

Journal Watch

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Low-dose isotretinoin in the treatment of acne vulgaris

Amichai B, Shemer A, Grunwald MH.
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Isotretinoin has been prescribed increasingly to moderate cases of acne that are unresponsive to conventional therapy. The classical recommended dose has been 0.5 to 1.0 mg/kg/day for four to eight months, which may cause many side effects that are dose dependent. This study looked into the efficacy and side effects of low-dose isotretinoin 20 mg per day for six months in 638 patients with moderate papulo-pustular acne.

Patients were evaluated every two months by the same physician. Complete blood counts, liver and lipid profiles were tested at baseline, four and ten weeks after commencement of treatment. Patients were divided into two age groups: 12-20 years and 21-35 years. It was found that 94.8% and 92.6% of the patients achieved significant improvement or complete remission, whereas 5.2% and 7.4% experienced treatment failure and required another course of isotretinoin in the two groups respectively. In the four-year follow-up, relapses were seen in 3.9% and 5.9% of the patients in the two groups respectively. In both groups, the most common side effects were mild cheilitis and xerosis in 91% and 43% of the patients respectively. Abnormal serum lipids values and liver enzymes were only seen in 4.2% and 4.8% respectively, compared with 10% in patients receiving the classical regimen. There was no statistically significant difference in improvement and relapse rates among the two groups and no difference was found between the two genders.

It was concluded that low-dose isotretinoin at a dose of 20 mg per day for six months was effective in treating moderate acne. Such regime was associated with a low incidence of side effects and at a lower cost.

A retrospective cohort study of Southeast Asian patients with large congenital melanocytic nevi and the risk of melanoma development

Chan YC, Giam YC.
J Am Acad Dermatol 2006;54:778-82.

In Caucasians with large congenital melanocytic nevi (LCMN), the life-time risk of developing melanoma is estimated to be 4.5-10%. This was a retrospective cohort study to determine the risk of melanoma development in patients with LCMN conducted in a predominantly Asian society in Singapore.

Thirty-nine patients (23 males and 16 females; mean age 18.8 years) with CMN that covered at least 5% of the body surface area (range: 5-40% and mean: 12.2%) were studied. Fifteen of them had giant CMN, which are CMN that were predicted to attain at least 20 cm diameter in adulthood. The diameter of the CMN in the rest of 24 patients ranged from 10 to 17 cm. The average period of follow-up was 16.9 years. Altogether, five skin biopsies were performed on patients who developed nodules from within the nevi. None of them showed dysplastic or malignant transformation. Seven patients with LCMN on the scalp, face or back received magnetic resonance imaging of the head or

thoracolumbar spine and none showed features of leptomeningeal melanocytosis. A retrospective search for malignancy using database of the National Cancer Registry in Singapore revealed no case of malignancy among all the patients studied.

It was concluded that the risk of melanoma in Asian patients with LCMN is low. However, the small sample size in this study made it difficult to estimate the life-time risk of developing melanoma in patients with LCMN.

A comparison of Q-switched alexandrite laser and intense pulsed light for the treatment of freckles and lentigines in Asian persons: a randomized, physician-blinded, split-face comparative trial

Wang CC, Sue YM, Yang CH, Chen CK.
J Am Acad Dermatol 2006;54:804-10.

This trial compared the efficacy and side effects of Q-switched alexandrite laser (QSAL) and intense pulsed light (IPL) for freckles and lentigines treatment in Asians.

It recruited 15 Taiwanese women with facial freckles and 17 with facial lentigines to receive on one cheek one session of QSAL and two sessions of IPL on the other cheek. Patients were given antibiotic ointment topically on the laser side till the lesions healed, then sunscreen to prevent post-inflammatory hyperpigmentation (PIH) and re-pigmentation. Evaluations were conducted at baseline and weeks 2, 4, 8 and 12 with digital photography documentation. The photographs were assessed by three independent, blinded physicians to evaluate the extent, the darkness, and the density of the pigmented lesions. It was found that the improvement rates after one session of QSAL was significantly higher than that after one and two sessions of IPL for patients with freckles. In patients with lentigines, the improvement rates after both treatments were

similar. PIH was noted in 28% of the patients within two to four weeks after QSAL and none after IPL. More patients with lentigines (47%) developed PIH after QSAL treatment than patients with freckles (7%) ($p=0.01$). The incidence of PIH caused by QSAL was significantly higher than that associated with IPL in patients with lentigines ($p=0.001$), but not in patients with freckles ($p=0.05$). Such a difference might be due to the melanocytic hyperplasia in lentigines in contrast to hyper-melanosis in freckles.

