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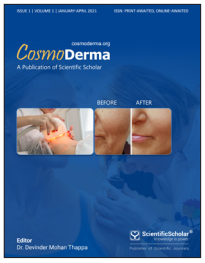

Focus

Cryotherapy in psoriasis – A novel therapeutic modality in the future scenario

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INTRODUCTION

Psoriasis is a chronic, disfiguring, inflammatory, and proliferative condition of the skin.[1] There is no cure for psoriasis and despite the availability of a wide array of treatment modalities, psoriasis has a remitting and relapsing course. To maintain remission, often long-term treatment with systemic and topical medication is required which predisposes the patients to serious adverse effects. To achieve adequate therapeutic response in a chronic disease like psoriasis, it is pertinent to address the issues of patient compliance by reducing the duration, adverse effects as well as cost of treatment, at the same time providing therapeutic efficacy equivalent to the widely used standard treatment modalities. This emphasizes the need to evaluate the role of newer treatment options. Cryotherapy being safe, effective, and also cost-effective provides a befitting and effective alternative in localized plaque psoriasis.

Cryotherapy involves the application of intense cold to diseased tissue to cause controlled and targeted destruction by rapid freezing. Its role in treating dermatological disorders including lupus erythematosus, warts, chancroid, herpes zoster, and epitheliomas was for the first time demonstrated in the late eighteenth century. The term "cryotherapy" was introduced in the year 1905, by Juliusberg. Today, cryotherapy has become an indispensable asset in the therapeutic armamentarium of dermatologists for treating a wide variety of benign and malignant skin lesions.

Cryotherapy is a common in-office procedure. For achieving maximum therapeutic response, the cooling and thawing rate in tissues should be regulated by the physician by selecting the type of cryogen and the appropriate cryosurgical method.[2]

CRYOGENS

Commonly used cryogens include liquid nitrogen, nitrous oxide, and solidified carbon dioxide (dry ice or carbon dioxide snow) with a boiling point of −196°C, −89°C, and −78°C, respectively.

CRYOTHERAPY METHODS

Various methods have been devised for the use of cryotherapy in various conditions. These methods include the spray technique or timed spot freeze technique, dipstick applicator method, cryoprobe method, and thermo-couple device.

The cryoprobe method is a contact method functioning on the principle of temperature exchange. Cryoprobes are made of copper because of their high conductivity and provide temperatures of −65 to −86°C with a moderate freezing speed of <100°C/min.[3] This method provides controlled and reproducible results by pressing the cryoprobe against the skin, thus inducing vessel contraction.[3] This makes it effective in treating chronic plaque psoriasis. The cryoprobe method is also best suited for vascular lesions.[3]

CRYOTHERAPY IN PSORIASIS – A NOVEL THERAPEUTIC APPROACH IN FUTURE SCENARIO

Psoriasis is a chronic disease requiring long-term treatment with systemic and topical medication. The popularly used systemic agents such as methotrexate, cyclosporine, azathioprine, mycophenolate mofetil, and retinoids act as a double-edged sword, providing remission at the expense of potential side effects, restricting their use in severe and recalcitrant psoriasis alone. Biologicals are effective in prolonging remission; however, the increased cost of treatment and the lack of long-term safety data regarding their use are major limiting factors.[4] The prolonged use of topical medications like glucocorticoids in chronic localized plaque psoriasis leads to atrophy, telangiectasia, and striae along with the increased risk of systemic absorption. Psoralen photochemotherapy with 8-methoxy psoralen and ultraviolet A radiation is associated with an increased risk of development of basal cell carcinoma and melanoma.

Cryotherapy has been found to be effective in the management of localized plaque psoriasis and provides a rapid, safe, and easy therapeutic alternative to currently used treatment modalities. Moreover, it is safe and effective in treating plaque psoriasis in pregnant or lactating females, and immunocompromised patients and elderly patients with hepatic, renal or other co-morbidities, where other commonly used systemic agents may be contraindicated.

