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Case Series: Carbon Dioxide Cryo-Assisted Surgery: Making the Difference in the Management of Keloids and Hypertrophic Scars in a Resource-Limited Setting

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ABSTRACT

Background: A number of illnesses and disorders, including both benign and malignant skin ailments, have been treated with cryosurgery in the past. For a variety of benign skin conditions, cryosurgery is an incredibly effective treatment. Family doctors are capable of swiftly learning the method with the right guidance and supervised practice. When it comes to treating lesions in the majority of non-hair-bearing body parts, cryosurgery works best for patients with light skin. Materials & Method: a six (6) months study in a Plastic Surgery Centre, with 136 patients treated with CO_2 Cryo-assisted surgery were monitored over a 5 year period. Result: From our study 85% of our wounds healed without regrowth or recurrence. The 15% which show evidence of regrowth (recurrence); and were injected with Intradermal 5 FluoroUracil and Triamcenolone in a ratio mix of 3:1. The scar was subsequently reviewed at 2-4 weekly interval. A heaping up scar is reinjected intra-lesionally and intradermally. Conclusion: Another alternative for frequently occurring dermatological lesions is cryosurgery, which is minimally invasive, fast, efficient, and requires little to no anesthesia. Cryosurgery is a fantastic advantage for patients and caregivers similarly, because it is less intrusive, requires no cones or sutures, and requires no post-operative care. Comparing CO2 to argon, helium, liquid nitrogen, nitrous oxide, and other gases, it is more readily available, less expensive, and has a longer shelf life.

Keywords: Cryosurgery, Cryoassisted, Liquid Nitrogen, Carbondioxide, Recurrence.

INTRODUCTION

The administration of therapeutic cold at extremely low temperatures (below 0°C) to destroy tissues in specific target areas is known as cryosurgery, a subfield of cryobiology and surgery.[1] and [2]. Cryoablation is a surgical technique that involves using extremely cold temperatures to eliminate tissue that is aberrant or damaged. Cryo, which means "icy cold," and surgery, which means "handwork" or "handiwork," are the Greek terms from which the phrase originates. Using extremely low temperatures to eliminate aberrant tissues, such as tumors, is a surgical technique known as cryosurgery, or cryotherapy. During the procedure, liquid nitrogen is most frequently used, however argon and carbon dioxide are also options. A number of illnesses and

conditions have previously been treated with cryosurgery, including many benign and cancerous skin diseases[3,4,5]. A process that involves freezing and destroying aberrant tissue using a cryoprobe or an extremely cold liquid. Compressed argon gas, liquid nitrogen, or liquid nitrous oxide are examples of coolants used to cool cryoprobes. Certain cancers and diseases that have the potential to develop into cancer can be treated with cryosurgery. Also known as cryotherapy and cryoablation1. Cryogen: Materials, fluids, or gases with exceptionally low boiling points less than -150oF are referred to as cryogenic materials. The gases that are most frequently used include argon, nitrous oxide, and liquid nitrogen. The gas carbon dioxide. It is difficult to sustain liquid nitrogen at temperatures below -80°C since it vaporizes and costs roughly N150,000 for a 25 kg cylinder. After the cylinder's seal has whether in use or not, evaporates after 72 hours of tampering. That suggests that, for that price, it has a 72-hour shelf life after being tampered with. The situation is different with CO2 gas because it is stable and does not evaporate. A cylinder I had lasted three years despite being tampered with. Cryotherapy's introduction to human medicine dates back to the 1960s, but in the 1980s, interest in its use to cancer treatment faded. Although cryosurgery is not a novel technique, the instruments employed to provide the necessary temperature shift are developing, resulting in extremely accurate target regions. Because of the increased accuracy, there is less collateral tissue injury, which promotes quicker healing and reduced scarring. The micro-applicator tips' accuracy keeps the adjacent healthy tissue from being damaged, causing the patient no discomfort. As a result, therapies are closely monitored and might be extended if needed. Additionally, three technological advances have resulted in a resurgence of interest in cryotherapy[4]. These include: (1) enhanced cryosurgical equipment, such as vacuum-insulated small-diameter probes supercooled to -200°C; (2) improved intraoperative ultrasonography as a technique for monitoring the tissue freezing process; and (3) advancements in minimally invasive surgery apparatus.

