AARS HOT TOPICS MEMBER NEWSLETTER

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TABLE OF CONTENTS

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Industry News

Foamix: Positive topline phase 3 results for topical minocycline foam. Practical Dermatology, DermWire. Wednesday, September 12, 2018. http://practicaldermatology.com/dermwire/2018/09/12/foamix-positive-topline-phase-3-results-for-topical-minocycline-foam

Foamix Pharmaceuticals' FMX101 topical minocycline foam for the treatment of moderate-to-severe acne has met primary endpoints of its third Phase 3 clinical trial. Foamix shared topline results of the clinical trial (FX2017-22), which met both co-primary endpoints of (1) absolute change from baseline in inflammatory lesion count at Week 12, and (2) Investigator Global Assessment ("IGA") treatment success at Week 12, defined as an IGA score of 0 or 1, and at least a 2-grade improvement (decrease) from baseline. The safety profile of FMX101 was found to be consistent with that determined from the two prior Phase 3 studies (FX2014-04 and FX2014-05). Foamix plans to continue to share data from this study as they become available over the remainder of 2018. "We are extremely pleased with the topline results of this confirmatory Phase 3 trial. These study results should support a finding that FMX101 appears to be safe and effective in the treatment of moderate-to-severe acne," says David Domzalski, CEO of Foamix. "This is the most significant milestone to date for Foamix and brings us closer to helping patients who struggle with the physical and psycho-social effects of acne. If approved, we believe FMX101 would be the first topical minocycline product available for patients in the United States." Mr. Domzalski says the company is now prepared to finalize efforts to submit the company's first NDA. "The data from this confirmatory Phase 3 study are impressive, and the reductions in inflammatory lesions and the proportions of subjects achieving treatment success highlight significant improvements in disease severity for those that received FMX101 in the study," states Iain A. Stuart, Ph.D., Senior Vice President, Research & Development, Foamix. "The strong body of clinical data we have generated with FMX101, including the results from this most recent Phase 3 trial, suggest that it may offer patients an efficacious treatment in a convenient and safe topical foam formulation. If approved, it has the potential to address a significant unmet need in this difficult to treat condition."

Allergan launches Spotlyte: Digital hub will educate consumers about medical aesthetic treatments. Practical Dermatology, DermWire. Wednesday, September 12, 2018. http://practicaldermatology.com/dermwire/2018/09/12/allergan-launches-spotlyte/?c=&t=

Allergan has launched Spotlyte, described as an innovative digital hub of curated content that helps consumers discover how medical aesthetic treatments may fit into their routines. Spotlyte is the first venture from the new Allergan-owned digital ventures unit, Project Moonwalker, which is dedicated to creating consumer facing businesses that unlock opportunities in the medical aesthetics category. Alexandra Wilkis Wilson, co-founder of Gilt Groupe and Glamsquad, and senior vice president of Consumer Strategy and Innovation at Allergan, leads the project. Spotlyte promised well-researched content, product reviews and insider profiles, together with the latest beauty news and trends, offering a holistic and informative lens into these worlds. Spotlyte will provide access to a team of trained specialists ready to offer real-time support and chat directly with anyone considering medical aesthetic treatments, as well as help connect readers to local licensed providers. In keeping with its stated goal of educating consumers and providing well researched and accurate information on medical aesthetics, the site is brand agnostic. "We have a unique position as industry leaders to identify emerging trends in real time and change the way that consumers engage with medical aesthetics," said Alexandra Wilkis Wilson. "I have spent most of my career focused on the consumer while creating powerful brands at the intersection of technology and lifestyle. The core goal of Project Moonwalker is to enable information flow and access. Spotlyte is the first step in changing how consumers can

become better educated on medical aesthetics." "As the market leader in medical aesthetics, we have the opportunity and the responsibility to properly educate consumers and mainstream the conversation around aesthetic treatments. We want to create an open dialogue by incorporating medical aesthetics into the overall aesthetics conversation," said Brent Saunders, CEO of Allergan. "We believe the medical aesthetics market will double in 5-7 years."

