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Journal Watch

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A prospective randomized controlled trial comparing infliximab and etanercept in patients with moderate to-severe chronic plaque-type psoriasis: the Psoriasis Infiximab vs. Etanercept Comparison Evaluation (PIECE) study

de Vries AC , Thio HB, de Kort WJ, Opmeer BC, van der Stok HM, de Jong EM, et al.
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There are no direct comparison data between infliximab and entanercept in the treatment of psoriasis. This study was a multicenter, randomised control trial done in the Netherlands to compare the efficacy, outcome of etanercept vs. infliximab in the management of moderate to severe chronic plaque psoriasis. Patients (age 18-75 years old) with Psoriasis Area and Severity Index (PASI) ≥10 and/or body surface area (BSA) ≥10% and/or PASI ≥8 plus a Skindex-29 score ≥35 were included. Etanercept 50 mg subcutaneously twice weekly or infliximab 5 mg per kg was given intravenously at week 0, 2, 6 and every 8 weeks.

Speed of onset of action was defined as proportion of patients reaching PASI 75 by week 6. It was achieved in 4.3% patients in the etanercept group and 52% patients in the infliximab group. PASI 75 was achieved in 22% of etanercept group and 76% of infliximab group (P<0.001) at 12 week. In the etanercept group, 35% compared to 72% of infliximab group (P=0.01) achieved PASI 75 at 24 weeks. Fifty percent of the etanercept group (n=5) and 67% of infliximab group (n=6) (P=0.65) achieved PASA 75 at 48 weeks. There was no significant difference in duration of remission between etanercept group (13.7 weeks) and infliximab group (15.5 weeks). Most side effects in both groups were mild. In conclusion, both treatments were effective. Infliximab has more rapid onset of action and a better short-term clinical response but there is no significant difference at 48 weeks with respect to duration of remission after cessation of treatment and maintenance treatment after 48 weeks.

Photodynamic therapy using intense pulsed light for treating actinic keratoses and photoaged skin of the dorsal hands: a randomized placebo-controlled study

Kohl E, Popp C, Zeman F, Unger P, Koller M, Landthaler M, et al.
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Actinic Keratosis (AK) is a common disease and studies have shown that it is found in 49% men and 28% women over 45 years of age. It has the potential to progress to squamous cell carcinoma in up to 20% of patients. Photodynamic therapy with intense pulsed light (IPL) combined with a photosensitiser was found to be effective in treatment of AK in facial skin but the thin skin on back of hands with lower density of skin appendages, less subcutaneous fat, more photoageing makes it difficult to treat AK in these areas.

This study was a randomised, placebo-controlled trial to study the efficacy of methyl aminolaevulinate-intense pulsed light (MAL-IPL)

on dorsal hands compared to IPL alone. Thirty-seven patients were recruited into both treatment groups: methyl aminolaevulinate (MAL) and IPL (wavelength ≥600 nm, 16.2 J cm^2, 20 ms, spot size 10-48 mm, 3 passes, double pulse with 40 ms delay, 20% overlap, Ellipse Flex PPT) (MAL-IPL) or placebo and IPL (placebo-IPL). Patients were given three treatments at 6-week intervals and followed up at 10 weeks after the last treatment.

Complete AK clearance rates per hand were 54.5% in the MAL-IPL group and 3% in the placebo-IPL group (P<0.0001) at 10 weeks after the last treatment. Complete AK clearance rates per lesion were 69% in MAL-IPL group and 15% in placebo-IPL group (P<0.001). Increased thickness of subepidemal collagen band, reduced wrinkle size, reduce skin roughness were found in both groups but without significant difference. Mottled pigmentation was significantly higher in MAL-IPL than Placebo-IPL group. In conclusion, MAL-IPL is more effective than Placebo-IPL in reducing AK on dorsal hands. Both treatments improved photoageing on the hand dorsum.

