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Date: 17 July 2019
Sources Searched: Medline, Embase.

Topical Tacrolimus

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Evidence Summary:

- To date no studies on the use or effect of topical tacrolimus during pregnancy have been published.
- Available safety data in pregnancy is based upon observational studies of oral tacrolimus following organ transplantation which reported no increased risk of congenital malformations, but an increased risk of prematurity, although possibly associated with maternal disease. Birth weight was found to be significantly decreased, although appropriate for gestational age.
- Systemic absorption of topical tacrolimus is very low in both 0.1% and 0.03% concentrations due to the large size of the molecule, although an impaired skin barrier associated with certain skin diseases may allow for increased systemic absorption.

Source: VESTERGAARD, C., WOLLENBERG, A., BARBAROT, S., CHRISTEN-ZAECH, S., DELEURAN, M., SPULS, P., FLOHR, C., TRZECIAK, M., VON KOBYLETZKI, L., SENESCHAL, J., PAUL, C., BIEBER, T., WERFEL, T., FÖLSTER-HOLST, R., DARSOW, U., GIELER, U., SVENSSON, Å., CORK, M., STALDER, J., DE RAEVE, L., KUNZ, B., SIMON, D., CHERNYSHOV, P., HIJNEN, D., GELMETTI, C., RING, J., TAIEB, A., DE BRUIN-WELLER, M. and THYSSEN, J.P., 2019. European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period. *Journal of the European Academy of Dermatology and Venereology : JEADV,* .

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1. European task force on atopic dermatitis position paper: treatment of parental atopic dermatitis during preconception, pregnancy and lactation period.

Author(s): Vestergaard, C; Wollenberg, A; Barbarot, S; Christen-Zaech, S; Deleuran, M; Spuls, P; Flohr, C; Trzeciak, M; von Kobyletzki, L; Seneschal, J; Paul, C; Bieber, T; Werfel, T; Fölster-Holst, R; Darsow, U; Gieler, U; Svensson, Å; Cork, M; Stalder, J-F; De Raeve, L; Kunz, B; Simon, D; Chernyshov, P; Hijnen, D; Gelmetti, C; Ring, J; Taieb, A; de Bruin-Weller, M; Thyssen, J P

Source: Journal of the European Academy of Dermatology and Venereology : JEADV; Jun 2019

Publication Date: Jun 2019

Publication Type(s): Journal Article

PubMedID: 31231864

Available at Journal of the European Academy of Dermatology and Venereology : JEADV - from Wiley Online Library Science , Technology and Medicine Collection 2017

Abstract: Atopic dermatitis (AD) is a common inflammatory skin disease that affects both children and adults, including a large number of adults of reproductive age. Several guidelines for the treatment of AD exist, yet specific recommendations for the treatment of pregnant or lactating women and for adults planning to have a child are often lacking. This position paper from the European Task force on Atopic Dermatitis (ETFAD) is based on up-to-date scientific literature on treating pregnant and lactating women as wells as adults with AD planning to have a child. It is based on the expert opinions of members of the ETFAD and on existing safety data on the proposed treatments, many of which are derived from patients with other inflammatory diseases or from transplantation medicine. For treating future parents, as well as pregnant and lactating women with AD, the use of topical treatments including moisturizers, topical corticosteroids, tacrolimus, antiseptics such as chlorhexidine, octenidine, potassium permanganate and sodium hypochlorite (bleach) is deemed to be safe. Ultraviolet (UV) therapy may also be used. Systemic treatment should be prescribed only after careful consideration. According to the opinion of the ETFAD, treatment should be restricted to systemic corticosteroids and cyclosporine A, and, in selected cases, azathioprine.

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2. Psoriasis in those planning a family, pregnant or breast-feeding. The Australasian Psoriasis Collaboration.

Author(s): Rademaker, Marius; Agnew, Karen; Andrews, Megan; Armour, Katherine; Baker, Chris; Foley, Peter; Frew, John; Gebauer, Kurt; Gupta, Monisha; Kennedy, Debra; Marshman, Gillian; Sullivan, John

Source: The Australasian journal of dermatology; May 2018; vol. 59 (no. 2); p. 86-100

