

Journal Watch

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Intralesional 5-fluorouracil in the treatment of keloids: An open clinical and histopathologic study

Kontochristopoulos G, Stefanaki C, Panagiotopoulos A, Stefanaki K, Argyrakos T, Petridis A, et al.
J Am Acad Dermatol 2005;52:474-9.

Twenty patients, 11 males and 9 females, aged 12 to 65 years were recruited to evaluate the efficacy of intralesional 5-fluorouracil (5-FU) in the treatment of keloids. The sizes of the lesions varied from 1 to >5 cm and numbers from 1 to >20, with durations varied from 0.2 to 20 years. Eleven patients had failed other treatments such as corticosteroid injections, silicone gel, surgical excision and cryotherapy.

All patients received once weekly intralesional 5-FU (50 mg/mL) with dosages depending on the extent of the lesions but not exceeding 100 mg per session. Ten patients had punch biopsies specimens taken from the injection sites before and after six sessions of 5-FU treatment. Treatment was terminated once the result was satisfactory and the mean number of treatment sessions was seven. Reduction in keloid volume was noted in 95% of the cases with two patients improved by 25%, eight patients by 50%, eight patients by 75% and one showed complete resolution. The response was found to correlate with the duration of the keloids. Histopathological improvement showing decrease in inflammation, diminution of hyalinized collagen fibers, less prominent vascularity and flattening of the dermal papillae without signs of atrophy were consistent with the improvement seen clinically. Pain, superficial

ulceration and hyperpigmentation were the complications most commonly seen. Recurrence was found to correlate with the duration but not the size of the keloids. It was shown that 82% of the patients having a disease duration of less than two years showed no relapse in one year, while 75% of those having a disease duration of more than two years relapsed in one year.

The authors concluded that intralesional 5-FU may play a role in the treatment of keloids but this therapy has a high recurrence rate.

Long-term treatment of atopic dermatitis with pimecrolimus cream 1% in infants does not interfere with the development of protective antibodies after vaccination

Papp KA, Breuer K, Meurer M, Ortonne JP, Potter PC, de Prost Y, et al.
J Am Acad Dermatol 2005;52:247-53.

This 2-year prospective study recruited 91 patients, aged 3 to 23 months, with mild to moderate atopic eczema, to evaluate the effect of pimecrolimus cream 1% on the development of post-vaccination protective antibodies.

Seventy-six patients received pimecrolimus twice daily for two years and 15 patients received control treatment (vehicle plus moderately potent corticosteroid) for the first year and pimecrolimus for the second year. Patients in the test group were instructed to use pimecrolimus to affected areas

at the first sign or symptom of flare. Moderately potent topical corticosteroids were allowed for flares not prevented by pimecrolimus applied in this manner. Vaccination history was obtained and the immune response to vaccination against tetanus, diphtheria, measles, and rubella was evaluated at month 18 and 24. Serum levels of tetanus- and diphtheria-neutralising antitoxins and levels of neutralising measles and rubella antibodies were measured. The results were compared with the sero-prevalence in the general age-matched paediatric populations reported in the literature. The sero-positive rates for the tested group irrespective of vaccination history were 93.6% for tetanus, 88.6% for diphtheria, 88.5% for measles, and 84.4% for rubella and were found to be comparable with those reported in literature. There was not any relationship between the development of an immune response to each vaccination and the usage of pimecrolimus during the vaccination period (within 28 days). This may be accounted for by the negligible systemic absorption of topically applied pimecrolimus.

It was thus concluded that topical pimecrolimus cream 1% treatment for atopic dermatitis in early childhood does not interfere with the development of a normal response to vaccinations. This study was sponsored by Novartis Pharma.

Mycosis fungoides – a retrospective study of 40 cases in Hong Kong

Ku LS, Lo KK.

Int J Dermatol 2005;44:215-20.

This is a multi-clinic, 35-year, retrospective study to determine the clinico-pathological characteristics, treatment and disease outcomes of 40 patients with mycosis fungoides (MF)/ Sezary syndrome in the Social Hygiene Service, Hong Kong.

