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Intralesional Delivery of Therapeutic Peptides and Enzymes- A Review

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Abstract : Intralesional injection is a non-routine technique used to inject medication directly into the keloid or skin lesions. The dermis as regular practice is targeted during intralesional injection. The intralesional and systemic use of peptide proteins is not only based on scientific studies but also on empirical base. The aim of the present review is o have brief glance on intralesional drug therapy, the technique to employ and its major application in various disorders and in congenital malformations by utilising therapeutic peptide proteins and enzymes in parenteral dosage from. The use of protein in different disorders has mostly been carried out on protein formulation consisting of an isolated or combination of protein enzymes including traditional and recombinant enzymes and also by rDNA technologies during clinical trial studies. The overview of these studies implies that protein and peptide therapy via intralesional route can avoid the adverse effect cause by radiotherapy and chemotherapy. Moreover it does require minimum dose to achieve maximum efficacy and should be utilized to minimize the risk of systemic circulation. Proteins like bacterial antigenic metabolites viz. collagenase, chondroitinase, botulinium toxin, BCG stain and their subsequent immunological products like cytokines, interferons and TNF factors are in prime interest for delivery via intralesional route through this study

Keywords : Intralesional, Percutaneous needle aponeurotomy, Proteins, Peptides, Enzyme therapeutics.

Introduction

In intralesional injection, there is direct administration of medication in percutaneous way into skin, skin lesions or in keloids. It has been a paramount part in dermatological studies since 1961. It is also termed as percutaneous needle aponeurotomy. This is typically performed in minor surgical room, employing local anaesthesia. The surgeon palpates the contracting cord or lesion and uses the bevel of a hypodermic needle placed blindly through the intact skin to 'saw' through the lesion, all the while maintaining the cord under tension. If enough of the lesion is divided, the remaining fibres will rupture and the affected joint will straighten to one degree or another.Intralesional injections are beneficial for a broad range of indications, are easily performed, and are comparatively safe[1, 2].Intralesional therapy is an approach in which medications are injected into a specific skin lesion or immediate below the skin to treat local skin tissues with minimal systemic effects and for faster therapeutic effect. Here skin works as a reservoir, enabling medication to deposit in the dermal layer of and subsequent medicaments being delivered over duration of time, resulting in prolonged therapy while avoiding or reducing the side effects of systemic therapy. It is often used for conditions such as acne, keloids and vitiligo. In frequent cases, intralesional therapy expels the need for long duration oral or topical therapy. It does have more efficacy as the injection works deep into the tissue where topical medications cannot

penetrate. Most occasionally intralesional therapy is combined with cryotherapy to operate on keloids and other dermatological conditions.

Mostly intralesional therapy is administered via needle, although a few physicians prefer jet injection devices (eg. Dermojet).Typically 30 gauge needles are employed, although 25-gauge needles are preferred. These needles are placed on 1 or 3 mlLuer-Lok syringes to prevent the needle detaching from the syringe under the force of injection. Sometimes the quantity of dose delivered is about in the tenths or even hundredths of a millilitre, and thus smaller syringe viz. one millilitre syringes permits for greater quantitative accuracy. 21 or 22 gauge bore needle is used to draw up the solution and subsequently to dilute the active medicaments with additives viz. saline buffer or lidocaine, and later it is separated and restored with that of small injecting needle. Thirty-gauge needles are the utmost desirable and widely utilised by dermatologists as they lowers discomfort when penetrating the skin, and prevent rapid injection, which is associated with increased pain. Rather smaller gauge needles provide greater precision in injecting the suitable dose of drug. [3, 4]

Injection technique

While dealing with intralesionaltherapy protective eye wear is strongly advised, since while treating with cystic type lesions, there is a chance of material to get discharge from the injection or the cyst from splashing into the eye.