Greek terms cryo, which means "icy cold," and surgery, which means "handwork" or "handiwork," are the roots of the word cryo. Extreme cold is used during cryosurgery, also known as cryotherapy, to remove aberrant tissues like tumors. Liquid nitrogen is most frequently utilized during the surgery, while argon and carbon dioxide are also options. Historically, cryosurgery has been used to treat a wide range of illnesses, including both benign and malignant skin ailments.[3, 4, 5]. For a variety of benign skin conditions, cryosurgery is a very successful treatment. Family doctors can quickly become proficient in the method with the right training and supervised practice. The majority of non-hair-bearing body parts can benefit from cryosurgery treatment of lesions, and patients with light skin are the greatest candidates for this procedure[1, 6.] The way cryosurgery operates is by using the damaging effects of extremely low temperatures on living cells. Ice crystals start to form inside the cells when their temperature drops below a specific point. Because of their lesser density, these crystals eventually shatter. split those cells apart. Once the blood arteries supplying the damaged tissue start to freeze, malignant development will suffer more damage1,7. Many illnesses and disorders, including skin ailments like warts, moles, skin tags, solar keratoses, and tiny skin malignancies, can be treated using cryosurgery.[7,8.] Three phases can be distinguished in the cryotherapy mode of action: (1) heat transfer, (2) cell damage, and (3) inflammation. The rapid transfer of heat from the skin to a heat sink is the process by which cryotherapy kills the targeted cells. With a boiling point of -196°C, liquid nitrogen is the most widely used cryogen. The temperature differential between the liquid nitrogen and the skin determines how quickly heat is transferred. While employing spray cryotherapy method, the liquid nitrogen is applied

directly to the skin, whereupon the heat from the skin is rapidly transferred to the liquid nitrogen through evaporation, also known as boiling heat transfer. The liquid nitrogen almost instantly evaporates (boils) as a result of this process. Conduction heat transfer happens while utilizing a cryoprobe for cryotherapy, where heat is transported by the copper-metal probe[9].

After the cell is frozen, cell damage happens during the thawing process. Ice crystals do not develop until -5°C to -10°C due to the hyperosmotic intracellular environment. Further harm is done to the cell membrane by the osmotic gradient that is created when water turns into ice, which concentrates extracellular solutes. Fast freezing and gradual thawing enhance epithelial cell tissue damage and are best suited for the management of cancer. Following a quick thaw, fibroblasts make less collagen[10]. Consequently, in places where scarring is likely, a quick thaw might be more appropriate for treating benign lesions or keloids[11]. Cell Damage When a steak is taken out of the freezer and defrosted, freeze damage is visible. The intracellular liquid that has leaked due to cell wall breakdown is represented by the steak juices that are visible when the meat has completely thawed. Additionally, by further concentrating electrolytes intracellularly, low temperature ensures maximum harm. To destroy keratinocytes as best as possible, they must be frozen at -50°C. Melanocytes are more sensitive and can be destroyed at as little as -5°C. This finding accounts for the hypopigmentation that occurs in darker-skinned individuals after cryotherapy. Usually, malignant skin tumors require -50°C, but benign lesions only need -20°C to -25°C[10]. The most efficient way to deliver cryogen is using self-pressurizing spray guns (Figure 2). These guns release a mixture of liquid and vapor cryogen droplets. Liquid nitrogen evaporatively transitions from the liquid to gas phase upon contact with the tissue. Research indicates that this method extracts more heat from treated tissue than using probes. The diameter of the needle orifice and the pressurizing gun's trigger regulate the spray droplet's volume and size. Probably the most widely used technique is spray cryotherapy. The majority of benign and some superficial neoplastic lesions can be treated with this technique. Each spray is pulsed to Avoiding overexpansion of the treatment site prevents complications[9]. Cryosurgery is a minimally invasive procedure that is frequently preferred over more traditional types of surgery due to its minimal pain, scarring, and cost; however, as with any medical treatment, there are risks involved, primarily that of damage to nearby healthy tissue. Damage to the skin's nerve tissue is of particular concern. Patients who undergo cryosurgery typically experience redness and mild to moderate localized pain, which is typically adequately relieved by oral administration of mild analgesics like ibuprofen, codeine, or acetaminophen (paracetamol). Blisters may form following cryosurgery, but these typically scab over and peel away within a few days. Hypopigmentation may occasionally occur, but this problem is usually temporary, and it normally goes away over several months as melanocytes migrate and re-pigment the area[3,6]. Inflammation is the final reaction to cryotherapy, and it is typically shown as erythema and edema.[12]. As a reaction to cell death, inflammation aids in the elimination of individual cells locally. Blisters may arise as a result of basement membrane dissociation brought on by a comprehensive cryotherapy treatment[1,9.]