Publication Date: May 2018

Publication Type(s): Journal Article Review

PubMedID: 28543445

Abstract: The Australasian Psoriasis Collaboration has reviewed the evidence for managing moderate to severe psoriasis in those who are pregnant or are breast-feeding, or planning a family. The severity of the psoriasis, associated comorbidities and specific anti-psoriasis treatment, along with other exposures, can have a deleterious effect on pregnancy outcomes. Psoriasis itself increases the risk of preterm and low birthweight babies, along with spontaneous and induced abortions, but no specific birth defects have been otherwise demonstrated. The baseline risk for a live born baby to have a major birth defect is 3%, and significant neuro-developmental problem is 5%. In Australia, pregnant women with psoriasis are more likely to be overweight or obese, depressed, or smoke in their first trimester, and are also less likely to take prenatal vitamins or supplements. Preconception counselling to improve maternal, pregnancy and baby health is therefore strongly encouraged. The topical and systemic therapies commonly used in psoriasis are each discussed separately, with regards to pregnancy exposure, breast-feeding and effects on male fertility and mutagenicity. The systemic therapies included are acitretin, adalimumab, apremilast, certolizumab, ciclosporin, etanercept, infliximab, ixekizumab, methotrexate, NBUVB, prednisone, PUVA, secukinumab and ustekinumab. The topical therapies include dithranol (anthralin), calcipotriol, coal tar, corticosteroids (weak, potent and super-potent), moisturisers, salicylic acid, tacrolimus, and tazarotene. As a general recommendation, effective drugs that have been widely used for years are preferable to newer alternatives with less foetal safety data. It is equally important to evaluate the risks of not treating, as severe untreated disease may negatively impact both mother and the foetus.

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3. Review of treatment options for psoriasis in pregnant or lactating women: from the Medical Board of the National Psoriasis Foundation.

Author(s): Bae, Yoon-Soo Cindy; Van Voorhees, Abby S; Hsu, Sylvia; Korman, Neil J; Lebwohl, Mark G; Young, Melody; Bebo, Bruce; Kimball, Alexa Boer; National Psoriasis Foundation

Source: Journal of the American Academy of Dermatology; Sep 2012; vol. 67 (no. 3); p. 459-477

Publication Date: Sep 2012

Publication Type(s): Journal Article Review

PubMedID: 22018758

Abstract:BACKGROUNDTreating psoriasis in pregnant and lactating women presents a special challenge. For ethical reasons, prospective randomized control trials have not been conducted in this patient population although these patients do encounter new-onset psoriasis in addition to flares and may require treatment throughout their pregnancies.OBJECTIVEOur aim was to arrive at consensus recommendations on treatment options for psoriasis in pregnant and lactating women.METHODSThe literature was reviewed regarding all psoriasis therapies in pregnant and lactating women.RESULTSTopical therapies including emollients and low- to moderate-potency topical steroids are first-line therapy for patients with limited psoriasis who are pregnant or breast-feeding. The consensus was that second-line treatment for pregnant women is narrowband ultraviolet B phototherapy or broadband ultraviolet B, if narrowband ultraviolet B is not available. Lastly, tumor necrosis factor-α inhibitors including adalimumab, etanercept, and infliximab may be used with caution as may cyclosporine and systemic steroids (in second and third trimesters). Some specific strategies may be used to minimize risk and exposure.LIMITATIONSThere are few evidence-based studies on treating psoriasis in pregnant and lactating women.CONCLUSIONSBecause there will always be a question of ethical concerns placing pregnant and lactating women in prospective clinical trials, investigation of both conventional and biologic agents are unlikely to ever be performed. Some of these medications used to treat psoriasis are known abortifacients, mutagens, or teratogens and must be clearly avoided but others can be used with relative confidence in select patients with appropriate counseling of risks and benefits.

Database: Medline

4. Managing the skin in pregnancy part 2. Pre-existing, new and postpartum skin conditions

Author(s): Wines N.

Source: Medicine Today; Sep 2016; vol. 17 (no. 9); p. 27-35

Publication Date: Sep 2016

Publication Type(s): Article

Abstract: Management of pre-existing skin conditions, such as acne, psoriasis and atopic eczema, and new conditions such as skin cancer may need to be modified during pregnancy, when many of the usual treatments are contraindicated. Management of postpartum nipple and breast problems can be helped by a simplified diagnostic approach and knowledge of medication safety during breastfeeding.Copyright © MedicineToday 2016.

Database: EMBASE

5. Safety of topical dermatologic medications in pregnancy

Author(s): Patel V.M.; Schwartz R.A.; Lambert W.C.

