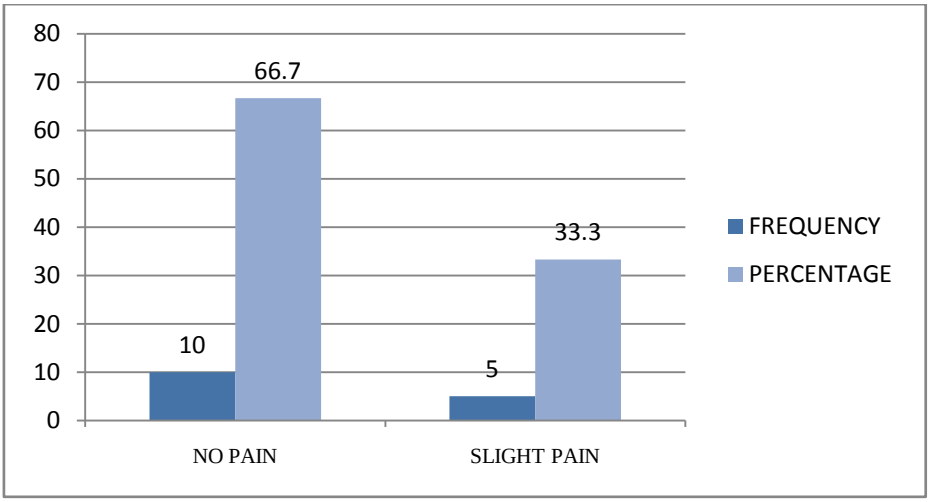
DISTRIBUTION OF SEX:



POST OPERATIVE PAIN 3RD DAY



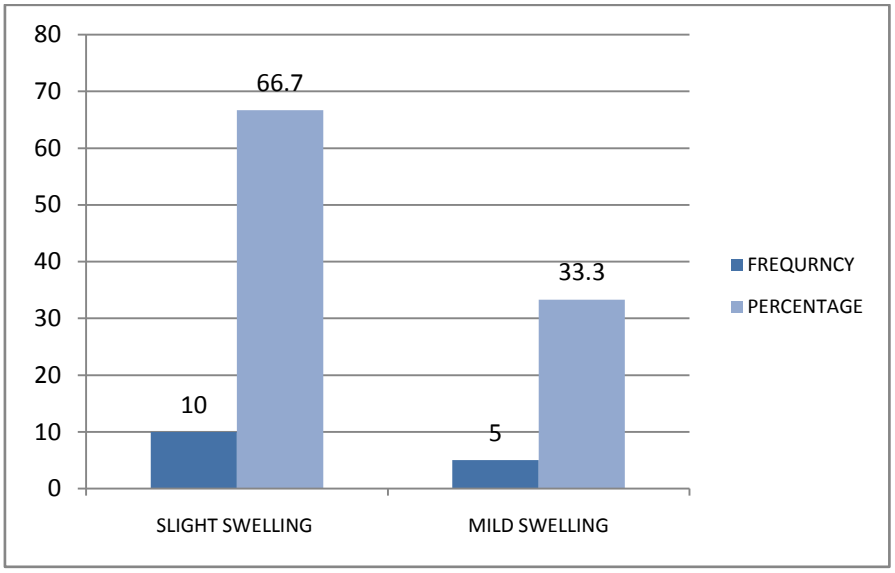
POST OPERATIVE DAY 1ST WEEK



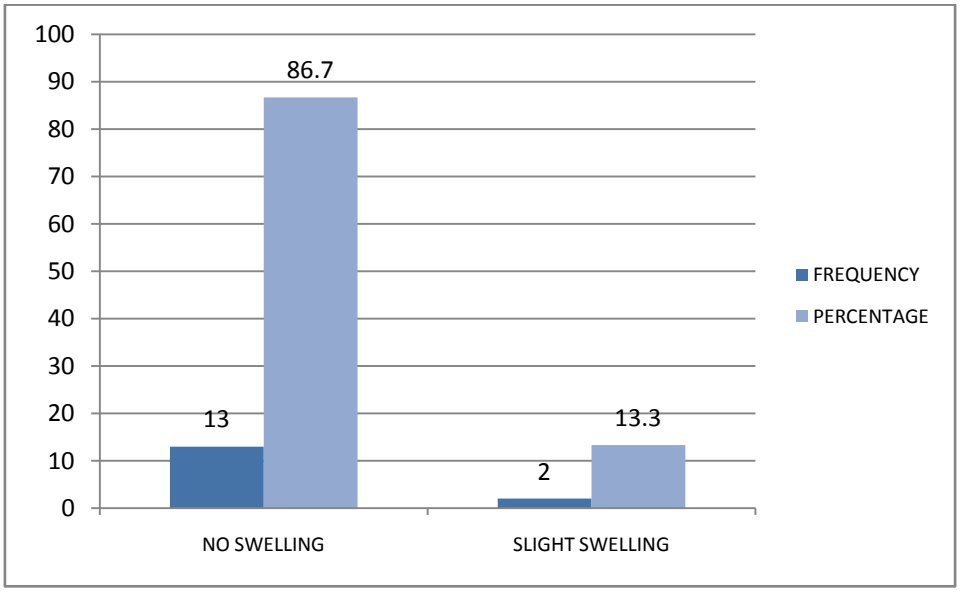
On the 3rd day after treatment 46.7% (7) of them had slight pain, 26.7 % (4) of them had mild pain, 20% (3) of them had severe pain and 6.7% (1) of them had very severe pain.