Candela acquires Ellipse. Practical Dermatology, DermWire. Tuesday, September 11, 2018. http://practicaldermatology.com/dermwire/2018/09/11/business-news-candela-acquires-ellipse/?c=&t=

Candela Corporation has acquired Ellipse, a Danish medical device company that manufactures and markets Intense Pulsed Light (IPL) and laser-based platforms for a wide variety of medical and aesthetic skin treatments. Financial terms of the agreement were not disclosed. "The acquisition of Ellipse allows Candela to strengthen its footprint in the multi-application space and provide our customers a comprehensive portfolio. Candela's best-in-class laser and energy-based technologies are now coupled with a trusted IPL technology that is well respected by physicians," states Geoffrey Crouse, Chief Executive Officer of Candela, in a news release. "Ellipse platforms will provide aesthetic practices with a fully scalable multi-application, multi-technology device. We look forward to Ellipse strengthening our portfolio as we continue to deliver our brand promise of Science, Results, Trust to our physicians and patients worldwide. The Ellipse product portfolio is consistent with our commitment to scientifically proven technologies backed by consistent clinical outcomes." Ellipse's products include Nordlys, a multi-application, multi-technology IPL and Nd:YAG platform for vascular and pigmented lesions, as well as hair removal. The Nordlys also offers a fractionated 1550 nm handpiece for skin resurfacing. Other products include an IPL-only system used for skin rejuvenation, facial veins and hair removal, as well as a fractional non-ablative laser system used for skin resurfacing. Ellipse's Selective Waveband Technology (SWTÒ) uniquely utilizes dual filtering on all IPL handpieces to focus on effective wavelengths and selectively deliver precise energy to the targeted area, using sub-millisecond pulses for some applications. "We are excited to join forces with Candela and market our strong technology platforms via Candela's expansive global footprint, along with its commitment to clinical excellence, quality and innovation," says Jacob Kildegaard Larsen, Chief Executive Officer at Ellipse. "As a physician who utilizes the Ellipse IPL platform and considers it a foundational technology for all dermatology practices, I am pleased that Candela can now offer the full spectrum of light, laser and energy-based solutions to physicians and patients worldwide," says Jill Waibel, MD, a board-certified dermatologist and Medical Director/Founder of Miami Dermatology and Laser Institute in Miami, Florida. "Candela and Ellipse are both physician acknowledged leaders in their respective categories. Bringing the companies together will herald a new era in device innovation that elevates patient care," concludes Christine Dierickx, MD, a Luxembourg based dermatologist, specializing in laser surgery and cosmetic dermatology.

New Medical News

Combination chemical peels are more effective than single chemical peel in treatment of mild-to-moderate acne vulgaris: A split face comparative clinical trial. Nofal E, Nofal A, Gharib K, et al. J Cosmet Dermatol. 2018 Sep 10. doi: 10.1111/jocd.12763. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30203434

Background: Successful management of acne involves choosing proper medication. Chemical peeling is a well-known option in treatment of acne vulgaris. Objective: To evaluate and compare the clinical efficacy and safety of combination chemical peels vs single peel in treatment of mild-to-moderate acne. Methods: The study included 45 patients with mild-to-moderate acne divided into three equal groups. Group A underwent combination sequential peels

with modified Jessner's solution (MJ) followed by trichloro acetic acid (TCA20%) on the right (Rt) side of the face vs TCA 30% on the left (Lt) side. Group B was treated by combination peels of salicylic (20%) mandelic (10%) (SM) mixture on the Rt half vs salicylic acid 30% on the Lt half. Group C underwent combination sequential peeling of MJ and TCA on the Rt side vs SM combination peels on the Lt side. All patients received six sessions with 2-week intervals and followed up for 3 months after the last session. Side effects were reported. Results: Both sides of the face showed significant improvement of acne lesions but improvement was significantly higher and earlier in sides treated by combination peels. Side effects were minimal. Conclusion: In conclusion, combination peels achieved a higher and earlier therapeutic response with a reasonable cost that is maintained for a relatively long periods than single peel. Combination sequential peels gave the best results.

Tretinoin loaded nanoemulsion for acne vulgaris: Fabrication, physicochemical and clinical efficacy assessments. Sabouri M, Samadi A, Ahmad Nasrollahi S, et al. Skin Pharmacol Physiol. 2018 Sep 10;31(6):316-323. doi: 10.1159/000488993. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30199861

Background and aim: Acne vulgaris is a common inflammatory skin condition which is treated using Tretinoin (TRE), a widely used retinoid. Nano emulations (NEs) are colloidal nano-sized particles that enhance the therapeutic efficacy of TRE and minimize adverse effects. This study is aimed at developing a TRE-loaded NE (NE-TRE) and at assessing the therapeutic effects of the formulation in acne vulgaris lesions, compared to conventional 0.05% TRE emulsion. Method: The high energy emulsification method was used to make NE-TRE. After obtaining stable NE, particle characterization and physicochemical properties were evaluated under accelerated conditions. Conducting a clinical study, we compared the therapeutic effects of NE-TRE and 0.05% TRE emulsion by comparing the number of acne lesions and porphyrin production in both sides of the face. Results and conclusion: We successfully developed stable nanoparticles. It was a stable oil-in-water emulsion with particle size of about 150 nm, and containing circular and separated particles. In a pilot clinical study, the number of acne lesions as well as the size and intensity of porphyrin production significantly reduced after topical application of NE-TRE This formula shows proper efficiency and good loading capacity of TRE in the drug delivery system.

