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Journal Watch

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Evidence-based treatments for female pattern hair loss: a summary of a Cochrane systematic review

van Zuuren EJ, Fedorowicz Z, Carter B.
Br J Dermatol 2012;167:995-1010.

This is a systematic review of randomised controlled trials to assess the evidence for the effectiveness and safety of the treatments available for female pattern hair loss (FPHL). Relevant studies that compared any type of intervention used to treat FPHL in 12 common electronic databases and trial registers, which included the Cochrane Library, MEDLINE, EMBASE, AMED, PsycINFO, LILACS and several ongoing trials registries, were searched. Of the 334 references retrieved from the searches, only twenty-two studies which examined 2349 participants were included and the treatment period ranged between 6 and 12 months. Most studies investigated minoxidil (n=10) and finasteride (n=4), others investigated regimens such as cyproterone, flutamide, systemic oestrogen, spironolactone etc. This review showed that the only intervention that appeared to be effective and safe for the treatment of FPHL was minoxidil. Pooled data from four studies showed that more participants treated with minoxidil reported a moderate improvement in their hair regrowth compared with placebo (RR 1.86, 95% CI 1.42-2.43). The 2% minoxidil applied twice daily illustrated a good safety profile and efficacy. More undesirable side-effects were associated with the twice daily use of 5% minoxidil. There is a lack of evidence for the effectiveness of some widely-used treatments such as spironolactone, cyproterone acetate, finasteride and laser comb therapy. The authors suggested the need of further well-designed trials investigating other treatment options. Studies to compare the efficacy of 2% minoxidil twice daily and 5% minoxidil once daily are needed as the latter will improve compliance.

Acitretin for the treatment of cutaneous T-cell lymphoma

Cheeley J, Sahn RE, DeLong LK, Parker SR.
J Am Acad Dermatol 2013;68:247-54.

Cutaneous T-cell lymphoma (CTCL) is a rare and heterogeneous group of disorder. Although most patients run an indolent course, the disease can lead to significant disfigurement and impact on quality of life. Retinoids are an attractive option for treating CTCL due to its non-immunosuppressive properties and ease of administration. Currently, bexarotene is the only FDA-approved systemic retinoid for treatment of CTCL but it is associated with multiple adverse effects. Acitretin, which has a better safety profile and is much cheaper, may be a good alternative. In this retrospective study, the authors aimed at studying the effectiveness of acitretin, either alone or in combination with other treatments in managing patients with CTCL.

Forty-one patients with CTCL were identified during the study period, 32 (29 mycosis fungoides, two Sezary syndrome, and one unclassified CTCL) of which had been prescribed acitretin (10-50 mg daily) for at least one month and were included for analysis. Six patients were given acitretin alone and the rest received combination of acitretin and

other CTCL therapies, namely topical nitrogen mustard and phototherapy. The majority of patients (69%) were stage IB/IIA. Fifty-nine percent of patients responded, of which, one achieved complete remission, 11 had more than 50% improvement and seven with partial improvement. Eight patients had stable disease with no new lesions, while five showed worsening of disease.

Acitretin were generally well-tolerated. Most patients experienced mild symptoms, namely alopecia, cheilitis, dyslipidaemia, xerosis and depression (9-22%). Five patients stopped acitretin due to alopecia, arthritis, gastrointestinal disturbance and perceived allergic reaction.

The authors concluded that acitretin was effective for early stage CTCL and generally well-tolerated. However, this study was limited by the small sample size and retrospective nature. Moreover, as most patients were on combination of treatment, this made the analysis of efficacy of acitretin on management of CTCL difficult.

Topical propranolol for treatment of superficial infantile haemangiomas

Xu G, Lv R, Zhao Z, Huo R.
J Am Acad Dermatol 2012;67:1210-3.

Infantile haemangiomas (IH) are common among children. Although most lesions involute spontaneously, some require active intervention to avoid functional and aesthetic complications. Since Léaute-Labrèze *et al* reported the beneficial effect of propranolol in patients with IH, subsequent reports also showed that systemic propranolol therapy was effective in halting progression and inducing regression of haemangiomas. However, reports on topical propranolol are lacking.