Source: Journal of Drugs in Dermatology; Jul 2016; vol. 15 (no. 7); p. 830-834

Publication Date: Jul 2016

Publication Type(s): Article

PubMedID: 27391632

Abstract: Dermatologic drugs should be employed with caution in women of childbearing age who are pregnant or considering pregnancy. Topical drugs have little systemic absorption. Therefore, they are deemed safer than oral or parenteral agents and less likely to harm the fetus. However, their safety profile must be assessed cautiously, as there is limited available data. In this article, we aggregate human and animal studies and provide recommendations on using topical dermatologic medications in pregnancy.Copyright © 2016 Journal of Drugs in Dermatology. All Rights Reserved.

Database: EMBASE

6. Treatment of atopic dermatitis in pregnancy

Author(s): Babalola O.; Strober B.E.

Source: Dermatologic Therapy; 2013; vol. 26 (no. 4); p. 293-301

Publication Date: 2013

Publication Type(s): Article

PubMedID: 23914886

Abstract: Atopic dermatitis (AD), also referred to as eczema, is one of the most frequently observed skin diseases in pregnant patients. The presentation and histopathology of this condition during pregnancy is identical to that of the non-pregnant individual. AD is a T-helper 2 dominant disease and may worsen during pregnancy, which favors this population of T-lymphocytes. AD management during pregnancy requires special precautions to avoid harming the fetus. Herein is an exploration of

the different options available for the treatment of the pregnant patient with AD. The management of concomitant bacterial and viral infections is also discussed. © 2013 Wiley Periodicals, Inc.

Database: EMBASE

7. Management of psoriasis in pregnancy

Author(s): Babalola O.; Strober B.E.

Source: Dermatologic Therapy; 2013; vol. 26 (no. 4); p. 285-292

Publication Date: 2013

Publication Type(s): Article

PubMedID: 23914885

Available at Dermatologic Therapy - from Wiley Online Library Science , Technology and Medicine Collection 2017

Abstract: Psoriasis is an inflammatory skin disorder not uncommonly seen in pregnant patients. Several drugs have been approved for its treatment in non-pregnant patients, but special precautions are necessary when selecting a treatment plan during pregnancy to prevent harmto the fetus and child. This article reviews the treatment options for the treatment of psoriasis in the pregnant and lactating patient. © 2013 Wiley Periodicals, Inc.

Database: EMBASE

8. Psoriasis in Pregnancy

Author(s): Sorin D.; Pavlovsky L.; David M.

Source: Current Dermatology Reports; 2012; vol. 1 (no. 4); p. 209-213

Publication Date: 2012

Publication Type(s): Review

Available at Current Dermatology Reports - from SpringerLink - Medicine

Available at Current Dermatology Reports - from Unpaywall

Abstract: Psoriasis in pregnant women requires special considerations in view of its course during pregnancy and postpartum period, the possible adverse outcomes, and the restricted basket of therapeutic measures that can be used. Most studies of pregnant psoriatic women have shown that psoriasis remained unaltered in approximately 25 % of pregnancies, improved in 50 %, and worsened in 25 %. In contrast, during the 3-month postpartum period, approximately 30 % remain unchanged, 10 % improved, and 60 % deteriorated. Psoriatic arthritis improved in the vast majority of pregnancies. Impetigo herpetiformis-a rare generalized pustular psoriasis-precipitated by pregnancy has been reported repeatedly. Moderate-to-severe psoriasis, especially when associated with comorbidities, may carry an increased risk for cesarean delivery, chronic hypertension, low birth weight, and recurrent abortions. For mild and limited disease, the use of topical mild-to-moderate-potency steroids (category C) may be used. For moderate-to-severe psoriasis, UVB phototherapy appears to be safe and effective. Anti-TNF alpha agents (category B) should not be given beyond 30 weeks of pregnancy. © 2012 Springer Science+Business Media, LLC.

Database: EMBASE

9. Atopic dermatitis in pregnancy: Current status and challenges

Author(s): Koutroulis I.; Papoutsis J.; Kroumpouzos G.