One week after treatment 66.7% (10) of the patients had no pain and 33.3% (5) of them left with slight pain. The pain score was significantly different from post-operative score through 1st week. The post- operative and 3 days pain score was significantly higher than 1 week

SWELLING 3RD DAY



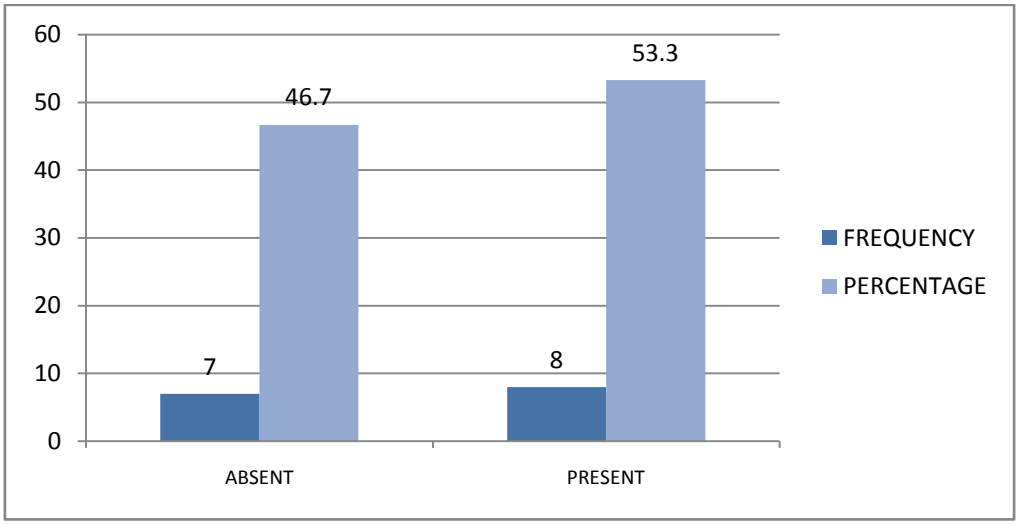
SWELLING 1ST WEEK



Swelling on 3rd day after treatment 66.7% (10)of the patients had slight swelling and 33.3% (5) of them had mild swelling.

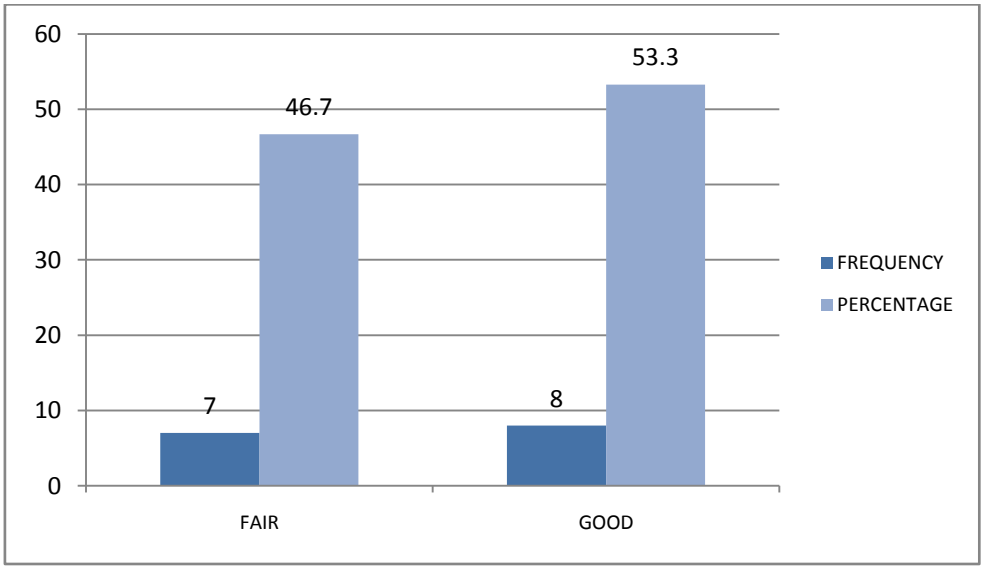
On 1st week post treatment 86.7% (13) of them had no swelling and 13.3 % (2) of the patients had slight swelling.

