Article **ECORFAN Journal**
December 2015 Vol.1 No.1 1-9

Therapeutic alternatives in ungueal psoriasis. Brief review of its pros and cons

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Received January 12, 2015; Accepted September 18, 2015

Abstract

Psoriasis is an inflammatory, autoimmune disease. Nail affection occurs in 40 to 50%, however, frequently the management is not adequate. Nowadays a wide range of therapeutic options are availa-ble that includes topic, intralesional or systemic drugs and also biologic agents; none has been 100% effective. Every option present advantages, and adverse effects, that must be considered based on the severity of nail compromise, clinical type of psoriasis and patient to treat.

Nail psoriasis, topic treatments, systemic treatments, biological agents, indications, side effects.

Citation: NAVARRO-DURÁN Llary, TORRES-GUERRERO Edoardo, GONZÁLEZ-MEDINA Elisa Monserrat, RAMOS-BETANCOURT Laura and LACY, Rosa María. Therapeutic alternatives in ungueal psoriasis. Brief review of its pros and cons. ECORFAN Journal-Republic of Guatemala 2015, 1-1: 1-9

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Introduction

Psoriasis is an autoimmune inflammatory disease that occurs in genetically susceptible individuals-mind. It comes with exacerbations and remissions and involves the development of injuries of varying severity that affect not only skin but also nails and joints [1]. Is estimated to affect about 2% of the world population [2]. This calculated figure may be far from the number of actual cases because a large percentage of the population is not in a position to go or no medical services, and that this condition may be underdiagnosed or subject to misdiagnoses [3].

Although the first concepts regarding the pathogenesis of psoriasis are mainly focused on keratinocyte hyperproliferation, deregulation of the immune system is now recognized as a critical factor in this disease. Studies have supported the concept that Interacci-tions between different cells and cytokines probably contribute to the initiation and perpetuation of skin inflammation. A basic theoretical sequence immunological events occurring in psoriasis are described below: antigenic stimuli contribute to the activation of dendritic cells and other innate immune cells in the skin; proinflammatory cytokines produced by the innate immune cells, including interferon alpha (IFN), active-ing stimulate myeloid dendritic cells in the skin; they produce cytokines such as IL interleukin IL -23 and -12 that stimulate attraction, activation and differentiation of T cells recruited These T cells produce cytokines that stimulate keratinocyte proliferation and production of proinflammatory cytokines and peptides that perpetuate the process inflammatory [4].

The nail involvement occurs in 40-50% of adult patients with psoriasis; up to 13% of pediatric patients with this disease and this prevalence increases to 87% in those with psoriatic arthritis [5, 6].

There is a positive association between psoriasis and nail the duration and severity of skin lesions [6]. 5% of the patients with psoriasis, nail lesions may occur without presenting cutaneous manifestations [7]. Despite its relative frequency, nail psoriasis often overlooked and not treated effectively. This has important implications for patients with negative impact on the fun-tioning and quality of life. In addition, it can be a predictor of future inflammatory damage arti-lar (precursor of psoriatic arthritis) and is a visible indicator of disease activity [8].

The nail apparatus consists of the following anatomical structures: the nail plate, the periungual folds, matrix and bed [9]. Clinical morphology depends on the anatomical location of the pathological process [1] may affect any element, whether the bed and / or the matrix. This results in different clinical signs.

The most common findings are alterations of the bed comprising the following:

Onycholysis: One of the most frequent alterations and features. A distal detachment of the sheet occurs with respect to the bed, in which a more or less large whitish area surrounded by an erythematous appearance collarette with an oil stain is observed. Sometimes the whitish hue takes a greenish or brown due to colonization by bacteria or fungi. Subungual hyperkeratosis: It is important because parakeratotic proliferation of cells, which results in a dense, powdery, whitish mass distally off the nail; and it is the most clinically confused with onychomycosis. Oil stains or salmon patch: It is the only exclusive nail psoriasis lesion. Round or oval areas are seen in the center of the sheet of orange color. Splinter hemorrhages: These are linear, with threadlike appearance. Usually they are seen only in the fingers [1, 6, 10].