In this retrospective study, the authors aimed at investigating the efficacy and safety of treating superficial haemangiomas with topical propranolol ointment. Twenty-five children with 28 superficial IH were treated with topical 1% propranolol ointment (10 mg oral propranolol crushed pills mixed with 1g petrolatum) thrice daily. Clinical response was based on subjective assessment of change in colour, size and surface tension, coupled with ultrasound measurement of depth at week 4, 12 and 24.

Ninety percent of patients responded to topical propranolol therapy, of which 57% showed good response. Patients who received treatment early responded better. Side-effects associated with systemic use of propranolol, namely bradycardia, hypotension, bronchospasm and hypoglycaemia, were not observed in this study.

The authors concluded that topical propranolol treatment is a safe and effective therapy for superficial IH, especially if it was initiated during the proliferative phase. This can also be used as an adjunct therapy during the wait-and-see period, which was the commonest approach in most cases of IH.

This study was limited by the small sample size, retrospective nature, lack of control arm and the potential bias due to unblinded assessment.

A long-term follow-up study of methotrexate in juvenile localised scleroderma (morphoea)

Zulian F, Vallongo C, Patrizi A, Belloni-Fortina A, Cutrone M, Alessio M, et al.
J Am Acad Dermatol 2012;67:1151-6.

Systemic steroid and methotrexate (MTX) have been used to treat localised scleroderma. In a recent double-blinded controlled trial, oral MTX (1.5 mg/m^2/week) and oral prednisolone (1 mg/kg/day) for the first three months were shown to be more effective in achieving and sustaining remission than oral prednisolone alone. However, the long-term efficacy and safety of MTX is not known.

This prospective study was the open extension of the above mentioned-controlled trial. The authors aimed at studying the long-term therapeutic role of MTX in children with localised scleroderma.

A total of 65 patients were treated with MTX (46 from steroid/MTX group and 19 from steroid alone group). Clinical response was determined using infrared thermography to assess the degree of inflammation and standardised computerised skin score system to assess the size of skin lesion.

Forty-eight patients (73.8%) responded, 10 (15.4%) relapsed after treatment with MTX for 24 months. Seven (10.8%) patients defaulted follow-up. Among those responders, MTX treatment was maintained for a mean of 27.5 months (18-30 months), 72.9% maintained in complete remission (CR) for a mean of 25 months after MTX discontinuation while the remaining 27.1% in CR with MTX. Moreover, longer MTX treatment was shown to be associated with lower relapse rate and lower incidence of disease flare during when the dose of MTX was tapered.

Methotrexate-related side-effects were reported in 48.3% of patients, including nausea, headache, hair loss, fatigue and transient elevation of liver enzyme. All these were mild and did not require dose modification or termination.

The authors concluded that long-term MTX therapy is effective and well-tolerated for morphoea. However, the objective assessment tools used in this study were not widely-used, which makes comparison with other studies difficult.

Topical paromomycin with or without gentamicin for cutaneous leishmaniasis

Ben Salah A, Ben Messaoud N, Guedri E, Zaatour A, Ben Alaya N, Bettaieb J, et al.
N Engl J Med 2013;368:524-32.

Cutaneous leishmaniasis is a disfiguring trypanosomal infection with a yearly incidence of 1.5 million cases worldwide. Leishmania major (L. major) is prevalent in Eurasia and Africa, and manifests as enlarging papulonodule that ulcerates and resolves in a three months (70%), with scarring and disfigurement. Paromomycin is an antibacterial aminoglycoside that has been evaluated to be useful systemically to treat visceral leishmaniasis and topically for cutaneous L. major.

A randomised, vehicle-controlled trial was conducted in Tunisia, to evaluate the efficacy of topical paromomycin in a hydrophilic base (15% paromomycin, with or without 5% gentamycin) compared with placebo. A total of 375 patients were recruited over four years. The patients included were of 5-65 years old, the majority were adult males who had a microbiologically confirmed ulcerative cutaneous leishmaniasis with five or fewer lesions. Treatment was given daily for 20 days.