SLOUGHING 1ST WEEK



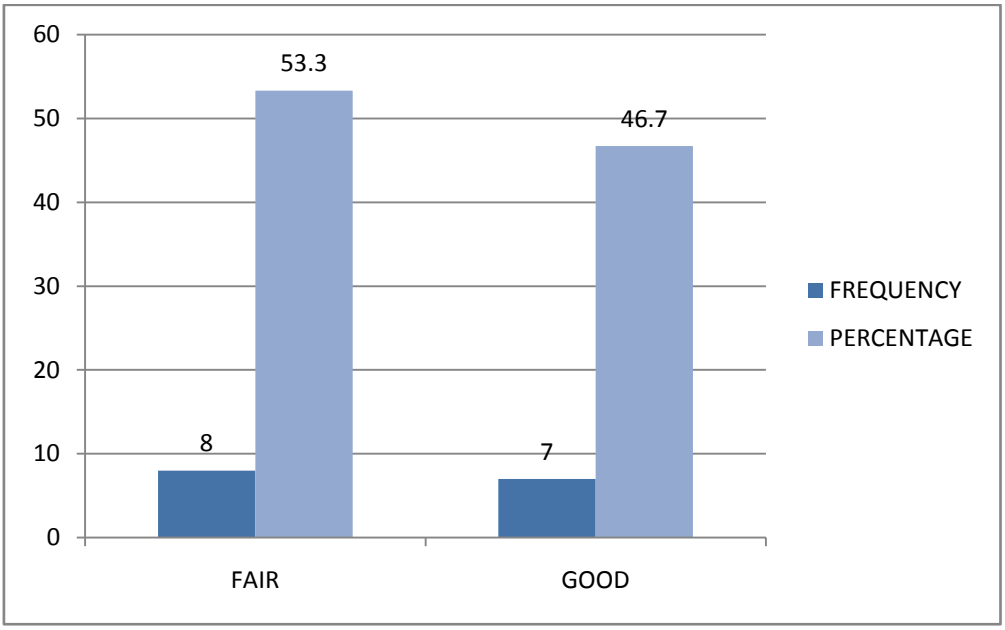
There was no slough formation in 46.7 %(7) of the patients on 1st week post treatment and 53.3%(8) of the patients had slough formation.

GRANULATION 2 WEEKS



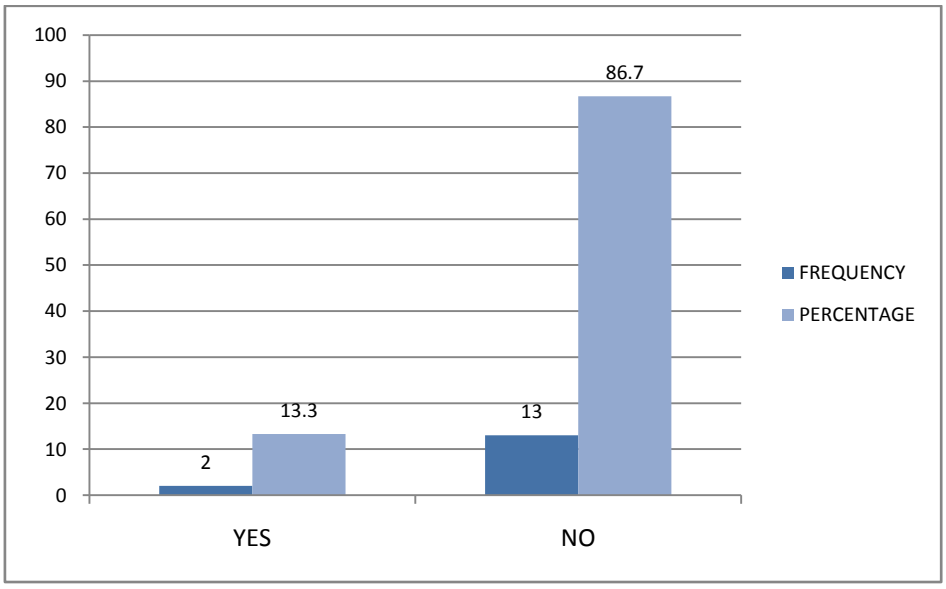
After 2 weeks post treatment 46.7% (7)of the patients had fair amount of granulation tissue formation and 53.3 %(8) of the patients had a good amount of granula.tion

EPITHELIZATION 1 MONTH



One month after treatment there was fair epithelization in 53.3% (8)of patients and 46.7%(7) of patients had good epithelization.

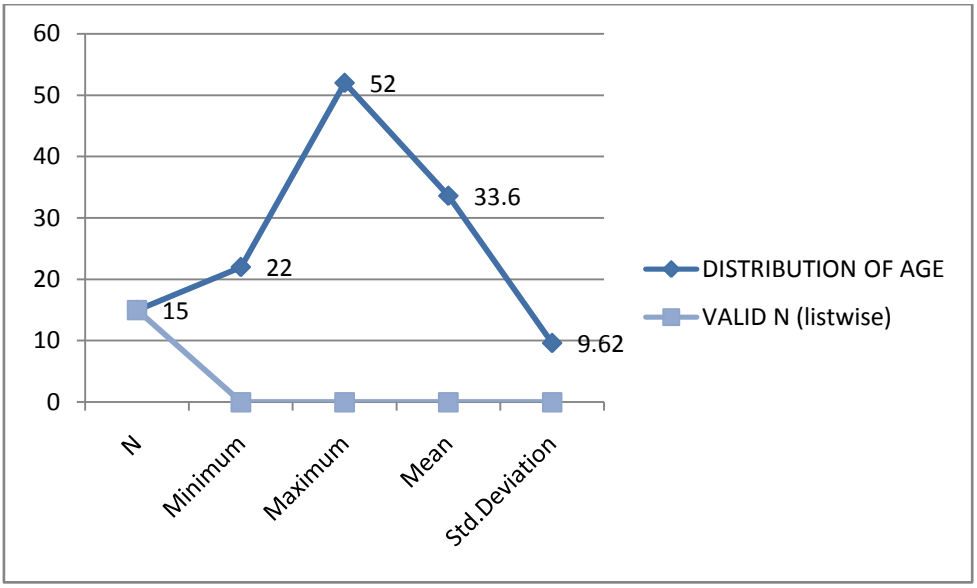
RECURRENCE 2 MONTH



There was recurrence of the lesion in 13.3%(2) after 2months and 86.7%(13) of them had no recurrence.