Source: Obstetrical and Gynecological Survey; Oct 2011; vol. 66 (no. 10); p. 654-663

Publication Date: Oct 2011

Publication Type(s): Review

PubMedID: 22112526

Abstract: Atopic dermatitis (AD) is the most common pregnancy dermatosis. This evidence-based review article provides an evaluation of AD in gestation. Our literature search revealed 4 epidemiologic studies on AD in pregnancy, and a total of 55 articles that provide the basis for this review. The limitations of epidemiologic studies included herein are critically reviewed. The management of AD in gestation is reviewed with an emphasis on drug safety. Further studies are required to determine whether it is the intrinsic ("nonallergic" or "atopiform dermatitis") and/or extrinsic (IgE-associated) AD that is affected by pregnancy, and to establish the postpartum prognosis of "new atopic dermatitis" (AD presenting for the first time in pregnancy). A revision of the diagnostic criteria will allow a more accurate confirmation of the prevalence of AD, and especially "new atopic dermatitis," in pregnancy as well as differentiation of AD from specific dermatoses of pregnancy, such as prurigo and pruritic folliculitis. Addressing the above issues and unraveling the etiopathogenesis of AD in pregnancy will help clarify a suggested overlap with the above specific dermatoses. Target Audience: Obstetricians & Gynecologists and Family Physicians Learning

Objectives: After the completing the CME activity, physicians should be better able to correctly diagnose and safely treat atopic dermatitis in pregnancy; differentiate atopic dermatitis from other pregnancy dermatoses; and appraise the controversies and challenges in the field. © 2011 by Lippincott Williams & Wilkins.

Database: EMBASE

10. Topical corticosteroids and topical calcineurin inhibitors in the treatment of atopic dermatitis: focus on percutaneous absorption.

Author(s): Pariser, David

Source: American journal of therapeutics; 2009; vol. 16 (no. 3); p. 264-273

Publication Date: 2009

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 19262357

Abstract: The 2 primary classes of drugs used to treat atopic dermatitis (AD) are topical corticosteroids (TCSs) and topical calcineurin inhibitors (TCIs). For maximum efficacy, topical agents must efficiently penetrate the skin but, for optimal safety, should not be absorbed into the bloodstream. TCSs, a mainstay in AD treatment for more than 50 years, can potentially be absorbed into the systemic circulation, particularly when used on young children, for prolonged periods, or on areas of thin and sensitive skin, such as the eyelids, face, and flexures. There is a risk of cutaneous and systemic adverse events, including suppression of the hypothalamic-pituitary-adrenal axis and related sequelae, especially when potent or superpotent TCSs are used for extended periods. Ideally, TCSs should be used for short periods (2-4 weeks), but clinical reality often necessitates longer use. TCIs also effectively and safely treat AD, with the most commonly observed local adverse events

being skin irritation and burning. These agents have demonstrated good penetration of the skin with minimal systemic absorption, as evidenced by low blood concentrations, and can be used safely on thin and sensitive skin. The use of mid-potency TCSs to treat acute flares involving skin of normal thickness, followed by the introduction of TCIs for maintenance therapy, constitutes an appropriate application of both drug classes. Pharmacists with a clear understanding of how both types of agents affect the systemic circulation have the opportunity to inform patients and caregivers about benefits and limitations of different therapeutic agents, address patient concerns about adverse events, and help patients understand how to use medical therapies appropriately.

Database: Medline

11. Skin and systemic pharmacokinetics of tacrolimus following topical application of tacrolimus ointment in adults with moderate to severe atopic dermatitis.

Author(s): Undre, N A; Moloney, F J; Ahmadi, S; Stevenson, P; Murphy, G M

Source: The British journal of dermatology; Mar 2009; vol. 160 (no. 3); p. 665-669

Publication Date: Mar 2009

Publication Type(s): Research Support, Non-u.s. Gov't Clinical Trial, Phase Ii Journal Article

PubMedID: 19076975

Available at The British journal of dermatology - from Wiley Online Library Science , Technology and Medicine Collection 2017

Abstract:BACKGROUNDSystemic exposure to tacrolimus following topical application of tacrolimus ointment is minimal. There are, however, no data on the distribution of tacrolimus in the skin.OBJECTIVESTo assess the distribution of tacrolimus in the skin and the systemic pharmacokinetics of tacrolimus in adults with moderate to severe atopic dermatitis after first and repeated application of tacrolimus ointment.METHODSWe investigated skin distribution of topically applied tacrolimus and systemic pharmacokinetics of percutaneously absorbed tacrolimus in adults with atopic dermatitis after topical application of tacrolimus 0.1% ointment twice daily for 2 weeks. Tacrolimus concentrations were assessed in full-thickness skin biopsies and blood samples.RESULTSOf 14 patients, 11 completed treatment and were analysed. Mean +/- SD tacrolimus concentrations in the skin at 24 h after first and last ointment applications were 94 +/- 20 and 595 +/- 98 ng cm(-3), respectively. At 168 h after stopping treatment, values were 97% lower than at 24 h after last application. Tacrolimus concentration decreased with increasing skin depth. Systemic tacrolimus exposure after ointment application was low and highly variable, with 31% of samples below the limit of quantification (0.025 ng mL(-1)) and 94% below 1 ng mL(-1). Blood concentrations at 24 h after the first and last ointment applications were 750 and 1800 times lower, respectively, than those in skin. Physicians' assessments showed that tacrolimus ointment was effective and well tolerated.CONCLUSIONSTacrolimus was primarily partitioned in the skin, with minimal systemic absorption after topical application, in patients with atopic dermatitis.