The safety and efficacy of four different fixed combination regimens of adapalene 0.1%/benzoyl peroxide 2.5% gel for the treatment of acne vulgaris: results from a randomized controlled study. Tan J, Bissonnette R, Gratton D, et al. Eur J Dermatol. 2018 Sep 6. doi: 10.1684/ejd.2018.3367. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30187864

Background: Combined use of a retinoid and antimicrobial is recommended for acne; however, local tolerability issues may compromise patient adherence and treatment outcome. Objectives: This multicentre, single-blinded controlled study was designed to determine whether modified adapalene/benzoyl peroxide (A/BPO, Epiduo®, Galderma, France) regimens improve local tolerability during the first four weeks of treatment without impairing efficacy at Week 12. Materials & methods: In total, 120 subjects with mild-to-moderate acne received, during the first four weeks, A/BPO daily overnight (A/BPO-EN), A/BPO daily for three hours (A/BPO-3h), A/BPO daily overnight and a provided moisturizer lotion (A/BPO-moisturizer), or A/BPO every other night (A/BPO-EoN). Local tolerance assessments included signs and symptoms, global worst score (GWS), and total sum score (TSS). Efficacy was assessed based on lesion counts, investigator global assessment (IGA), and total lesion count reduction. Adherence, subject satisfaction, and overall safety were also assessed. Results: The mean TSS was significantly reduced at Week 1 with A/BPO-EoN vs. A/BPO-EN ($p<0.05$), and A/BPO-EoN led to the lowest GWS and a decrease in severity of stinging/burning and erythema ($p<0.05$). The A/BPO-moisturizer regimen prevented dryness and scaling compared

with the A/BPO-EN regimen. The median decrease in lesions from baseline was similar in all groups: up to 67% for total, 72% for inflammatory, and 70% for non-inflammatory lesion counts. Adherence, IGA, patient satisfaction, and overall safety were excellent. Conclusion: Modulating treatment regimens during the first four weeks improved local tolerability without impacting overall efficacy outcome after 12 weeks and may improve treatment adherence during the first weeks of therapy.

Efficacy and safety of 2% supramolecular salicylic acid compared with 5% benzoyl peroxide/0.1% adapalene in the acne treatment: A randomized, split-face, open-label, single-center study. Zheng Y, Yin S, Xia Y, et al. Cutan Ocul Toxicol. 2018 Sep 3:1-21. doi: 10.1080/15569527.2018.1518329. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30173582

Background: Topical drugs for mild to moderate acne include adapalene (ADA) and benzoyl peroxide (BPO). Supramolecular salicylic acid (SSA), a modified SA preparation, is considered as a new effective therapeutic scheme. Objectives: To compare the safety and efficacy of 2% supramolecular SA (2%SSA) with 0.01% adapalene plus 5% benzoyl peroxide (5%BPO+0.1%ADA) for treatment of facial acne. Materials and methods: This was an open-label, split face, randomized and single center clinical trial. Subjects with mild to moderate acne were enrolled. 2% SSA cream were randomly applied on one side of the face while 5%BPO+0.1%ADA gel was applied on opposite side for 28 days. The numbers of acne lesions, along with side effects of the targeted area were evaluated by the investigators at day 0, day 14 and day 28. Skin water content, TEWL and skin lightening indexes were measured at the same time. Results: A total of 31 of acne patients completed the trial. Dates showed that 2% SSA had similar effects to 5%BPO+0.1%ADA in reducing papules/pustules (47.9% vs. 49.8%), non-inflammatory lesions (43.1% vs. 42.7%) and total lesions (44.1% vs. 45.6%; all P>0.05) at day 28. The skin barrier (skin hydration value and TEWL value), skin brightness (L*-value) and erythema (a*-values) indicators showed no statistically differences in the left and right sides of the face (P>0.05). Conclusion: This study demonstrated that 2% SSA has a similar efficacy with 5%BPO+0.1%ADA in mild to moderate acne treatment. This might be a useful pilot study that could be used to support further larger clinical trials.