Pre-Injection

1. The lesion and surrounding areas shall be cleaned with a spirit swab and allowed to dry.
2. The injection site shall be treated with a local anaesthetics agent, which shall not to be injected straight into the lesion rather applied around the surrounding area of the skin lesion.

Injection

1. Drug is injected intralesionally into cutaneous or nodal lesions which are visible, and those can be detected by ultrasound waves. With single insertion point, it is injected so that the needle radial would reach maximum and allows within the lesion to achieve equal and total dispersion. Sometimes multiple insertion points also being used if a lesion is too large than the radial reach of the needle.
2. Drug shall be injected equally and completely within the lesion by pulling the needle rear without leaving the lesion. The needle shall be directed again more times if necessary while injecting the remaining of the dose of drug. It shall be continued until the whole dose is equally and completely dispersed.
3. When needle is intended to be removed, it shall be taken out slowly to avoid leakage at the insertion point from the lesion.
4. Steps 1-2 shall be repeated under pre-injection and steps 1-3 under injection for other lesions to be operated.
5. A new needle shall be used as the needle is completely removed from a lesion and also at each time when a different lesion is to be treated.

Post-Injection

6. At the injection site(s) little force shall be applied for at least 30 seconds with sterile gauze.
7. Injection site(s) is and the peripheral area shall be swabbed with spirit.
8. Gloves shall be changed and the injected lesion(s) and covered with an absorbent cotton-pad and dry dressing.
9. The outer part of dressing should be wiped with spirit.
10. Patients must be advised to keep the injection site(s) covered for almost first week after each treatment visit or longer if the injection site exudates or drains and about changing the dressing if it falls off.

To disinfect the skin, a 60–70% alcohol-based solution (isopropyl alcohol or ethanol) on a single-use swab or cotton-wool ball shall be applied at site of injection followed by inserting the hypodermic single use needle at a 45 degree to 90 degree angle into the lesion to the level of mid-dermis, and then the drug should slowly be injected. Once needle deposited correctly into the mid-dermis, of the skin visibly may rises slightly and blanches.

Drugs being used for intralesional delivery

Corticosteroids

Since the 1960s, corticosteroid injections remained a worldwide welcome treatment for various pathological scars, and in inflammatory conditions. Corticosteroids like hydrocortisone, betamethasone valerate and methyl-prednisolone aceponate have an important role because of their potent anti-inflammatory activity along with immunosuppressive effects and of anti-proliferative effects on epidermal cells producing keratin. They also suppress collagen synthesis by fibroblasts.This treatment is being continued a vital role in the management of keloids.[7]The thing is corticosteroid should be intralesionally injected at the exact depth of lesion in the mid-dermis to forbear from irreversible shrivel of the epidermis.[8]By considering the size and site of the lesion and the age of the patient, the prescribed dose would be from 10 to 40 mg/ml, and the treatment interval can be about 4 to 6 weeks to several months or till the scar is in flat appearance.[9]Injections may be repeated once every 3-4 weeks depending on the bulkiness of the keloid and the therapeutic response. [10,11]Generally, one commences with a concentration of 5 mg/ml working up to the full concentration of 40 mg/ml, if necessary, when there is no response. If required, the injection can be repeated every 4-6 weeks.[12]

In the treatment for alopecia areata procedure includes the intralesional injection of a steroid solution of triamcinolone immediate below the epidermal, employing a 1-ml tuberculin syringe and a 1-inch needle of 30-gauge. Usually about 0.1 ml of drug is generally injected to each site, and injections are dispersed out to cover the target site. In result, the cortisone removes the confused immune cells and permits the hair to grow.[13] It may include burning sensation for up to three to five minutes after corticosteroid injection; provided higher the concentration of corticosteroid, the greater the discomfort of injection. Hence, corticosteroids are made less concentration by dilution just before injection to achieve patient compliance. Isotonic saline is most frequently used diluents for all corticosteroids, but some physicians also prefer with the local anaesthetic lidocaine.