The primary end-point was treatment cure (50% reduction of index lesion by 6 weeks, complete re-epithelialisation by 14 weeks, and absence of relapse by 24 weeks). It was found that the cure rates for paromomycin groups were similar, 81% (95% CI 73-87) for paromomycin-gentamycin and 82% (95% CI 74-87) for paromomycin alone; and significantly lower, 58% (95% CI 50-67) in placebo group ($P<0.001$). Patients treated with paromomycin (with or without gentamycin) suffered from mild-to-moderate inflammatory reactions on applications sites (22% vesiculation, 6% erythema), as opposed to 7% vesiculation and 2% erythema in placebo group. However, no observed renal impairment or ototoxicity resulted and there was no treatment withdrawal or suspension due to side-effects. The efficacy against non-ulcerative disease or disease due to other leishmania species remains to be investigated.

An audit of partner notification for syphilis and HIV

Armstrong H, Fernando I.
Int J STD AIDS 2012;23:825-6.

Partner notification (PN) is important in syphilis and HIV management in current epidemics. The aim of this study is to assess the PN outcome of newly-diagnosed syphilis and HIV patients. The study was conducted in Edinburgh over 18 months. The clinical notes of patients newly-diagnosed with syphilis and HIV were reviewed and the outcome of PN recorded. The traceable partner was defined if the genito-urinary medicine department or the index patients could contact them.

A total of 105 new syphilis cases were diagnosed. Ninety-one cases were men and 87% were men who have sex with men (MSM). The median age was 36 (range 18-81) and 83% were suffering from infectious syphilis. There were 423 sexual contacts in these 105 index patients, 37% (156/423) had traceable partners. In these traceable partners, 78% (121/156) were informed that they had the exposure risk. However, only 58% (91/156) had the blood test for screening. Finally 22% (34/156) had tested positive for syphilis.

A total of 44 new HIV cases were diagnosed. The majority (80%) were asymptomatic and seven patients presented as AIDS with either presence of an AIDS -defining illness or CD4 count <200 cell/μL. About 89% (39/44) were men and 90% of whom were MSM. The median age was 33 years (range 19-63 years). There were 188 sexual contacts noted in these 44 index patients and 52% (97/188) had traceable partners. In these traceable partners, 90% (90/97) were informed they had the exposure risk. However, only 57% (59/97) had the blood test for screening. Finally 23% (24/97) had positive HIV testing.

Since the British Association for Sexual Health and HIV aimed at the target of at least 60% of traceable partners should be attending blood screening, the authors concluded that they should further review and improve the partner notification.

What is the role of a full physical examination in the management of asymptomatic patients with late syphilis?

Dabis R, Radcliffe K.
Int J STD AIDS 2012;23:901-2.

A full physical examination is generally recommended in the management of late syphilis patients to detect neurological or cardiovascular complications. The aim of this study was to review whether a full physical examination including cardiovascular and neurological examination had been carried out in asymptomatic late syphilis patients and the effect of this on subsequent management. The study was conducted in a genitourinary medicine department in Birmingham, UK from 1994 to 2010. Of the total of 648 medical notes identified with the diagnosis of late syphilis, only 480 records were reviewed. The remaining were excluded because of unavailable records, false positive results, early syphilis, defaulted follow-up, previously treated and unclear written notes. Within these 480 records, the majority were heterosexual men (50%) and heterosexual women (43%). The remaining were men who have sex with men (6%) and sexual orientation not mentioned (1%). All were HIV negative.

A total of 295 asymptomatic late syphilis patients were identified and only 2% (7/295) had an abnormality on physical examination. One had reduced vibratory sensation. However, subsequent cerebrospinal fluid examination did not review any evidence of neurosyphilis. Six patients had cardiovascular abnormality detected, however, all these were clinical insignificant. All these seven patients were treated as late latent syphilis.

In conclusion, the performance of a full physical examination in asymptomatic patients with late syphilis added no additional benefit in diagnosing cardiovascular and neurological complications of late syphilis.

Association of psoriasis with stroke and myocardial infarction: meta-analysis of cohort studies

Xu T, Zhang YH.
Br J Dermatol 2012;167:1345-50.