There were 27 males and 13 females and the mean age at diagnosis was 56.4, about 10 years

younger than that in the West and Japan. The incidence in Hong Kong was estimated to be 0.044 per 100,000. The average duration from onset of symptoms to diagnosis was 95.6 months and that from first seen by dermatologists to diagnosis was 12.7 months. Eighty-five percent of the patients presented with patches and plaques without lymph node or visceral involvement. Pruritus was absent in 40% of the patients. An average of 1.48 biopsies were needed to establish the diagnosis and only 58% of the MF skin biopsies were reported as histologically diagnostic of MF. Four most frequently encountered histological features that attained statistical significance were atypical lymphocytes, epidermotropism, interface changes and Pautrier's microabscesses. Eighty percent of the patients were in stage IA & IB disease. Sixty-nine percent of all patients were treated with psoralen-UVA as their initial therapy and the complete response rate and relapse rate were 78.3% and 66.6% respectively. Disease progression to more advanced stages was only seen in 15% of the patients. The 5-year survival rates for the whole group and stages IA & 1B patients were 88.8% and 100% respectively.

In conclusion, MF is rare among Hong Kong Chinese and majority presented as skin-limited non-progressive disease.

Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis

Chalmers RJ, Kirby B, Smith A, Burrows P, Little R, Horan M, et al.

Br J Dermatol 2005;152:444-50.

Repeated liver biopsies are recommended to monitor psoriatic patients receiving long-term methotrexate. However, another suggestion is to monitor the serum procollagen III aminopeptide

(PIIINP) serially followed by selective liver biopsies. A multi-centre audit was conducted to compare the health costs and outcomes between the two approaches.

For a period of 24 months, 166 patients from two intervention groups were monitored by serial serum PIIINP measurement and then subjected to selective liver biopsies if the serum PIIINP was raised. On the other hand, 87 patients from two control groups were monitored by the standard guideline using repeated liver biopsies.

The need for liver biopsy was reduced by sevenfold in the intervention groups (respectively 0.04 and 0.02 biopsies/patient/year) as compared to the two control groups (0.26 and 0.30 biopsies/patient/year). Clinical management was altered in one out of five patients biopsied in the intervention groups as compared to one out of 16 patients in the control groups.

It is concluded that PIIINP monitoring is cost saving in reducing unnecessary liver biopsies in psoriatic patients receiving long-term methotrexate.

Histologic and ultrastructural analysis of ultraviolet B laser and light source treatment of leukoderma in striae distensae

Goldberg DJ, Marmur ES, Schmults C, Hussain M, Phelps R.
Dermatol Surg 2005;31:385-7.

Ultraviolet B (UVB) laser and light source emitting UVB have been shown to induce repigmentation of striae distensae. This study analysed the histologic and ultrastructural changes of melanocytes after treatment with an UVB-emitting laser and light source.

A total of ten subjects were selected. They were between 20 and 45 years old, with hypopigmented striae for at least two years and occurred on the

trunk or extremities. Five were treated with XeCl excimer UVB laser emitting monochromatic laser light at 308 nm. The other five were treated with a UVB light source. Treatment started at their minimal erythema dose and treatment dose was increased by 10% each treatment until post-treatment erythema occurred. Treatment was continued until 10 treatments were completed with either full repigmentation or until there was a 75% or greater increase in pigment in the treatment area. Biopsies were taken before and six months after the last treatment. The histologic and ultrastructural changes in melanocytes were analysed using standard and electron microscopy. All patients showed some persistence of clinically significant pigmentation at six months after the last treatment. In addition, biopsy analysis showed an increase in melanin content, hypertrophy and increased number of melanocytes in all patients. Such findings were correlated with the persistence of pigment and no difference was found between laser and light source.

The authors concluded that repigmentation of striae distensae was due to not only the increase in size and melanin content, but also the number of melanocytes, as shown histologically and ultrastructurally. The increase in number of melanocytes might account for the relative long-lasting repigmentation effect.

Photodynamic therapy: new treatment for therapy-resistant plantar warts

Schroeter CA, Pleunis J, van Nispen tot Pannerden C, Reineke T, Neumann HA.
Dermatol Surg 2005;31:71-5.