ISSN-On line: 2414-8849

These lesions can present isolated or associated with lesions of the matrix, in which case it can be observed pits or dimples, which are usually multiple and irre gular-punctate depressions, which are caused by transient focal involvement of the proximal matrix. These dimples correspond to paraqueratosis islets that by eliminating the appearance of the nail, leave blues-making in the film. Trachyonychia appears as the result of a permanent alteration of the proximal matrix, where a rough, dull surface is observed. Other related findings are leukonychia (partial or total white coloration of the nail plate, due to the involvement of the intermediate parent), Beau lines (horizontal depressions that represent involvement of the proximal or intermediate matrix along its length) and red crescent (involvement of the distal matrix) [1, 6, 10].

This condition resembles other onicodistrofias, the most common differential diagnosis of onychomycosis, so it is recommended to rule out this disease before treatment instituted (and if confirmed, must be resolved first), and in patients with psoriasis of the nails the risk of a fungal superinfection increases to 27% [10], plus there are hypotheses that suggest that onychomycosis can be a factor that aggravates or perpetuates psoriatic nail dystrophy [11].

In a publication by Fischer-Levancini, it was reported that up to 50% of patients with nail psoriasis referred pain associated with these events [5], a finding consistent with an en-study by De Jong et al, with a total of 1728 patients with nail psoriasis, who reported the presence of this symptom as much as 51.8% of the total and recorded more than 90% patients concerned about their aesthetic appearance. The activities of daily living were negatively affected in 58.9% of patients and a similar number (56.1%) reported that nail psoriasis inhibited normal activities of cleaning staff.

Regarding professional activities, 47.9% of these patients were adversely affected [12].

Therapeutic strategies and resources.

So far, it has a wide range of drug options for the treatment of nail psoriasis, something that represents a therapeutic challenge for dermatologists, and motivates the search for new solutions thereof including topical medications, intralesional, and systemic with biological action; none of which has been 100% effective. Each of these options has advantages and themselves, these side effects to be taken into account depending on the degree and type of nail condition of the patient being treated; not to mention the variability in costs.

Table 1 topical and systemic treatments tested until now are listed.

Due to many factors, treatment of nail psoriasis is complicated. On the one hand, this is due to the slow growth of this Annex and the difficulty in penetrating topical treatments; besides there are few available topical treatments. Meanwhile, oral medica-ments have limited use because of its systemic toxicity, in addition to the literature reports little attachment to them when the nails are the only affected (or where skin lesions are not important structure for the patient in the presence of nail lesions) [13, 14, 15].

For local treatment, steroid injections are considered the measure of choice. These drugs have anti-inflammatory, immunosuppressive and antiproliferative effects (which sig-nifica that these drugs act on all aspects of the disease physiopathogenic) [16].

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However, these infiltrations generate great pain, influence the development of atrophy, hipocromías, superinfection, inclusion cysts and tendon ruptures, so many PATIENT-tes discontinue treatment. Given the above, such as UL-esteem traquioniquias intense treatment option recommended only in severe cases and only if the condition is one or two fingers. Triamcinolone acetonide is the most commonly used agent bimonthly, at doses of 2.5 to 10 mg / ml to a maximum of four injection points (two in the proximal nail fold and two on the side fold) for 6 months [17] .

As another alternative within this family of drugs, clobetasol propionate concentrated-ing to 0.05% cream or gel, it is used twice a week for 4 months. The disadvantages are the percentage improvement reported (51%) and side effects (may cause atrophy, de-pigmentation, and telangiectasia presence of bone resorption) [12,17]. This same steroid at a concentration of 8% lacquer in scheme application once daily for the first week and second week onwards with applications 2-3 times a week for up to 9 months has proven both have adequate penetration into the bed and matrix, without adverse effects, with good results [18]. However, in Mexico there is available a commercial formulation of this substance, and although it can be appealed to the master formulations to address this issue, candidal superinfection has been reported after treatment with this steroid (Figs. 1-A and 1- B) [10].

Other topical therapeutic modalities used include 5 - fluorouracil, which is used dissolved in a 1% solution of propylene glycol or urea cream with 20% applied twice a day for at least six months. This drug is a pyrimidine analog that acts by irreversible inhibition of DNA synthesis, blocking cell proliferation [19].

Its use is recommended especially in the presence of dimples and subungual hyperkeratosis; besides improving dystrophies origin matrix up to 50% [20]; in cam-bio, clearly worse onycholysis, so it is suggested to avoid its application to this manifest-ing and as side effects can cause irritation and hyperpigmentation (Fig. 2) [10, 21,22].