Two anomalies connected to wound healing are keloids and hypertrophic scars, particularly in the skin of the negroids. Trauma is typically implicated, whether it is overt or occasionally hidden. One important component in the formation of keloids is wound care. Technique: tension wounding parallel to the lines rather than perpendicular to ST-RSTL. The most prevalent factor seems to be genetic predisposition. These people are referred to as keloid formers, typically develop keloids in multiple body locations the formation and growth of the

keloid scar are largely dependent on a number of factors, including the tension of the suture closure, the presence of contamination and infection, the overuse of diarthermy, the cleanliness or contamination of the incision, the surgeon's experience, racial factors, the anatomical site of the injury, its vascularity, and its diameter and depth.

MATERIALS AND METHOD

This study was carried out at Life Forte Renaissance Plastic Surgery Centre, Port Harcourt, Nigeria. It serves both low and high income social class. Patients present directly, and referral from both the Government and Private hospitals. All patients were treated outpatient basis. The facility has 3 Cryo machines: a cryopen which is portable cordless and hand held. An analogue Metrum Cryoflex machine and a computerised Metrum Cryoflex.

The Procedure (Cryo-Assisted Surgery)

Together with other surgical methods like excision, cryoassisted surgery can be carried out independently or as a standalone treatment. Either intralesional or core excision is the usual method for keloids surgical excision. A significant factor in preventing recurrence is preventing new damage to the healthy, normal skin in the vicinity. A 5 mm keloid skin cuff is left behind after our surgery. The boundaries of this 5 mm cuff of keloid skin are used for suturing to adjacent edges. Since the keratinocytes in the surrounding normal skin are already sensitized, any trauma to these primed keratinocytes causes an exaggerated hypersensitivity reaction that results in fibroplasia, which is the cause of excessive collagen deposition and keloids that grow again. This is notably noticeable when an adult ear lobule with an existing burst ear ring bore reopens, especially if the primary ear lobe was present during infancy. This seems to be the most typical reason for keloids in the earlobes. With cryoassisted surgery, the damaged tissue is removed with the least amount of harm to the surrounding healthy tissue. After that, cryo-freeze the edges and thaw them twice for five minutes. Next, use inert Prolene 4/0 suture to sew the edges. Following freezing and thawing, the typical cryosurgery leaves a raw wound that continues to leak serum, is unattractive, and occasionally smells. Suturing inside the boundaries of the keloidal skin edge is done with cryoassisted procedures, and the wound heals in 10 to 21 days to heal.

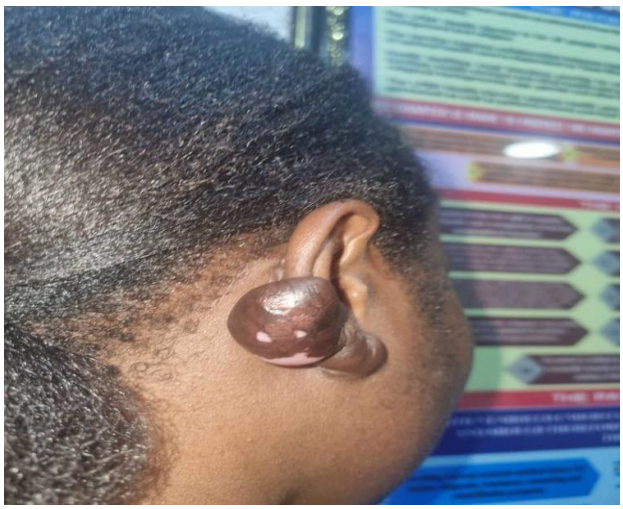

Plate 1: Right ear lobule keloid.