The aim of this study is to evaluate the possibility of using photodynamic therapy (PDT) to treat recalcitrant plantar warts.

A total of 31 patients with 48 therapy-resistant plantar warts were randomly selected. The mean

age was 29 years (range 6-74). The mean number of warts per patient was 1.5 (range 1-4) and the mean duration of warts was 33 months (range 1-156 months). Each wart was scrapped using a blunt scalpel down to papillary dermis. Then δ -aminolevulinic acid in 20% diflucortolone base was applied topically to the warts for four to eight hours, followed by light irradiation for 15 to 20 minutes. Patients were retreated every two to four weeks if warts persisted.

The total clearance rate was 88% and the average number of treatment session per wart was 2.3. Older patients had a lower clearance rate (p value in the univariate logistic regression model: 0.0781). On the other hand, longer irradiation time (p=0.1338) and larger size of warts (p=0.1679) tended to have higher clearance rates. No correlation was found between complete clearance and duration of warts, mean treatment energy, number of treatments and the mean incubation time (p values between 0.27 and 0.70). Out of 111 treatment sessions, the reported adverse effects included pain (18%), tingling (10%), itching (6%) and hypopigmentation (1%).

The author concluded that recalcitrant plantar warts could be successfully treated with PDT and without serious adverse effects. Further studies should be needed to compare PDT with standard treatments for previously untreated warts.

Sexually transmitted infections among brothel-based sex workers in Bangladesh: high prevalence of asymptomatic infection

Nessa K, Waris SA, Alam A, Huq M, Nahar S, Chawdhury FA, et al.
Sex Transm Dis 2005;32:13-9.

This is a cross-sectional study on sexually transmitted infections (STIs) prevalence among

sex workers (SWs) in four randomly selected brothels in Bangladesh between August 2002 and April 2003. All SWs were eligible for participating in the study irrespective of symptoms. The participants were assessed on the knowledge of STIs and HIV and their prevention. Gynaecological examination, investigations including wet film, Gram's stain, gonococcal culture, chlamydia PCR tests and serology for syphilis were performed. HIV was not tested because the SWs were already enrolled in the HIV-surveillance program.

Totally 439 SWs were enrolled in the study and 95% returned for treatment and counselling. 218 (49.6%) were symptomatic and 221 (50.4%) were asymptomatic. No significant differences were found between the two groups in sexual behaviour and knowledge. Majority (99.1%) had knowledge about STIs and HIV, and 43% knew about their prevention methods. Although 96% had negotiated for condom use, only 29% always used condom with their clients.

The commonest symptoms were lower abdominal pain (28.9%), dyspareunia (25.5%), vaginal discharge (20.5%), dysuria (14.4%), vaginal itching (9.8%) and genital ulcer (1.8%). Abnormal vaginal discharge was the commonest finding on speculum examination in both symptomatic and asymptomatic cases. Gonococcal infection was found in 17.5% while 15.5% had chlamydial infection. There was no significant difference between the prevalence of these two diseases in the symptomatic and asymptomatic groups. Genital wart was found in 5.7%. Vesicles were found in 3%. Positive syphilis serology was found in 31.5% and 6.6% had active syphilis (RPR > 1:8). Cervical infections were associated with younger age and condom use. Vaginal discharge, dyspareunia and endocervical mucopus were significantly associated with gonococcal and chlamydial cervical infections.

Topical phenytoin suspension and normal saline in the treatment of leprosy trophic ulcers: a randomised, double-blind, comparative study

Bhatia A, Nanda S, Gupta U, Gupta S, Reddy BS. *J Dermatol Treat* 2004;15:321-7.

The authors conducted a prospective, parallel, double-blind, randomised study in 45 leprosy patients with acute, simple trophic ulcers. Acute simple ulcer was defined as ulcer involving only skin and subcutaneous tissue without bone for less than three months. The subjects were randomised into three groups to receive four weeks of treatment. Two groups received daily 2% and 4% phenytoin wound dressing respectively; the control group received daily normal saline (NS) dressing. Phenytoin sodium powder was dissolved into NS to prepare a suspension for dressing. The end point was measured by percentage reduction in surface area of ulcer, appearance of healthy granulation tissue, cessation of discharge, negative bacterial culture and the overall clinical grading of healing. The result was assessed weekly by a blinded investigator.