Derivatives of vitamin D (Fig. 3), such as calcipotriol, tacalcitol and calcitriol, interac-They act with vitamin D receptors, promote cell differentiation and immunomodulation, while inhibit cell proliferation and expression of cutaneous lymphocyte associated antigen (CLA, for its acronym in English -Associated Cutaneous Lymphocyte Antigen), which translates clinically in improved nail bed alterations [16], acting positi-tively in reducing hyperkeratosis, however, its effects are limited to the parent company level, observed in a study conducted by Urbina and Sudy in Chile, little improvement pique-teado [23] so it should always be combined with corticosteroids, which raises even the cost of treatment. Recommended treatment schemes are: Calcipotriol twice daily or calcipotriol + betamethasone once a day for 3 months [24, 25].

Tazarotene (third generation derivative of retinoic acid from [Fig. 4]), exerts its effect by activating and regulating gene transcription, which modulate and induce the expression of epidermal growth factor, promote epidermal cell differentiation, exert effects immunomodulatory and regulate the growth of hyperproliferative epithelia; so it is an excellent modality for the treatment of disorders such as psoriasis [16].

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This drug presentation hydrophilic ointment gel or 0.1% applied once daily has been shown to significantly improve subungual hyperkeratosis, onycholysis, oil spots and the dimples, after 12 weeks of daily use. Side effects were rare and were Prolon-gada improvement (especially hyperkeratosis) to stop treatment, but remember that it is contraindicated in pregnancy (teratogenicity), it is expensive and not very effective in removing other changes resulting from damage to the nail matrix [5, 26, 27].

Tacrolimus is a macrolide immunosuppressant that acts by inhibiting calcineurin phosphatase. This lock prevents lymphocytes can dephosphorylate the cytoplasmic subunit of nuclear factor of activated T cells (NFAT by its acronym Nuclear Factor of Activated T Cells), which in turn prevents transcription of numerous inflammatory cytokines [19]. In studies with this drug has been observed generally good response, however, it has also been a frequent association with acute paronychia, aspect to take into consideration with-[14].

As for systemic treatment, it has cyclosporine, which is considered a PROFAR-maco, which acts by binding to cyclophilin, exerting a similar tacrolimus effect (Figs. 5-A and 5-B) [16]. This drug dose of 5 mg / kg daily produces improved nail lesions. However, due to their profile of liver and kidney toxicity, there is no justification to indicate it to isolated nail psoriasis [28]. In a study investigating the efficacy and safety of methotrexate (which blocks cell division in S phase and exerts an anti-inflammatory effect by the increase in tissue levels of adenosine) at doses of 15 mg / week and cyclosporin 5mg / kg was compared after 6 months of treatment, concluded that both drugs were equally effective in nail psoriasis. However, methotrexate was more effective in lesions of the matrix, whereas cyclosporin was more effective on the injury bed [16, 29].

Besides the above, we must not forget the major side effects associated with methotrexate, such as pancytopenia (by myelotoxicity) and liver toxicity, same that occurs with long-term treatment (as in the case of psoriasis) [16].

Among the physical treatment modalities are photochemotherapy with 8-MOP (I put-xipsoraleno), same as minister topically or orally, with subsequent exposure to UVA rays and generates good results, especially when the damage to nail apparatus It presents with pustules and / or hyperkeratosis, but on the contrary, onycholysis worsens [5, 10]. Until the advent of the derivatives of vitamin D, this was one of the handiest therapeutic strategies [10]; however, remember the side effects that include fotooni-cólisis and burns of the periungual tissues, this method can also predispose photosensitivity reactions, as well as exposing the patient to the side effects of psoralens (when they are indicate systemically), not to mention that UVA is limited number of sessions, beyond which it can no longer exposed [19], so that if a relapse occurs at the end of this treatment, not It is possible to re-use this mode.

Also, good results with photodynamic therapy and laser dye, which have shown to be effective in correcting alterations in both the bed and matrix are mentioned; However, the former has the disadvantage of discomfort and pain associated with their application and both are to the disadvantage of its cost (taking into account that talking about long-term treatment) [5].

At present there are relatively few studies that have examined the use of modifiers specific biological response in the treatment of nail psoriasis.

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These compounds work by means of mechanisms including interaction with receptors that alter or block the activation and differentiation of T cells, as well as, inhibit the release of cytokines and eliminate pathogenic B cells. The main target of action of these drugs created by bioengineering is the Tumor Necrosis Factor (TNF) [16]. Current evidence suggests that TNF as inhibitors infliximab, adalimumab and etanercept are effective for this pur-site, but have a very high cost and its use is not approved for the treatment of nail ma-isolated manifestations; [30] besides their dosing schedules are com-plex, for example infliximab (which in turn, is the antibody with the best results have been observed with the most experience trials have) the dosage is 5 mg / kg, intravenous infusion at weeks 0, 2, 6 and every 8 weeks until week 38-46 [31].

