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Journal Watch

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Treatment of dyshidrotic hand dermatitis with intradermal botulinum toxin

Swartling C, Naver H, Lindberg M, Anveden I.
J Am Acad Dermatol 2002;47:667-71.

As hyperhidrosis was an exacerbating factor in about 40% of pompholyx hand dermatitis, an open study was undertaken to assess the efficacy of intradermal botulinum toxin A (Btx A) on this dermatitis. Ten subjects with bilateral vesicular hand eczema were given intradermal Btx A on one hand, using the untreated side as control. Under regional nerve block, two units (U) of Botox® (0.02 ml, 100 U/ml) were injected every 15 mm on the volar aspect of the palm and fingers, giving a density of 0.8 U/cm^2. The mean total dose of Botox® given was 162 U.

Subjective assessment showed that seven of the ten patients had good or very good response at follow-up five to six weeks after the treatment. Six of these seven patients reported increased hand perspiration or aggravation of eczema in summer. Itching also decreased by a mean of 39% on the treated side on a visual analogue scale, compared to an increase of 52% on the control side. Objective assessment also showed a decrease in disease activity and improvement in clinical signs.

The authors suggested that Btx A was a valuable alternative for refractory vesicular hand eczema, especially if it was associated with increased sweating or exacerbation during summer.

A randomized, double-blind, placebo-controlled phase III study evaluating efficacy and tolerability of two courses of alefacept in patients with chronic plaque psoriasis

Krueger GG, Papp KA, Stough DB, Loven KH, Gulliver WP, Ellis CN.
J Am Acad Dermatol 2002;47:821-33.

Alefacept is a human fusion protein comprising the first extracellular domain of the lymphocyte function-associated antigen-3 fused to part of IgG_1. It would bind to CD2 on T-cells, inhibiting their activation and proliferation.

This randomized, double-blind placebo-controlled study assessed the efficacy and side effect profile of alefacept in 553 patients with chronic plaque psoriasis. All patients were at least 16 years of age and had psoriasis for over 12 months involving at least 10% body surface area. It included two 12-week treatment courses, comprising of once-weekly intravenous alefacept 7.5 mg or placebo, and a 12-week follow-up period after each course. The second course was given if the subject's psoriasis was not clear after the first 12-week follow-up period, CD4 count was at or above lower limit of normal, and no prohibited medications were taken. After the first course, 28% of alefacept-treated group and 8% of the placebo group attained a 75% or more decrease in the psoriasis area severity index (PASI) ($P<0.001$). For the patients given two courses of alefacept,

40% of them attained a 75% or more decrease in PASI while 71% attained a 50% or more decrease during the study duration. The treatment was well tolerated, with chills occurring more commonly in the first course (10% of treated group versus 1% of the placebo group). There was no significant difference in laboratory parameters between the treatment and placebo group. The authors suggested that alefacept was an effective therapeutic option for psoriasis.

Treatment of chronic actinic dermatitis with tacrolimus ointment

Uetsu N, Okamoto H, Fujii K, Doi R, Horio T.
J Am Acad Dermatol 2002;47:881-4.

This was an open study to investigate the efficacy of 0.1% tacrolimus ointment in treating patients with chronic actinic dermatitis (CAD). Six male patients (aged 51 to 80) with CAD not responding to topical corticosteroids, sunscreen and oral antihistamines were recruited. All were hypersensitive to both ultraviolet A and B by phototesting. They were instructed to apply 0.1% tacrolimus ointment twice daily to facial and neck lesions. The duration of follow-up ranged from six months to two and a half years. Clinical improvement was noted two weeks after initiation of treatment in all patients with decrease in pruritus, erythema, swelling and scaling. There were more substantial reduction in signs and symptoms four weeks onwards. Tacrolimus ointment was applied once daily if necessary after four weeks. The drug was well tolerated although all patients developed transient mild irritation at the onset. The authors suggested that tacrolimus was more effective than low- to mid-potency corticosteroids in the treatment of facial lesions of CAD. Further investigations on its efficacy and tolerability in patients with CAD might be warranted.

A randomized, observer-blinded trial of twice vs. three times weekly narrow band ultraviolet B phototherapy for chronic plaque psoriasis

Cameron H, Dawe RS, Yule S, Murphy J, Ibbotson SH, Ferguson J.
Br J Dermatol 2002;147:973-8.

