

Journal Watch

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Comparison of localised high-dose UVA1 irradiation versus topical cream psoralen-UVA for treatment of chronic vesicular dyshidrotic eczema

Petering H, Breuer C, Herbst R, Kapp A, Werfel T. *J Am Acad Dermatol* 2003;50:68-72.

Localised photochemotherapy, using 8-methoxypsoralen (MOP) gel or cream combined with UVA irradiation, has been used to treat severe hand eczema. However, it may provoke phototoxic reactions followed by long-lasting hyperpigmentation. This study compared the efficacy of localised high-dose UVA1 irradiation with topical cream PUVA in the treatment of chronic vesicular dyshidrotic eczema.

Twenty-seven patients had recurrent and recalcitrant bilateral vesicular dyshidrotic eczema for a mean duration between six months and five years. Localised UVA1 was irradiated to one hand five times weekly for three weeks, starting at a dose of 30 J/cm², then increasing up to a maximum of 130 J/cm² and reaching a cumulative dose of 1720 J/cm². On the opposite hand, 8-MOP cream PUVA was delivered at an initial dose of 2 J/cm² and increasing up to a maximum of 10 J/cm² and reaching a cumulative dose of 130 J/cm². The disease severity was scored using the Dyshidrosis Area and Severity Index. Twenty-four patients showed good response to either therapy. There was a significant decrease in the severity score after treatment ($p < 0.05$) for both methods. However, there was no difference between localised UVA1 irradiation and topical cream PUVA.

This study showed that both cream PUVA and UVA1 irradiation are equally effective in treating dyshidrotic eczema on hands and feet. UVA1 irradiation has additional benefit of less phototoxic reactions and potentially less carcinogenicity. However, the study sample is small and further study is necessary to evaluate the efficacy and safety of UVA1 therapy.

Acitretin treatment in (pre)malignant skin disorders of renal transplant recipients: Histologic and immunohistochemical effects

Smit JV, de Sevaux RG, Blokk WA, van de Kerkhof PC, Hoitsma AJ, de Jong EM. *J Am Acad Dermatol* 2004;50:189-96.

The incidences of premalignant and malignant cutaneous lesions are high in renal transplant recipients. Acitretin treatment was reported to reduce the number of new squamous cell carcinomas (SCC) and actinic keratoses (AK). This study investigated the histologic and immunohistochemical effects of acitretin on AK.

A total of 33 renal transplant recipients received acitretin in doses up to 0.4 mg/kg/day for 12 weeks. The inclusion criteria included a history of at least one cutaneous SCC and ≥ 10 AKs, or ≥ 20 AKs if no previous history of SCC. Skin biopsies were taken from clinically evident AK lesions, before and after three months of treatment. Histologic and immunohistochemical parameters were analysed for dysplasia, epidermal thickness, proliferation, differentiation, apoptosis, and

dermal inflammation. Following acitretin treatment, the epidermal thickness was significantly reduced ($p=0.002$) and the normal differentiation parameter K10 was increased ($p=0.02$). Other parameters did not change. There was also an increase in markers for retinoid-induced keratinization including K13 ($p=0.006$) and K19 ($p=0.05$) after acitretin treatment.

Acitretin can alter keratinization, lead to peeling of the hypertrophic stratum corneum and then improves AK clinically. However, rapid recurrence can be anticipated after stopping acitretin treatment, since there is no significant change in proliferation and dysplasia. However, it was not mentioned whether the authors recommended the use of acitretin in such condition.

Twice weekly fluticasone propionate added to emollient maintenance treatment to reduce risk of relapse in atopic dermatitis: randomised, double-blind, parallel group study

Berth-Jones J, Damstra RJ, Golsch S, Livden JK, Van Hooft O, Allegra F, et al.
Br Med J 2003;326:1367-72.

This was a randomised, double-blind, parallel group study to evaluate the efficacy and safety of using fluticasone propionate cream or ointment in maintaining remission of moderate to severe atopic dermatitis. A total of 376 adult patients were recruited during a flare, which was treated with fluticasone propionate cream 0.05% or ointment 0.005%, once or twice daily, for four weeks. The disease activity of 295 patients was brought under control and subsequently went into a maintenance phase. Either placebo or fluticasone propionate cream or ointment, were applied twice weekly to all healed sites of potential relapse and any new occurring sites, in addition to emollients. The severity was assessed by the three item severity score, which was the sum of three signs: erythema, oedema or papulations,

and excoriations; each scored from 0 to 3. Remission was defined as an index lesion score of one or lower.