So it has recently tested a water soluble nail lacquer containing hidroxipropilqui-cough (copolymer of glucosamine and N-acetylglucosamine units linked by glucosídi-cos links; very abundant in crustaceans, fungi and insects), horsetail extract (Equisetum vense ar-rich silicates, which bind to the nail keratin reinforcing structure) and methyl sulfonyl methane (which gives elasticity to the nail and reduces their fragility). This product is effective for strengthening nails and reduces their roughness; plus it has some antimicrobial activity which has resulted in combination with antifungals such as ciclopirox to treat onychomycosis. In a clinical trial conducted to verify if this lacquer was able to improve the signs of nail psoriasis, dimples and decreasing the degree of onychodystrophy it was shown without any adverse effects (except mild irritation periungual folds) will report ; although in some cases observed in the authors' experience, no significant changes (unpublished data) [32,33, 34] showed.

Conclusions

The condition of the nails in patients with psoriasis is very common, with the percentage involvement is between 10 and 78%. The fingernails and in turn are affected more than usual is that it affects more than a fingernail.

Current therapy is often ineffective or generates modest results and includes the application of topical agents or local steroid injections are very painful. Furthermore, systemic therapies are generally not recommended for patients with nail disease only. Added to this, one of the problems by checking the level of evidence available treatments is the lack of sufficient studies in literature, in addition to the validity between the different trials reported.

It is not yet has a "gold standard" in the treatment of this manifestation, sometimes as in-capacitating or as traumatic for some patients, so the choice of therapeutic approach based on the points raised in this article I allow to individualize, choosing those tools and best suited to each patient therapeutic combinations (in the case of being necessary), taking into account (among other things) the degree of nail condition -and cutaneous-, there is-State General health, the presence or absence of comorbidities, and prescribed treatments for each of them (with the consequent potential interactions) and possible side effects in each case.

References

[1] Jiaravuthisan MM, Sasseville D, Vender RB et al. *Psoriasis of the nail: anatomy, pathology, clinical presentation, and a review of the literature on therapy*. J Am Acad Dermatol 2007; 57: 1–27.

ISSN-On line: 2414-8849

[2] Amaya GM, Barba F, Blancas GF, Gómez FM. *Consenso mexicano para el manejo de la terapia biológica en psoriasis*. Rev Cent Dermatol Pascua 2004;13: 172-184.

[3] Podsowa N. *Revisión del IPC Sobre la Psoriasis. Enfoque en América Latina*. Diciembre 2009.

[4] Nestle FO, Kaplan DH, Barker J. *Psoriasis*. N Engl J Med 2009; 361:496.

[5] Fischer-Levancini C, Sánchez-Regaña M, Llambí F, Collgros H, Expósito-Serrano V, Umbert-Millet P. *Psoriasis ungueal. Tratamiento con ungüento hidrófilo de tazaroteno al 0.1%*. Actas Dermosifilogr 2012; 103 (8): 725 – 728.

[6] Reich K. *Approach to managing patients with nail psoriasis*. JEADV 2009; 23(Suppl. 1): 15–21.

[7] Grover C, Reddy BS, Uma CK. *Biopsy and histopathology in diagnosing nail psoriasis*. Br J Dermatol 2005; 153: 1153–1158.

[8] Wilson FC, Icen M, Crowson. *Incidence and clinical predictors of psoriatic arthritis in patients with psoriasis: a population-based study*. Arthritis Rheum 2009; 61: 233–239.

[9] Tosti A, Piraccini BM: *Nail Disorders*. En: Bolognia J, Jorizzo J, Rappini R. Dermatology. 1era. Ed. Madrid. Mosby Elsevier, 2008; 1061-1078.

[10] Sánchez-Regaña M y Umbert P. *Aspectos diagnósticos y terapéuticos de la psoriasis ungueal*. Actas Dermosifiliogr. 2008; 99: 34-43.

[11] Van der Velden HMJ, Klaassen KMG, van de Kekrhof PCM, Pasch M. *Fingernail psoriasis reconsidered: A case-control study*. J Am Acad Dermatol 2013; 69: 245 – 252.

