Role of Intralesional Injection in The Treatment of Psoriasis.

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Abstract:
Psoriasis is a chronic multisystemic inflammatory disease. The pathogenesis of psoriasis is multifactorial with genetic and environmental background. The burden of psoriasis on the sufferers depends on the percentage of body affection, associated comorbidities, response to and inevitable side effects of the treatment. The choice of treatment relies on the percentage of body affection, generalized or localized. The first line for localized plaque psoriasis is topical therapy as steroids, vitamin D analogues, keratolytic and emollients. However, some plaques are resistant to these topical drugs, especially thick hyperkeratotic plaques, plaques on palm, sole and scalp and nail psoriasis. Intralesional injection guarantee direct delivery of adequate doses of the drugs in the lesion with overcoming the barriers that impact the absorption of applied topical drugs and avoiding the side effects of systemic drugs. This article will review the different drugs available for intralesional injection in the treatment of psoriasis.

Key words: Psoriasis, intralesional injection, Corticosteroids, Methotrexate, Botulinum toxin, Secukinumab.
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Abbreviations:
TAC: triamcinolone acetonide MTX : Methotrexate. CyA: Cyclosporine.
5- FU : 5-Flurouracil. BoNT: Botulinum toxin.

Introduction:

Psoriasis is a chronic inflammatory autoimmune skin disease affected by genetic and various environmental factors.[1] Prevalence of psoriasis is 1–3% in the global population. Moderate to severe psoriasis has a high negative impact on patients' quality of life.[2] Plaque psoriasis is the most prevalent type, presented as well-demarcated, erythematous oval or rounded plaques covered with silvery scales.[3]

Topical therapy plays an important role in treatment of psoriasis. It is the gold standard treatment in mild psoriasis and is recommended as adjuvant to phototherapy and systemic therapy in moderate and severe psoriasis.[4] Currently approved topical treatments include corticosteroids (used alone or in combination regimens), vitamin D analogues, combined corticosteroid/vitamin D (calcipotriol) formulations, vitamin A derivatives (tazarotene), anthralin, and newer formulations of tar.[5] Histologically, psoriasis is characterized by epidermal thickening, which may render the local absorption of drugs [6]

Intralesional therapy is the injection of a higher concentration of a drug directly into skin lesions without significant systemic absorption. The rationale for this technique is the establishment of a subepidermal depot which bypasses the superficial barrier zone. [7]

Intralesional drug therapy is most suitable for scalp, nail, and localized and recalcitrant plaque psoriasis. However, there are specific drugs, which can be used for this purpose, under strict monitoring such as corticosteroids, methotrexate, cyclosporine and etc. [8]

This review aims to provide an overview of the role of intralesional injection in the treatment of psoriasis by examining its mechanisms of action, indications, clinical efficacy, safety profile, and current evidence, while highlighting emerging therapeutic agents and future directions for research.

I.Corticosteroids.

Intralesional corticosteroids injection is a traditional modality that appears to be a relatively safe and effective treatment for psoriatic nails especially in nail matrix involvement. Injection doses, concentrations and injection frequencies have not been standardized. Various side effects such as injection side atrophy, disappearance of the phalanx under injection or tendon rupture. Intralesional triamcinolone acetonide (TAC) injection in nail matrix at concentration of 5 mg/ml every 4 weeks for finger nails and every 8 weeks for

toes nail improved Nail area and severity index at the 5th injection.[9]

Attwa E, etal. Conducted a comparative study between intralesional TAC versus intralesional 5-flurouracil (5-FU) in localized plaque psoriasis. They injected TAC at a concentration of 10 mg/ml with a maximum dose of 20 mg per session at a dosage of 0.1 ml/cm2. While 5-FU injected at a concentration of 50 mg/ml with a maximum dose of 150 mg per session at a dosage of 0.1 ml/cm2. Both drugs were injected every 2 weeks for 3 sessions. The percentage of improvement in TAC side (89%) was significantly more than the percentage of improvement in 5-FU side (67%).[10]

II. Methotrexate.

Intralesional Methotrexate (MTX) injection in nail psoriasis was documented for the first time in 2011. Saricaoglu et al. reported its use in a single nail of a patient. The injection was given into the proximal nail fold (2.5 mg into each side of the nail weekly for 6 weeks). Improvement of subungual hyperkeratosis and pitting were observed.[11]