Database: Medline

12. Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases

Author(s): Lam J.; Dohil M.A.; Polifka J.E.

Source: Journal of the American Academy of Dermatology; Aug 2008; vol. 59 (no. 2); p. 295-315

Publication Date: Aug 2008

Publication Type(s): Review

PubMedID: 18410980

Abstract: In patients with psoriasis, there is an increased availability of drugs for treatment. However, there are important questions about drug safety for mothers with psoriasis and their fetuses. Currently, there are limited safety data for many of the medications used. In this article, we review current pregnancy risk information for medications commonly used in the treatment of psoriasis. In addition, a list of teratology information resources is included to help practicing clinicians find up-to-date information regarding the safety of the medications they prescribe. © 2008 American Academy of Dermatology, Inc.

Database: EMBASE

13. The safety of tacrolimus ointment for the treatment of atopic dermatitis: a review.

Author(s): Rustin, M H A

Source: The British journal of dermatology; Nov 2007; vol. 157 (no. 5); p. 861-873

Publication Date: Nov 2007

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Review

PubMedID: 17854353

Abstract: Tacrolimus ointment is a topical calcineurin inhibitor (TCI) that was developed specifically for the treatment of atopic dermatitis (AD). It is one of the most extensively tested dermatological

products, with more than 19 000 patients (including approximately 7600 children) having participated in the tacrolimus ointment clinical development programme. Recent regulatory reviews have focused on the potential risk of malignancy with TCIs, based on their mode of action and the effects of systemic tacrolimus when given to transplant recipients. Studies have shown, however, that the systemic absorption of tacrolimus when applied topically is very low, with blood concentrations being below the level of quantification in most patients. Moreover, TCIs are not associated with a decrease in immunocompetence in the skin and there is no increase in the incidence of infections with long-term treatment. More than 5.4 million prescriptions for tacrolimus ointment have been issued worldwide, with no evidence of an increased risk of malignancy in adults or children compared with the general population. Similarly, epidemiological studies have failed to demonstrate an increased incidence of skin cancer in patients using TCIs. The most common adverse events (AEs) that occur with tacrolimus ointment treatment are transient application-site reactions, such as burning or pruritus. These complications are related to disease severity, and decrease in frequency over time as AD improves. The incidence of nonapplication-site AEs does not increase with long-term treatment, and most such events occurring in clinical trials were considered to be unrelated to therapy. Although it is important that clinicians are aware of the recent changes in product labelling, extensive clinical trials continue to show that tacrolimus ointment is well tolerated, and is generally an effective therapy for suitable patients with AD.

Database: Medline

14. Blood concentrations, tolerability and efficacy of pimecrolimus cream 1% in Japanese infants and children with atopic dermatitis.

Author(s): Eichenfield, Lawrence F; Ho, Vincent; Matsunaga, Janice; Leclerc, Patricia; Paul, Carle; Hanifin, Jon M