It was concluded that both QSAL and IPL were effective in the treatment of freckles and lentigines in Asians. The risk of PIH caused by QSAL was higher in patients with lentigines than freckles.

Folic acid supplementation during treatment of psoriasis with methotrexate: a randomized, double-blind, placebo-controlled trial

A Salim, E Tan, A Ilchysyn, Berth-Jones J.
Br J Dermatol 2006;154:1169-74.

The issue of folic acid (FA) supplementation during treatment of psoriasis with methotrexate (MTX) remains controversial. This study was a randomized, double-blind, placebo-controlled trial to evaluate the effects of FA supplementation on the therapeutic response of psoriasis to MTX.

Twenty-two psoriatic patients on MTX treatment were recruited. Patients were randomized to receive either FA 5 mg once daily or placebo for 12 weeks. The dose of MTX was not allowed to change throughout the study. Patients were assessed using the Psoriasis Area and Severity Index (PASI), horizontal visual analogue scale (VAS) and Dermatology Life Quality Index (DLQI) at 3-week interval.

The mean PASI in the FA group increased from 6.4 at baseline to 10.8 at 12 weeks with a mean change of 4.4. In contrast, the mean PASI in the

placebo group decreased from 9.8 at baseline to 9.2 at 12 weeks with a mean change of -0.6. The difference in the mean change of PASI, VAS and DLQI were all significant ($p < 0.05$). Few adverse effects were reported. The mean lymphocyte count rose from 2.07 to 2.12 x 10⁹/L while it decreased from 1.89 to 1.42 x 10⁹/L in the placebo group ($p < 0.05$).

It was concluded that FA supplementation during MTX treatment reduces the efficacy of MTX in the treatment of psoriasis. The main drawback of this study was the small sample size and short duration of the study. It was not certain whether FA reduces MTX toxicity to a degree greater than reduction in its efficacy. A larger trial of longer duration was needed to evaluate this possibility.

Influence of treatment of erosive lichen planus of the vulva on its prognosis

Cooper SM, Wojnarowska F.
Arch Dermatol 2006;142:289-94.

One hundred and fourteen women with a definite clinical diagnosis of erosive lichen planus of the vulva (ELPV) were studied to evaluate the clinical features, response to treatment and clinical course.

The mean age of self-reported vulval symptoms was 56.9 years (range: 27-79 years) and the mean age at diagnosis was 62.1 years (range: 29-82 years). The onset of vulval disease was as follows: pre-menopausal: 19 cases (17%); peri-menopausal: 17 cases (15%); post-menopausal: 78 cases (68%). Vulval pain (91 cases; 80%) and pruritus (74 cases; 65%) were the most common symptoms. Vulval erosions and white reticulations were seen in 111 cases (97%) and 94 cases (82%) respectively. Oral lichen planus (LP), perianal LP and cutaneous LP were seen in 67 cases (59%), 32 cases (28%) and 22 (19%) respectively. Scarring was present in 118 (95%) women as follows: mild: 25 cases (22%), moderate: 53 cases (46%), severe: 30 cases (26%).

Ultra-potent topical steroids (0.05% clobetasol propionate ointment) were effective in improving symptoms in 89 cases (94%). Sixty-three of these cases (71%) were symptom-free during treatment. Systemic treatments were not consistently effective. Vulval symptoms were improved in 86 cases (75%) cases (symptom-free: 62 cases (54%); partial response: 24 cases (21%); no change: 18 cases (16%); worse: 10 cases (9%)). The clinical signs except scarring resolved in only 10 cases (9%). Squamous cell carcinoma developed in three (3%) cases.

It was concluded that ultra-potent topical steroids were effective in treating ELPV and with time, symptomatic improvement can be seen in three-quarters of cases, and healing of erosions seen in 50% cases.

Combination of oral terbinafine and topical ciclopirox compared to oral terbinafine for the treatment of onychomycosis

Avner S, Nir N, Henri T.
J Dermatol Treat 2005;16:327-30.