Thiol/disulfide homeostasis as a marker of oxidative stress in rosacea: a controlled spectrophotometric study. Sener S, Akbas A, Kılınc F, et al. Cutan Ocul Toxicol. 2018 Sep 3:1-15. doi: 10.1080/15569527.2018.1517124. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30173569

Background: Rosacea is the chronic inflammatory disease of the facial skin. Although its etiology is not clear yet, inflammatory processes triggered by oxidative stress and oxidation of lipids have been suggested to have a role. While studies on the relationship between inflammation and oxidative stress are ongoing, thiol metabolism and its role in oxidative stress have also begun to be investigated. Thiols are among the key molecules of protein metabolism in the organism and they are firstly consumed antioxidants in case of oxidative stress. Thiols regulate intracellular redox metabolism and protect keratinocytes against the results of oxidative alterations in the stratum corneum. There is a balance known as dynamic thiol/disulfide homeostasis between thiols and their oxidized forms; disulfides. Aim: This study aimed to determine the effects of oxidative stress on protein metabolism in rosacea patients by investigating thiol/disulfide homeostasis using a newly developed and fully automated method. Determination of plasma thiol levels provides important clues regarding the extent of free radical-mediated oxidation of proteins causing damage in rosacea. Methods: The study included 50 rosacea patients who were diagnosed clinically or histopathologically with rosacea and 42 age- and gender-matched healthy controls. Serum plasma levels of native thiol, total thiol, and disulfide were determined. The following ratios were calculated: Disulfide/native thiol ratio, disulfide/total thiol ratio, and native thiol/total thiol ratio. Results: The mean age was 41.8±10.5 in the rosacea patients

(35 females) and 42.5±10.3 years in the control group (33 females). The mean disulfide level was found to be significantly higher in the rosacea patients than in the control group (23.4±5.5 µM/L and 17.3±6.2µM/L, respectively; $p < 0.001$). The mean disulfide/native thiol ratio (0.055±0.016 vs. 0.041±0.017) and the mean disulfide/total thiol ratio (0.049±0.012 vs.0.037±0.013) were significantly higher and the mean native thiol/total thiol ratio (0.884±0.118 vs. 0.923±0.027) was significantly lower in the patients as compared with the controls ($p < 0.05$ for all). Conclusion: In rosacea patients, the thiol/disulfide balance was observed to shift towards disulfides, which could be considered an indicator of oxidative stress in rosacea.

Expression of inflammatory and fibrogenetic markers in acne hypertrophic scar formation: focusing on role of TGF-β and IGF-1R. Yang JH, Yoon JY, Moon J, et al. Arch Dermatol Res. 2018 Oct;310(8):665-673. doi: 10.1007/s00403-018-1856-2. Epub 2018 Aug 29. https://www.ncbi.nlm.nih.gov/pubmed/30167815

Acne vulgaris is a universal skin disease and it may leave a scar when the original skin lesion disappears. These scars can cause cosmetic problems and psychological burden, leading to poor quality of life of patients. Acne scars are classified into atrophic scars and hypertrophic scars. As most of the acne scars are atrophic, many studies have been conducted focusing on the treatment of atrophic lesions. This study was conducted to investigate the underlying pathogenesis of acne hypertrophic scars by identifying roles of fibrogenetic and inflammatory markers. Skin biopsy samples were obtained from hypertrophic scars of face and back and from adjacent normal tissues as control group. Some samples from back were immature hypertrophic scars and the other samples were in mature stages. Immunohistochemistry staining and quantitative PCR were performed for fibrogenetic and inflammatory markers. Both in mature and immature hypertrophic scars, vimentin and α-SMA were increased. Production of TGF-β3 protein as well as transcription of TGF-β3 was also significantly elevated. In contrast, expression of TGF-β1 showed no increase. Instead, expression levels of SMAD2 and SMAD4 were increased. Elevations of CD45RO, TNF-α and IL-4 and reduction of IL-10 were observed. In immature hypertrophic scars, IGF-1R and insulin-degrading enzyme expression were increased. Increased apoptosis was observed in immature stages of hypertrophic scars but not in mature stages. Elevations of TGF-β3, SMAD2 and SMAD4 in hypertrophic scars and increase of IGF-1R in immature stages may give some clues for acne hypertrophic scar formation.