Source: The Journal of dermatology; Apr 2007; vol. 34 (no. 4); p. 231-236

Publication Date: Apr 2007

Publication Type(s): Clinical Trial Multicenter Study Journal Article

PubMedID: 17352719

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Abstract: Pimecrolimus cream 1% is a topical calcineurin inhibitor for the treatment of atopic dermatitis. Minimal systemic exposure to pimecrolimus has been previously observed in Caucasian pediatric patients treated with the cream twice daily for up to 1 year. The objective of this open-label, non-comparative, multicenter study was to assess the systemic exposure, tolerability and efficacy of pimecrolimus cream 1% when used twice daily for 3 weeks in pediatric patients of Japanese background. The patient cohort consisted of 17 Japanese infants and children (age range, 3.6 months to 11.6 years) with atopic dermatitis of at least mild severity affecting >or=10% of the total body surface area (range, 10-48%). Pimecrolimus cream 1% was applied twice daily for 3 weeks. Blood levels of pimecrolimus were determined on days 1, 10 and 22. Safety and tolerability were evaluated by monitoring adverse events, laboratory parameters, physical condition and vital signs. Efficacy parameters included the Eczema Area and Severity Index, the Investigators' Global Assessment and the pruritus score. The median exposure to pimecrolimus cream 1% was 22 treatment days (range, 9-29 treatment days). Pimecrolimus blood concentrations were <0.5 ng/mL in 94% of samples on day 1, in 93% of samples on day 10 and in 100% of samples on day 22, with no indication of an increase with increasing body surface area treated (up to 48% of the total body surface area). No drug-related systemic adverse events or serious adverse events were reported. Treatment was effective according to all efficacy parameters. The findings of this study indicate that the use of pimecrolimus cream 1% results in minimal systemic absorption of the active ingredient in pediatric patients of Japanese background with extensive disease.

Database: Medline

15. Safety of topical calcineurin inhibitors in atopic dermatitis: evaluation of the evidence.

Author(s): Spergel, Jonathan M; Leung, Donald Y M

Source: Current allergy and asthma reports; Jul 2006; vol. 6 (no. 4); p. 270-274

Publication Date: Jul 2006

Publication Type(s): Journal Article Review

PubMedID: 16822378

Available at Current allergy and asthma reports - from SpringerLink - Medicine

Available at Current allergy and asthma reports - from ProQuest (Health Research Premium) - NHS Version

Abstract: Topical calcineurin inhibitors (pimecrolimus, Elidel, East Hanover, NJ; and tacrolimus, Protopic, Tokyo, Japan) have been approved for the use in atopic dermatitis since the year 2000. These compounds represent a relatively safe class of topical anti-inflammatory, nonsteroidal therapy. However, in January of 2006, the US Food and Drug Administration issued a black box warning on these compounds about possible concerns of increased long-term malignancy risk due to systemic immunosuppression. To date, studies from clinical trials, systemic absorption, and post-marketing surveillance show no evidence for this systemic immunosuppression or increased risk for any malignancy.

Database: Medline

16. Tacrolimus: Focusing on atopic dermatitis

Author(s): Carroll C.L.; Fleischer Jr. A.B.

Source: Drugs of Today; Jul 2006; vol. 42 (no. 7); p. 431-439

Publication Date: Jul 2006

Publication Type(s): Review

PubMedID: 16894398

Abstract: Tacrolimus ointment is an effective treatment for atopic dermatitis. As a calcineurin inhibitor, it works through the FK-binding protein, inhibiting calcineurin and preventing dephosphorylation of nuclear factor of activated T cells (NFAT). Systemic absorption from the drug is minimal, allowing a favorable safety profile. In head-to-head clinical trials with pimecrolimus, tacrolimus proved to be a more effective treatment. Tacrolimus ointment has also been compared to standard topical corticosteroid treatments and is equally effective if not superior to several topical steroids. Overall, tacrolimus ointment is a safe and effective treatment for atopic dermatitis and can be used as an adjunctive treatment to standard management with topical corticosteroids.

Database: EMBASE

17. Tacrolimus ointment: a review of its use in atopic dermatitis and its clinical potential in other inflammatory skin conditions.

Author(s): Simpson, Dene; Noble, Stuart

Source: Drugs; 2005; vol. 65 (no. 6); p. 827-858

Publication Date: 2005

Publication Type(s): Comparative Study Journal Article Review

PubMedID: 15819596

Available at Drugs - from SpringerLink - Medicine

Abstract: Tacrolimus ointment (Protopic) is a topically applied macrolide lactone immunomodulator effective in the treatment of atopic dermatitis. Its mechanism of action primarily involves calcineurin inhibition, which interrupts cytokine gene expression and leads to the downregulation of T-cell activity. Tacrolimus ointment (0.03% and 0.1% for adults and 0.03% for children) is an effective treatment for atopic dermatitis of the trunk and limbs, as well as sensitive skin areas such as the face. Its efficacy is similar to or greater than that of hydrocortisone acetate 1%, hydrocortisone butyrate 0.1% and betamethsone valerate 0.12% ointments and pimecrolimus 1% cream. Systemic absorption of tacrolimus from the ointment is minimal, and adverse events, which are mostly associated with the application site and include skin burning and pruritus, tend to resolve early in treatment. Unlike topical corticosteroids, tacrolimus ointment is not associated with skin atrophy, and it is a well tolerated treatment for adults or children with atopic dermatitis, particularly when long-term treatment is indicated or the face or skin-fold regions are involved.

