

Journal Watch

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Treatment of chronic erosive oral lichen planus with low concentrations of topical tacrolimus: an open prospective study

Olivier V, Lacour JP, Mousnier A, Garraffo R, Monteil RA, Ortonne JP.
Arch Dermatol 2002;138:1335-8.

An open prospective study investigating the efficacy and safety of topical tacrolimus on chronic erosive oral lichen planus (EOLP) was performed. Ten patients with histologically proven, refractory EOLP were treated with topical tacrolimus mouthwashes, 0.1 mg/100 mL distilled water, four times daily for six months. No other treatments were allowed during the study and all preceding treatments were stopped four weeks before the study. Symptoms of spontaneous and meal-induced pain were assessed on a visual analogue scale separately (0 to 4). The extent of eroded surface area was documented and scored (1-4). The sum of these three scores constituted the clinical score. The patients were assessed monthly during treatment, and at nine and 12 months.

Two patients were excluded because of non-compliance. Of the remaining eight patients (mean age 58.1 years, range 34-74), one did not respond while seven reported a decrease in symptoms by the first month. The mean score decreased from a baseline of 7.00 to 5.43 (22.43% decrease) at one month and to 3.43 (51% decrease) at six months. Three patients reported transient tingling after treatment, while two patients experienced dryness of the mouth. The

whole-blood concentration of tacrolimus was below the detectable level (1.5 ng/mL) in all cases. Six patients relapsed at nine months (within a mean of 38.6 days after cessation of treatment) and all relapsed at 12 months.

The authors concluded that topical tacrolimus provided rapid palliation in EOLP and suggested confirmation by a larger study. However, the risk of malignant transformation in EOLP treated by topical tacrolimus still needs further assessment.

Viral disease transmitted by laser-generated plume (aerosol)

Garden JM, O'Banion MK, Bakus AD, Olson C.
Arch Dermatol 2002;138:1303-7.

There has been increasing concern regarding the presence of infectious material in the plume generated by lasers. This study aimed to evaluate the presence of viral material in the plume of carbon dioxide laser and its transmissibility.

Bovine cutaneous fibropapillomas excised from cattle were exposed to carbon dioxide laser at three different settings: (1) 12 W, 2 mm spot size, continuous mode; (2) 4W, 2 mm spot size, continuous mode; (3) 8 W, 0.2 mm spot size, 0.1 second pulse duration. The laser-generated plume was collected via a vacuum suction line. The material collected from the plume was evaluated for the presence of viral DNA by gel electrophoresis and then hybridization. It was also inoculated onto the skin of three calves.

Bovine papillomavirus (BPV) DNA was detected in the laser plume at all three laser settings. Tumours were induced by inoculating material from the laser plume for all laser parameter settings and they were clinically and histologically typical of bovine cutaneous fibropapillomas. Biochemical analysis of the DNA from an induced lesion and a laser plume sample showed the same viral DNA type, giving proof that the growths indeed were induced by material from the laser plume.

These findings therefore suggest that there is a possibility of transmission of papillomavirus via the laser plume, emphasizing the need for safety precautions during laser therapy. However, whether the effect of clinical exposure to laser plume containing infectious material is the same as inoculation is unknown.

Frequency of facial basal cell carcinoma does not correlate with site-specific UV exposure

Heckmann M, Zogelmeier F, Konz B.
Arch Dermatol 2002;138:1494-7.

A retrospective analysis of the distribution and histopathological features of facial basal cell carcinoma (BCC) in relation to ultraviolet (UV) light exposure was performed. The anatomical site was carefully documented. The periorbital area was divided into four quadrants (upper, lower, lateral and medial) and the nose was similarly divided into four segments (basal segment of the nose adjacent to the nasolabial fold on either side, the apex, and the dorsum/bridge of the nose).

A total of 3065 BCCs in 2785 patients were studied (mean age 63.2 years, range 20-101). The top three sites were as follows: the nose 1373 (44.8%), orbital area 386 (12.6%), and ears 269 (8.8%). Of the 1373 nasal BCCs, the distribution was as follows: base 851 (62%), apex 292 (21.3%), and dorsum 230 (16.8%). Of the 386 orbital

BCCs, 225 (58.3%) occurred in the medial quadrant while 24 (6.2%) in the lateral quadrant. Finally, there were totally 269 auricular BCCs, of which 105 (39.0%) were located on the pre-auricular area, 99 (36.8%) on the retroauricular fold and 65 (24.2%) on the helix. There was no difference in distribution between older (>63 years of age) and younger patients. There was no correlation between site and histological type.

Although the dorsum and apex of the nose, lateral quadrant of the orbit, and helix of the ears were more prominent and exposed, they were comparatively less frequently affected. The authors therefore concluded that the cumulative effect of UV light exposure alone at a particular site correlated poorly with the development of BCC. They suggested that site-specific textural qualities of facial skin might be a potential cofactor.