Origanum vulgare L. essential oil as a potential anti-acne topical nanoemulsion-in vitro and in vivo study. Taleb MH, Abdeltawab NF, Shamma RN, et al. Molecules. 2018 Aug 28;23(9). pii: E2164. doi: 10.3390/molecules23092164. https://www.ncbi.nlm.nih.gov/pubmed/30154336

Antibiotics are often prescribed in acne treatment; however, Propionibacterium acnes and Staphylococcus epidermidis, the two of the major acne-associated bacteria, developed antibiotic resistance. Essential oils (EOs) present a natural, safe, efficacious and multifunctional alternative treatment. This study aimed to assess the potential anti-acne activity of selected seven EOs commonly used in Mediterranean folk medicine. Antimicrobial activity screening of these oils showed oregano to exhibit the strongest antimicrobial activity with minimum inhibitory concentration (MIC) of 0.34 mg/mL and minimum bactericidal concentration (MBC) of 0.67 mg/mL against P. acnes; and MIC of 0.67 mg/mL and MBC of 1.34 mg/mL against S. epidermidis. The composition of the most effective EOs (oregano and thyme) was determined using gas chromatography-mass spectrometry (GC-MS). Monoterpenoid phenols predominated oregano and thyme EO with thymol percentile 99 and 72, respectively. Thymol showed MIC 0.70 mg/mL against both P. acnes and S. epidermidis whereas MBC was 1.40 and 2.80 mg/mL against P. acnes and S. epidermidis, respectively. Moreover, oregano exhibited the strongest anti-biofilm effect against S. epidermidis with MBIC 1.34 mg/mL and killing dynamic time of 12 and 8 h against P. acnes and S. epidermidis, respectively. Oregano,

the most effective EO, was formulated and tested as a nanoemulsion in an acne animal mouse model. The formulation showed superior healing and antimicrobial effects compared to the reference antibiotic. Collectively, our data suggested that oregano oil nanoemulsion is a potential natural and effective alternative for treating acne and overcoming the emerging antibiotic resistance.

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Disruption of mesoderm formation during cardiac differentiation due to developmental exposure to 13-cis-retinoic acid. Liu Q, Van Bortle K, Zhang Y, et al. Sci Rep. 2018 Aug 28;8(1):12960. doi: 10.1038/s41598-018-31192-0. https://www.ncbi.nlm.nih.gov/pubmed/30154523

13-cis-retinoic acid (isotretinoin, INN) is an oral pharmaceutical drug used for the treatment of skin acne, and is also a known teratogen. In this study, the molecular mechanisms underlying INN-induced developmental toxicity during early cardiac differentiation were investigated using both human induced pluripotent stem cells (hiPSCs) and human embryonic stem cells (hESCs). Pre-exposure of hiPSCs and hESCs to a sublethal concentration of INN did not influence cell proliferation and pluripotency. However, mesodermal differentiation was disrupted when INN was included in the medium during differentiation. Transcriptomic profiling by RNA-seq revealed that INN exposure leads to aberrant expression of genes involved in several signaling pathways that control early mesoderm differentiation, such as TGF-beta signaling. In addition, genome-wide chromatin accessibility profiling by ATAC-seq suggested that INN-exposure leads to enhanced DNA-binding of specific transcription factors (TFs), including HNF1B, SOX10 and NFIC, often in close spatial proximity to genes that are dysregulated in response to INN treatment. Altogether, these results identify potential molecular mechanisms underlying INN-induced perturbation during mesodermal differentiation in the context of cardiac development. This study further highlights the utility of human stem cells as an alternative system for investigating congenital diseases of newborns that arise as a result of maternal drug exposure during pregnancy.

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A novel topical minocycline foam for the treatment of moderate-to-severe acne vulgaris: Results of two randomized, double-blind, phase 3 studies. Gold LS, Dhawan S, Weiss J, et al. J Am Acad Dermatol. 2018 Aug 27. pii: S0190-9622(18)32474-5. doi: 10.1016/j.jaad.2018.08.020. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30165171

Background: FMX101 4% is a topical minocycline foam for the treatment of moderate-to-severe acne. Objective: Evaluate the efficacy and safety of FMX101 4% in treating moderate-to-severe acne vulgaris. Methods: Two identical Phase 3 studies were conducted. Subjects were randomized 2:1 to once-daily FMX101 4% or foam vehicle for 12 weeks. The co-primary end points were the change in inflammatory lesion count from baseline and the rate of IGA treatment success (score of 0 or 1 for "clear" or "almost clear," with ≥2-grade improvement) at Week 12. Results: 961 subjects were enrolled (Study 04, N=466; Study 05, N=495). Compared with vehicle, FMX101 4% demonstrated significantly greater reduction in inflammatory lesions in both studies (P<.05) and a greater IGA treatment success rate in Study 05 (P<.05). Pooled analyses of the 2 studies demonstrated statistical significance for both co-primary end points (all P<.05). Noninflammatory lesion count was also significantly reduced with FMX101 4% vs vehicle in both studies. FMX101 4% was generally safe and well tolerated. Skin-related adverse events were reported in <1% of FMX101 4% subjects. Limitations: Longer-term efficacy and safety outcomes are needed (ongoing). Conclusion: FMX101 4% topical minocycline foam appears to be a safe and efficacious treatment for moderate-to-severe acne.