Pediatric contact dermatitis registry data on contact allergy in children with atopic dermatitis

Jacob SE, McGowan M, Silverberg NB, Pelletier JL, Fonacier L, Mousdicas N, et al.
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This retrospective case review studied 1142 patch test cases of children younger than 18 years in the United States. The objective was to elucidate the associations and sensitisation among patients with concomitant atopic dermatitis (AD) and allergic contact dermatitis (ACD), using data from the Pediatric Contact Dermatitis Registry.

Patch-tested patients with AD were 1.3 years younger (10.5 years in the AD group vs 11.8 years in the non-AD group; P<0.001). Atopic dermatitis was more significantly likely in Asian patch-test patients (OR, 1.92; 95% CI, 1.2-3.1; P=0.008) or African-American patients (OR, 4.09; 95% CI, 2.7-6.2; P<0.001). Patch testing was more likely to be performed in patients with generalised AD with (OR, 4.68; 95% CI, 3.50-6.30; P<0.001). There was a significantly longer history of dermatitis in patients with AD as compared to those without AD, 3.5 years vs 1.8 years (P<0.001).

Patient with AD had different reaction profiles to those without AD. In contrast to patients without AD; the odds ratio of positive patch test of the following substances were: cocamidopropyl betaine (CAPB): OR: 7.4 (P=0.008); wool alcohol: OR: 4.2 (P=0.047), lanolin: OR: 4 (P=0.053), tixocortol pivalate: OR: 5.3 (P=0.02) and parthenolide: OR: 7.6 (P=0.006). Patients with AD had a statistically significantly lower OR of having a positive patch test to methylisothiazolinone, cobalt and potassium dichromate when compared with the non-AD group.

This study provides information on the relationship between atopic dermatitis and allergic contact dermatitis in paediatric patch-tested patients in the United States. Concomitant undiagnosed ACD may result in treatment resistant disease in patients with AD. Physicians must beware of the diagnosis of ACD in patients with AD as patients can avoid detected allergens that could potentially aggravate the cutaneous symptoms.

Phototherapy for vitiligo a systematic review and meta-analysis

Bae JM, Jung HM, Hong BY, Lee JH, Choi WJ, Lee JH, et al.
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This systemic review and meta-analysis was performed to estimate the treatment response of vitiligo to phototherapy. The meta-analysis included 35 prospective studies. The outcome of interest was the repigmentation rate.

Repigmentation was graded based on a quartile scale with at least mild (>=25% repigmentation), at least moderate (>=50% repigmentation), and marked (>=75% repigmentation) responses. Subgroup analyses were performed to investigate the treatment response to NBUVB phototherapy by body site, (1) face and neck, (2) trunk, (3) extremities, and (4) hands and feet.

For NBUVB phototherapy, a mild response (>=25% repigmentation) was seen in 62.1% of 130 patients (95% CI: 46.9%-77.3%) in three studies at 3 months; at 6 months: this was seen in 74.2% of 232 patients (95% CI: 68.5%-79.8%) from 11 studies; and at 12 months: 8 studies reported a mild response in 75% of 512 patients (95% CI: 60.9%-89.2%). There was a marked response (>=75% repigmentation) to NBUVB phototherapy in 13.0% (95% CI, 2.1%-23.9%) of 106 patients in two studies at 3 months, in 19.2% (95% CI, 11.4%-27.0%) of 266 patients in 13 studies at 6 months and 35.7% (95% CI, 21.5%-49.9%) of 540 patients in 9 studies at 12 months.

For PUVA phototherapy, there was an at least mild response in 51.4% (95% CI, 28.1%-74.7%) of 103 patients in four studies at 6 months; and 61.6% (95% CI, 20.2%-100%) of 72 patients in three studies at 12 months. A marked response to PUVA was achieved in 8.5% (95% CI, 0%-18.3%) of 88 patients in 3 studies at 6 months and 13.6% (95% CI, 4.2%-22.9%) of 72 patients in 3 studies at 12 months.