Cryotherapy with nitrous oxide using the cryoprobe method has been used successfully in the treatment of localized plaque psoriasis. The psoriatic plaque to be treated is first cleansed with povidone-iodine. After drying, a lubricating gel (usually E.C.G. gel) is applied over the treatment site to ensure uniform contact of the cryoprobe with the psoriatic plaque. In one session, two to three freeze-thaw cycles are given with 2–3 s freeze time and 10 s thaw time using the pre-cooled cryoprobe of appropriate size and shape. Weekly sessions of cryotherapy thus given successfully induce remission in psoriatic plaques after an average of 6–10 sessions.

MECHANISM OF ACTION OF CRYOTHERAPY IN PSORIASIS

Cryonecrosis

Three major phases occur at the cellular level during cryonecrosis as follows:

Immediate phase

Intracellular and extracellular ice crystals form during the freezing phase. The thawing phase is equally damaging to the cells, resulting in cell bursts due to endosmosis and intracellular re-crystallization. Following different mechanisms operate simultaneously leading to cell necrosis:

1. Ice crystal formation
2. Dehydration and solute concentration
3. Protein denaturation
4. Thermal shock

Delayed phase

It occurs within a few hours of the final freeze-thaw cycle and is characterized by cryotherapy-induced vascular stasis due to localized vasoconstriction, increased blood viscosity, and microvascular endothelial damage that produces prothrombotic microenvironment causing occlusion of papillary dermal capillaries, resulting in ischemia.

Late immunological phase

Local inflammation develops within 24 h of treatment and results in immunologically mediated tissue destruction.

Cryo-immunomodulation

Recent studies reveal that cryoablation can trigger both immunostimulatory and immunosuppressive responses.[5] The role of suppressor T-cells (now referred to as regulatory T-cells) in causing immunosuppression following cryosurgery has been suggested by various studies.[5]

Although the exact mechanism of action of cryotherapy in treating psoriatic plaques is not known, various mechanisms proposed are as follows:[6]

1. Normal re-epithelialization following physical destruction of psoriatic lesions
2. Shortening of elongated dermal papillae
3. Reverse Koebner phenomenon
4. The creation of a scarred or altered dermis inhospitable to psoriasis by being less accepting for the immune cells thought to be pathogenic for psoriasis.

Cryoimmunomodulation plays a pivotal role in regulating the aberrant immune response involved in the pathogenesis of various autoimmune diseases including psoriasis. The

technique and rate of freezing cycles, the number of freeze-thaw cycles, and the size of cryolesion play a role in precise mechanisms of the watershed between immunosuppression and immunostimulation after cryoablation.[7,8]

Both necrosis and apoptosis play a role in cell death after cryoablation with a significantly different impact on the immune response.[7] Controlled cryoablation by inducing keratinocyte apoptosis skews the immune response toward Th2 helper T cell response, which releases anti-inflammatory cytokines.[7] Furthermore, cryotherapy by promoting apoptosis and apoptotic cell uptake apparently corrects the defect in clearance of apoptotic cells underlying various autoimmune diseases and thereby, induces "self-tolerance," modulates phagocyte function, inhibits pro-inflammatory cytokine release, and increases the production of anti-inflammatory cytokines such as interleukin (IL)-4, IL-5, IL-10, and transforming growth factor beta-1 (TGF-β1).[9,10]

Microvessel damage and thrombosis induced by cryoablation delay the infiltration of blood-borne dendritic cells, allowing the local macrophages to rapidly clear the cellular debris. Macrophages lack the ability of cross-presentation of antigens and therefore are less effective in priming the Th1 cells than the dendritic cells, thereby favoring an anti-inflammatory immune response.[7] Physiologically, after apoptotic cell uptake, the tissue macrophages produce cytokines such as TGF-β, prostaglandin E2, and platelet-activating factor that dampen the activation of adaptive immune cells.[9] Thus, macrophages actively suppress immune responses rather than present antigens in a tolerogenic manner.