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FoxO1 enhances differentiation and apoptosis in human primary keratinocytes. Shi G, Liao PY, Cai XL, et al. Exp Dermatol. 2018 Aug 25. doi: 10.1111/exd.13775. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30144329

Forkhead box-O1 (FoxO1) is a key nutrient- and growth factor-dependent regulator of metabolism, but its functional role in human primary keratinocytes (HPKs) is less known. To investigate the role of FoxO1 in HPKs and effect of insulin-like growth factor 1 (IGF-1) and isotretinoin on FoxO1 expression. HPKs were treated with 1.2 mM calcium chloride, 1-20 ng/ml IGF-1 and 0.1-10 μM isotretinoin. Recombinant adenovirus expressing FoxO1 or FKHR shRNA lentivirus transfection was introduced to upregulate or silence FoxO1 expression. Epidermal FoxO1 immunostaining was lower in acne lesion than in normal skin. FoxO1 overexpression induced involucrin expression, G2/M arrest and apoptosis but suppressed proliferation, while FoxO1 silencing decreased involucrin expression but increased proliferation, S phase and viable cells in HPKs. IGF-1 downregulated FoxO1 and involucrin but upregulated p-Akt expression in HPKs, which was blocked by pre-treatment with LY294002. Isotretinoin enhanced FoxO1, p53 and p21 but inhibited p-FoxO1 and involucrin expression in HPKs. These results demonstrate that FoxO1 promotes differentiation and apoptosis in HPKs. IGF-1 may reduce keratinocyte differentiation through PI3K/Akt/FoxO1 pathway, while isotretinoin can reinforce FoxO1 expression. FoxO1 may be involved in acne pathogenesis and could serve as a potential therapeutic target.

Calprotectin can play an inflammatory role in acne vulgaris. Korkmaz S, Fıçıcıoğlu SK. Postepy Dermatol Alergol. 2018 Aug;35(4):397-399. doi: 10.5114/ada.2017.71286. Epub 2018 Aug 21. https://www.ncbi.nlm.nih.gov/pubmed/30206454

Introduction: Acne vulgaris (AV) is a chronic inflammatory disorder of the pilosebaceous unit. Although various mechanisms have been indicated in the etiopathogenesis of acne vulgaris, the exact pathophysiology is still unknown. Aim: To investigate the level of calprotectin in acne vulgaris and its levels relationship with disease severity. Material and methods: A total of 66 AV patients, who were divided into 33 mild and 33 moderate-severe cases, and 30 healthy controls were enrolled in the study. Disease severity was assessed using the Global Acne Score. According to this scale, patients whose Global Acne Score was 1-18 had mild acne, those with a score of 19-30 had moderate acne, those with a score of 31-38 had severe acne, and those with a score greater than 39 had very severe acne. Serum calprotectin levels of all participants were measured by enzyme-linked immunosorbent assay method. Results: The serum calprotectin levels in the moderate-severe AV group were significantly higher than that of the mild AV group ($p < 0.001$). In addition, the serum calprotectin level in the mild AV group was significantly higher than that of the healthy control group ($p = 0.047$). However, in the Spearman's correlation analysis, the serum calprotectin level and GAS were not correlated in AV patients ($p = 0.171$, $r = 0.179$). Conclusions: Serum calprotectin levels are increased in mild and moderate AV patients.

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Efficacy of folic acid and vitamin B12 replacement therapies in the reduction of adverse effects of Isotretinoin: a randomized controlled trial. Ghiasi M, Mortazavi H, Jafari M. Skinmed. 2018 Jul 1;16(4):239-245. eCollection 2018. https://www.ncbi.nlm.nih.gov/pubmed/30207526