In addition, regarding treatment response to NBUVB phototherapy by body site, the most responsive body site was the face and neck. A marked response was seen on the face and neck in 44.2% (95% CI, 24.2%-64.2%) of 153 patients in five studies. The treatment responses on hands and feet were extremely low, with a mild response observed in only 11.0% of patients.

The authors concluded that longer treatment duration should be encouraged to enhance the treatment response to phototherapy for vitiligo. A period of at least six months of treatment is required to determine the responsiveness to phototherapy. The most responsive body site was the face and neck. It is essential to reassure and encourage patient to achieve maximum treatment response.

Clinical markers of vitiligo activity

Benzekri L, Gauthier Y.
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The clinical course of vitiligo is difficult to predict. Currently, disease activity is mainly determined by history of progression, Koebner phenomenon, or negativity of mini-grafting test. All these assessments are imprecise, time consuming and non-immediate. So far, histological studies of the edge of viliginous lesions, although invasive, have been considered the most reliable method. It has been found that in active lesions, there is a progressive loss of pigment, prominent inflammatory reaction and absence of melanocytic detachment. In this study, the authors aimed at developing a rapid, non-invasive and accurate tool to assess vitiligo activity.

In this cross-sectional prospective study, patients with non-segmental vitiligo who failed various medical treatments and had stopped treatment for one year were recruited. Patients were assessed systematically by visualisation under daylight and Wood's lamp. They were scored using Vitiligo European Task Force (VETF) scoring system, and photographed using serial digital images to whole body and individual lesions. Clinically they were classified into amelanotic with sharply demarcated border (ASDB) if they showed pigmented areas and achromia only or hypomelanotic with poorly defined border (HPDB) if there were pigmented, hypochromic and achromic areas. They were re-assessed after one year by blinded observers to evaluate for disease progression. Skin biopsies were also taken from vilitiginous areas, perilesional margin and nearby normal skin.

A total of 71 patients were included of which two were lost to follow-up. Forty-six of them showed disease progression in one year while 23 cases remained stable. It was found that those with stable disease were statistically associated with ASDB type, absence of family history of vitiligo and less than 10% body surface area involvement. Histologically, there was a lack inflammatory infiltrate and a reduced expression E-cadherin at the membrane of keratinocytes. However, skin type and the presence of Koebner phenomenon was not associated with disease activity.

The authors concluded that the presence of hypochromic edge and poorly-demarcated borders under Wood's light at first visit could accurately predict vitiligo activity, which also correlated with histological finding. With this simple non-invasive assessment, physicians can decide on suitable treatment and predict treatment outcome. However, this study was limited by small sample size, cross-sectional nature and disease activity was sometimes site-dependent.

Isotretinoin treatment for acne and risk of depression: a systematic review and meta-analysis

Huang YC, Cheng YC
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Isotretinoin is the most effective treatment for severe and nodulocystic acne. However, after the first report on its possible induction of depressive symptoms in 1983, its relationship with depression remains controversial. In this study, the authors examined this relationship using an evidence-based meta-analysis.

All controlled or prospective non-controlled trials involving more than 15 acne patients on isotretinoin, with documentation of depression prevalence or depressive score, published before 30 September, 2016 and quality score more than 12 were included. The primary outcome of this study was to examine the prevalence of depression or change in depressive score after isotretinoin therapy.

Out of 172 studies screened, 31 studies met the inclusion criteria: three population-based studies, 8 controlled studies, and 20 prospective open-label studies. In the controlled trials, the change in depression score from baseline was similar in those who received isotretinoin and alternative treatment. On the other hand, there was a significant decrease in depression prevalence (relative risk [RR] 0.588, 95% CI 0.382-0.904) and reduction in depression score (SMD -0.335, 95% CI -0.498 to -0.172) after isotretinoin treatment. Only one populational study showed an increase in depression, but that study was subjected to sampling bias.

The authors concluded that isotretinoin treatment for acne at standard therapeutic dose did not increase the risk of depression. In fact, after pooling analysis, a significant decrease in depressive score was observed. Although individual susceptibility to depression under isotretinoin use cannot be ruled out, current evidence showed that isotretinoin is safe for acne patients.