REVIEW OF LITERATURE: ROLE OF CRYOTHERAPY IN PSORIASIS REVISITED

Various studies in the literature support the role of cryotherapy in localized chronic plaque psoriasis. The salient

Table 1: Comparison and salient features of various studies.

Study title	Author name	Outcome	Side-effects
Cryotherapy of psoriasis.[6]	Scoggins	Response rate of 67–80%, in 35 patients with more than 220 psoriatic plaques.	
Cryotherapy for psoriasis.[11]	Nouri *et al.*	In a total of nine patients of chronic plaque psoriasis, • Complete resolution (100%): 5 patients • Substantial resolution (75-80%): 2 patients • Mild-to-Moderate resolution: 1 patient	Hypopigmentation, atrophy, secondary bacterial infection
Cryotherapy in Psoriasis.[12]	Taweel *et al.*	Conducted on 50 patients with chronic plaque psoriasis. Response: No-response ratio of 6:1 • Complete resolution: 31 patients (62%) • Moderate resolution: 9 patients (18%) • Mild resolution: 5 patients (10%) • No resolution: 5 patients (10%)	Only side effect observed was hypopigmentation
Cryotherapy as a treatment for psoriasis.[13]	Shamsadini *et al.*	Conducted on 63 patients of chronic plaque psoriasis, with cryotherapy on 217 psoriatic plaques compared to 193 untreated psoriatic plaques as control. • Complete resolution: 4 patients (6.35%) • Mild-to-moderate resolution: 19 patients (30.1%) • No improvement: 40 patients (63.5%)	
Cryotherapy in chronic plaque psoriasis: An effective therapeutic modality[14]	Kumar *et al.*	Conducted on 50 patients of chronic plaque psoriasis with cryotherapy on 183 psoriatic plaques (Psoriasis vulgaris-128; Palmoplantar-55) compared to 160 untreated psoriatic plaques (Psoriasis vulgaris-108; Palmoplantar-52) as control. G5- Complete resolution-128 patients (psoriasis vulgaris-68; palmoplantar-40) G4- (76–90%) Resolution-25 patients (psoriasis vulgaris-18; palmoplantar-7) G3- (51–75%) Resolution-19 patients (psoriasis vulgaris-16; palmoplantar-3) G4- (26–50%) Resolution-4 patients (psoriasis vulgaris-2; palmoplantar-2) G1- (up to 25%) Resolution-0 patients G0- No Response-7 patients (psoriasis vulgaris-4; palmoplantar-3)	Blistering, mottled pigmentation, Koebner phenomenon

features of the various studies have been summarized in Table 1.[6,11-14] Scoggins in 1987 was the first to evaluate the role of cryotherapy in the treatment of psoriasis.[6]

Stone proposed that dermal papillae of psoriasis are elongated with a nine-fold increase in volume and are hence prone to edema that produces a spurt of inflammation. Cryotherapy, similar to other therapeutic modalities of psoriasis including laser, appears to shorten the dermal papillae or edema.[15] Cryotherapy being safe, effective, and cost effective provides a befitting and effective alternative in localized plaque psoriasis and can also be used in treatment of palmoplantar psoriasis.

COMPLICATIONS

Cryotherapy is a safe treatment modality, devoid of any systemic adverse effects. However, few local side effects may occur, all of them being mild and transient in nature. Acute complications include pain during cryotherapy that is mild to moderate in nature, not lasting for more than a few minutes after the procedure. Cryotherapy may result in edema or blistering, within 1–2 days that subside in a few days. Erosion may form that heals with hyperpigmented crust formation within 1–2 weeks.[3] Secondary infection after the procedure can be avoided by maintaining adequate hygiene and appropriate local or oral antibiotic treatment, in case of erosion or blister formation. Chronic complications include hyperpigmentation, more pronounced around the margins of the treated site and rarely, altered sensation. Few permanent or long-lasting complications like hypopigmentation may result due to melanocyte destruction at a temperature of −4°C.[3] However, it heals with mottled pigmentation, leading to uniform hyperpigmentation over time. Other rare side effects include atrophy, hypertrophic scar, or keloid formation.[14]

CONTRAINDICATIONS

Various relative and absolute contraindications of cryotherapy[3] have been listed in Table 2.