One study compared the efficacy of intralesional MTX versus triamcinolone acetate and reported no significant difference in the results between both drugs. But, MTX yielded more persistent improvement at 6 months with fewer adverse effects.[12] For nail psoriasis, a 2.5-mg methotrexate injection into each side of the nail at a point 2.5 mm proximal and lateral to the junction of proximal and lateral nail folds.[13]

A novel therapeutic approach for psoriasis involving microneedling-assisted percutaneous delivery of chitosan-coated hollow mesoporous silica nanoparticles containing MTX (MTX@HMSN/CS). The MTX@HMSN/CS-loaded MNs successfully penetrate the psoriasiform thickened epidermis, allowing MTX@HMSN/CS to be accurately delivered to the site of skin lesion. MTX was then released continuously from HMSN/CS for at least one week to maintain effective therapeutic drug concentration for skin lesion with long-term anti-proliferative and anti-inflammatory effects.[14]

III. **Cyclosporine**.

Oral intake of cyclosporine (CyA) is associated with risk for hypertension and renal toxicity, thus the need for safe topical delivery of CyA is a necessity. (15)

Intralesional CyA was investigated for the 1st time in treatment of plaque psoriasis in 1988, by Powles AV, et al. The intravenous cyclosporine solution 50mg/ml was diluted with 2 parts of normal saline. Then, Cyclosporine was injected intralesional in psoriatic plaques in six occasions for 12 days. Every 1-2 cm plaque received 0.2-.05 ml of cyclosporine. Other plaques were injected with normal saline as control. Marked improvement in plaque erythema, thickness, and scales in cyclosporine -treated plaques than control after one week from the start and continued to the second week. Cyclosporine yielded few side effects as flare around psoriatic plaques lasted only for 1 hour and some scabs in the centre of plaques.[16]

Two years later, Ho VC, et al. supported the same efficacy of cyclosporine in treatment of plaque psoriasis with additional histopathological evidence of reduction in epidermal thickness, antigen presenting cells and dermal monocytes and mast cells.[17]

Mittal J, etal. Injected cyclosporine intramatrical in nail psoriasis at a concentration of 50mg/ml in comparison to intramatrical injection of TAC and MTX. Cyclosporine induced less improvement in comparison to TAC and MTX, with more side effects as post-injection pain last for few hours.[18]

VI. 5-Flurouracil.

5-Flurouracil (5-FU) is an antimetabolite that inhibits deoxyribonucleic acid synthesis as well as ribonucleic acid processing and therefore decreases epidermal proliferation. It has been widely used topically, intravenously, and intralesionally in various dermatological and nondermatological diseases. It is available as a solution, cream and as sustained-release preparation for intralesional use in various concentrations (0.5%, 1%, and 5%).[19]

Intralesional injection of 5% 5-FU was given weekly for a total of three injections for localized psoriatic plaque. 5-FU was injected intralesional in a dosage of 0.1 ml/cm2. After three injections of 5-FU, 57.5% of patients showed excellent (70%-90%) improvement, 30% of patients had moderate (30%-70%) improvement, and only 12.5% of patients did not respond to treatment. At the end of follow-up period of 10 weeks after last injection (12th week), 10% of patients had clearance (>90% resolution).[20]

O.1 ml of 5-FU (Utoral® 250 mg/5 ml, Korea limited pharm, Korea), was injected in nail matrix and nail bed monthly for 3 months in comparison to intralesional TAC and MTX. 5-FU showed reduction in target NASI score, but less than that of TAC and MTX. Subungual hematoma and nail fold hyperpigmentation were observed in 1 patient (6.7%) of the intralesional 5-FU group.[21]

V. **IL-17A inhibitors**.

For the first time, He F, et al. injected secukinumab (IL-17A inhibitor) intralesional in the nail matrix of 2 patients with isolated nail psoriasis. Secukinumab (150 mg/ml) was diluted with sterilized water for injection to reduce local irritation. The dosage was 0.1 ml diluted secukinumab per fingernail and three different concentrations 7.5, 15 and 30 mg/ml, respectively, were injected from the second to fourth fingers of the left hand. The total dose was 5.25 mg every time and repeated every 2 weeks for 12 weeks. The right-hand nails received no therapy. There was marked improvement in left nail psoriasis at 6 weeks with 80% improvement in one nail in comparison to the right-hand nails. Both the patients felt transient and bearable pain while receiving injection, without any major discomfort.[22]