DESCRIPTIVES

Descriptive statistics



15 patients were enrolled in the study minimum age was 22 and the maximum age was 52, mean=33.60, SD= 9.620.

NPar Tests

Chi-Square Test

Test Statistics					
	post op pain 3rd day	**post op day 1st week**	**swelling 3rd day**	**swelling 1st week**	**sloughing 1st week**
Chi-Square	5.000[a]	1.667[b]	1.667[b]	8.067[b]	.067[b]
df	3	1	1	1	1
Asymp. Sig.	.172	.197	.197	.005	.796
a. 4 cells (100.0%) have expected frequencies less than 5. The minimum expected cell frequencyis 3.8.					
b. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 7.5.					

Test Statistics			
	granulation 2weeks	**epithelization 1 month**	**recurrence 2 month**
Chi-Square	.067[b]	.067[b]	8.067[b]
Df	1	1	1
Asymp. Sig.	.796	.796	.005
a. 4 cells (100.0%) have expected frequencies less than 5. The minimum expected cell frequency is 3.8.			
b. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 7.5.			

NPar Tests

One-Sample Kolmogorov-Smirnov Test				
		post op pain 3rd day	**post op day 1st week**	**swelling 3rd day**
	N	15	15	15
Normal Parameters[a,,b]	Mean	1.87	.33	1.33
	Std. Deviation	.990	.488	.488
Most Extreme Differences	Absolute	.276	.419	.419
	Positive	.276	.419	.419
	Negative	-.191	-.247	-.247
	Kolmogorov-Smirnov Z	1.069	1.624	1.624
	Asymp. Sig. (2-tailed)	.204	.010	.010
a. Test distribution is Normal.				
b. Calculated from data.				

One-Sample Kolmogorov-Smirnov Test				
		swelling 1st week	sloughing 1st week	granulation 2weeks
	N	15	15	15
Normal Parameters[a,,b]	Mean	.13	.53	1.53
	Std. Deviation	.352	.516	.516
Most Extreme Differences	Absolute	.514	.350	.350
	Positive	.514	.316	.316
	Negative	-.352	-.350	-.350
	Kolmogorov-Smirnov Z	1.992	1.357	1.357
	Asymp. Sig. (2-tailed)	.001	.050	.050
a. Test distribution is Normal.				
b. Calculated from data.				

One-Sample Kolmogorov-Smirnov Test			
		epithelization 1 month	recurrence 2 month
	N	15	15
Normal Parameters[a,,b]	Mean	1.47	1.87
	Std. Deviation	.516	.352
Most Extreme Differences	Absolute	.350	.514
	Positive	.350	.352
	Negative	-.316	-.514
	Kolmogorov-Smirnov Z	1.357	1.992
	Asymp. Sig. (2-tailed)	.050	.001
a. Test distribution is Normal.			
b. Calculated from data.			

DISCUSSION

This Critique was undertaken to evaluate the efficacy of cryosurgery, as a treatment modality in management of benign and premalignant oral lesion which is of size greater than 1 cm and to evaluate the post operative clinical outcome of oral lesion using liquid nitrogen with cryogun spray through open method. Our clinical study was done on 15 out- patients with the respective lesion. a regular follow up was done at 3rd day,1stweek,2nd week, 1st month and 2nd month to evaluate the post operative pain, swelling,granulation tissue formation, epithelization and recurrence. This study presents a series of cases that demonstrate the clinical efficacy of cryosurgery as an alternative to conventional surgical technique to treat most common oral lesion, this technique is well tolerated by patients due to the rapid healing and minimal bleeding, can be performed in absence of anesthesia and is extremely an useful alternative in patients to whom minor surgery is contraindicated due to age or medical history. It is the simple procedure to perform, minimally invasive, low cost and very effective.

Destruction of the diseased tissue in the appropriate position by means of freezing is well established in many branches of surgery. The tissues are apparently unaltered at thaw but progressive necrosis happens. There is controversy as to whether tissue death is principally due to the direct effects of freezing or to subsequent ischemia. Studies at the ultra structural level show that

ice crystals are formed within the cells during cryosurgery in which resultant cell damage is osmotic rather than mechanical and that microcirculatory changes are secondary in terms of the chronological development of tissue necrosis. The experiments carried out on intact tissues under conditions similar to those used in clinical cryosurgery have clarified some of the mechanisms involved in tissue destruction. It has been shown, using freeze substitution and electron microscopy, which ice crystals form intracellularly during cryosurgery although evidence from freezing isolated cells would suggest that the freezing rates used clinically would be more likely to result in extracellular ice. It appears that cells in close contact in living tissues behave differently to those suspended in liquids. Repeat freeze results in rather large intracellular ice crystals and it is this increase in size which appears to be more lethal following this technique. The changes occurring in the living tissues immediately after thaw have been described both in epithelium and muscle[(5)].