Anticancer agents with local anaesthetics

Since 1970, bleomycin injection via intralesional route is known for fruitful therapy of recalcitrant verrucae, but the major pitfall is the moderate to severe discomfort associated with the injection. Procedural distress can be minimised by using bleomycin in reconstitution form with lidocaine. It results with minimal morbidity, and patient compliance can be achieved.[14]Increasing popularity is gained by intralesionalbleomycin in the past decade for treatment of warts in different regions as other aspects are not very effective.[15]Further synergistic combination of intralesional 5-fluorouracil, lidocaine and epinephrine is proved to be effective in treating skin warts.[16]

Keloids and scars treatment

Keloids are a type of skin disorder in which the skin grows beyond its limit of the original cured or uncured wound. Certain keloids with unknown origin and without recognition also may occur. In general, keloids are resulted due to atypical wound healing involving extreme fibroblast participation and then unequal distribution of collagen.Steroids like triamcinolone with or without 5-fluorouracil, verapamil- a calcium channel blocker by intralesional route is advocated to treat skin acne, cyst and keloids while recent approaches like intralesional skin-cryotherapy (by using liquid nitrogen with active medicinal agent), bleomycin, interferons are being used as novel intralesional therapy.[17]

Proteins, peptides and enzymes as drug for intralesional therapy

Steroidal medication into a Peyronie's plaque and in scars is being practiced since the 1950s. , Since it was thought that steroids had anti-scarring properties and hence could be utilised as potent medicinal agents at that time. But the initial studies indicated improvement up to 60% of patients although neither study reported in the literature had patients exposed to placebo treatment, nor were there any objective measures made of the improvement. One more reason for steroid injection to become less popular is that steroids can cause muscular atrophy, and thereby may resulting weakening of the penile tissues. Therefore, excluding in very extreme exceptions the use of intralesional steroids were completely withdrawn.[6]

These things made for researcher to pay attention towards intralesional route of therapeutic peptide and enzyme, including rDNA generated recombinants and synthetic protein which assured maximum therapeutic

efficacy due to optimal skin absorption and with minimal side effects. Some of therapeutic enzymes, peptides and proteins are summarised below.

Orgotein (superoxide dismutase).

Being a super oxide dismutase, this enzyme was employed in minimising the injury caused by free radicals. Since, free radicals are secreted from tissue when those get injured and probably may induce more scar formation. Hence understood mechanism for orgotein is to interfere with this process and hopefully resulting suppression in scarring formation. Orgotein also supposed to carry anti-inflammatory properties, and hence first employed in the treatment of inflammatory bladder disorders, in early 1974. Orgotein exerts its mechanism of action by breaking down of superoxide free radicals in to hydrogen peroxide and oxygen molecules, thus suppressing inflammation and fibrosis. Therefore it was hypothesised that direct injections of orgotein into these penile plaques may reduce their sizes and also help with pain. In this regard two studies were carried out in 1981, which showed promise about this enzyme, in which it showed that his 23 patients had significant reduction of the in duration size, pain and penile deviation on erection[18], while it is also showed in 19 of his 22 patients, a restoration of normal or near normal sexual function.[19]

Collagenase

This enzyme produced by the bacterial species *Clostridium*, majorly *Clostridium histiolyticum*, and its purified endotoxin collagenase has been approved by the FDA. 'Xiaflex' a well-known brands in the treatment of Dupuytren's contracture and Peyronie's disease. It is extrapolated that intralesional administration of these lytic enzymes into the fibrotic lesions on the palmar aponeurosis, extension deficits of the digits have been checked in remarkable decrease pre and post treatment. Dupuytren's contracture and Peyronie's disease are assumed to be similar in their undisclosed physiology, since both do involve fibrotic lesions affecting normal function; hence it was suggested that this way of therapy could be extrapolated. Certain literature denoted a pilot study[20], designed to reveal the safety and feasibility of collagenase in vitro specimens, it was estimated that collagenase successfully managed in dissolving plaque tissue, with maintaining elasticity of muscle, vascular smooth muscle or the myelin sheath. It was concluded by authors for extrapolating application of collagenase is potentially active proteolytic enzyme in dissolving the diseased plaque tissue.[21]