The study demonstrated that phenytoin dressing was superior to NS. The reduction of ulcer size, appearance of granulation tissue was significantly better in the treatment groups. Eleven patients in each treatment group showed complete healing comparing to none in the control. No significant difference was found between the two treatment groups. No adverse effect was reported.

The author concluded that topical phenytoin can significantly promote wound healing in acute, simple trophic ulcers of leprosy and is a cost-effective treatment option to prevent morbidity and mortality of patient.

Clobetasol proprionate shampoo 0.05% and calcipotriol solution 0.005%: A randomised comparison of efficacy and safety in subjects with scalp psoriasis

Reygagne P, Mrowietz U, Decroix J, de Waard-van der Spek FB, Acebes LO, Figueiredo A, et al. *J Dermatol Treat* 2005;16:31-6.

This multicentre, randomised, investigator-masked parallel group study compared the efficacy and safety of the short contact therapy with 0.05% clobetasol proprionate (CP) shampoo with 0.005% calcipotriol solution in treating scalp psoriasis.

151 subjects with moderate to severe scalp psoriasis were randomised to receive CP shampoo or calcipotriol solution for four weeks. CP shampoo was applied once daily on a dry scalp and left for 15 minutes before rinsed off. Calcipotriol solution was applied twice daily without rinsing. The efficacy was measured by the global severity score (GSS) and the total severity score (TSS). 137 subjects completed the study. Seven of those who withdrew from the study belonged to the calcipotriol group because of adverse reaction. The study demonstrated the efficacy of CP shampoo was superior to calcipotriol solution in terms of TSS and GSS. CP shampoo was more effective in reducing symptoms such as erythema, plaque thickening, adherent desquamation and pruritus. Side effects were more common in the calcipotriol group. Among which, burning sensation was statistically more significant. Other adverse effects such as telangiectasia and cutaneous atrophy were not different significantly between the two groups.

The authors concluded that short contact therapy with CP shampoo was more effective and well-tolerated than calcipotriol solution in the management of scalp psoriasis. The short contact

therapy with high potent topical steroid minimised its potential side effects. Extended long-term continuous use of topical steroid of high potency is not recommended. The regime of CP shampoo in actual practice has to be determined. This study was funded by Galderma R&D.

Biological effects of bexarotene in cutaneous T-cell lymphoma

Budgin JB, Richardson SK, Newton SB, Wysocka M, Zaki MH, Benoit B, et al.
Arch Dermatol 2005;141:315-21.

Bexarotene is a novel third-generation retinoid X receptor-selective retinoid. Its effects on malignant peripheral blood T cells in patients with Sezary syndrome (SS) and high tumour burden (>50% peripheral blood mononuclear cells PBMCs) were studied. Bexarotene was incubated with PBMCs from these patients at concentrations of 1 μ M and 10 μ M for 48, 72, and 96 hours. The effects on apoptosis, interleukin-4 (IL-4) levels and γ -interferon (γ -IFN) were measured.

Nine patients were studied. No apoptosis was seen at 48 hours. Apoptosis of the PBMCs at 72 hours incubation was seen with 1 μ M and 10 μ M bexarotene in three (33%) patients and six (67%) patients respectively. No apoptosis was observed in three (33%) samples with either concentration.

Apoptosis of the PBMCs was also increased when interferon- α was added but no synergistic effect was seen with bexarotene. A 50% decrease in IL-4 production was seen in five (45%) samples when 10 μ M bexarotene was added, while in the remaining six samples IL-4 production was increased by bexarotene. IL-4 production remained unchanged in three (27%) samples. This correlated with resistance to apoptosis. The production of γ -IFN was increased by interleukin-2 (IL-2), but the

combination of bexarotene and IL-2 did not lead to a further increase in production of γ -IFN.