Efficacy of glycolic acid peels in the treatment of melasma

Hurley ME, Guevara IL, Gonzales RM, Pandya AG.
Arch Dermatol 2002;138:1578-82.

This was a prospective trial comparing the effectiveness of using 4% hydroquinone cream and 20-30% glycolic acid peels to 4% hydroquinone cream alone in melasma.

Twenty-one Hispanic women with bilateral epidermal and mixed melasma were recruited. Their mean age was 40 years (range: 18 to 65). The trial was of eight weeks' duration, during which 20-30% glycolic acid peels were applied to one side of the face every two weeks, in addition to application of 4% hydroquinone twice daily to the whole face. A sunscreen with sun protective factor 25 was used in the morning. Pigmentation was assessed subjectively using a linear analog scale and physician and patient global evaluation. Objective assessment was done by mexameter and the melasma area and severity index (MASI score).

Eighteen patients completed the study. Half of them were of Fitzpatrick skin type IV and the other half type V. Both combined treatment and hydroquinone alone achieved a significant reduction in pigmentation ($P < 0.001$). When assessed by mexameter and MASI score, there was no significant difference between combination treatment and hydroquinone monotherapy. When assessed by the physician, eight patients improved more on the peeled side while seven improved more on the non-peeled side. However, eleven patients thought there was greater improvement on the peeled side, and four thought the non-peeled side improved more. The authors concluded that addition of glycolic acid peels did not augment the bleaching effect of 4% hydroquinone.

The relevance of these findings to Chinese patients is uncertain. In addition, the optimum duration of combination treatment is not known and further trials with a longer study period should be carried out.

Treatment of mycosis fungoides/Sezary syndrome: the University of California, San Francisco (UCSF) approach

Zackheim HS.

Int J Dermatol 2003;42:53-6.

In UCSF, the first-line treatment for patch stage mycosis fungoides (MF) was class I topical corticosteroids usually 0.05% clobetasol. UVB was used to treat patch stage MF in children and adolescents, and hypopigmented MF. PUVA was used to treat patch and plaque stage MF. It was more effective than UVB due to deeper penetration. Topical nitrogen mustard and carmustine were usually effective in patch and early plaque MF. However, the former was associated with a high rate of allergic reactions and also carried risk of skin cancer while the latter was only used as a back-up treatment for topical

corticosteroid failures. Total skin electron beam was the choice in UCSF for patients with widespread plaques and/or tumour stage disease. Recurrence in the form of early stage disease in six to twelve months might occur but this could be managed with conservative therapy. Total skin electron beam could be repeated two to three times at a reduced dose.

Those who failed topical therapy, phototherapies and radiation were candidates for systemic therapies. Methotrexate was their usual first line agent. Most responding patients would show improvement at or below 50 mg per week. For more resistant and advanced MF, interferon- α , systemic bexarotene, denileukin diftitox (a diphtheria fusion toxin), or multi-agent chemotherapies such as CHOP were used. For lymphomatoid papulosis, the symptoms were usually mild and treatment was not needed. If treatment was indicated, low-dose methotrexate (7.5 to 20 mg per week) was their first choice.

Value of histopathology in vitiligo

Montes LF, Abulafia J, Wilborn WH, Hyde BM, Montes CM.

Int J Dermatol 2003;42:57-61.

There were few publications on the histopathological features of vitiligo. This study identified the microscopic alterations important in the histologic diagnosis of vitiligo. Twenty skin biopsy specimens from 10 men and 10 women with vitiligo as well as five skin specimens from horses with vitiligo were studied using light microscopy and electron microscopy. Light microscopy revealed inflammatory changes in the borders of the new lesions in actively spreading vitiligo. There was partial or complete lack of melanin as a result of the disappearance of melanocytes through a degenerative process involving vacuolization. The stratum corneum was slightly thicker than in normal skin. The keratinocytes showed vacuolization close to the

basement membrane which had thickening and duplication. The upper dermis was infiltrated by T lymphocytes, often in a perivascular manner. The number of Langerhans' cells was increased while Merkel cell was absent.

Most of these changes were confirmed by electron microscopy, which also demonstrated ultra-structural changes like dilated endoplasmic reticulum, swelling of axons, discontinuation of axon membranes and reduplication of Schwann cells' cytoplasmic organelles. The findings of a superficial dermal inflammatory infiltrate in areas of melanocyte loss supported the use of topical corticosteroids and PUVA on new or spreading vitiliginous lesions. Moreover, evaluation of the inflammatory infiltrates might be helpful in predicting the prognosis of vitiligo in future. Nevertheless the authors did not explain why horse skin was used in this human study.

Assessment of histologic criteria in the diagnosis of mycosis fungoides

Naraghi ZS, Seirafi H, Valikhani M, Farnaghi F, Kavusi S, Dowlati Y.