Plate 2: Intra-lesional excision is done with a 5mm margin cuff of keloid skin.

Plate 3: Cryotherapy in process.

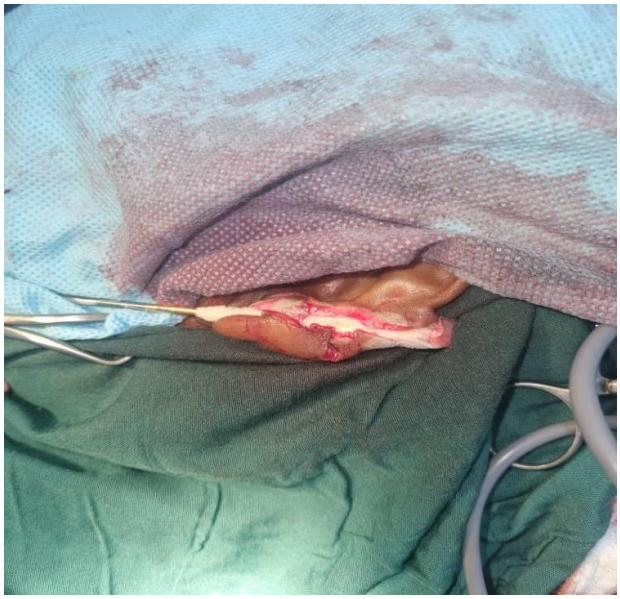

Plate 4: Cryotherapy in process.

Plate 5: Skin edges allowed to thaw before suturing with prolene 4/0.

Plate 6: Suturing completed.

Table 4.1: Summary Table for patients treated with Cryo-Assisted Surgeries

S/No	Clinical Features	Males	Percentages (%)	Females	Percentages (%)
1	Keloid Formers with leisions at multiple Sites	76	69.00	60	31.00

RESULTS

Table 2: Summary for Percentage distribution of Wound Healing in Keloids Formers Patients

S/No	Wound Healing	Percentages (%)
1	Wounds healed without regrowth or recurrence	85.00
2	Evidence of regrowth (recurrence);	15.00
Complications		
4	Wound Regrowth (recurrence)	15.000
5	Hypopigmentation	5.00
6	Atrophic skin	5.00

The number of our patients treated with cryo-assisted surgery for keloids were 136 patients over a 6 months period, 76 were males and 60 females. 24 were keloid formers, who had lesions at multiple sites. 18% had had a positive family history. Age range 2 years to 86 years. Timely removal of sutures between 5-7 days is critical. Suturing should not be under tension.

Prophylactic antibiotherapy is essential as to leave no room for infection. Careful use of diarthermy and haemostatic sutures, not to leave a mass of devitalized tissue is done to prevent infection. Sutures were removed from 5-7 days for head and neck surgeries; 10-14 days for the trunk (chest, abdomen and back) and 14-21 days for the upper and lower limbs.