Database: Medline

18. Topical tacrolimus: a review of its uses in dermatology.

Author(s): Woo, Denise K; James, William D

Source: Dermatitis : contact, atopic, occupational, drug; Mar 2005; vol. 16 (no. 1); p. 6-21

Publication Date: Mar 2005

Publication Type(s): Journal Article Review

PubMedID: 15996345

Available at Dermatitis : contact, atopic, occupational, drug - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Abstract: Tacrolimus is one of the newer immunosuppressants that act by inhibiting T-cell activation and cytokine release. It is approved for the treatment of atopic dermatitis, and its safety and efficacy have been extensively studied in large-scale randomized controlled trials and open-label studies worldwide involving over 12,000 patients and up to 3 years of follow-up. Since its introduction, anecdotal reports and case series have found topical tacrolimus also to be effective and well tolerated in patients with a variety of other skin disorders, including other types of eczema, papulosquamous disorders, disorders of cornification, rosacea, other inflammatory skin conditions, vesiculobullous diseases, vitiligo, connective-tissue diseases, graft-versus-host disease, and follicular disorders. This paper reviews the currently available evidence on the use of topical tacrolimus for these conditions, as well as its safety profile and cost-effectiveness. Tacrolimus does appear to offer a safe and efficacious alternative that minimizes the need for topical glucocorticoids and does not cause skin atrophy. However, the risk of systemic absorption is increased with generalized disruption of the skin barrier. Further large-scale studies are needed to clarify the efficacy of topical tacrolimus in a variety of conditions for which anecdotal reports of success exist, especially in regard to

different racial groups and in comparison to (as well as in combination with) other existing therapies. Long-term safety data should continue to be monitored and reported.

Database: Medline

19. Tacrolimus ointment: a new therapy for atopic dermatitis--review of the literature.

Author(s): Pustisek, Nives; Lipozencić, Jasna; Ljubojević, Suzana

Source: Acta dermatovenerologica Croatica : ADC; Mar 2002; vol. 10 (no. 1); p. 25-32

Publication Date: Mar 2002

Publication Type(s): Journal Article Review

PubMedID: 12137728

Abstract: Atopic dermatitis is a chronic inflammatory skin disease characterized by severe pruritus, typical morphology and distribution of skin lesions, and personal and family history of atopy. The management of atopic dermatitis is directed at preventing the inflammation, itch, and secondary lesions. Therapy relies on general management measures, anti-inflammatory agents, antiprurites, antibiotics, and immunosuppressants. Treatment options for patients with severe or longstanding disease, extensive body surface area involvement of facial lesions are limited. Tacrolimus ointment is the first in the class of topical immunomodulators that has been formulated for the treatment of atopic dermatitis in children (2 to 15 years of age) and adult patients. The mechanism of action of tacrolimus in atopic dermatitis seems to involve T-cells, Langerhans cells, mast cells and basophiles. Experimental evidence suggests that tacrolimus inhibits T-lymphocytes activation by binding to an intracellular protein, FKBP-12. This binding phenomenon inhibits the ability of calcineurin to activate the promotor region of the gene for IL-2, IL-3, IL-4, IL-5, interferon gamma, tumor necrosis factor alpha, and granulocyte macrophage colony-stimulating factor, all of which participate in the early immune response and play a role in the pathogenesis of atopic dermatitis. Tacrolimus ointment is not atrophogenic, and is associated with minimal systemic absorption. There were no consistent changes in any laboratory variable during topical tacrolimus therapy. The most common adverse events associated with its use were transient skin burning and pruritus at the site of application. Tacrolimus ointment is safe and efficacious therapy for the treatment of pediatric and adult patients with atopic dermatitis on all skin regions including the face, neck and intertriginous areas. An overview is given of tacrolimus in atopic dermatitis.

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20. Safety and efficacy of 1 year of tacrolimus ointment monotherapy in adults with atopic dermatitis. The European Tacrolimus Ointment Study Group.