Previous studies have reported elevated homocysteine levels and folic acid and/or vitamin B12 deficiencies after isotretinoin therapy, which increase the risk of cardiovascular and neuropsychiatric disorders. Homocysteine is

metabolized in the liver, a process requiring folate and vitamin B12. We conducted a randomized controlled trial to investigate whether folate and vitamin B12 replacement therapy with isotretinoin would be useful for preventing hyperhomocysteinemia. A total of 66 patients with acne were randomized into two groups: group A took isotretinoin, folic acid, and vitamin B12, whereas group B took isotretinoin alone. Treatment was continued for 2 months. Blood homocysteine, folic acid, and vitamin B12 levels were measured before and after treatment. In group A, a significant decrease in homocysteine level was observed after treatment (P=.0004), although it was still within the normal range. Folic acid and vitamin B12 levels significantly increased (P=.0026 and P=.0002, respectively). In group B, no significant changes were observed in the levels of homocysteine and vitamin B12, but folic acid levels decreased significantly (P=.02). We concluded that folic acid and vitamin B12 supplementation during isotretinoin therapy could be useful for preventing folate deficiency and improving blood homocysteine levels; this might as a result reduce the risks for cardiovascular and neuropsychiatric disorders in patients taking isotretinoin.

Clinical Reviews

Adverse cutaneous reactions to skin care products on the face vary with age, but not with sex. Huang LN, Zhong YP, Liu D, et al. Contact Dermatitis. 2018 Sep 12. doi: 10.1111/cod.13102. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30206954

Background: Adverse skin reactions to skin care products have been increasing in recent years. However, to date, these reactions have not been well characterized. Objective: To describe the symptoms, clinical signs and frequency of adverse cutaneous reactions to skin care products on the face in males vs females of various ages. Patients and methods: All outpatients diagnosed with adverse cutaneous reactions to skin care products on the face examined by dermatologists at the Dermatology Hospital of South Medical University between November 1, 2016 and October 31, 2017, employing a questionnaire and an interview, were eligible. The associations of adverse cutaneous reactions with age and sex were analysed. Results: A total of 433 outpatients, accounting for 0.12% of all outpatients, were assessed. Of these, 223 patients, including 204 females and 19 males, aged 4 to 75 years, were eventually diagnosed with adverse reactions to skin care products on the face. Eighty-two per cent of patients experienced pruritus, 80% showed erythema, and 48% showed visible swelling. The incidence rates of both xerosis and oedema correlated positively with age, whereas acne-like lesions were negatively associated with age, but not with sex. Conclusions: Our results indicate that pruritus, xerosis and erythema are common adverse cutaneous reactions to facial skin care products. These reactions vary with age, but not with sex. Vigorous safety testing should precede the marketing of skin care products.

Hidradenitis suppurativa/acne inversa: A practical framework for treatment optimization - systematic review and recommendations from the HS ALLIANCE working group. Zouboulis CC, Bechara FG, Dickinson-Blok JL, et al. J Eur Acad Dermatol Venereol. 2018 Sep 3. doi: 10.1111/jdv.15233. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30176066

Hidradenitis suppurativa (HS)/acne inversa is a debilitating chronic disease that remains poorly understood and difficult to manage. Clinical practice is variable and there is a need for international, evidence-based and easily applicable consensus on HS management. We report here the findings of a systematic literature review, which were subsequently used as a basis for the development of international consensus recommendations for the management of patients with HS. A systematic literature review was performed for each of nine clinical questions in HS (defined by an expert steering committee), covering comorbidity assessment, therapy (medical, surgical and combinations), and

response to treatment. Included articles underwent data extraction and were graded according to the Oxford Centre for Evidence-based Medicine criteria. Evidence-based recommendations were then drafted, refined, and voted upon, using a modified Delphi process. Overall, 5,310 articles were screened, 171 articles analyzed, and 65 used to derive recommendations. These articles included six randomized controlled trials plus cohort studies and case series. The highest level of evidence concerned dosing recommendations for topical clindamycin in mild disease (with systemic tetracyclines for more frequent/widespread lesions) and biologic therapy (especially adalimumab) as second-line agents (following conventional therapy failure). Good-quality evidence was available for the hidradenitis suppurativa clinical response (HiSCR) as a dichotomous outcome measure in inflammatory areas under treatment. Lower-level evidence supported recommendations for topical triclosan and oral zinc in mild-to-moderate HS, systemic clindamycin and rifampicin in moderate HS and intravenous ertapenem in selected patients with more severe disease. Intralesional or systemic steroids may also be considered. Local surgical excision is suggested for mild-to-moderate HS, with wide excision for more extensive disease. Despite a paucity of good quality data on management decisions in HS, this systematic review has enabled the development of robust and easily applicable clinical recommendations for international physicians based on graded evidence.