The efficacy of a combination therapy of oral terbinafine and topical ciclopirox nail lacquer was compared with oral terbinafine monotherapy for the treatment of onychomycosis caused by dermatophytes. Patients were randomized to receive either a combination of 16 weeks of oral terbinafine 250 mg daily and nine months of topical ciclopirox nail lacquer once daily, or 16 weeks of oral terbinafine 250 mg daily alone. If only fingernails were involved, oral terbinafine was given for eight weeks instead. They were monitored at 0, 3, 6 and 9 months for clinical improvement, direct smear and mycological culture. Complete blood count and liver function test were monitored before and every six weeks till the end of oral terbinafine therapy.

Thirty-four patients were randomized to the combination therapy group and another 34

patients to monotherapy group. All had mycologically confirmed toe nail onychomycosis without lunula involvement and six had concomitant finger nail infection. *Trichophyton rubrum* was the commonest organism (n=65) and *Trichophyton mentagrophytes* accounted for the rest. The commonest clinical presentation was distal and lateral subungual onychomycosis (n=54), followed by white superficial onychomycosis (n=10) and proximal subungual onychomycosis (n=4).

After nine months of treatment, the complete cure rate (clinical and mycological cure rate) was 67.6% in the combination therapy group and 50% in the monotherapy group. The difference was not significant. The clinical cure and mycological cure rates were respectively 82.4% and 88.2% for the combination therapy group, and 58.8% and 64.7% for the monotherapy group. The difference in the clinical cure and mycological cure rates between the two groups were statistically significant (both $p < 0.05$). Younger age and shorter disease duration were significant prognostic indicators for both mycological cure and complete cure in the combination therapy group only ($p < 0.05$).

The authors concluded that the combination therapy of topical ciclopirox nail lacquer and oral terbinafine is a safe and more effective treatment for onychomycosis than oral terbinafine monotherapy.

A randomized, investigator-masked clinical evaluation of the efficacy and safety of clobetasol propionate 0.05% shampoo and tar blend 1% shampoo in the treatment of moderate to severe scalp psoriasis

Griffiths CEM, Finlay AY, Fleming CJ, Barker JNWN, Mizzi F, Arsonnaud S.
J Dermatol Treat 2006;17:90-5.

This was a multicentre, randomized parallel group

investigator blinded study to compare the efficacy, safety and cosmetic acceptance of clobetasol propionate 0.05% shampoo against tar blend 1% shampoo. The inclusion criteria were ≥ 18 years of age and with $\geq 15\%$ of the scalp area affected by moderate to severe psoriasis. Concurrent systemic treatment or aggravating drugs were not allowed. Clobetasol propionate shampoo was applied to dry scalp once daily for 15 minutes and then rinsed off. Tar shampoo was applied twice weekly to wet scalp before rinsing off. The subjects were assessed at baseline, week 2 and 4. The primary endpoint was the Total Severity Score (TSS) and Global Severity Score (GSS) at week 4. The secondary efficacy endpoints were scores for plaque thickness, desquamation, erythema and pruritus. The subjective global assessment of improvement and the scalp area involvement were also assessed. Cutaneous, ocular and overall systemic side effects were assessed.

A total of 162 subjects were randomized to clobetasol propionate shampoo (n=121) and tar blend shampoo (n=41) at a ratio of 3:1. Clobetasol propionate shampoo was superior to tar blend shampoo for TSS and GSS at week 4 and at week 2 (both $p = 0.0001$). The improvement of plaque thickness, desquamation, pruritus and erythema at week 4 was statistically significant in favour of clobetasol propionate ($p \leq 0.0002$). In the clobetasol propionate group, the area of scalp involvement decreased from 48% to 29%, comparing to 54% to 46% in tar shampoo at week 4 ($p = 0.0007$). Clobetasol shampoo had a significantly better cosmetic acceptability ($p \leq 0.017$) and subjective global assessment of improvement ($p < 0.001$) than tar shampoo. Significant changes for cutaneous atrophy, telangiectasia, blood pressure or ocular safety were not observed. However, more adverse effects were reported in the clobetasol propionate group (8%): itching, stinging and burning of the scalp, headache, tingling sensation after rinsing hair; and moderate to unacceptable worsening of psoriasis. One patient withdrew from the study due to intense itching and burning of the scalp.

The authors concluded that clobetasol propionate shampoo once daily is superior to tar shampoo twice weekly in treating moderate to severe scalp psoriasis because of increased efficacy and patient acceptance. This study received assistance from the Galderma Medical Affairs.

Value of sentinel node status as a prognostic factor in melanoma: prospective observational study

Kettlewell S, Moyes C, Bray C, Soutar D, MacKay A, Byrne D, et al.
Br Med J 2006;332:1423-5.