This was an observer-blinded, randomized study to investigate the efficacy of twice weekly versus thrice weekly narrow band-UVB (NB-UVB) phototherapy. One hundred and thirteen patients, skin phototype I to III, with plaque psoriasis were randomized to receive either the twice weekly (58 patients) or thrice weekly (55 patients) regimen. NB-UVB was initially delivered at 70% of the minimal erythema dose and continued with an increment of 10% or 20% per session depending on skin types and erythema responses. There was no limit to the number of sessions and treatment was continued till clearance or for four sessions after reaching minimal residual activity. Forty patients in the twice weekly group and 44 patients in the thrice weekly group achieved complete clearance or minimal residual activity respectively ($p=0.21$). It took the former group 1.5 times longer in duration than the latter to attain clearance or minimal residual activity, a geometric mean of 88 versus 58 days ($p<0.0001$). Time to relapse, defined as the relapse of psoriasis leading to the use of therapies other than emollient alone, was not significantly different between the two groups. The proportion of patients with erythema was similar between the groups. It was therefore concluded that thrice weekly NB-UVB treatment achieved clearance of chronic plaque psoriasis more quickly than twice weekly treatment in a skin phototype I-to-III population.

Guidelines for the management of lichen sclerosus

Neill SM, Tatnall FM, Cox NH.
Br J Dermatol 2002;147:640-9.

Lichen sclerosus (LS) affects the anogenital area of paediatric and adult patients. Extragenital LS may also occur. Clinically active LS i.e. ecchymosis, hyperkeratosis and progressing atrophy should be treated. Ultrapotent topical corticosteroid ointment such as clobetasol propionate is the recommended and first line treatment for adult LS. Less potent topical corticosteroids like betamethasone dipropionate may be used in paediatric anogenital LS. Topical testosterone has been shown to be less effective than clobetasol propionate in recent research. Surgery should be reserved for malignancy and complications such as meatal stenosis. Cryotherapy, photodynamic therapy, laser therapy have been used with some success. For treatment failures, one should consider non-compliance to treatment, additional problems like contact allergy to medications, superimposed candidiasis and intraepithelial neoplasia. Mechanical problems due to scarring, such as phimosis or meatal stenosis, are also possible causes of treatment failure. The authors suggested follow-up in three months to assess compliance, response to treatment and for malignancy screening. It is stated that malignancy, if occurs, will do so rapidly. The patients can be reassessed six months later and then discharged to their primary care physicians if treatment response is satisfactory. Any persistent ulceration or new growth should be re-examined by an appropriate specialist for possible malignancy. For those patients with poorly controlled LS, long-term specialist follow-up is indicated. These patients usually have histological features of both LS and lichen planus. A small proportion may develop squamous cell carcinoma.

Frequent use of tobacco and alcohol in Chinese psoriasis patients

Zhang X, Wang H, Te-shao H, Yang S, Wang F.
Int J Dermatol 2002;41:659-62.

This was a case-control study conducted in northern China, recruiting 789 Chinese psoriatic patients and 789 healthy Chinese controls. It was the largest research on the effects of smoking and alcohol drinking on psoriasis in Chinese population. It analysed the patients' demographic data, the extent and severity of psoriasis, their smoking habit and alcohol consumption. The results showed that males in the case group consumed significantly more alcohol and tobacco than those in the control group ($p<10^{-6}$). Positive smoking history was present in 48.9% of case group versus 29.1% of control group. Positive drinking history was present in 29.8% of case group versus 9.2% of control group. In the female case and control groups, there is a significant difference in alcohol consumption ($p<10^{-4}$) but not in tobacco use ($p=0.4$). A significant dose-dependent effect between the amount of smoking and the severity of psoriasis was also demonstrated. Smoking was found to enhance chemotaxis and adherence of neutrophilic granulocytes. Release of peroxidases and other enzymes was also stimulated. These played an important role in the development and exacerbation of psoriasis. Furthermore, alcohol consumption could induce vasodilation, enhance vessel permeability and promote neutrophilic granulocytes migration and infiltration. Alcohol use also increased arachidonic acid content, suppressed adenyl cyclase and decreased cAMP. All these might induce epidermal cells proliferation. The authors suggested that restriction in alcohol and tobacco consumption might reduce the severity and frequency of psoriasis in Chinese.

Treatment of necrobiosis lipoidica with topical psoralen plus ultraviolet A

De Rie MA, Sommer A, Hoekzema R, Neumann HAM.