[12] De Jong EM, Seegers BA, Gulinck MK. *Psoriasis of the nails associated with disability in a large number of patients: results of a recent interview with 1728 patients*. Dermatology 1996; 193: 300–303.

[13] Radtke MA, Beikert FC, Augustin M. *Nail psoriasis – a treatment challenge*. JDDG 2013; 11(3): 203-220.

[14] Crowley J, Weinberg JM, Wu JJ, Robertson AD, Van Voorhees AS. *Treatment of Nail Psoriasis. Best practice recommendations from the medical board of the National Psoriasis Foundation*. JAMA Dermatol 2014; 150 (12): E1 – E8.

[15] Edwards F, de Berker D, *Nail psoriasis. Clinical presentation and best practice recommendations*. Drugs 2009; 69: 2351–2361.
16.- Arenas R. *Dermatología. Atlas, diagnóstico y tratamiento*. 5ta Ed. México. Mc Graw Hill, 2013: 609 – 619.

[17] Oram Y, Akkaya D. *Treatment of Nail Psoriasis: Common Concepts and New Trends*. Dermatology Research and Practice, vol. 2013; Art. ID 180496: 01-13.

[18] Nakamura RC, Abreu LD, Duque-Estrada B, Tamler C, Leverone AP. *Comparison of nail lacquer clobetasol efficacy at 0.05%, 1% and 8% in nail psoriasis treatment: prospective, controlled and randomized pilot study*. An Bras Dermatol 2012; 87(2): 203 - 211.

[19] van de Kerkhof P, Nestlé FO. *Psoriasis*. En: Bolognia J, Jorizzo J, Schaffer JV. Dermatology. 3rd. Ed. New York. Elsevier Saunders, 2012: 135 – 156.

[20] Baran R, Dawber RPR. *Diseases of the nails and their management*. 2nd. Ed. Oxford. Blackwell Scientific Publications, 1994: 135 – 142.

ISSN-On line: 2414-8849

[21] Frederiksson T. *Topically applied fluorouracil in the treatment of psoriatic nails*. Arch Dermatol. 1974; 110: 735.

[22] Fritz K. *Psoriasis of the nails. Successful topical treatment with 5-fluorouracil*. Z Hautkr 1988;64: 1083-1088.

[23] Urbina F, Sudy E. *Tratamiento de la psoriasis ungueal con calcipotriol tópico en cura oclusiva*. Actas Dermosifilogr 2001; 92: 527 – 529.

[24] Sanchez Regaña M, Márquez G, Umbert P. *Nail psoriasis: a combined treatment with 8% clobetasol nail lacquer and tacalcitol oinment*. J Eur Acad Dermatol Venereol. 2008; 22: 963-969.

[25] Sánchez Regaña M, Ojeda R, Umbert P. *Empleo de calcipotriol tópico en la psoriasis ungueal*. Piel. 2002;17: 104-108.

[26] Scher RK, Stiller M, Zhu YI. *Tazarotene 0,1 % gel in the treatment of fingernails psoriasis: a double-blind, randomized, vehicle-controlled study*. Cutis. 2001;68: 355-358.

[27] Rigopoulos D, Gregoriou S, Katsambas A. *Treatment of psoriatic nails with tazarotene cream 0,1 % vs. clobetasol propionate 0,05 % cream: a double-blind study.* Acta Derm Venereol. 2007;87: 167-168.

[28] Ojeda R, Sánchez Regaña M, Massana J, Oliete R, Umbert P. *Clinical experience with the use of cyclosporin A in psoriasis. Results of a retrospective study*. J Dermatol Treat. 2005;16: 338-341.

[29] Gumusel M, Ozdemir I, Bodur S. *Evaluation of the efficacy of methotrexate and cyclosporine therapies on psoriatic nails: a one-blind, randomized study*. JEADV 2011; 25: 1080–1084.

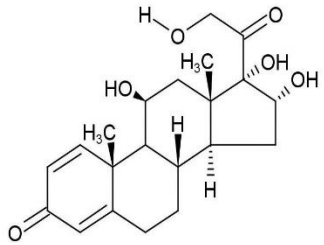
[30] Tan EST, Chong WS, Liang Tey HL. *Nail psoriasis*. Am J Clin Dermatol 2012; 6: 13.

[31] Zaiac M. *The role of the biological agents in the treatment of nail psoriasis*. Am J Clin Dermatol 2010; 11 suppl 1: 27-29.