Author(s): Reitamo, S; Wollenberg, A; Schöpf, E; Perrot, J L; Marks, R; Ruzicka, T; Christophers, E; Kapp, A; Lahfa, M; Rubins, A; Jablonska, S; Rustin, M

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Abstract:OBJECTIVETo investigate the safety and efficacy of using 0.1% tacrolimus ointment for long-term treatment of atopic dermatitis.DESIGNOpen-label, noncomparative study with 6 to 12 months of follow-up.SETTINGSOutpatient departments in 30 study centers in 11 European countries.PATIENTSWe enrolled 316 patients aged 18 years and older with moderate to severe atopic dermatitis, 200 for 6 months and 116 for 12 months; 77.5% of patients completed the study.INTERVENTIONTwice-daily application of 0.1% tacrolimus ointment on all affected skin. Visits were scheduled on day 1; after 1, 2, and 4 weeks of treatment; and monthly thereafter.MAIN OUTCOME MEASURESSafety assessments included monitoring of adverse events, clinical laboratory values, and tacrolimus blood concentrations. Efficacy end points included a combined score (modified Eczema Area and Severity Index) and an investigator's global assessment.RESULTSLocal irritation, adverse events such as burning sensation (47% of patients), pruritus (24% of patients), and erythema (12% of patients) were common but tended to occur only when initiating treatment. Laboratory values showed no marked changes over time. Systemic absorption was minimal, with the maximum tacrolimus blood concentration being less than 1 ng/mL in 76% of patients. All efficacy end points showed improvement. The mean (SD) modified Eczema Area and Severity Index score was 23.7 (12.6) at day 1, 13.5 (11.3) at week 1, 6.1 (9.2) at month 6, and 6.1 (8.1) at month 12. Marked or excellent improvement or clearance of disease was reported in 54%, 81%, and 86% of patients at week 1, month 6, and month 12, respectively.CONCLUSIONUp to 1 year of tacrolimus ointment use was safe and effective in patients with atopic dermatitis. Arch Dermatol. 2000;136:999-1006

Database: Medline

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#	Database	Search term	Results
1	Medline	(Tacrolimus).ti,ab	15120
2	Medline	exp TACROLIMUS/	15314
3	Medline	(fujimycin OR FK506).ti,ab	5860
4	Medline	(1 OR 2 OR 3)	23813
5	Medline	exp "ADMINISTRATION, TOPICAL"/	84189
6	Medline	exp OINTMENTS/	12598
7	Medline	(ointment*).ti,ab	11317
8	Medline	(topical).ti,ab	91065
9	Medline	(cutaneous*).ti,ab	143694
10	Medline	(5 OR 6 OR 7 OR 8 OR 9)	292873
11	Medline	exp "SKIN ABSORPTION"/	11349
12	Medline	(systemic* ADJ2 (absorption OR absorb*)).ti,ab	3178
13	Medline	(11 OR 12)	14306
14	Medline	(4 AND 10 AND 13)	107
15	Medline	(pregnan*).ti,ab	468278
16	Medline	exp PREGNANCY/	867138
17	Medline	(15 OR 16)	968233

18	Medline	(4 AND 10 AND 17)	19
19	EMBASE	(Tacrolimus).ti,ab	30393
20	EMBASE	exp TACROLIMUS/	75360
21	EMBASE	(fujimycin OR FK506).ti,ab	7172
22	EMBASE	(19 OR 20 OR 21)	78918
23	EMBASE	exp "TOPICAL DRUG ADMINISTRATION"/	103026
24	EMBASE	exp OINTMENTS/	11273
25	EMBASE	(ointment*).ti,ab	14877
26	EMBASE	(topical).ti,ab	123031
27	EMBASE	(cutaneous*).ti,ab	185831
28	EMBASE	(23 OR 24 OR 25 OR 26 OR 27)	382275
29	EMBASE	exp "SKIN ABSORPTION"/	6793
30	EMBASE	(systemic* ADJ2 (absorption OR absorb*)).ti,ab	3652
31	EMBASE	exp "DRUG ABSORPTION"/	80855
32	EMBASE	(29 OR 30 OR 31)	88710
33	EMBASE	exp TACROLIMUS/tp	3811
34	EMBASE	(pregnan*).ti,ab	599015
36	EMBASE	exp PREGNANCY/	636088
37	EMBASE	(34 OR 36)	853842

38	EMBASE	(33 AND 37)	53
39	EMBASE	(22 AND 28 AND 37)	64
40	EMBASE	(38 OR 39)	90
41	EMBASE	(22 AND 28 AND 32)	252
42	EMBASE	*"DRUG ABSORPTION"/	22508
43	EMBASE	(33 AND 42)	5