He F, et al. conducted another study on 6 patients and reported that degree of improvement was superior in nail bed than nail matrix and no statistically significant difference in degree of improvement between three different concentrations of secukinumab.[23]

VI. **Botulinum Toxin**.

Botulinum toxin (BoNT) is a neurotoxin produced by Clostridium botulinum, a Gram-positive, rod-shaped anaerobic bacterium. [24] Botulinum toxin bind certain complexes in the presynaptic membrane to prevent the release of neurotransmitters such as CGRP, substance P and others. [25]

Chen S-Q, et al. found increased cutaneous nerve fibers density in psoriatic skin in comparison to normal skin. Those nerve fibrs were distributed around the keratinocytes.[26] Sensory nerves such as nociceptive neurons secrete a plenity of neuropeptides as CGRP, substance P and nerve growth factor. These neurotransmitters stimulate release of IL- and IL-23. IL-23 stimulates the differentiation of Th17 cells .[27]

Immunohistochemical study has shown that these neuropeptides present an increased level in psoriatic lesions,[28] along with an upregulation of their corresponding receptors.[29] CGRP proved its ability to stimulate direct epidermal proliferation in a tissue engineered model for psoriasis.[30] Sensory neurons can regulate IL-23 expression in the pathology of psoriasis through neuron-derived CGRP.[31] Multiple studies reported that after central or peripheral nerve injury (such as cerebrovascular accident, trauma, polio, epidural nerve block, etc.), the psoriasis plaques in neurological dysfunction skin were improved or got completely remission. [32-34] Denervation of psoriatic skin attenuates immune system activation in psoriasis as T cell activation, TNF signialling and IL-17 secretion.[35] All these factors points to the impilication of nerveous system and neuropeptides in pathogensis of psoriasis. BoNT is a neurotoxin that inhibit release of neuropetides from their specific neurons, Thus BoNT can be helpfull in management of psoriasis.[36]

Zanchi M, et al. were the first researchers to inject BoNT-A in patients with inverse psoriasis, in 2008.[37] The authors injected 2.4 U of BoNT-A (BOTOX¨, Allergan Inc.) at points 2.8 cm2 apart, in 15 patients with plaque psoriasis. 13 of 15 patients (87%) showed improvement in erythema intensity and infiltration that lasted till 12-weeks in some patients and maintained in one patient till 3 years. Khattab FM, etal. enrolled thirty- five patients with bilateral symmetrical plaque psoriasis. One hundred units BoNT-A vial (Refinex, made in China) was diluted with 5 ml of sterile saline. One side of the body was injected of BoNT-A once with a dose of 2.4 U at 2.8 cm2 distance. The plaques were assessed clinically every 4 weeks till 16 weeks post-injection and followed up till 6 months post-injection. The degree of improvement was 85% at 16 weeks post-injection. [38] Several studies reported good efficacy of BoNT in treatment of psoriasis. [39-41]

References.

1. Zhou X, Chen Y, Cui L, Shi Y, Guo C. Advances in the pathogenesis of psoriasis: from keratinocyte perspective. Cell Death Dis. 2022;13(1):81.

2. Ruggiero A, Fabbrocini G, Cacciapuoti S, Cinelli E, Gallo L, Megna M. ocular manifestations in psoriasis screening (OcMaPS) questionnaire: A useful tool to reveal misdiagnosed ocular involvement in psoriasis. J Clin Med. 2021;10(5):1031.

3. **Chen W-Y, Chen S-C, Hsu S-Y, Lin Y-A, Shih C-M, Huang C-Y, et al.** Annoying psoriasis and atopic dermatitis: A narrative review. *Int J Mol Sci*. 2022;23(9):4898.

4. Ramic L, Sator P. Topical treatment of psoriasis vulgaris. J Dtsch Dermatol Ges. 2023;21(6):631-42.

5. Segaert S, Calzavara-Pinton P, de la Cueva P, Jalili A, Lons Danic D, Pink AE, et al. Long-term topical management of psoriasis: the road ahead. J Dermatolog Treat. 2022;33(1):111-20.