The application of cryotherapy to oral surgery has been facilitated by the development of keeler arul probe. preliminary experiments with these applicators indicated that the probe could be used most effectively in oral surgery, especially for the eradication of superficial lesion by necrosis, with discomfort both during and tissue reaction, eliminating bleeding, and reduced discomfort both during and after the operation. To test the effectiveness of the cryoprobe in this field and compare the results with excision and

suture, and electro surgery. Cryosurgery would appear to have advantage over excision and suture for small lesion, or superficial lesion close to vital structures which are to be left intact if possible. Eventhough healing is delayed, it is not associated with prolonged discomfort, hemorrhage and resultant scar formation and wound contraction is minimal. Electrosurgery would appear to have no peculiar advantage over cryosurgery, except, in the treatment of gingival lesions and few advantages over excision and suture except in the preservation of sulcus depth. If cryosurgery is to become the valuable tool in oral surgery that is formally suggest by this investigation, there are two important factors that should govern its uses- it should not be used for lesion more than 3 cm in diameter, or lesions partly impossible to reach to the probe, all lesions should be treated by freezing for two minutes and thawing and re-freezing to be certain of achieving a satisfactory tissue kill. Improved instrumentations and the increase in freezing by local physical means, or other, simultaneous applications, will further enhance the value of the cryoprobe in outpatient oral surgery[3]

Cryosurgery has been recommended for the removal of superficial mucosal lesions in the oral cavity . More recently, carbon dioxide lasers, which emit far infra-red radiation, have been used as an alternative form of treatment . Comparisons of the effectiveness of cryosurgery, laser surgery and electro- cautery have been reported in the treatment of cervical mucosal lesions. In these studies the quality of healing following use of the CO2 laser have

been subjectively assessed to be "excellent", with high cure rates being reported the effectiveness and the healing response following use of the 2 techniques was compared by producing lesions on the lateral border of sheep tongues. Cryosurgery produced more extensive lesions with a marked inflammatory reaction but no differences in the time course of healing were evident. Laser surgery was as effective as cryosurgery in the removal of superficial tissues but caused less swelling and, therefore, may be advantageous in some clinical situations. Cryosurgery and CO 2 laser surgery has an advantage that are readily apparent, both techniques are easily used in treating mucosal lesions, hemorrhage is controlled during the procedure and they are relatively painless. Cryosurgery has become established as an effective means of treatment for leukoplakia, whereas carbon dioxide laser surgery is a more recent development and has been recommended for clinical use. This latter technique is confined to hospital treatment due to the size of lasers presently available. The use of the Nd-YAG laser on oral mucosa has been evaluated. This instrument differs from the CO2 laser in that emits radiation in the near infra-red, with bands at 1064 nm and 1318 nm. As such, there is a greater extinction length in the mucosa and the Nd-YAG laser causes deeper tissue coagulation rather than surface vaporization. The miniature CO2 laser may be useful in the treatment of oral lesions, comparable to that of cryosurgery. A serious disadvantage with both techniques in the management of any mucosal disease is the lack of an

opportunity to sample the lesion and examine it microscopically in order to determine the nature of the lesion being treated[12].

Cryosurgery is a successful mode of therapy for the conditions which have traditionally presented problems in the management of leukoplakia,vascular malformation and certain extensive surface lesions like lichen planus. The technique of freezing has been used to treat hemangiomas , Applications of selected freezing have been employed to treat leukoplakia and hyperkeratosis, With the advancement in cryosurgical technique and equipment,it was utilized in pyogenic granuloma, angioma, fibroma, keratoacanthoma. Lichen planus was treated with cryotherapy with good results .cryosurgery is also used to treat salivary gland neoplasm cryosurgery is an effective, simple, predictable, relatively self limiting and safe method for almost all types of oral lesions. As it causes necrosis and sloughing as part of treatment ,delayed healing is an intensive problem with this technique else, it is free from complications such as pain, hemorrhage ,infection, unconditional damage to adjacent structures ,or scar formation that are seen with knife excision or electro surgery[9] . In our study 15 patients were enrolled with benign and premalignant lesion among which , there were 5 mucocele lesions, 2 traumatic fibroma, 1 leukoplakia, 2 erythroplakia, 3 lichen planus, 2 Apthous ulcers were seen. The site of occurrence of the lesion varied in different subjects the lesions were present on the buccal mucosa, floor of the tongue, upper vestibule, lower vestibule. Post-treatment follow up

was done at 3rd day, 1st week and 1st month and 2nd month to evaluate the intensity of pain, swelling, sloughing, granulation, epithilization and recurrence. There were good response after treatment and comparing the 3rd and 1st week there were a reasonable amount of reduction in pain and swelling and sloughing was present , on the 2nd week granulation flesh was healthy, after a month reepithelialization phase was good. In 15 cases recurrence was seen in 2 cases one in lichen planus other in erythroplakia. The other lesions had no recurrence and responded well under open method cryosurgery treatment.

Cryosurgery supports in treating orofacial lesions is a great extent some vascular malformations like Cavernous hemangioma when treated with cryosurgery produces shows complete regression of these malformations, whether of skin or of mucosa, with minimal scarring. Cryosurgery is very effective in cases of strawberry nevi where it reduces the excessive bleeding and ulceration or overwhelming parental demands. Capillary nevi also responds to cryosurgery. Lymphangiomas with fibrous element are usually less responsive to cryosurgery. It is a satisfactory alternative to excision or cautery for treating the Granulomatous and hyperplastic conditions like papillary hyperplasia of the palate, fibrous epulis, fibroepithelial polyps, myeloid epulides and viral warts. In case of Denture hyperplasia for a say if lesion is present in the lower labial sulcus, hyperplastic folds may be multiple and relatively broad based. Simple excision in may leads to loss of sulcus depth, which