[32] Cantoresi F, Sorgi P. *Improvement of psoriatic onychodystrophy by a water-soluble nail lacquer*. JEADV 2009; 23: 832- 834.

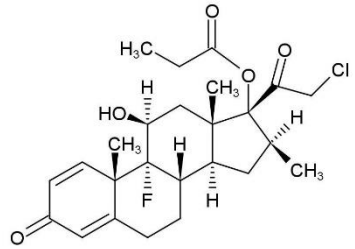
[33] Xua X, Zhuanga X, Chengb B, Xua J, Longc G, Zhang H. *Manufacture and properties of cellulose/O-hydroxyethyl chitosan blend fibers*. Carbohydrate Polymers 2010; 81: 541–544.

[34] Bohn M, Kraemer K. *Dermatopharmacology of ciclopirox nail lacquer topical solution 8% in the treatment of onychomycosis*. J Am Acad Dermatol 2000;43: S57-S69.



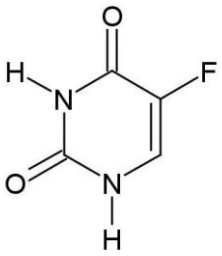
TRIAMCINOLONA

Figura 1A



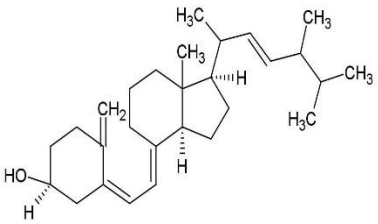
CLOBETASOL

Figura 1B



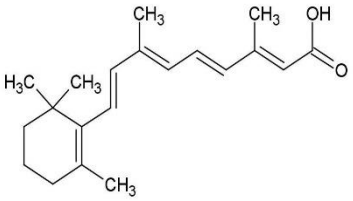
5-fluorouracilo

Figura 2



VITAMINA D
(CALCIFEROL)

Figura 3



ÁCIDO RETINOICO

Figura 4

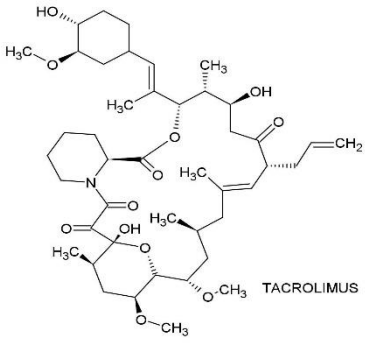
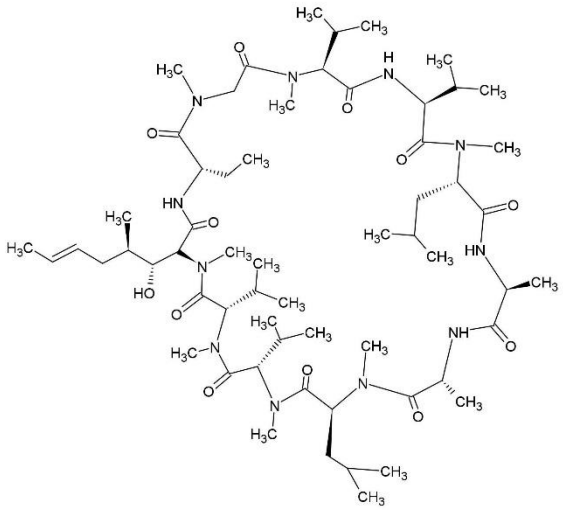


Figura 5A



CICLOSPORINA A

Figrua 5B

Tratamiento de aplicación tópica o intralesional	**Nivel de evidencia**
- Ciclosporina tópica al 70% en aceite de maíz	IB
- Ungüento tópico de tacrolimus al 1%	III
- Clobetasol al 0.05, 0.1 y 0.8% en laca	III
- Tazaroteno en gel al 0.1%	III
- Calcipotriol (con o sin betametasona)	IIB
- Fototerapia (con psoraleno y/ o acitretina)	III
- Luz pulsada de 595nm	III
- Terapia fotodinámica con MAL*	III
- Rayos Grenz	IIB
- Inyección intralesional de corticoides	IV
Tratamientos Sistémicos y Biológicos	
- Metotrexato	IIA
- Ciclosporina	III
- Acitretina	III
- Apremilast	IB
- Adalimumab	IB
- Etanercept	IIA
- Golimumab	IB
- Infliximab	IB
- Ustekinumab	IB
- Ixekinumab	IB
- Secukinumab	IB

ISSN-On line: 2414-8849