This is a meta-analysis of cohort studies to evaluate the association between psoriasis and a composite vascular endpoint including stroke and myocardial infarction (MI). A systematic literature search of MEDLINE (Pubmed), EMBASE and Cochrane Library from March 2012 for cohort studies describing the association of psoriasis with stroke and MI using the search terms psoriasis, cerebral infarction, stroke, brain infarction, MI and cohort studies were performed. Two hundred unique citations were retrieved and finally seven cohort studies were included in this meta-analysis. The selected studies were conducted in the U.K., Taiwan, Denmark, U.S.A. and Netherlands between 2006 and 2012 with a follow-up ranging from five to 18 years. Three studies focused on MI, two focused on stroke and two on both. Potential publication bias was assessed by Egger's test and Begg's test. This analysis showed an overall 20% increase in the association of psoriasis with composite vascular endpoint (RR 1.2; 95% CI 1.1-1.31). Subgroup analysis maintained that psoriasis significantly increased the risk of stroke (RR 1.21; 95% CI 1.04-1.4) and MI (RR 1.22; 95% CI 1.05-1.42) separately. The authors concluded that psoriasis significantly raised the risk of stroke and MI and that this increase was probably not related to conventional cardiovascular risk factors.

Experience with molluscum contagiosum and associated inflammatory reactions in a paediatric dermatology practice

Berger EM, Orlow SJ, Patel RR, Schaffer JV.
Arch Dermatol 2012;148:1257-64.

This retrospective study is carried out in the Paediatric Dermatology Faculty Practice at the New York University School of Medicine. The authors aimed to find out the implication of inflammatory reactions to molluscum contagiosum (MC) infections. The interaction between atopic dermatitis (AD) and MC infections was also studied.

A total of 696 patients with MC infection were found over a five-year period. The mean age at presentation was 5.5 years. There were 307 patients (44.1%) with a history of atopy, including 259 patients (37.2%) with AD. For those with history of AD, 65.3% had active dermatitis, with 53.9% at sites of MC infection only. There were significantly more AD patients with more than 50 MC lesions than those without AD (19.7% vs. 5.0%, $p<0.001$). Patients with inflamed MC lesions were found to be significantly less likely to have more lesions over the following 3 months than those without inflamed lesions (5.2% vs. 18.4%, $p<0.03$). Molluscum dermatitis was noted in 270 patients (38.8%), of which AD patients were more prone to have that than non-AD patients (50.6% vs. 31.8%, $p<0.001$). There were 34 patients presented with a Gianotti-Crosti syndrome-like reaction (GCLR). An obvious reduction in number of MC lesions (50%-95%) in the 9 patients with GCLR was noted. Inflamed MC lesions were more common in patients with GCLR than in those without (64.7% vs. 20.1%, $p<0.001$). The most common treatment employed was Cantharidin (n=475).

This study is limited by the retrospective and record review nature. However, it showed that MC was more commonly seen in children with AD and they tended to have a larger number of MC lesions. It was also observed that GCLR in patients was a good prognostic sign in terms of MC clearance.

Incidence of hidradenitis suppurativa and associated factors: a population-based study of Olmsted County, Minnesota

Vazquez BG, Alikhan A, Weaver AL, Wetter DA, Davis MD.
J Invest Dermatol 2013;133:97-103.

Hidradenitis suppurativa (HS) is considered as a rare disease, however the chronic and debilitating nature of the disease warrants further epidemiological study. This study is based on population-based data from a well-studied US county.

A total of 268 patients were diagnosed with HS for the first time during the period 1968-2008. The age and sex-adjusted annual incidence of HS was 6.0/100,000 person-years (95%CI: 5.2-6.7). The incidence was significantly greater in women than men (8.2/100,000 [95%CI: 7.0-9.3] vs. 3.8/100,000 [95%CI: 3.0-4.7]). There was an increase incidence from 4.3/100,000 (95%CI: 2.8-5.8) during 1970-1979 to 9.6/100,000 (95%CI: 7.8-11.3) during 2000-2008. Women had significantly more axillary (67.7% vs. 46.8%, p=0.001), upper torso (24.9% vs. 2.5%, p<0.001) and groin (73.0% vs. 60.8%, p=0.047) involvement than men. Men had significantly more perineal or perianal disease than women (20.3% vs. 5.8%, P<0.001). Acne was noted in 36.2% of patients and pilonidal disease was found in 6% of patients. Depression was diagnosed in 42.9% of HS patients. Only male gender was associated with disease severity (p=0.015) after adjusted for age; BMI, acne, pilonidal disease and depression were not associated with severity of HS.