may result in need of further management such as vestibuloplasty in the elderly and debilitated, in such issue cryosurgery may be used. Necrosis of the hyperplastic tissue may be achieved with minimal alteration of sulcus depth. Mucus retention cysts and antral polyps respond to cryosurgery without recurrence and detectable scarring. Cryosurgery for oral cancer benefits localized tissue destruction in superficial accessible lesions. It is the treatment of choice in recurrent nasopharyngeal carcinoma, It should not be the primary treatment of oral cancer except in very early lesions of anterior part of palate and in patients who are considered unfit for other forms of treatment. In the management of basal cell carcinoma the ulcers at the inner canthus or in cases where there are multiple lesions, cryosurgery is a sound alternative to surgery and radiotherapy provided the tumor has not invaded deeper structures. Cryosurgery in herpetic or aphthous ulcers used for their eradication, gave very satisfactory results. There was no intra or postoperative bleeding, no surgical defects, minimal scarring, and no infection following treatment[(1)].

Chronic facial pain can be treated by cryogenic block , The duration of the block is related to the distance in which the nerve must regenerate from the point of freezing to the innervated area and in this series in which peripheral branches of the trigeminal nerve were frozen, The extended nerve block which follows cryoanalgesia has been shown to be associated with Antrograde degeneration. The management of chronic pain is often expremental,

and employs techniques which interrupt or modify pain path- ways but which do not incapacitate the whole patient. As the response to treatment of patients with chronic pain is often unpredictable, it is desirable to select techniques which do not produce irreversible damage to the nerve or trigger secondary neuralgia. Above all cryoanalgesia appears to offer advantages over other methods of long term nerve block or neurectomy, and may result in prolonged relief in some patients[(6)].

Pain in tempromandibular joints is a common clinical problems, cryoanalgia provides a short term relief of intractable neurogenic pain in the TMJ with some long term relief. The main advantages of the procedure are that the intra-atricular structures are not damaged and case procedure with minimal morbidity. Disadvantage include it have only a temporary relief under certain circumstances, with unpredictable outcomes, there is a good chance of pain recurrence. The procedure may be repeated but there may a decreasing in response. Cryoanalgesia is useful adjunct to the management of extremely unmanageable pain localized to the TMJ. A suggested management protocol would involve as initial conservative treatment followed by arthrocentesis and arthroscopy. If these techniques fail and the patient responds to intra- articlar bupivicaine, then cryoanalgesia should be considered[(8)].

Cryotherapy in management of lesion in bone ,on comparing the histological response of normal bone to freezing gives hope that cryosurgery may have a significant role in the treatment of

neoplastic and infiltrative lesions involving the calcified tissues of the jaws. Relatively only a little is known, however, of the response of abnormal cells within the bone and this will be obviously governing the ultimate outlook for this form of therapy. In assessing the freezing procedures in soft tissue one can usually see a well defined frozen zone and palpate the size of the ice ball formed. The zone of freezing is much harder to define in bone, and the ice ball cannot be palpated. The insertion of thermocouples to the register tissue temperature is more difficult in bone than in soft tissue and it is necessary to drill access holes. To help in overcoming these problems in evaluation, it was decided to attempt to use thermography. The use of this method, which monitors infra red emission and does not appear to have been previously described in relationship to cryosurgery. The clinical information available indicates that sound repair of the bony cavities can occur after curettage of a lesion and cryosurgery of the surrounding region. Primary union of overlying soft tissue incisions can take place. The factors which contribute to the inhibition of osteogenesis and inadequate repair of the bone after freezing in certain cases require careful study[(3)].

Though cryosurgery have many advantages such as minimal general disturbance to the patient, particularly well accepted by children and elder patients, Low complication rate, minimal volume of tissue destruction, Particularly suited to extensive superficial lesions ,Treatment may be repeated as often as necessary without

increase in scarring, offers quality management of wide areas of premalignant change, May be used as an alternate to surgery and/or radiotherapy in palliative tumor control , Cryosurgery is a very safe, easy to perform, and relatively inexpensive technique for treating various oral lesions in an out-patient clinic, it have its own disadvantages and limitations as follows:

Difficulty in judging the extent of the lesion can lead to involvement of an inadequate amount of tissue, use is minimally confined to surface lesions of no more than a certain depth, surgical access is required for deeper lesions. The depth of destruction is limited although the base of the lesion is refrozen after excision of frozen tissue. Certain tissue seems to have a greater resistance to freezing than others, cryosurgery is non-specific in its destructive effects. In lesion of tongue the procedure can limit its functions. Healing is slow, Extensive cryosurgery procedures may produce considerable scarring. Following healing by secondary intention, loss of normal anatomy can lead to limitation of mouth opening, speech disturbances and prosthetic problems, as in the case of widespread keratoses, after extensive cryosurgery severe pain can be troublesome and narcotic analgesics may be required. If a biopsy is not taken prior to cryosurgery, the true nature of the lesion may not be found.