6. Negrutiu M, Danescu S, Popa T, Focsan M, Vesa SC, Szasz F, et al. Imaging Approach in the Diagnostics and Evaluation of the Psoriasis Plaque: A Preliminary Study and Literature Review. Diagnostics (Basel). 2024;14(10):969.

7. Deshmukh NS, Belgaumkar VA, Mhaske CB, Doshi BR. Intralesional drug therapy in dermatology. Indian J Dermatol Venereol Leprol. 2017;83(1):127-32.

8. Sathyan S, Agarwal K, Podder I, Patil A, Kircik L, Weinberg J, et al. Intralesional Mode of Drug Administration in Psoriasis. J Drugs Dermatol. 2022;21(2):186-90.

9. Grover C, Kharghoria G, Bansal S. Triamcinolone acetonide injections in nail psoriasis: A pragmatic analysis. kin Appendage Disord. 2024;10(1):50-9.

10. Attwa E, Khater MH, Selim HM, Essam R. Comparative efficacy of intralesional 5 flurouracil and intralesional triamcinolone acetonide in localized plaque psoriasis. Dermatol Ther. 2022;35(11): e15796.

11. Sarıcaoglu H, Oz A, Turan H. Nail psoriasis successfully treated with intralesional methotrexate: Case report. Dermatology. 2011;222(1):5-7.

12. Starace M, Alessandrini A, Iorizzo M, D'Altobrando A, Ferrari T, Bruni F, et al. A pilot study of intralesional methotrexate injections versus triamcinolone acetonide in patients affected by nail matrix psoriasis. Clin Exp Dermatol. 2022;47(6):1165-8.

13. Choudhary P, Mehta RD, Ghiya BC, Sharma D. Treatment of nail psoriasis with intramatrical methotrexate: An uncontrolled prospective study of 20 patients. J Am Acad Dermatol. 2021;84(2):526-8.

14. Du H, Yang J, Li M, Xia Y, Li Y, Zhu J, et al. Microneedle-assisted percutaneous delivery of methotrexate-loaded nanoparticles enabling sustained anti-inflammatory effects in psoriasis therapy. J Mater Chem B. 2024;12(10):2618-27.

15. Sadeghi S, Kalantari Y, Seirafianpour F, Goodarzi A. A systematic review of the efficacy and safety of topical cyclosporine in dermatology. Dermatologic therapy. 2022; 35(6):e15490.

16. Powles AV, Baker BS, McFadden J, Rutman AJ, Griffiths CEM, Fry L, et al. Intralesional injection of cyclosporin in psoriasis. Lancet. 1988;1(8584):537

17. Ho VC, Griffiths CE, Ellis CN, Gupta AK, McCuaig CC, Nickoloff BJ, et al. Intralesional cyclosporine in the treatment of psoriasis. A clinical, immunologic, and pharmacokinetic study. J Am Acad Dermatol. 1990;22(1):94-100.

18. Mittal J, Mahajan BB. Intramatricial injections for nail psoriasis: An open-label comparative study of triamcinolone, methotrexate, and cyclosporine. Indian J Dermatol Venereol Leprol. 2018;84(4):419-23.

19. Mahdy MNI., Nofal A, Khater EMG, Different Uses of 5-FLUROURACIL in Dermatology. The Egyptian Journal of Hospital Medicine. 2022. 89(1): 5498-5500.

20. Mahajan BB, Singla M. Evaluation of intralesional 5% 5-fluorouracil in resistant localized plaque psoriasis. Indian Dermatol Online J. 2014;5(3):287-90.

21. Abdelmeniem IM, El Eryan IM, Nofal A, Fouda I, Omar SS. Topical calcipotriol combined with urea 20% versus intralesional injection of triamcinolone acetonide, 5-fluorouracil, and methotrexate in the treatment of nail psoriasis: A comparative study. Dermatol Ther. 2022;35(9):e15660.

22. He F, Long F, Tu J, Yin Z. Intramatricial low-dose secukinumab injection for nail psoriasis. Indian J Dermatol Venereol Leprol. 2021;87(1):116-9.

23. He F, Long FY, Zhang ZQ, Xia RY, Lu Y, Yin ZQ. Intramatricial injection of anti-interleukin-17A antibody for six patients with nail psoriasis. Clin Exp Dermatol. 2022;47(2):432-3.