This was a single centre prospective observational study done at Scotland. The objective was to determine the prognostic value of sentinel node status in melanoma.

A total of 482 patients were recruited from 1996 to 2003. These patients had wide excision of primary melanoma, with tumour thickness of at least 1 mm and without clinical or biochemical metastasis. Sentinel node biopsy was performed within eight weeks from the surgery of the primary tumour. Sentinel nodes were identified by lymphoscintigraphy, γ probe, and intraoperative blue dye and examined by both conventional histopathology and immunopathology. Cox model for multivariate analysis was used to determine the prognostic significance of sentinel node status for survival as compared with other known prognostic factors.

One or more sentinel nodes were identified in 472 patients. There were 207 men and 265 women, with a median age 54 years. The median number of sentinel nodes identified was two (range one to five). One hundred and five patients (22%) had one or more positive sentinel nodes. At mean follow-up of 42 months, 44 (42%) were alive and disease free, 12 (11%) were alive with recurrence, and 46 (44%) died of melanoma. Of the 367 patients with negative sentinel node involvement, 299 (82%) were alive and disease free, 24 (6.5%)

were alive with recurrence and 31 (8.4%) died of melanoma. The survival difference between positive and negative sentinel node biopsy was highly significant for all levels of tumour thickness greater than 1 mm ($p < 0.001$). Multivariate analysis showed that sentinel node status was independent of tumour thickness and ulceration. Clark levels, age at melanoma diagnosis, sex and body site of primary tumour did not give extra prognostic value.

In conclusion, sentinel node status is a highly significant prognostic factor in melanoma and should be considered as a staging procedure in centres entering patients into adjuvant studies.

Comparison of the surgical outcomes of punch incision and elliptical excision in treating epidermal inclusion cysts: a prospective, randomized study

Lee HE, Yang CH, Chen CH, Hong HS, Kuan YZ.
Derm Surg 2006;32:520-5.

This was a prospective, randomized study, done in Taiwan, to compare traditional elliptical surgical excision with punch excision for epidermal inclusion cysts. The cosmetic results, operative time, patient satisfaction, complications and long term recurrence were studied.

A total of 60 patients were recruited. Exclusion criteria were clinically infected or inflamed cysts, recurrent cysts, uncertain diagnosis or those who could not be followed up. The size or the location of a cyst did not affect the case selection. Either traditional elliptical surgical excision using the standard procedures or punch excision was assigned to patients on a random basis. During the punch excision, using 3, 4 or 5 mm dermal punch biopsies trephines, a small round incision was made in the middle of the cyst. Lateral pressure was applied to the base of the cyst to express the contents. The cyst wall was then removed through the punch opening followed by

wound closures. All the procedures were performed by the same dermatologist during the study period. Telephone interviews were completed for all participated patients after a follow-up period of 14 to 29 months.

Twenty-nine patients, 16 males and 13 females, average age 36.8 years, were assigned to elliptical surgical excision. Thirty-one patients, 21 males and 10 females, average age 38.2 years, were assigned to punch excision. The mean original size was 1.06 cm for the surgical excision group and 1.14 cm for the punch excision group. The former had a mean length of wound of 2.34 cm and operation time of 21.6 minutes while they were respectively 0.73 cm and 12.7 minutes for the latter ($p < 0.0001$ for both). Two patients of the surgical excision group had complications of prolonged erythema and inflammation over the operative wounds while one patient of the punch excision group had recurrence. Twelve of the 31 patients in the punch excision group were highly satisfied with the cosmetic results.

The authors concluded that punch excision produces a better cosmetic result for removing epidermal inclusion cysts and the recurrence rate was low. This technique is especially useful for cysts measuring 1 to 2 cm that are located on a cosmetically concerned site.

The epidemiology of childhood alopecia areata in China: a study of 226 patients

Xiao FL, Yang S, Liu JB, He PP, Yang J, Cui Y, et al. *Pediatr Dermatol* 2006;23:13-8.

A survey of 226 children with alopecia areata (AA) less than 16 years old was performed at 1st Hospital of Anhui Medical University in China. It studied the clinical and epidemiological profile of AA in childhood. Family history and heritability were also studied.