It was therefore concluded that bexarotene induces apoptosis in T lymphocytes in patients with SS. However, there is a subset of patients who are resistant to these effects. Inhibition of IL-4 by bexarotene is seen in those who demonstrate apoptosis with bexarotene.

Long-term follow-up of patients with early-stage cutaneous T-cell lymphoma who achieved complete remission with psoralen plus UVA monotherapy

Querfeld C, Rosen ST, Kuzel TM, Kirby KA, Roenigk HH, Prinz BM, et al.
Arch Dermatol 2005;141:305-11.

The long-term outcome of 66 patients with stage IA, IB or IIA mycosis fungoides (MF) successfully treated with psoralen-UVA monotherapy (PUVA) was evaluated in this retrospective study.

The age at presentation varied between 22 and 89 years (median 57 years in the non-relapse group and 54 years for the relapse patients). Thirty-three patients relapsed while thirty-three cases who stayed in remission. The median disease-free interval for relapse and non-relapse patients was 39 months (range 2-127 months) and 84 months (range 5-238 months respectively). The male to female ratio was 1:1.4 and 1:1.8 respectively.

The median cumulative PUVA dose was higher in non-relapse patients when compared to relapse cases (186 J/cm² vs 108 J/cm²; P=0.03) and relapse status was not affected by clinical stage. The median time to complete remission (CR) was four months.

For stage IA cases, the actuarial survival rates for 5, 10, and 15 years were 94%, 82% and 82%

respectively and in stage IB/IIA patients, were 80%, 69%, and 58% respectively. The median follow-up time was 94 months (range 5-242 months). For stage IA, disease free survival rates at 5 years and 10 years were 56% and 30% and for stage IB/IIA, 74% and 50% respectively. No statistical difference in overall survival was detected between non-relapse cases and relapse cases. Twelve out of the 33 relapse patients responded to PUVA and remained disease-free. Chronic photodamage was present in 18 (27%) patients and skin malignancy (squamous cell carcinoma, Bowen's disease, basal cell carcinoma) developed in 17 (26%) patients.

The authors concluded that PUVA is effective in inducing remission in MF but needs to be balanced against the risk of photodamage and skin malignancy. In addition, long-term survival is not affected by the relapse status.

Patch testing with egg represents a useful integration to diagnosis of egg allergy in children with atopic dermatitis

Giusti F, Seidenari S.

Pediatr Dermatol 2005;22:109-11.

The role of patch testing with egg together with skin prick tests in children with atopic dermatitis was investigated in this study. These results were

compared to a repeated open food challenge with egg, after a three to four weeks egg, milk and peanut elimination diet.

Eighty-five patients with atopic dermatitis (37 boys, 48 girls) with an average age of 6 ± 3.9 years (range 6 months to 14 years) were studied. There was a 77% agreement between skin prick tests and patch tests for egg white, being positive in 15 and 16 children respectively. Patch testing of egg yolk and/or egg white was positive in 36.5% and for skin prick tests, 18.8% cases were positive. There was an eczematous response in 26 cases (30.6%) after food challenge. A positive patch test and skin prick test was found in 77% and 46% of these cases respectively. Eight of these children reacted to both tests and twelve children showed a response to patch testing only. Four children reacted to skin prick test alone. However, 18% of those cases who did not react to open food challenge with egg showed a positive patch test and 7% had a positive skin prick test. Patch testing had a higher sensitivity than skin prick test (79.6% vs 46.2%) but the specificity was lower than skin prick testing (81.4% vs 93.2%).

It was concluded that patch testing combined with skin prick tests will increase the detection rate for egg allergy. However, practical problems such as lack of a commercial preparation for food in patch testing and variations in allergen quality when testing with fresh food remain to be overcome.



Web sites of Dermatology & Venereology in Hong Kong

The homepage of The Hong Kong Society of Dermatology & Venereology
<http://www.medicine.org.hk/hksdv/>

Hong Kong Journal of Dermatology & Venereology
 (Official Publication of The Hong Kong Society of Dermatology & Venereology)
<http://www.medicine.org.hk/hksdv/bulletin.htm>

The homepage of The Asian Dermatological Association
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