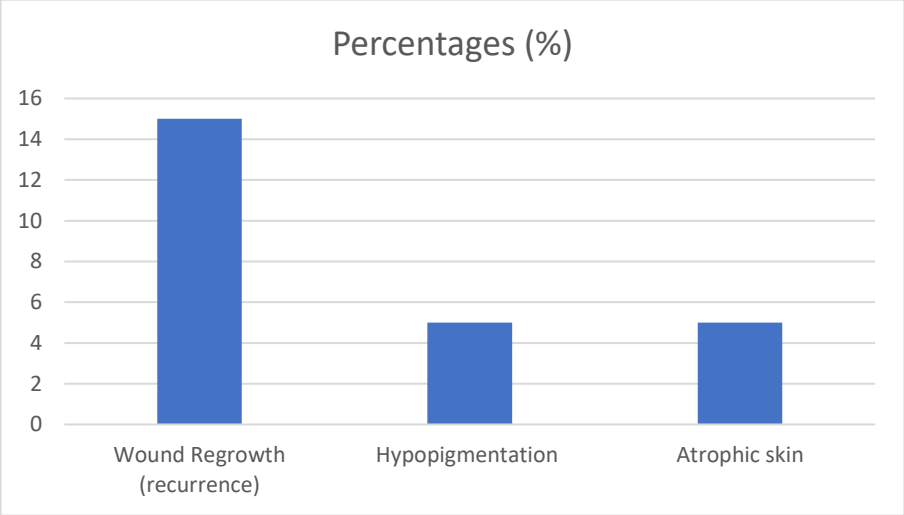

Figure 1: Bar Chat of Various Complications during Wound Healing Process

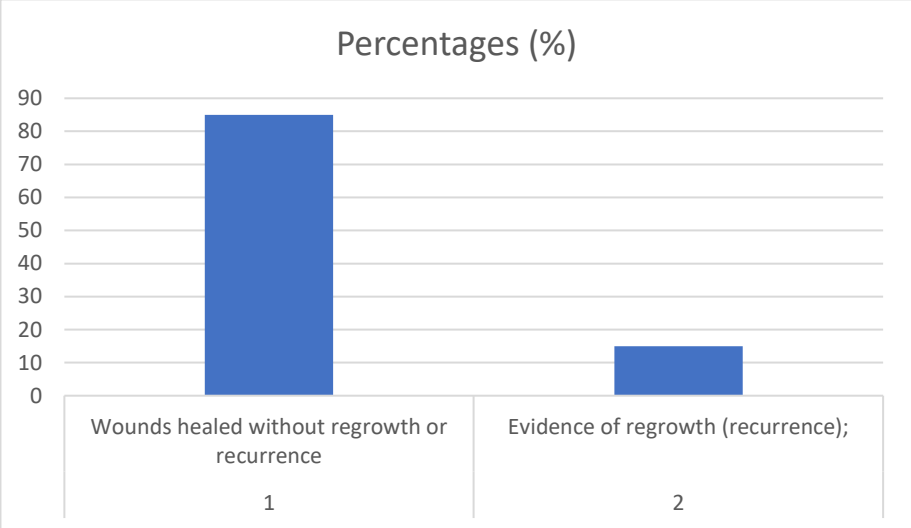

Figure 2: Phases of Wound Healing

From our study 85% of our wounds healed without regrowth or recurrence. The 15% which show evidence of regrowth (recurrence); and were injected with Intradermal 5 FluoroUracil and Triamcenolone in a ratio mix of 3:1. The scar was subsequently reviewed at 2-4 weekly interval. A heaping up scar is reinjected intra-lesionally and intradermally. Complications observed were recurrence 15%, hypopigmentation 5%, atrophic skin 5%. This was discontinued if the scar is thinning out or becoming hypopigmented. Our recurrence rate was monitored for up to 5 years. Our recurrence rate was 15%. Our follow up series of up to 5 years was recurrence free in 85%; even for keloid formers, hence our publishing of this series for multi-centre study and further evaluation.