Int J Dermatol 2003;42:45-52.

The pathologic diagnosis of early mycosis fungoides (MF) could be very difficult and its histologic features might merge into those of other inflammatory dermatoses.

In this study, the histologic features of skin biopsy specimens from 30 MF patients were analyzed. Subsequently the histologic features of 24 patients with patch stage MF were compared with those from 24 non-MF patients whose histologic patterns were suspicious of MF. The most common histologic patterns encountered were lichenoid, followed by spongiotic-lichenoid and psoriasiform. It was found that Pautrier's microabscesses, haloed lymphocytes, disproportionate epidermotropism, larger

epidermal lymphocytes, absence of dyskeratosis, hyperconvoluted dermal and epidermal lymphocytes, and papillary dermal fibrosis could be used to distinguish MF from its inflammatory imitators. Epidermotropism was a sensitive but non-specific feature whilst disproportionate epidermotropism was significantly more specific although not as sensitive. The two most specific attributes in the epidermis were Pautrier's microabscesses, and the presence of lymphocytes being larger than dermal lymphocytes. Dermal fibrosis was a feature in late atrophic lesions, and was not a sign in early patches. Dermal oedema and vasculopathy were neither specific nor sensitive.

The value of individual pathologic features in the diagnosis of early MF was generally poor, and the gold standard in the diagnosis was still clinicopathologic correlation. However, the authors did not address the possibility that, among those 24 non-MF controls histologically suspicious of MF, some might turn out to be MF on long term follow-up.

Prevalence of atopic dermatitis in Japanese adults

Muto T, Hsieh SD, Sakurai Y, Yoshinaga H, Suto H, Okumura K, et al.

Br J Dermatol 2003;148:117-21.

There has been a paucity of studies on the prevalence of atopic dermatitis in adult patients worldwide. This questionnaire-based study covered 12,193 persons who were mostly government officials or dependent family members visiting a medical centre in Tokyo for annual comprehensive health check-ups between September 1997 and August 1998. The U.K. Working Party's diagnostic criteria for atopic dermatitis were used because these criteria had been validated both in hospital and general population settings. A total of 10,762 persons

aged 30 or more was included in the analysis. Three quarters were male. Thirty-seven percent and 38% were in their 40's and 50's respectively.

This study shown that the point prevalence of atopic dermatitis was 2.8% and 3.1% respectively for men and women, without any statistically significant difference between them and among the different age groups of either gender. The lifetime prevalence of atopic dermatitis was 3.1% and 3.7% respectively for men and women, with no significant statistical difference between the genders. It was shown that 93.4% of those who ever had atopic dermatitis had an episode of atopic dermatitis in the previous year. Comparing with previous Japanese studies, there was a remarkable increase in the prevalence of atopic dermatitis from less than 0.1% in 1966-72 to 0.5% in 1988-92, and 2.9% in the present study. Nevertheless, one major drawback in the present study is the difficulty in generalising the figure to the whole Japanese population. The subjects chosen were mainly government officials and their family members who might only represent a particular social class in Japan.

Photodynamic therapy with topical methyl aminolaevulinate for actinic keratosis: results of a prospective randomised multicenter trial

Pariser DM, Lowe NJ, Stewart DM, Jarratt MT, Lucky AW, Pariser RJ, et al.
J Am Acad Dermatol 2003;48:227-32.

This prospective randomized, double-blind, placebo-controlled study evaluated the effectiveness and tolerability of using photodynamic therapy (PDT) with topical methyl aminolaevulinate (MAL) cream for actinic keratosis (AK). MAL might have greater skin penetration and selectivity for neoplastic tissue than topical 5-aminolaevulinic acid.

Eighty patients (70 males and 10 females) with a mean age of 65 years (range: 31 to 84) were recruited. Forty-two patients with 260 AKs were treated with MAL PDT while 38 patients with 242 AKs were given placebo PDT. The topical cream was applied to the lesion under occlusion for at least three hours before illumination with red light (570-670 nm, light dose 75 J/cm²). Treatment was repeated one week afterwards. The result was evaluated three months later with intent-to-treat analysis. Significantly more patients (82%) in the MAL group had their AKs resolved completely than those (21%) in the placebo group. For individual lesions, more AKs also resolved with MAL PDT (89%) than placebo treatment (38%). A good or excellent cosmetic result was achieved subjectively and objectively in over 90% of the MAL group. Side effects with MAL PDT were local phototoxicity reactions, like burning sensation, erythema, crusting and pain. Two patients discontinued MAL PDT because of the adverse effects. One patient in the MAL PDT was lost to follow-up.

The authors concluded that PDT with topical MAL was effective for treating AKs with tolerable side effects and favourable cosmetic outcome. Further studies to compare its efficacy with other modalities of treatments are warranted.