After 16 weeks of maintenance treatment, 133 patients remained in remission (87 fluticasone propionate; 46 emollient alone), 135 patients relapsed (40 fluticasone propionate; 95 emollient) and 27 patients discontinued. Patients using fluticasone propionate cream or ointment were less likely to experience a relapse: (median time to relapse for fluticasone propionate and emollient was 16 weeks and six weeks respectively); hazard ratio 5.8 for cream (95% CI 3.1 to 10.8, $p<0.001$) and 1.9 for ointment (95% CI 1.2 to 3.2, $p=0.010$). There was no difference in adverse effect between the groups.

It was concluded that the use of fluticasone propionate twice weekly in addition to emollient, can effectively maintain remission in patients with moderate to severe atopic dermatitis. However, the study failed to explain the difference in efficacy between cream and ointment formulation. Nevertheless, this study highlighted an important step towards successful long term management of atopic dermatitis. In future studies, it may be useful to explore the use of lower potency topical corticosteroid and extend the study to include children. The study was funded by Glaxo Wellcome (now GlaxoSmithKline) R & D, United Kingdom.

Safety and efficacy of 4% hydroquinone combined with 10% glycolic acid, antioxidants, and sunscreen in the treatment of melasma

Guevara IL, Pandya AG.
Int J Dermatol 2003;42:966-72.

This was a randomised, double-blind, single-center study to compare the efficacy and safety of combination of 4% hydroquinone, 10% buffered

glycolic acid, vitamin C, vitamin E and sunscreen in the treatment of melasma. Thirty-nine Hispanic women, aged 18 to 50 years, with Fitzpatrick skin types III to V and bilateral epidermal melasma were recruited. Two-third of the patients were randomised to apply a cream containing the above ingredients twice daily on the whole face for 12 weeks and the rest of the patients applied a cream containing sunscreen only. The patients were evaluated using a mexameter and the melasma area and severity index (MASI). Adverse effects were assessed by a blind investigator using a four-point scale (0, none; 1, mild; 2, moderate; 3, severe), for burning, itching, redness, dryness and peeling.

Thirty-five patients completed the study and the mexameter results showed a significant decrease in pigmentation in the case group ($p < 0.0001$). Fifteen of 20 patients in the case group improved while only 2 of 15 patients in the control group improved. Reduction of MASI scales were also significant ($p = 0.01$). Irritation in the form of mild to moderate erythema was more common in the case group (85%), but all were able to continue with the addition of moisturiser cream. Thus, combination of 4% hydroquinone, 10% buffered glycolic acid, vitamin C and E, and sunscreen were more effective in treating melasma than using sunscreen alone although mild to moderate irritation is more common in the former. This study was granted by ICN Pharmaceuticals.

Itraconazole in the treatment of seborrhoeic dermatitis: a new treatment modality

Baysal V, Yildirim M, Ozcanli C, Ceyhan AM.
Int J Dermatol 2004;43:63-6.

Thirty-two adult patients with clinically seborrhoeic dermatitis not responding to at least one month of topical corticosteroid were recruited for this study. The patients applied 1% hydrocortisone cream twice daily on the scalp,

face and pre-sternal area for the first month and then stopped. Itraconazole 200 mg daily was given during the first week of the first month and the first two days of each subsequent month for 11 months. No other topical or oral medications were allowed as therapy for seborrhoeic dermatitis. The same doctor assessed the patients under standard lighting conditions 2 months after the last month of itraconazole therapy. The scalp, face and chest were graded for erythema, papules and scales and the condition was evaluated as complete clearing ($> 71\%$), marked improvement (51-70%), moderate improvement (26-50%), and slight improvement ($< 25\%$).