In conclusion HS is a rare disease and associated with current or history of smoking, obesity and gender. There are significant differences in the site of involvement between men and women and patients are more likely to be depressed. This study is limited by geographical restriction, which might not represent the populations in other parts of the US or other countries.

Oral cyclophosphamide without corticosteroids to treat mucous membrane pemphigoid

Munyangango EM, Le Roux-Villet C, Doan S, Pascal F, Soued I, Alexandre M, et al.
Br J Dermatol 2013;168:381-90.

This is a retrospective study carried out in France between November 2003 and December 2006 to evaluate the efficacy and safety of daily oral cyclophosphamide (CYC) without corticosteroids as therapy for severe mucous membrane pemphigoid (MMP). Thirteen patients (six women and seven men) were finally included for analysis during the study period. Cyclophosphamide was started at 2 mg/kg daily in these patients. They were examined every month to evaluate disease activity in the skin and mucous membrane according to a scoring system. Complete remission (CR) was defined as no active lesions and disease control (DC) was defined as ≥40% but <100% reduction of that score. The overall response rate was 69% (9/13 patients) after 52 weeks of CYC and median time to DC was 8 weeks (range 4-52 weeks). Seven patients (54%) achieved CR, the median time to CR being 24 weeks (range 16-52 weeks) and they remained in CR at week 52. Cyclophosphamide treatment achieved CR of severe active ocular lesions in a much shorter time (12-36 weeks) than other active lesions. Although transient lymphopenia was the most common side-effect (10/13 patients), leading to cessation of CYC in six patients, serious side-effects such as haemorrhagic cystitis, infections or secondary malignancies did not occur. The authors concluded that CYC without corticosteroids had rapid DC in patients with severe refractory MMP and was safe. This study is limited by the small sample size and retrospective nature.

Infantile haemangioma: treatment with short course systemic corticosteroid therapy as an alternative for propranolol

Nieuwenhuis K, de Laat PC, Janmohamed SR, Madern GC, Oranje AP.
Pediatr Dermatology 2013;30:64-70.

Propranolol has been increasingly used as first-line treatment for infantile haemangiomas (IH) since 2008. High-dose continuous corticosteroid therapy was considered as the second-line treatment with only 30% of cases having a favourable and persistent response. A single-centre retrospective case study was performed in the Netherlands to evaluate the efficacy and safety of intermittent high-dose corticosteroids in the treatment of IH. Twenty-one children with IH treated with prednisolone 3 mg/kg/day (divided into 3 times per day, each course for 2-3 weeks then tapered over 10 days, repeat if indicated) during 1994-2009 were included. Two blinded investigators interpreted the results independently according to the Hemangioma Activity Score (HAS). The study included 16 females and six males, most lesions were on head and neck with ulceration.

The mean duration of treatment was two weeks (range 1-6 weeks) and number of courses of treatment required was two (range 1-5). The median cumulative dose of prednisolone used was 91 mg/kg, compared to 500-750 mg/kg in high-dose continuous therapy for 6-9 months. Infantile haemangioma growth was stabilised with 62% of cases achieving a good response (>50% reduction in HAS) and 23% achieving favourable response (30-50% reduction in HAS). About 57% of children suffered from minor, short-termed side-effects. The side-effect profile was related proportionally to the cumulative dose (all patients receiving three or more courses developed side-effects), but no persistent side-effects were noted after a median follow-up of 61 months.

In summary, the authors concluded that intermittent high-dose corticosteroid therapy was an effective and safe treatment for IH. It could be adopted as the second-line therapy for IH in cases where propranolol failed or was contraindicated. This study is limited by retrospective nature and small sample size.