Complication categorized as immediate complication includes bleeding, blistering, edema, pain, vascular head ache, vasovagal syncope. Delayed complications includes excessive

granulation, infection is rare but possible with delayed healing tendon repture due to deeper freezing on extensor surface of fingers , ulceration, temporary complications include altered sensation may occur when damage in particular nerve, More profound freezing causes Wallerian degeneration which is followed by regeneration, as the nerve sheath architecture remains intact. This is also the reason for reduced sensation following cryosurgery, caution is required with lesion over nerve trunks. Peripheral nerve fibers may be painful following moderate freezing of adjacent structures, possibly due to the action of cellular breakdown products , hyperpigmentations may occur, increased risk with aggressive freezing hypertrophic scaring may occur , Scarring of facial skin if freezing is done for longer than 20–30 seconds. Healing occurs with reduction in pigmentation in such cases. Pyogenic granuloma rarely occurs. Permanent complications may include alopecia, atrophy, cartiladge necrosis, hypopigmentations.

There are some more contraindications such as cold intolerance, cold urticaria, cryoglobulinemia, dysfibrinogenemia, agammaglobulinemia, Raynaud's and collagen diseases, pyoderma gangrenosum, patients undergoing hemodialysis or immunosuppressive therapy, patients with platelet alterations or with multiple myeloma[(1)]. After all cryosurgery in treating oral lesions overweighs with its advantages.

CONCLUSION

Cryosurgery is the use liquid nitrogen were extreme cold is produced to destroy abnormal tissue. Cryosurgery is very safe, easy to perform and relatively inexpensive technique for treating various oral lesions in out-patient clinic it is very useful for oral lesion as the oral mucosa is humid which makes it an ideal site for freezing. With recent development of better equipment this mode of therapy appears to have a promising role in the management of benign mucosal lesion, more reasonable with adequate success, the procedure is relatively more acceptable and has shown to have , faster recovery. Though cryosurgery have some difficulties like portability of the cryogenic agent and storage of highly volatile material, it require special storage container for short-term storage and canister for dispensing the liquid from the container during its use, its advantages are numerous , this technique provide a bloodless field , less pain when compared to conventional surgery, anesthesia is optional, excellent cosmetic results , low cost, low risk of infection, minimal wound care, no need of suture removal, no work or sports restrictions, short preparation time, useful in pregnancy. In this study the open method used to treat lesion with cryogen spray using liquid nitrogen has shown significantly good results in achieving complete regression of the benign and premalignant lesion of oral cavity.

BIBLOGRAPHY

1. Bansal A, Jain S, Gupta S. Cryosurgery in the treatment of oro-facial lesions. Indian Journal of Dental Research. 2012 Mar 1;23(2):297.

2. Farah CS, Savage NW. Cryotherapy for treatment of oral lesions. Australian dental journal. 2006 Mar;51(1):2-5.

3. Bradley PF, Fisher AD. The cryosurgery of bone. An experimental and clinical assessment. British Journal of Oral Surgery. 1975 Nov 1;13(2):111-27.

4. Ameerally PJ, Colver GB. Cutaneous cryotherapy in maxillofacial surgery. Journal of Oral and Maxillofacial Surgery. 2007 Sep 1;65(9):1785-92.

5. Whittaker DK. Mechanisms of tissue destruction following cryosurgery. Annals of the Royal College of Surgeons of England. 1984 Sep;66(5):313.

6. Barnard D, Lloyd J, Evans J. Cryoanalgesia in the management of chronic facial pain. Journal of maxillofacial surgery. 1981 Jan 1;9:101-2.

7. Goss AN. Cryoneurotomy for intractable temporomandibular joint pain. British Journal of Oral and Maxillofacial Surgery. 1988 Feb 1;26(1):26-31.

8. Sidebottom AJ, Carey EC, Madahar AK. Cryoanalgesia in the management of intractable pain in the temporomandibular joint: a five-year retrospective review. British Journal of Oral and Maxillofacial Surgery. 2011 Dec 1;49(8):653-6.

9. Narula R, Malik B. Role Of Cryosurgery In The Management Of Benign And Premalignant Lesions Of The Maxillofacial Region. Indian Journal of Dental Sciences. 2012 Jun 1;4(2).

10. Darbandi A, Shahbaz NA. Effect of cryotherapy on physiologic pigmentation of oral mucosa: a preliminary study. Journal of Dentistry of Tehran University of Medical Sciences. 2004;1(2):49-52.

11. McCreary CE, McCartan BE. Clinical management of oral lichen planus. British Journal of Oral and Maxillofacial Surgery. 1999 Oct 1;37(5):338-43.

12. Kardos TB, Ferguson MM. Comparison of cryosurgery and the carbon dioxide laser in mucosal healing. International journal of oral and maxillofacial surgery. 1991 Apr 1;20(2):108-11.

13. Syed Nayeema, Dr.M.Subha: Cryotherapy- a Novel treatment modality in oral lesions, International Journal of Pharmacy and Pharmaceutical Sciences 2013 (5) 4-5

14. Bekke JP, Baart JA. Six years' experience with cryosurgery in the oral cavity. International journal of oral surgery. 1979 Aug 1;8(4):251-70.