Twenty-eight patients completed the study and there was significant clinical improvement starting from the end of the first month ($p = 0.001$) and the improvement was maintained till the end of the study. Final global evaluation at the 12th month showed that 19 patients showed complete improvement, six showed moderate improvement, and three patients showed slight improvement. There were no haematologic or biochemical abnormalities observed during the study. The authors concluded that this treatment modality can be used as alternative therapy in patients not responding to or unwilling to use conventional topical therapy.

Verrucae vulgares: flashlamp-pumped pulsed dye laser treatment in 134 patients

Kopera D.
Int J Dermatol 2003;42:905-8.

The author reported her experience with 585-nm flashlamp-pumped pulsed dye laser (FPDL) for the treatment of verrucae vulgares over a 18 months' duration. It recruited 134 voluntary patients (mean age 25; range 4-65 years) with recalcitrant or untreated verrucae vulgares to receive FPDL treatment. The following parameters

were used: spot diameter, 7 mm; pulse duration, 450 us; fluence, 8 J/cm². Eight patients were lost to follow-up. The rest 126 patients received a mean of 3.38 treatment sessions (range, 1-8) with a mean interval of 3.26 weeks. Overall, 62.69% of patients showed total remission, 21.42% showed partial remission and 9.52% of the patients did not respond.

It was found that verrucae in the extremities responded poorer than the rest of the body. Those in the palms required less treatment sessions than those in the feet (3.37 vs 4.7). After a median of 3.37 treatments, 71.42% of palmer warts resolved, whereas only 46.15% of plantar warts resolved after a median of 4.7 sessions. The burning sensation following each treatment was well tolerated by most patients (93.66%). The result of FPDL treatment for viral warts is comparable to other modalities of treatment, including topical salicylic acid, cauterisation and cryotherapy. It is more expensive but requires less compliance. It is not associated with post-treatment complications like pain or wound and blister formation.

The dermoscopic classification of atypical melanocytic naevi (Clark naevi) is useful to discriminate benign from malignant melanocytic lesions

Blum A, Soyer HP, Garbe C, Kerl H, Rassner G, Hofmann-wellenhof R.

Br J Dermatol 2003;149:1159-64.

This was a German study to investigate the sensitivity and specificity of the dermoscopic classification of atypical melanocytic naevi in identifying melanoma in patients with multiple naevi. It studied 254 melanocytic lesions from 108 females and 97 males. Digital dermoscopic images of all 254 melanocytic lesions were documented at a magnification of 20-fold before excision. Lesions on soles, palms, subungual and

mucosal sites were excluded due to site-specific dermoscopic features.

All melanocytic lesions were classified using the dermoscopic classification of atypical melanocytic naevi into seven types namely: reticular, globular, homogenous or combinations of any two or three of these types. The distribution of the pigmentation was classified as uniform, central hyper- or hypopigmented, eccentric hyper- or hypopigmented, and multi-focal hyper- or hypopigmented. Histopathologically, 179 (70.5%) were benign naevi and 75 (29.5%) were malignant melanoma. Reticular, homogenous and reticular-homogenous types were significantly more frequent in naevi than in melanoma. None of the melanoma showed globular or homogenous type, whereas 86.7% of them were of the three-structure type (reticular, globular and homogeneous) ($p < 0.001$). When using the three-structure pattern as a malignancy indicator, the sensitivity and specificity to pick up melanoma was 86.7% and 87.7% respectively. Regarding the distribution of the pigment, the uniformly pigmented and centrally hyperpigmented type were significantly more frequent in naevi than in melanoma, whereas the eccentric peripheral hyperpigmented and multifocal patchy hyper- or hypopigmented type was significantly more frequent in melanoma ($p < 0.001$). It is therefore recommended that the three-structure type should be excised, whereas the peripheral hyperpigmentation type should either be excised or follow-up within three months.

A novel targeted T-cell modulator, efalizumab, for plaque psoriasis

Lebwohl M, Tying SK, Hamilton TK, Toth D, Glazer S, Tawfik NH et al for the Efalizumab Study Group. N Engl J Med 2003;349:2004-13.

Efalizumab, a humanised monoclonal antibody, inhibits the interaction between leukocyte-function-associated antigen type 1 (LFA-1) and

intercellular adhesion molecules, which is an important step in the pathogenesis of psoriasis. This was a phase III, multicentre, randomised, placebo-controlled, double-blind study, investigating the efficacy and safety of efalizumab in the treatment of moderate to severe psoriasis.