DISCUSSION

Table 1 in this present study shows the outcome for patients treated with Cryo-Assisted Surgeries, the number of our patients treated with cryo-assisted surgery for keloids were 136 patients over a 6 months period, 76 were males and 60 females, 24 were keloid formers, who had lesions at multiple sites while 18% had had a positive family history. . Age range 2 years to 86 years. Timely removal of sutures between 5-7 days is critical. Suturing should not be under tension. Prophylactic antibiotherapy is essential as to leave no room for infection. Careful use of diarthermy and haemostatic sutures, not to leave a mass of devitalized tissue is done to prevent infection. Sutures were removed from 5-7 days for head and neck surgeries; 10-14 days for the trunk (chest, abdomen and back) and 14-21 days for the upper and lower limbs. From our study 85% of our wounds healed without regrowth or recurrence. This findings is in line with outcome of Engy and Colleagues[15] who find that their study included 45 adult Egyptian cases of keloids. Their ages ranged from 20 to 55, and their mean age was 33.69 (± 11.02 standard deviation). Of the groups under investigation, 21 cases (46.7%) were male and 24 cases (53.3%) were female. The body had keloids in several places, including the back, breast, and ears. A keloid's causes can include surgery, trauma, ear piercings, and spontaneous growth. Eight instances (17.8%) had undergone prior treatment, nine cases (20%) had multiple keloids, and 31 cases (80%) had keloid over bony prominences.[15] From this present study complications observed were recurrence 15%, hypopigmentation 5%, atrophic skin 5%. This was discontinued if the scar is thinning out or becoming hypopigmented. Our recurrence rate was monitored for up to 5 years. Our recurrence rate was 15%. Our follow up series of up to 5 years was recurrence free in 85%; even for keloid formers, hence our publishing of this series for multi-centre study and further evaluation. The outcome this investigation also concurs with the work done by Engy and Colleagues[15] who reported that the total number of patients studied, 25 (55.6%) experienced adverse effects in the form of ulceration, discomfort, itching, hypopigmentation, and hyperpigmentation, and 20 (44.4%) did not experience any side effects or complications. In their study, the most common side effects were greater discomfort and itching immediately following the treatment, which disappeared within a week at most. This study's conclusion is consistent with that of Reinholz et al., who found that > 90% of their participants experienced local unfavorable effects, such as ulceration, telangiectasia, and hyperpigmentation[19.] From our study 85% of our wounds healed without regrowth or recurrence. The 15% which show evidence of regrowth (recurrence); and were injected with Intradermal 5 FluoroUracil and Triamcenolone in a ratio mix of 3:1. The scar was subsequently reviewed at 2-4 weekly interval. A heaping up scar is reinjected intra-lesionally and intradermally. This outcome also agrees with the findings of Alexander et al., study, they produced positive outcomes by using intralesional injection rather than suspension application[16]. Alegre-Sánchez et al., stated that TAC in suspension form has a higher affinity than cream or ointment and may therefore more easily flow through the micro-channels created by fractional ablative lasers[17]. However, our results conflict with those of Danielsen and Colleagues (18), who found that intralesional verapamil was not as effective as IL TAC. There were considerably higher recurrence rates at the 12-month follow-up in a double-blind controlled experiment that compared identically timed TAC 5 mg/ml with 4 monthly doses of verapamil in 14 keloid lesions. The hazard ratio for recurrence was 8.44 (95% CI 1.62–44.05).18 Liquid nitrogen has a boiling temperature of -196oC (-320.8oF), while CO2 has a boiling point of -57oC (-70.6oF). Consequently, compared to CO_2, liquid nitrogen exhibits substantially faster pull-down rates. When liquid nitrogen is used instead of CO2, the frost produced has the same time and quality. CO_2 and N2 have different chemical characteristics,

with CO_2 being more reactive. Carbon dioxide has the ability to react with metals to generate carbonates and with water to form carbonic acid. Compared to other gases, N_2 is far less reactive and does not react with many other chemicals. In our environment, using CO2 is preferred since its advantages outweigh its disadvantages. One advantage of CO_2 is that it is less erratic. A cylinder costs roughly 10% of the price of liquid and can last up to three years. nitrogen. Additionally, it's difficult to find liquid nitrogen on the market. Problems might arise with any operation. One can categorize complications into four groups: (1) acute, (2) delayed, (3) prolonged-temporary, and (4) permanent. Hemorrhage, infection (2.2%), and extensive granulation tissue formation are examples of delayed consequences. Complications that are prolonged but transitory include milia, hyperpigmentation, and altered feeling. Alopecia, atrophy, keloids, scarring, hypopigmentation, and ectropion the outward twisting of a portion or the entire eyelid away from the eye are examples of long-term consequences.[12, 13]. Cryotherapy's introduction to human medicine dates back to the 1960s, but in the 1980s, interest in its use to cancer treatment faded. Although cryosurgery is not a novel technique, the instruments employed to provide the necessary temperature shift are developing, resulting in extremely accurate target regions.