15. Yeh CJ. Simple cryosurgical treatment for oral lesions. International Journal of Oral & Maxillofacial Surgery. 2000 Jun;29(3):212-6.
16. Gage AA, Koepf S, Wehrle D, Emmings F. Cryotherapy for cancer of the lip and oral cavity. Cancer. 1965 Dec;18(12):1646-51.
17. Loitz GA, O'Leary JP. Erosive lichen planus of the tongue treated by cryosurgery. Journal of Oral and Maxillofacial Surgery. 1986 Jul 1;44(7):580-2.
18. Chen HM, Cheng SJ, Lin HP, Yu CH, Wu YC, Chiang CP. Cryogun cryotherapy for oral leukoplakia and adjacent melanosis lesions. Journal of Oral Pathology & Medicine. 2015 Sep;44(8):607-13.
19. Gongloff RK. Treatment of intraoral hemangiomas with nitrous oxide cryosurgery. Oral Surgery, Oral Medicine, Oral Pathology. 1983 Jul 1;56(1):20-4.
20. Prasad M, Kale TP, Halli R, Kotrashetti SM, Baliga SD. Liquid nitrogen cryotherapy in the management of oral lesions: a retrospective clinical study. Journal of maxillofacial and oral surgery. 2009 Mar 1;8(1):40-2.
21. Garg A, Tripathi A, Chowdhry S, Sharma A, Biswas G. Cryosurgery: Painless and fearless management of mucocele in young patient. Journal of clinical and diagnostic research: JCDR. 2014 Aug;8(8):ZD04.

22. Sako K, Marchetta FC, Hayes RL. Cryotherapy of intraoral leukoplakia. The American Journal of Surgery. 1972 Oct 1;124(4):482-4.

23. Tal H, Cohen MA, Lemmer J. Clinical and histological changes following cryotherapy in a case of widespread oral leukoplakia. International Journal of Oral and Maxillofacial Surgery. 1982 Feb 1;11(1):64-8.

24. Toida M, Ishimaru JI, Hobo N. A simple cryosurgical method for treatment of oral mucous cysts. International journal of oral and maxillofacial surgery. 1993 Dec 1;22(6):353-5.

25. Yu CH, Chen HM, Chang CC, Hung HY, Hsiao CK, Chiang CP. Cotton-swab cryotherapy for oral leukoplakia. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck. 2009 Aug;31(8):983-8.

26. J sunitha ,Cryotherapy –A review ,Journal of clinical and Diagnostic research , January 2010 4(2) 2325-2329

27. Tonietto L, Borges HO, Martins CA, Silva DN, Sant'Ana Filho M. Enucleation and liquid nitrogen cryotherapy in the treatment of keratocystic odontogenic tumors: a case series. Journal of Oral and Maxillofacial Surgery. 2011 Jun 1;69(6):e112-7.

28. Lin HP, Chen HM, Cheng SJ, Yu CH, Chiang CP. Cryogun cryotherapy for oral leukoplakia. Head & neck. 2012 Sep;34(9):1306-11.

29. Rezende KM, Moraes PD, Oliveira LB, Thomaz LA, Junqueira JL, Bönecker M. Cryosurgery as an effective alternative for treatment of oral lesions in children. Brazilian dental journal. 2014;25(4):352-6.

30. Daveinthiran Thanabalan, the Use Of Cryosurgery In The Management Of Oral Lesions, International Journal of Scientific Research 3(5):362-371 · June 2012

CASE SHEET

Patient Name: O.P. No:

Age/Sex: Date :

Occupation:

Address:

Phone No:

Chief Complaint:

History Of Present Illness:

Past Medical History:

Past Dental History:

Personal History:

Diet:

Habits:

Oral Hygiene:

General Physical Examination:

Vital Signs:

Blood Pressure:

Pulse:

Respiratory Rate:

Temperature:

Extra Oral Examination:

Facial Symmetry:

Jaws:

Tmj:

Lips:

Cheeks:

Mouth Opening:

Lymph Nodes:

Intra Oral Examination:

Teeth:

Soft Tissue:

Examination Of The Lesion:

Inspection:

Site:

Size:

Shape:

Surface Over The Swelling:

Surrounding Area:

Colour:

Palpation:

Site:

Site & Extent :

Shape:

Surface:

Fixity To Underlying & Overlying Structures:

Consistency:

Raise In Temperature:

Any Other Findings:

Provisional Diagnosis:

Differential Diagnosis:

Investigations:

Treatment Planned:

Final Diagnosis:

Surgical Notes:

Surgeon:

Assistant Surgeon:

Signature Of Staff

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PATIENT CONSENT FORM

O.P. NO:

I …….. , voluntarily consent for the use of liquid nitrogen cryotherapy for the treatment of intraoral lesions as a part of the on going study. The nature and the effect of the procedure have been explained to me.

I also consent to the administration of anesthetics as may be necessary. I accept all risks involved in these procedure.

I have been informed regarding the details and associated complications of the procedure(s).

I consent to the photographing of the procedure.

I have fully understood the procedure and I consent to such procedure by my own free will.

Date : Patient's signature

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ஒப்புதல் படிவம்

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DENTAL COLLEGE & HOSPITAL

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Affiliated to The Tamilnadu Dr.M.G.R Medical University
A Unit of Adhiparasakthi Charitable, Medical, Educational & Cultural Trust

This Ethical Committee has undergone the research Protocol submitted by Dr.S.Duraimurugan, Post Graduate Student, Department of Oral & Maxillofacial Surgery, under the title "Liquid Nitrogen Cryotherapy in Management of Oral lesions" Ref no : 2016-MDS-BrIII-GOK-06/APDCH under the guidance of Dr. D.Durairaj for consideration of approval to proceed with the study.

This Committee has discussed about the Material being involved with the study, the Qualification of the investigator, the present norms and recommendations from the Clinical Research Scientific body and comes to a conclusion that this Research protocol fulfils the Specific requirements and the Committee authorizes the proposal.

Principal

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