Chondroitinases

In treatment of spinal injuries during accidental conditions chondroitinases are advocated to be used where they have been reported to promote regenerating spinal cord. The enzyme is expected to exert its action by eliminating glial scar and accumulated chondroitin sulfate which are supposed to inhibit axon growth of neuron.[22]Chondroitinases have been concluded in promoting healing and regeneration of injured spinal cord and hence could be applied in the treatment of spinal injuries. Hyaluronidase also has shown its application in the reforming in damaged nerve tissue as it also has similar hydrolytic activity on chondroitin sulphate.

Botulinum toxin A (BTA)

Botulinum toxin A (BTA) an attenuated antigenic protein from *Clostridium botulinum*, which immobilizes the local muscles, reduces skin tension caused by muscle pull, and hence diminishes injury and further subsequent inflammation. Effective regulation and balance between fibroblast proliferation process and apoptosis provided with reduction in the tensile force while synthesis of fibroblast (cicatrisation) may represent a newer therapeutic for treatment of keloids. In-vitro studies have investigated that cultured fibroblasts found a characteristic behaviour in their differential cell-cycle distribution, which explains improvement of cell cycles in the presence of BTA and thus the incidental appearance of hypertrophic scar and also prohibit the development of hypertrophic scars.[23]Zhibo *et al*. (2009)carried out a prospective, uncontrolled study to assess the effects of BTA in the treatment of keloids.[24] Xiao *et al*. (2009) studied 19 patients with hypertrophic scars who undergone intralesional injections of BTA (2.5 units/cm of lesion at 1-month intervals) for three months.[25] At six-month follow up, all of the patients showed remarkable improvement of the scars and the therapeutic compliance was very high. After the BTA injections there was significantly reduction in the conditions like erythema, pruritus, and pliability score was observed than before.Certain reports also conclude that using intramuscular BTA in therapy of scar revision on the face helps to reduce the development of a widened scar.[26]

Bleomycin

Bleomycin is also a microbial origin glycopeptides isolated from *Streptomyces verticillus* exerts its mechanism of action by creating breaks in single and double stranded DNA. It is a potent cytotoxic agent, indicated its application in various types of melanomas and carcinomas in tumour oncology. It has been shown its efficacy in the treatment of cutaneous warts, particularly those located in and surrounds the nails.[27]It has also shown its notable remark in the treatment therapy of genital warts including giant condylomas and warts of oral cavity. Intralesionallybleomycin is administered in these cutaneous warts for specific course period and can be coupled with other drug for effective treatment of such cutaneous warts.

BCG antigen

Viral warts are among most commonly and frequently observed disorders. Etiological reason for this dermatological disease is a parasite called human papilloma virus (HPV) which is notorious for its contagious nature. It can affect people of both sexes, without any particular age group. Usually these warts may heal spontaneously, although that takes a long time. However, in certain cases healing do not happen its own even after long duration of follow up. Undesirable characters of such warts are often frustrating, and they raise a great therapeutic challenge in dermatology, being non-respondent to conventional treatment.

Recently, to overcome with this challenge, dermatologists have come up with different strategies that are being investigated with each passing day. Most of these pioneered strategies act by boosting the immune power to combat the menace of warts; so they are rightly indicated as immuno-modulators.Lyophilized powdered form of BCG vaccine is intralesionally advocated by diluting with 1 ml of normal isotonic saline, supplied with the vial of BCG vaccine. After reconstitution, 0.1 ml of this BCG vaccine is given intralesionally or intrademally (as per criteria) with the help of routine insulin syringe.[28]