This meta-analysis was limited by the lack of randomised controlled trials and a large inter-study variation was observed.

Anorectal pathology amongst HIV infected patients attending the Douala General Hospital: a cross-sectional study

Luma HN, Eloumou AFB, Fualefeh-Morfaw EA, Malongue A, Temfack E, Lekpa FK, et al.
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It is estimated that around 35.3 million people were living with HIV/AIDS (PLHIV) in 2012. The advancement of highly active anti-retroviral

therapy (HAART) alters the natural course of HIV infection from fatal disease to chronic illness. Ano-rectal pathologies (ARP) have become one of the commonest manifestations in PLHIV. This study was aimed to determine the prevalence and determinants of ARP in HIV infected patients attending a hospital-based HIV treatment centre in Africa.

During the four-month study period, HIV-infected patients who were receiving care in hospital including those attending outpatient clinics, pharmacy or on admission as in-patients were recruited consecutively after signing a written consent. A total of 430 HIV-infected were invited and 390 (90.7%) were analysed in the study. There was no difference in epidemiological data between those who accepted or refused. In the patient group participated in the study, the median duration of HIV diagnosis was three years (IQR: 2-5) and the CD4 count of the last six months was 411 (IQR: 234-601) cell/ml. Eight-four percent were on HAART with a median duration of treatment of two years (IQR: 1-4).

The prevalence of at least one ARP was 22.8% (95% CI: 18.7-27.3) with 7.4 % having more than one ARP. Haemorrhoids (10.3%) and proctitis (10%) were the commonest ARPs, followed by anal fissure (3.6%) and perianal excoriation (3.1%). From multi-variate analysis, the likelihood of having at least one ARP was increased by low CD4 count (<350 cells/ml; OR: 2.1; 95% CI: 1.1-4.2), in-patients (OR: 2.3; 95% CI: 1.2-4.3), not on HAART (OR: 2.2; 95% CI: 1.1-4.6), more than one sexual partner (OR: 2.4; 95% CI: 1.3-4.2) and having anal sex (OR: 5.0; 95% CI: 1.7-15.1).

The authors concluded that ARP was common and should be actively investigated and treated to improve the quality of life in PLHIV.

Detecting asymptomatic *Trichomonas vaginalis* in females using the BD Probe Tec™ *Trichomonas vaginalis* Q^x nucleic acid amplification test

Lord E, Newnham T, Dorrell L, Jesuthasan G, Clarke L, Jeffery K, et al.
Int J STD AIDS 2017;28:357-61.

Trichomonas vaginalis (TV) infection affects mainly women who are up to 15 times more likely to be infected than men and up to 50% are asymptomatic. Traditionally, TV is tested for by using wet-mount microscopy, acridine orange staining with fluorescence microscopy (AOS) or culture. Nucleic acid amplification test (NAAT) is now replacing culture as the gold standard for diagnosis. The aims of this study were to investigate local rates of asymptomatic TV using BDQ^x and to determine whether demographic and clinical data could be used to further delineate screening policies.

During the six-month study period, a total of 5775 BDQ^x tests for TV were performed of which 0.57% (33/5775) were positive. Three patients did not undergo BDQ^x testing, but were diagnosed with TV by using wet-mount microscopy, leading to a total of 36 patients with TV. Nineteen patients were tested with both wet-mount and BDQ^x and 58% (11/19) had concordant positive results. Of the remaining eight patients (42%) who had discordant results, all had negative microscopy and were positive on BDQ^x. Of the 33 patients diagnosed with TV by BDQ^x, 22 were symptomatic (vulval irritation, discharge, dysuria and pelvic pain). However, the risk factors for TV infection between symptomatic and asymptomatic groups were not statistically significant.

Although BDQ^x was highly sensitive and specific, the authors concluded that universal screening with this may not justified due to a low TV prevalence. Focusing screening symptomatic women, asymptomatic women who are HIV positive, aged >25 years or black ethnicity might be more appropriate.