The role of nutrition in inflammatory pilosebaceous disorders: Implication of the skin-gut axis. Maarouf M, Platto JF, Shi VY. Australas J Dermatol. 2018 Sep 3. doi: 10.1111/ajd.12909. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30175843

Nutrition plays a critical role in the manifestation and management of inflammatory pilosebaceous disorders. There is rich potential for insight into the impact of dietary effects on the pathophysiology of inflammatory pilosebaceous disorders including acne vulgaris, hidradenitis suppurativa, rosacea, and the closely related seborrhoeic dermatitis. Acne vulgaris and hidradenitis suppurativa are thought to have similar diet-modulating pathogenic pathways. Western diet influences Acne vulgaris and hidradenitis suppurativa by increasing insulin and modulating FOX01/mTOR, resulting in over-expression of cytokeratins, hyperproliferation of keratinocytes, and hypercornification of the follicular wall. Key receptors in rosacea are alternatively activated by UV radiation, hot beverages, spicy foods, vanilla, cinnamon, caffeine, alcohol, cold temperatures, and niacin- and formalin-containing foods, to increase oedema and flushing, resulting in erythema, telangiectasia, and warmth, characteristic features of the condition. Seborrhoeic dermatitis, while not a follicular disorder, is closely related, and can be modulated by dietary influences, such as biotin and probiotics. This overview summarizes the role that nutrition plays on these disorders, and identifies dietary modifications as potential adjunctive therapies.

Safety and effectiveness of amoxicillin in the treatment of inflammatory acne. Guzman AK, Choi JK, James WD. Int J Womens Dermatol. 2018 8;4(3):174-175. doi: 10.1016/j.ijwd.2018.03.006. eCollection 2018 Sep. https://www.ncbi.nlm.nih.gov/pubmed/30175221

Acne is a common skin disease that predominantly affects teenagers and young adults. Systemic antibiotic therapy, including tetracyclines, macrolides, and trimethoprim-sulfamethoxazole, is indicated in moderate-to-severe inflammatory disease. However, in certain cases, these antibiotics and other commonly prescribed treatments including oral contraceptives, spironolactone, and isotretinoin may be prohibited, especially in cases of pregnancy and drug intolerance. In this retrospective study, we assessed the safety and efficacy of systemic amoxicillin, which has a favorable tolerability profile and compatibility with pregnancy in the treatment of inflammatory acne.

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A rare dermatologic disease in pregnancy: Rosacea fulminans- case report and review of the literature. Demir O, Tas IS, Gunay B, Ugurlucan FG. Open Access Maced J Med Sci. 2018 Aug 4;6(8):1438-1441. doi: 10.3889/oamjms.2018.267. eCollection 2018 Aug 20. https://www.ncbi.nlm.nih.gov/pubmed/30159072

Background: Rosacea is a common, chronic disorder that can present with a variety of cutaneous or ocular manifestations. Skin involvement primarily affects the central face, with findings such as persistent centrofacial redness, papules, pustules, flushing, telangiectasia, and phymatous skin changes. The pathways that lead to the development of rosacea are not well understood. The relationship of pyoderma faciale (also known as rosacea fulminans) to rosacea also is uncertain. We aimed to write this article with the aim of showing how a pregnant patient who has been aggravated by the degree of lesions on the face during the first trimester of pregnancy is treated and to show what is in the literature in this issue. Case report: A 22-year-old woman complained of painful erythema, papules and pustules on the face. She had fever and malaise during the sixth week of her first pregnancy and a history of the mild eruption and seborrhea before her pregnancy with flaring over the preceding 4 weeks. Dermatologic examination revealed red erythema of all involved facial areas; the lesions consisted of papules, pustules and nodules. The case was diagnosed as rosacea fulminans (pyoderma faciale) by these findings. In the literature, there are some effective therapeutic options such as retinoids, tetracyclines, antiandrogenic contraceptives, and dapsone and these were not used because they are contraindicated in pregnancy. Amoxicillin-clavulanic acid 1 gr/day, wet compresses, and a fusidic acid cream were started. After the activity of the disease had been suppressed for 10 days, antibiotic was stopped, and the other treatment options were applied topically for the next month. One month after cessation of treatment, the lesions had disappeared with only mild erythema remaining. There was minimally flushing on the face and no telangiectasia. Conclusion: In conclusion, there is no substantial evidence as to the mechanism by which pregnancy may trigger this conditioner whether the gender of the fetus influences the development of rosacea fulminans, but is generally accepted that hormonal changes in pregnancy play an important role. The pathogenesis of rosacea fulminans remains uncertain, but it is obvious that the further basic and clinical research is required to optimize the management of this rare facial dermatosis.

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