There were 131 boys and 95 girls (age range 2 to 15 years, median 11 years) with an age of onset between one to 15 years (median 10 years). Most (192, 84.96%) of the cases had patchy alopecia with under 50% involvement, whereas 20 cases (8.85%) had 50-99% involvement and eight cases (3.54%) and six cases (2.65%) had alopecia totalis and universalis respectively. Boys were affected more severely with extensive AA in 19.08% of boys as compared to 9.47% of girls respectively. There was no significant difference in age of onset and duration of AA between the two sexes. A previous history of AA was reported in 67 (29.6%) cases with greater severity in early onset and recurrent AA. The median duration of AA was significantly longer in recurrent cases than in primary cases (three months vs one month). Associated diseases (thyroid disease, atopic dermatitis, vitiligo, psoriasis) were seen in six cases.

A positive family history was present in 25 (11.06%) cases. In the first, second and third degree relatives, the prevalence rate for AA was 2.87%, 0.40%, 0.13% respectively, while the corresponding heritability of AA were 51.20%, 46.25%, 25.65% respectively.

The findings from this study showed that most patients had limited AA and there was a male preponderance. It was concluded that genetic factors are important in AA.

Impairment of skin barrier function is not inherent in atopic dermatitis patients: a prospective study conducted in newborns

Kikuchi K, Kobayashi H, O'goshi K, Tagami H. *Pediatr Dermatol* 2006;23:109-13.

Twenty-four full-term, newborn infants between two and 14 days of age (median five days) were examined to determine whether the barrier

dysfunction of the stratum corneum was inherent in patients with atopic dermatitis (AD). The transepidermal water loss (TEWL) and high-frequency conductance were measured to determine water barrier function of SC and the hydration state of the skin surface respectively. They were examined again at one, three and six months.

There was a family history of atopy in 19 cases. Apart from physiological xerosis, no skin lesions were seen on first examination. At two to three months, eczematous lesions were found in four of the 19 cases with a family history of atopy. There was no significant difference in skin surface hydration of the cheek and forearm between the four infants who developed AD, the 15 cases with a family history who remained normal and the five cases with no family history of atopy. The barrier function only became abnormal (increased TEWL value) with the onset of AD. There was no significant difference in skin surface lipid levels between these three groups. In cases with AD, the TEWL on the flexor surface of the forearm was significantly higher at three months than those without AD irrespective of family history of atopy. There was however, no difference at birth in TEWL between those who subsequently developed AD and those who remained normal.

It was therefore concluded that the decreased barrier function seen in AD cases is not inherent but results from skin changes during dermatitis.

Prevalence of sexually transmitted infections among long-distance truck drivers in Tongling, China

Chen XS, Yin YP, Gong XD, Liang GJ, Zhang WY, Pomeroy G, et al.

Int J STD AIDS 2006;17:304-8.

This was a cross-sectional study conducted among long-distance truck drivers in Tongling of Anhui Province in East China. This study consisted of a structured questionnaire, blood

and urine samples collection. Blood samples were tested for syphilis, using rapid plasma regain and confirmed by *Treponema pallidum* haemagglutination assay. HIV test were done using ELISA technique and confirmed by Western blot. Herpes simplex virus 2 (HSV-2) infection was detected by anti-HSV-2 specific IgG antibodies using ELISA HSV-2 kit. Urine samples were tested for *Neisseria gonorrhoea* and *Chlamydia trachomatis* using polymerase chain reaction. The study was integrated into a routine physical check to avoid stigmatisation.

A total of 550 truck drivers participated in the study (age: 20 to 53 years; mean: 32.5 years). There were 93.4% of participants who achieved up to secondary or high school education level. They had been working in the industry from less than one year to 30 years (median: 6 years), 71.8% were married and 90% were local residents. Majority (96.5%) was aware of sexually transmitted infections and HIV, and 91.1% knew about their harmfulness. Only 35.6% (149 of 418) used condom during their last sexual intercourse and 76.6% (236 of 308) used condom for <50% of sexual intercourse.

The prevalence of gonorrhoea and chlamydial infections were 8.1% (43 of 530) and 10.6% (56 of 530) respectively. Eleven of 530 (2.1%) had co-infection. Four (0.7%) were infected with syphilis and 4.4% (24 of 545) were HSV-2 antibody positive. No HIV infection was detected. Univariate analyses showed that absence of condom use during the last sexual intercourse was significantly associated with gonorrhoea infection ($p=0.04$), and high educational level was associated with syphilis infection ($p=0.03$).

This study showed high prevalence rates of *Chlamydia trachomatis* and gonorrhoea infection, but low prevalence rates of syphilis and HSV-2 infection among truck drivers in China. There was a need for health education, behavioural change interventions in this high-risk population.