Nicotinamide

Nicotinamide is also known as vitamin B3 and orally available inexpensive agent without significant side effects. Since nicotinamide and its derivatives are potent components, hence patient with leishmaniasis would be benefited from therapeutic use of such components, optionally in combination along anti-parasitic category drugs. According to another preferable representation of the above defined use, the medicament is desirable for an administration of this compound by intralesional, intravenous, topical or oral route.Thus it concluded that the medicament is suitable to be administered at the sites of parasite-caused skin lesions hence intralesionally in patients with leishmania infections.[29]

Interferons

Interferon Alfa-2b injection also known as Intron-A was first reported at the American Urological Association summit held in 2003. The studies investigated that use of 5 million units of Intron-A administered every two weeks resulted in remarkable significance in deformity of Peyroni's disease. The work reports are mostly from Europe, which have not revealed any significant benefit with Interferon injections ranging from 1-5 million units per injection. The rationale for interferon use is much the same as that for verapamil, in that it biological modifies fibroblast behaviour. The major pitfall with interferon injections that were reported was flu-like symptoms in the Europe, but was not observed in the USA multi-centre trial, and although intron-A is costlier than verapamil, it is not an unaffordable drug.[7] During kenalog or Interferon Alfa-2bintralesional injection trials a dual behaviour of first decreases and then increase in genetic expressions of PDGF BB mRNAs is observed. Gene expressions of PDGF BB in situ were higher in hypertrophic scars than in normal skin. The estimated mechanism of Interferon Alfa-2b in regard of ameliorating hypertrophic scar is reduction in mitotic division and inhibiting proliferation of fibroblasts in hypertrophic scars by prohibiting PDGF gene expression.[30, 31]

Stewart C A *et al.*(2015) reported that treatment with intralesional Interferon Alpha-2b provided a greater than 20% reduction in curvature in the majority of men with Peyronie's disease. This improvement was free of location of plaque.[32]

Interferon Alfa-n3 also known as Alferon N (derived human leukocyte) is synthesised from pooled human leukocytes unitswith Sendai virus induced by incomplete infection to generate Interferon Alfa-n3. Human interferon alpha proteins are a sterile lipophobic formulation for use by injection in natural and purified form. Alferon N intralesional injection involves Interferon Alfa proteins being comprised about 166 amino acids ranging in molecular weights from 16,000 to 27,000 Daltons.

Intralesional injection of Alfron N found most advantageous in Condylomataacuminata which are known for their contagious, benign epithelial tumorogenic growth in the genital and perianal regions of men and women caused due to human papilloma-viruses (HPVs).[33]

TalimogeneLaherparepvec

IMLYGIC (talimogenelaherparepvec) is novel sterile complex viral peptide suspension introduced as intralesional injection and which is indicated in oncolytic viral warts. IMLYGIC is a live, attenuated HSV-1 that has been genetically engineered to express peptide huGM-CSF. The production of IMLYGIC is done by genetic modification involving parental virus -a primary isolate by using recombinant methods IMLYGIC composed of residual components of VERO cells including deoxyribose nucleic acid and protein and trace quantities of foetal bovine serum. IMLYGIC is a genetically engineered peptide suspension indicated in oncogenic viral wart therapy. It also indicated in the local treatment of unrespectablecutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.[34]

Cytokines, Intraleukines and TNF

The intralesional or more specifically intratumoral injection of Intraleukin-2 (IL2) has shown beneficial effects in cutaneous melanoma patients with nonresponsive melanomas or continuous reappearance even after surgery. It is investigated that the intralesional injection of L19-IL2, combination of immunocytokine of IL2 and the fragment human monoclonal antibody L19, resulted in combating not only over tumour progression, but also delayed period to distant metastasis and evidenced circulating immune cell populations.[35] In preclinical studies of cancer models a notable synergistic result of the L19-IL2 combination has been observed. Moreover L19-TNF, a second clinical-stage immuno-cytokine combination study also has produced remarkable advantages, based on the same L19 antibody fused to TNF.[36]

Other than these proteins entities there are several peptide proteins and enzymes which are preferentially could be given via intralesional route on which are either in pipeline process of preformulation studies or awaiting approvals of FDA. Few of those are claimed here.