CONCLUSION

Management of psoriasis is often challenging requiring prolonged continuous treatment which often leads to significant side effects. Cryotherapy is a rapid, safe, and easy therapeutic option for localized psoriasis that can be carried out as a simple office procedure in treating localized plaque psoriasis as well as, palmoplantar psoriasis. However, the role of cryotherapy is limited to localized psoriasis. At the same time, large-scale studies are required to validate the role as well as to standardize the treatment protocol of cryotherapy in treating psoriasis.

Table 2: Contraindications of cryotherapy.

Relative Contraindications	Absolute Contraindications
i. Keloidal tendency	i. Use of cryotherapy near eye margins leads to ectropion formation.
ii. Collagen vascular diseases	ii. Use of cryotherapy for a lesion located in an area with compromised circulation.
iii. Patients with sensory loss at lesional sites	iii. Sclerosing BCC or recurrent BCC or squamous cell carcinoma located in high risk areas like temple or nasolabial folds.
iv. Peripheral vascular disease	iv. Proven sensitivity or adverse reaction to cryotherapy.
v. Peripheral neuropathy	v. Cold urticaria, cryoglobulinemia, Raynaud's disease.
iv. Melanoma	

BCC: Basal cell carcinoma

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REFERENCES

1. Griffiths CE, Barker JN. Psoriasis. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's textbook of dermatology. 8th ed. Oxford: Blackwell Publishing; 2010. p. 20-1.
2. Theodorescu D. Cancer cryotherapy: Evolution and biology. Rev Urol 2004;6:S9-19.
3. Sharma VK, Khandpur S. Guidelines for cryotherapy. Indian J Dermatol Venereol Leprol 2009;75:90-100.
4. Smith CH, Anstey AV, Barker JN, Burden AD, Chalmers RJ, Chandler D, *et al.* British association of dermatologists guidelines for use of biological interventions in psoriasis 2005. Br J Dermatol 2005;153:486-97.
5. Wing MG, Rogers K, Jacob G, Rees RC. Characterisation of suppressor cells generated following cryosurgery of an HSV-2-induced fibrosarcoma. Cancer Immunol Immunother 1988;26:169-75.
6. Scoggins RB. Cryotherapy of psoriasis. Arch Dermatol 1987;123:427-8.
7. Sabel MS. Cryo-immunology: A review of the literature and proposed mechanisms for stimulatory versus suppressive immune responses. Cryobiology 2009;58:1-11.
8. Sabel MS, Su G, Griffith KA, Chang AE. Rate of freeze alters the immunologic response after cryoablation of breast cancer. Ann Surg Oncol 2010;17:1187-93.

9. Viorritto IC, Nikolov NP, Siegel RM. Autoimmunity versus tolerance: Can dying cells tip the balance? Clin Immunol 2007;122:125-34.
10. Savill J, Dransfield I, Gregory C, Haslett C. A blast from the past: Clearance of apoptotic cells regulates immune responses. Nat Rev Immunol 2002;2:965-7.
11. Nouri K, Chartier TK, Eaglstein WH, Taylor JR. Cryotherapy for psoriasis. Arch Dermatol 1997;133:1608-9.
12. Taweel AE, Kotb M, Wahab AA, Kamal A, Ali A. Cryotherapy in psoriasis. Gulf J Dermatol 1999;6:46-8.
13. Shamsadini S, Varesvazirian M, Shamsadini A. Cryotherapy as a treatment for psoriasis. Dermatol Online J 2005;11:21.
14. Kumar R, Mahajan M, Mahajan BB. Cryotherapy in chronic plaque psoriasis: An effective therapeutic modality. Egypt J Dermatol Venerol 2024;44:73-9.
15. Stone OJ. The elongated dermal papillae of psoriasis. Dermatome shaving, cautery, laser, pressure, tape, cryotherapy. Int J dermatol 1990;29:187-9.

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