Narrowband UVB and psoralen-UVA in the treatment of early-stage mycosis fungoides: a retrospective study

Diederens PV, van Weelden H, Sanders CJ, Toonstra J, van Vloten WA.
J Am Acad Dermatol 2003;48:215-9.

This retrospective study compared the effectiveness of narrowband UVB (NB-UVB) and psoralen-UVA (PUVA) in treating early-stage mycosis fungoides (MF). All cases were in either stage Ia or Ib. NB-UVB was given to 21 patients (mean age 45 years)

and PUVA to 35 patients (mean age 53 years) between 1982 and 1998. Both were administered twice weekly according to their respective regimens.

The mean duration of therapy was 14 months for NBUVB and 11 months for PUVA. NBUVB induced complete remission (no disease activity) in 81% (17 out of 21 patients) and partial remission (decrease of disease activity more than 50%) in 19% (4 out of 21). PUVA induced complete remission in 71% (25 out of 35 patients) and partial remission in 29% (10 out of 35). The mean follow-up duration was 77 months for NBUVB and 45 months for PUVA. The mean time to relapse was 24.5 months for NBUVB-treated cases and 22.8 months for PUVA-treated cases. Side effects included burning sensation, pruritus, and post-inflammatory hyperpigmentation in a few patients treated with NBUVB. Side effects with PUVA included nausea, headache, post-treatment burning sensation and pain in a few patients.

The authors concluded that NBUVB was an effective therapy for early-stage MF and could be started initially. If there was a lack of response or disease progression, PUVA could be used then. However the follow-up period is too short to look for chronic side effects and, in view of its retrospective design, a randomised controlled trial is necessary to give conclusive evidence.

Actinic degeneration and pigmentary change in association with psoralen and UVA treatment: a 20-year prospective study

Stern RS.

J Am Acad Dermatol 2003;48:61-7.

Psoralen and UVA (PUVA) treatment was known to induce actinic degeneration and pigmentary changes known as PUVA lentiginos. The present study was based upon the cohort of the PUVA Follow Up Study which was started in 1975 with

originally 1380 patients enrolled. The purpose was to analyse the risk factors for the development of actinic degeneration and pigmentary changes over the past two decades. There were 842 patients remained in the cohort at the end of 1998, of whom 599 underwent the standardised dermatologic examination of their hands and buttocks for serial changes.

The percentage of patients with moderate or severe actinic degeneration increased from 15.6% in 1977 to 61.4% in 1998 at hands, and from 2.2% to 21.3% at buttocks. The percentage of patients with moderate or severe pigmentary changes increased from 15.6% in 1977 to 58.6% in 1998 at hands, and from 12.6% to 24.7% at buttocks. The number of PUVA sessions was the most important risk factor for deterioration of actinic degeneration and pigmentary changes by univariate and multivariate analysis. Withholding PUVA for at least five years did not reduce the risk of actinic degeneration on the buttocks, signifying a persistent change.

The author concluded that PUVA was associated with long term complications of actinic degeneration and pigmentary changes, the risks of which were related to the number of sessions given. These, in addition to a higher risk of skin cancers, are important messages to convey while counselling patients for PUVA therapy.

Treatment of reticular leg veins with a 1064 nm long-pulsed Nd:YAG laser

Omura NE, Dover JS, Arndt KA, Kauvar AN.

J Am Acad Dermatol 2003;48:76-81.

The use of a single 50 millisecond pass of 1064 nm Nd:YAG laser with a fluence of 100 J/cm² in treating reticular leg veins was studied.

Twenty female volunteers aged 23 to 69 years were recruited for this prospective controlled study.

Twenty-four veins sized one to three mm in diameter were treated. A single vessel was treated in seventeen patients, two vessels in two patients, and three vessels in one patient. The control area was selected from a matched site on the contralateral leg. Topical anaesthetic cream and post-laser compression stockings were given for 11 patients. Pre-cooling and post-cooling at 4°C for several seconds were given using the contact cooling handpiece. Pre-laser, one-month and three-month post-laser treatment photographs were taken and evaluated by three nontreating physicians for clearing and side effects. No immediate clinical endpoint was noted in most subjects.

Greater than 50% clearance was found in 21 out of 24 vessels (87.5%) and greater than 75%

clearance in 16 of 24 vessels (66.7%) at three months. Three quarters of the larger vessels (2.0-3.0 mm in diameter) had more than 75% clearance whereas only half of the smaller vessels (1.0-1.5 mm) reached the same degree of clearance.

Side effects included treatment discomfort, superficial thrombus formation, transient bruising, matting and transient hyperpigmentation. More thrombus formation was noted in the group with compression stockings. The authors concluded that long-pulsed Nd:YAG laser at the study settings were effective for reticular leg veins and further research was warranted. However, the authors did not explain why larger vessels responded better than smaller vessels.