Table-1: Protein /enzymes are being given via intralesional route

S. No	Protein/ Enzymes	Indications	References
1	CIGB-300 (A Synthetic peptide)	In advanced cervical cancer	37, 38
2	Recomb. Human Epidermal Growth Factor (rHEGT)	In Chronic diabetic foot ulcers	39
3	Rituximab	In the treatment of Refractory Oral Pemphigus Vulgaris.	40
4	Bevacizumab	In patients with HIV-associated Kaposi's sarcoma in the upper airway.	41
5	Alefacept	In Psoriasis	42
6	Insulin-like growth factor-I (IGF-I)	Intreatment of superficial digital flexor tendonitis in thoroughbred racehorses	43
7	Infliximab	Non-infectious cutaneous granulomas	44
8	Papain	In keloid scar	45
9	Hyaluronidase	In oral sub-mucous fibrosis (OSF)	46
10	Placentrix	In OSF, as biogenic stimulators and as anti-inflammatory agent.	46, 47
11	Chymotrypsin	Asaproteolytic and anti-inflammatory agent.	48
12	Tissue Plasminogen Activator and Intracoronary Heparin	In patients with Unstable Angina and Coronary Thrombus Undergoing PTCA.	49

The field of oncology research has very good examples of the use of enzyme-protein therapeutics. Recent ongoing studies have shown that PEGylated arginine deaminase, is an degrading arginine, resulting in

inhibition of human melanoma and hepatocellular carcinomas, which are auxotrophic for arginine owing to a lack of arginosuccinatesynthetase activity.[50] Recently, another PEGylated enzyme, Oncaspar1 (pegaspargase), already in use in the clinic, has shown better results for the treatment of children with newly diagnosed acute lymphoblastic leukemia than the native, bacterial asparaginase.[51] Normal healthy cells can produce asparagine, but cancer cells are not and die in the presence of this asparagines degrading enzyme. In spite of the higher pharmacy cost of PEG-asparaginase, the total cost of the treatment is almost equal to the one with the native enzyme.[52]Asparaginase and PEG-asparaginaseare effective adjuncts to standard chemotherapy in oncology.

Intralesional immunomodulators for treatment of viral and carcinogenic warts

Cancer chemotherapy and antiviral therapy both required systemic way of treatment to cure tumours and warts. This perspective needs varieties of agents and factors for targeting these tumours and warts. For this reason, bacteria, bacterial derived drugs, toxic agents, bacterial vectors are being studied. Most generally used bacterial vector in order to carry foreign DNA into the tumor cells are *Bifido bacterium, Salmonella choleraesuis***,** *Salmonella typhi*, *Listeria monocytogenes, Vibrio cholera***,** and *Escherichia coli*. For example DNA from non-pathogenic or attenuated strains of Salmonella has been used to squash melanoma.[53]Immunotherapy is a propitious therapy for the treatment of perennial and resistant sort of warts which could lead to resolve without any physical changes or scarring additionally, would raise the host response against the causative agent, thereby leading to total resolution and minimal recurrence. A number of studies have been done since longwhere immunotherapy has been tried with variable success.

Intralesional protein and peptide candidates for vaccine which are antigenic in nature involved in immunomodulation and induction of immune system and resulting in regression of warts.[54]These immunomodulatory vaccines are composed ofbacterial type of vector which essentially do contain a gene carries a drug or prodrug activating enzyme and liposome contain tumor markers. This mode of therapy specifically chemotherapy employs the capability of the immune system to ascend delayed type hypersensitivity by various injected antigenic proteins towards wart or tumor tissue. Different vaccines with antigenic proteins or peptides have been used with varied results as summarized in table 2.