Br J Dermatol 2002;147:743-7.

A multicentre prospective study on the effect of topical psoralen plus ultraviolet A (PUVA) on necrobiosis lipoidica was undertaken. Thirty patients (27 women and three men) with biopsy-confirmed necrobiosis lipoidica were recruited. Thirteen of them were insulin-dependent diabetic. All subjects were treated previously with topical and/or intra-lesional corticosteroids without success. Twice weekly topical PUVA using an aqueous gel containing 0.005% psoralen was delivered using a standard Waldmann hand and foot PUVA 200 machine. The initial dose was 0.5 J cm^{-2} and was increased per session by 12.5% to a maximum of 10 J cm^{-2}. Clinical photographs were taken and results were classified as complete clearance (healing of ulceration and disappearance of erythema), improvement or worsening. A mean number of 20 (range 5-42) treatment sessions and a mean cumulative UVA dose of 69.4 J cm^{-2} (range 3.6-207.9) were delivered. Seventeen percent of the patients showed complete clearance after a mean of 22 treatment sessions (range 15-30), 37% showed improvement, 33% showed no effect and 13% worsened. High-frequency (20 MHz) ultrasound analysis was performed in 10 patients to assess the thickness and density of the lesional dermis. No difference was detected before and after topical PUVA. This study demonstrated that topical PUVA might be a useful therapeutic option for patients with necrobiosis lipoidica failing to respond to local corticosteroids.

A clinical study of childhood alopecia areata in Singapore

Tan E, Tay YK, Giam YC.

Pediatr Dermatol 2002;19:298-301.

An epidemiological study of alopecia areata (AA) affecting children before 16 years of age was performed. Totally 392 children were seen over a four-year period, accounting for 11.1% of the total number of AA cases diagnosed over this period. There were 323 (82.4%) cases with mild (less than 50%) involvement, and 69 (17.6%) cases with severe (over 50%) involvement. The male-to-female ratio was 1.4:1 and the duration of illness was less than six months in most (71.7%). The mean age at diagnosis was 11.2 years. Twenty-four patients (6.1%) had previous episodes of AA, of whom 15 cases presented with severe involvement. Nail changes were present in 33 (8.4%) patients. Thirty-three patients (8.4%) had a positive family history. An atopic history was noted in 104 patients (26.6%) but it had no correlation with the disease severity. Association with autoimmune diseases such as vitiligo and thyroid disorders was uncommon. Topical steroids were the first-line therapy. Intralesional triamcinolone was used in 280 cases with mild AA, of whom 160 (57.1%) and 211 (75.4%) showed a greater than 50% response at 12 and 24 weeks respectively. Nine patients with severe AA of less than one-year duration received oral prednisolone at a starting dose of 0.5 mg/kg/day and tapered over three to five months. Five cases showed more than 50% response at six months. Immunotherapy with squaric acid dibutyl ester resulted in more than 50% response at six months in 74.1% of 54 severe cases treated. Young age of onset, extensive AA, history of previous episodes and Down's syndrome were associated with poor response to therapy.

Congenital nevocytic nevi: follow-up of a Swedish birth register sample regarding etiologic factors, discomfort and removal rate

Berg P, Lindelof B.
Pediatr Dermatol 2002;19: 293-7.

The aims of this study were to investigate the frequency of removal of congenital melanocytic naevi (CMN), effect of maternal illness and smoking on the incidence of CMN, and its psychosocial effects. A questionnaire was sent to a sample of 185 persons registered in the Swedish Medical Birth Register as having CMN.

There were 150 respondents with a median age of 14 years (range 5-27 years). One hundred and twenty-eight respondents (85.3%) had true CMN while the remaining ones were other lesions like haemangiomas or café au lait spots. Fifty-one patients (39.8%) had undergone removal of CMN, of which 10 had large CMN and 41 had small CMN. The median age at operation was 9.7 years (range 0-25 years) and larger lesions were excised more often and earlier. Maternal illness and smoking in pregnancy were not associated with an increased incidence of CMN in the newborn. The presence of CMN resulted in extra precautions against sun exposure in 30% of respondents. Eight percent of subjects with true CMN felt that it affected their social activities. The median time for follow-up was 14 years and malignant melanoma was not reported in this sample.

The clonal nature of pityriasis lichenoides

Weinberg JM, Kristal L, Chooback L, Honig PJ, Kramer EM, Lessin SR.
Arch Dermatol 2002;138:1063-7.

Pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC) are believed to be benign cutaneous lymphocytic infiltrates and have been speculated to be related. This study investigated the T-cell clones in both PLEVA and PLC by using polymerase chain reaction/denaturing gradient gel electrophoresis (PCR/DGGE).

Twenty-seven skin tissue samples with histological diagnosis of PLEVA (14) and PLC (13) were analysed by PCR/DGGE. T-cell receptor rearrangements were detected in eight (57%) of PLEVA specimens, while only one (8%) PLC specimen showed T-cell receptor rearrangements. These findings suggested that monoclonal expansion was more common in PLEVA, while the lymphocytic infiltrate in PLC was predominantly polyclonal. It was therefore speculated that PLEVA might arise from a subset of T-cells in PLC and that these clones were the result of a variable host response to various pathogenic factors. In PLC, a small number of these clonal T-cells were present, often below the level of sensitivity of PCR. A greater influx of these monoclonal T-cells in the infiltrate resulted in the clinical features of PLEVA and recognition of the T-cell clone by PCR. This hypothesis still requires more supporting evidence, for example, from analysis of both PLEVA and PLC lesions from individual patients to delineate the clonal evolution proposed.

Correlations between clinical patterns and causes of erythema multiforme majus, Stevens-Johnson syndrome, and toxic epidermal necrolysis

Auquier-Dunant A, Mockenhaupt M, Naldi L, Correia O, Schroder W, Roujeau JC.
Arch Dermatol 2002;138:1019-24.

A multinational prospective case-control study was performed to investigate the relationship among erythema multiforme majus (EMM), Stevens-Johnson syndrome (SJS), and toxic

epidermal necrolysis (TEN) in terms of their clinical patterns and aetiology. The authors defined EMM as consisting of acrally distributed typical targets or raised atypical targets. SJS was characterised by widespread blisters on macules and flat atypical targets. The area of involvement for both EMM and SJS was less than 10% body surface area. Totally 552 patients and 1720 control subjects were recruited. Of the former, there were 88 EMM, 150 SJS, 108 SJS-TEN overlap, 114 TEN and 92 unclassified cases. Compared to SJS, TEN and SJS-TEN overlap, patients with EMM were younger (median 24 vs 45 years) and were nearly never associated with collagen vascular disease, HIV infection, and cancer. Involvement of two or more mucous membranes and fever over 38.5°C were less common. However, recurrence rate was 10-fold higher for EMM (30%).

SJS, SJS-TEN overlap and TEN were associated with a drug aetiology in 64%, 66% and 65% of cases respectively. Herpes infection was associated with EMM (29% for recent herpes, 17% for recurrent herpes) and SJS (6% cases for recent herpes, 10% for recurrent herpes). Only 18% of EMM cases were associated with drug exposure. TEN and SJS-TEN overlap were not associated with herpes infection. These findings suggested that EMM differed from SJS and TEN in severity and aetiology, with practical implications for managing these conditions.

Local treatments for cutaneous warts: systematic review

Gibbs S, Harvey I, Sterling J, Stark R.
BMJ 2002;325:461-8.

A meta-analysis was conducted to evaluate the effectiveness of different local therapies for cutaneous warts. All studies which randomized subjects to different interventions were examined. The main outcome used was the complete clearance of lesions. Totally 50 trials were included but most were generally of poor quality. Heterogeneity in methodology also affected data pooling. The best evidence came from six placebo-controlled trials for topical salicylic acid with a clearance rate of 75% (144 of 191) in treated cases versus 48% (89 of 185) in controls (odds ratio OR=3.91; 95% confidence interval, 95% CI=2.40-6.36). For cryosurgery, no significant difference in cure rates was found in two small trials comparing it with placebo or no treatment (OR=0.82, 95% CI=0.16-4.24). Two larger trials showed that there was no significant difference in cure rate between salicylic acid and cryosurgery (OR=1.15, 95% CI=0.72-1.82). Other trials mainly compared different regimens of cryosurgery. One trial revealed no significant benefit of prolonging three weekly cryotherapy beyond three months (about four freezes). Some evidence existed for the efficacy of topical dinitrochlorobenzene versus placebo in two small trials (OR=6.67, 95% CI=2.44-18.23). No consistent result was obtained for intralesional bleomycin in five studies. The evidence for the effectiveness of topical fluorouracil, intralesional interferons, photodynamic therapy and pulsed dye laser was limited.