Because of the increased accuracy, there is less collateral tissue injury, which promotes quicker healing and reduced scarring. Excess collagen at the location of a healed skin injury causes keloids, which are an overgrowth of dense fibrous tissue. Raised scars frequently have a deeper hue than the surrounding skin. When it goes beyond the confines of the initial wound and shows no signs of healing, it can be interpreted as the skin's aggressive healing response. Keloids are a condition that affects people regardless of their gender, age, or ethnicity. They are most common among people of pigmented races who have a positive family history of the condition. Patients with keloids experience both physical and psychological problems. If a keloid causes pruritus or pain, it can significantly lower a person's quality of life. Its mere look alone can also induce emotional tension and anxiety. Similar to an aberrant proliferation of scar tissue, a hypertrophic scar is limited to the area surrounding the initial incision. The scar eventually reverts to its normal state, and the extra tissue may hurt or itch. In contrast to keloids, hypertrophic scars are not related to age, gender, or inheritance, and they are not linked to any particular skin conditions or abnormalities. Hypertrophic scars, like keloids, can, nevertheless, also result in emotional and bodily pain.

Hypertrophic scars and keloids can result from any piercing or abrading damage to the skin, including burns, traumatic wounds, immunization sites, and surgical incisions. This might make the question of how to heal these scars widespread and worldwide. Uncertainty surrounds the pathogenesis of hypertrophic scars and keloids. There may be differing degrees of success with different therapies because scars can grow over a spectrum of wound kinds and patient skin types. The idea of abnormalities in the control of fibroblast proliferation and its production of extracellular matrix is the most widely accepted notion about the creation of keloids. This may involve the uncontrollably high synthesis of collagen and extracellular matrix caused by growth factors or cytokines. This could lead to an uncontrollably persistent scar formation environment, or in the case of an excessive matrix, this could manifest as hypertrophic or keloid scarring. Unusual cutaneous reactions to dermal damage include keloids and hypertrophic scars. Both entities beyond the initial borders of the wound. The ensuing physical and psychological repercussions can be crippling, and they are cosmetically disfiguring. There is currently no proven cure for keloids or hypertrophic scars, and no one treatment approach

works for everyone. On the other hand, carbon dioxide (CO2) cryosurgery provides a less invasive, highly curative, and minimally recurrent scar therapy option. This is especially crucial because thicker skin parts like the shoulders and upper chest are frequently the sites of prominent hypertrophic scars and extensive keloids. Because there was insufficient initial wound care in a context with limited resources, there may be a higher chance of scarring. Tensile skin forces, foreign body confinement, and care. When scar tissue grows forcefully outside the original wound borders, an aberrant reaction to wound healing results in keloids [20]. Although there is debate and difficulty in treating keloid scars, many therapy techniques are more effective than one 21. Triamcinolone acetonide (TAC) inhibits the proliferation of fibroblasts and wound inflammatory factors by transforming growth factor-beta (TGF-b) expression reduction and collagen breakdown and fibroblast apoptosis stimulation, which results in a decrease in fibroblast density [22]. Microthermal Zones (MTZs), which are formed by tissue vaporization and take the shape of rows encircled by normal skin, are produced by fractional CO2 lasers (FCL) and promote wound healing.[23] Many medications can be delivered by FCL. as corticosteroids, also referred to as LADD (laser-assisted drug delivery) 24,15. Trichloroacetic acid (TCA) causes alterations in the epidermis and dermis' ultrastructure. TCA enhances collagen and elastin's morphologic appearance. It can be utilized for keloids because it normalizes elastic tissue that was damaged by overproduction of collagen I and III by acting through the deposition of new collagen. [26]

CONCLUSION

Cryosurgey provides another option for commonly-seen dermatological lesions that is quick, effective, less invasive, and requires little to no anaesthesia. One needs to know lesions may need to be treated multiple times before resolution. Cryosurgery is less invasive, with no post-operative care; bloodless surgery, and does not require sutures and cones; thus, a wonderful benefit for both patients and caregivers CO_2 is more convenient, cheaper, cost effective, lasts longer, when compared to Nitrous oxide, Liquid nitrogen, argon and helium.

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- Conflict of Interest: There is no conflict of interest.
- Sponsorship / Financial Support: Nil.

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