Table-2: Intralesional immunomodulator agents

S. No.	Intralesional immunomodulators	Dose/duration	References
1	MMR vaccine	0.1 ml/lesion, 1-3 Weekly, Up To 3-6 Weeks/Till Complete Resolution	55
2	Mycobacterium indicus antigen	0.1 ml/lesion, weekly till 10 weeks or complete resolution	56
3	Mycobacterium w antigen	For cutaneous warts, 0.1 ml intradermal into 3-5 warts or all warts, followed by 0.1 ml intralesional, 2-4 weekly, maximum 10 sittings	56
4	BCG vaccine	0.1 ml/lesion every 2 weeks, till 5 doses Or complete resolution of warts (this dose is also used for palliation in melanoma)	57
5	Candida antigen	0.1-0.3 ml (1:1000), repeated after 3 weeks until complete resolution/4 weeks	58
6	Trichophyton antigen	For cutaneous and genital warts, 0.3 ml injected into largest wart every 3 weeks, maximum of 5 sitting	56
7	PPD or Tuberculin test antigen	0.1 ml/lesion injected 1-3 weekly till complete resolution/12 weeks	56

Future of protein based enzymes like superoxide dismutase, catalase enzymes may help to reduce organ injury in hemorrhagic shock.[14]Human butyril-cholinesterase, a natural serum detoxification enzyme, acts to break down acetylcholine. It could be useful for the treatment of cocaine overdose, as demonstrated by recent results. Re-construction of the enzyme based on structure has resulted in higher activity toward

cocaine.[15]Directed evolution has also marked in even more efficient optimization of butyril-cholinesterase;[17] directed evolution assures for the most powerful tool yet in the development of protein based drugs.[18]

Side effects, complications, and pitfalls

The most and curable common side effects of intralesional injections of protein drugs are generally local. These may include atrophy, hypopigmentation, and rarely, sterile abscess formation. Atrophy and pigment changes usually resolve over several weeks but occasionally persist longer and are sometimes permanent. Micronized crystals of active drug entity remain in skin for weeks and even months, so some physicians suggest injecting sterile saline into persistently atrophic sites in an attempt to activate the drug and clear it from the skin more quickly.[3]However, there are no clinical studies that support this practice. Darkly pigmented skin is most susceptible to hypopigmentation and depigmentation; caution should be used when injecting these patients and the patients should be advised of this potential complication.

Formed sterile abscess may require drainage, and this is usually accomplished by stabbing the abscess with a number 11 blade. Systemic antibiotics usually are not necessary if the abscess has been drained completely.

Conclusion

Intralesional therapy of proteins such as enzymes, peptide and peptidomimetic drugs are less invasive procedure and gaining more popularity among European and Asian countries. Intralesional peptides and enzymes have proven to be very effective for certain disease presentations with very notable therapeutic significance and success. Uses of protein, peptide and enzymes have been extended for treating cancer, congenital disorders viz. Duptryen's disease and also in viral infections. Proteins in combination with drug also have potential to induce synergistic effect for treatment of various disorders and to minimise adverse effects. Advancements in biotechnology and genetic engineering over the past ten years have boosted pharma-biotech companies to produce safer, cheaper therapeutic peptides and enzymes with enhanced potency and specificity. Some enzymes are in different phases of clinical trials.

Along with these advances, changes in orphan drug laws and new initiatives by the FDA have been effective in facilitating efforts to develop therapeutic peptides and enzymes via intralesional route of delivery. This synergy has had a beneficial effect on the development of treatments for both rare and common disorders.

Abbreviations:

rDNA (Recombinant Deoxyribose Nucleic Acid), BCG (Bacillus CalmatteGuarine), TNF (Tumor Necrosis Factor), HPV (Human Papilloma Virus), FDA (Food and Drug Administration), PEG (Poly-ethylene Glycol).

Conflict of Interests

The authors declare that there is no conflict of interest

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