Five hundred and ninety-seven patients participated in the study. They were randomised to receive subcutaneous injection of placebo or efalizumab at a dose of 1 or 2 mg/kg once every week for 12 weeks. From week 12 to 24, additional efalizumab treatment or placebo was given depending on the initial response. Efalizumab was discontinued at week 24 and patients were followed until week 36. The percentages of patients achieving an improvement of at least 75% (PASI 75) or 50% (PASI 50) in the psoriasis area and severity index (PASI) score from their baseline, were determined.

At week 12, patients receiving efalizumab at either dose showed significant improvement ($p < 0.001$): PASI 75 respectively 22% (1 mg/kg), 28% (2 mg/kg) and 5% (placebo). From week 12 to 24, the initial good responders (who was able to achieve PASI 50 at week 12) could maintain their improvement in 77% of patients if efalizumab was continued, as compared to 20% of patients if switched to placebo ($p < 0.001$). At week 36, 30% of patients could maintain an improvement of PASI 50. The adverse effects included nonspecific infection (13%), worsening psoriasis (9%), pruritus (6%) and arthritis (5%).

The study concluded that efalizumab is an effective treatment for moderate to severe psoriasis. The response can be maintained by extending treatment from 12 to 24 weeks. However, it should be noted that 9% of patients developed worsening in psoriasis. It is worthwhile to identify the subset of patients who will be benefited or paradoxically worsened by efalizumab therapy. This study was supported by Genentech Inc.

Two hundred ninety-six cases of onychomycosis in children and teenagers: a 10-year laboratory survey

Lateur N, Mortaki A, Andre J.

Pediatr Dermatol 2003;20: 385-8.

This study investigated the epidemiology of onychomycosis in children and teenagers. Nail samples from patients with nail problems were taken over a 10-year period and were examined by direct microscopy and culture. Only patients less than 17 years old were considered as children and their samples studied.

A total of 21,557 nail samples were collected during this period, of which 963 (4.5%) were from children. Onychomycosis was diagnosed in 296 (30.74%) of nails sampled in paediatric cases. There was a male preponderance (166 boys, 130 girls) and onychomycosis became more common with increasing age (75% affected cases were over six years old). The age distribution was as follows: two to six years old: 43 patients; six to twelve years old: 104 patients; 12 to 17 years old: 125 patients. In addition, there were 24 patients less than two years of age (youngest: six weeks old). Toenails were more frequently affected in all subset of patients.

The pathogen was identified in 189 samples (63.85%). Dermatophytes were only slightly more common than yeasts (24 vs 19 cases) in those under six years of age. In those over six years of age, dermatophytes were the main pathogen. *Trichophyton rubrum* was the main pathogen in both groups (142 cases), while *Candida* spp. (37 cases) was the next most common. *Scopulariopsis* spp. was detected in only one case.

It was therefore concluded that the toenails are most commonly affected in children with onychomycosis and that the clinical picture in those over six years old is similar to that of adults with *Trichophyton rubrum* being the main pathogen.

Erythema dyschromicum perstans in prepubertal children

Silverberg NB, Herz J, Wagner A, Paller AS.
Pediatr Dermatol 2003;20:398-403.

Erythema dyschromicum perstans (EDP) is characterised by slate-gray oval macules and patches with erythematous borders that range in diameter from 0.5 to 3 cm. Eight patients with EDP were identified by reviewing their medical, photographic and/or histological records. Five of these patients were available for follow-up and the clinical course was evaluated by telephone interview.

The trunk and the neck were the most commonly affected sites. Regardless of the patients' race, most lesions were grey in colour. The ethnic distribution of the patients was as follows: Caucasian: 5; Hispanic: 2; African-American: 1. The average age of onset was 5.2 years, with an equal sex distribution (4 males, 4 females). The average age of the lesions at presentation was 3.4 months (range 2 to 6 months). It was noted that the lesions appeared between July and December in all cases. The lesions varied from 0.5 to 2 cm in size and were not preceded by an inflammatory phase. Two patients had received amoxicillin and one with anticonvulsants prior to onset of the lesions. Apart from two patients who were treated with mid-potency topical steroids, and one with selenium sulphide lotion, treatment was conservative.