24.. Park MY, Ahn KY. Scientific review of the aesthetic uses of botulinum toxin type A. Arch Craniofac Surg. 2021;22(1):1-10.

25. Carr WW, Jain N, Sublett JW. Immunogenicity of botulinum toxin formulations: potential therapeutic implications. Adv Ther. 2021;38(10):5046-64.

26. Chen SQ, Chen XY, Cui YZ, Yan BX, Zhou Y, Wang ZY, et al. Cutaneous nerve fibers participate in the progression of psoriasis by linking epidermal keratinocytes and immunocytes. Cell Mol Life Sci. 2022;79(5):267.

27. Zhang X, He Y. The role of nociceptive neurons in the pathogenesis of psoriasis. Front Immunol. 2020;11:1984.

28. Kubanov AA, Katunina OR, Chikin VV. Expression of neuropeptides, neurotrophins, and neurotransmitters in the skin of patients with atopic dermatitis and psoriasis. bull exp biol med. 2015;159(3):318-22.

29. Smolyannikova VA, Kubanova AA, Karamova AE, Nefedova MA, Chikin VV. Role of the skin expression of neuropeptides, neurotrophins and their receptors in the pathogenesis of dermatoses. Arkh Patol. 2015; 77(4):33-9.

30. Pepin R, Ringuet J, Beaudet MJ, Bellenfant S, Galbraith T, Veillette H, et al. Sensory neurons increase keratinocyte proliferation through CGRP release in a tissue engineered in vitro model of innervation in psoriasis. Acta Biomater. 2024;182:1-13.

31. Zhang X, Cao J, Zhao S, Yang X, Dong J, Tan Y, et al. Nociceptive sensory fibers drive interleukin-23 production in a murine model of psoriasis via calcitonin gene-related peptide. Front Immunol. 2021; 12:743675.

32. Zhu TH, Nakamura M, Farahnik B, Abrouk M, Lee K, Singh R, et al. The role of the nervous system in the pathophysiology of psoriasis: a review of cases of psoriasis remission or improvement following denervation injury. Am J Clin Dermatol. 2016;17(3):257-63.

33. Lee EB, Reynolds KA, Pithadia DJ, Thiyanaratnam J, Wu JJ. Clearance of psoriasis after ischemic stroke. Cutis. 2019;103(2):74-6.

34. Azimi E, Lerner EA, Elmariah SB. Altered manifestations of skin disease at sites affected by neurological deficit. Br J Dermatol. 2015;172(4):988-93.

35. Qin B, Sun C, Chen L, Wang S, Yang J, Xie Z, et al. The nerve injuries attenuate the persistence of psoriatic lesions. J Dermatol Sci. 2021;102(2):85-93.

36. Amalia SN, Uchiyama A, Baral H, Inoue Y, Yamazaki S, Fujiwara C, et al. Suppression of neuropeptide by botulinum toxin improves imiquimod-induced psoriasis-like dermatitis via the regulation of neuroimmune system. J Dermatol Sci. 2021;101(1):58-68.

37. Zanchi M, Favot F, Bizzarini M, Piai M, Donini M, Sedona P. Botulinum toxin type-A for the treatment of inverse psoriasis. J Eur Acad Dermatol Venereol. 2008; 22(4):431-6.

38. Khattab FM, Samir MA. Botulinum toxin type-A versus 5-fluorouracil in the treatment of plaque psoriasis: Comparative study. J Cosmet Dermatol. 2021;20(10):3128-32.

39. Aschenbeck KA, Hordinsky MK, Kennedy WR, Wendelschafer-Crabb G, Ericson ME, Kavand S, et al. Neuromodulatory treatment of recalcitrant plaque psoriasis with onabotulinumtoxinA. J Am Acad Dermatol. 2018;79(6):1156-9.

40. González C, Franco M, Londoño A, Valenzuela F. Breaking paradigms in the treatment of psoriasis: Use of botulinum toxin for the treatment of plaque psoriasis. Dermatol Ther. 2020;33(6):e14319.

41. Juntongjin P, Srisinlapakig S, Nitayavardhana S. Botulinum toxin injection shows promise in nail psoriasis: A comparative randomized controlled trial. JAAD Int. 2024;16:105-11.