Complete remission was reported in all five patients after an average time of 2.5 years (range 1 to 5 years). No recurrence was reported at an average follow-up time of 3.5 years after clearance (range 1 to 7 years). The authors concluded that EDP in children is more likely to resolve within two to three years, in contrast to its persistent course in adults. As there was no oriental patient in this series, it is not known whether this is applicable to patients in our locality.

Histopathologic features of alopecia areata: a new look

Whiting DA.
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This study was performed to define the changes in histological features in the different stages of alopecia areata. Fifty patients with various types of alopecia areata (patch, diffuse, ophiasis, universalis, confluent types) were studied. Four-millimeter punch biopsy specimens were taken from the scalp at different stages of alopecia. Follicular units, anagen, telogen, catagen, terminal and vellus hairs were counted. In addition, the presence of an inflammatory infiltrate was noted.

Twenty-one men and 29 women were studied (mean age 33 years). Histological features did not vary between patients of different race, sex, age, type, or total duration of alopecia. The duration of the current episode was the main factor affecting the histological features. In acute disease, an inflammatory infiltrate was found around the hair bulb and lower follicle. On the other hand, this was centered on miniaturised hairs in the upper dermis in chronic disease.

Total follicular counts were similar between the different types of alopecia areata. However, there was a significant decrease in anagen count with increasing severity of alopecia areata. The loss of anagen hairs was greatest in early, acute disease, with a corresponding increase in telogen and vellus hairs. In subacute disease, there was a gradual loss of terminal hairs and increased catagen and telogen hairs. These ratios varied with repeated episodes of alopecia areata. In chronic disease, decreased terminal hairs and increased miniaturised hairs with variable inflammation were present. This was reversed in the recovery stage.

The authors concluded that the histological features vary with different stages of alopecia

areata and this condition may be considered in the presence of increased numbers of telogen hairs or miniaturised hairs in the absence of an inflammatory infiltrate.

Safety of cyclooxygenase 2 inhibitors and increased leukotriene synthesis in chronic idiopathic urticaria with sensitivity to non-steroidal anti-inflammatory drugs

Zembowicz A, Mastalerz L, Setkowicz M, Radziszewski W, Szczeklik A.
Arch Dermatol 2003;139:1577-82.

The safety of cyclooxygenase 2 inhibitors in patients with chronic idiopathic urticaria (CIU) and non-steroidal anti-inflammatory drug (NSAID) sensitivity was investigated. Patients were given placebo on day 1. On day 2, patients with sensitivity to aspirin were selected by an aspirin challenge test (up to 500 mg). These patients then entered into a double-blind, randomised, placebo-controlled, cross-over trial with celecoxib (up to 300 mg) and rofecoxib (up to 37.5 mg) on day 8 and day 15. After completion of the trial, seven patients were given naproxen sodium (500 mg) as positive

control. Parameters studied included skin examination (measured by modified PASI score), urine leukotriene E4 (LTE4), serum tryptase and skin biopsy with mast cell count.

Thirty-six patients (10 males, 26 females; mean age 39 years) were recruited. Eighteen patients developed a rash consistent with urticaria and/or angioedema after taking aspirin (maximum PASI score averaged 12.3 ± 9.8). However, none of these patients developed a skin eruption after taking celecoxib or rofecoxib. Urinary levels of LTE4 and serum tryptase levels were elevated in aspirin-sensitive patients when compared to non-sensitive patients. There was a positive correlation between baseline urinary LTE4, and extent of skin eruption. Naproxen induced a response in five of the seven patients with aspirin-sensitivity. There was also an increase in urinary LTE4 levels two hours after the onset of the urticaria. On histological examination, there was no correlation between the number of mast cells and the severity of skin eruption or serum tryptase levels.

It was concluded that cyclooxygenase 2 inhibitors do not affect CIU patients with NSAID sensitivity. In addition, there is associated overproduction of cysteinyl leukotrienes in patients with CIU and NSAID sensitivity.