Psoriasis Research Review™

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Issue 48 - 2018

In this issue:

Abbreviations used in this issue:

aOR = adjusted odds ratio; **BSA** = body surface area; **DLQI** = Dermatology Life Quality Index; **EQ-5D-3L** = EuroQol-5 dimensions-3 levels; **HR** = hazard ratio; **IGA** = Investigator's Global Assessment; **MS** = multiple sclerosis; **OR** = odds ratio; **PASI** = Psoriasis Area and Severity Index; **PGA** = Physician's Global Assessment; **RCT** = randomised controlled trial; **TNF** = tumour necrosis factor; **UVB** = ultraviolet B.

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Welcome to issue 48 of Psoriasis Research Review.

According to the compelling findings of a Danish study, psoriasis patients on topical treatments may benefit from a smartphone app reminding them to apply their medication. Following on, we discover that male psoriasis patients exhibit significantly lower serum levels of testosterone, higher levels of estradiol, and impaired erectile function compared with healthy controls. Other topics in this issue include trends in biologic use and psoriasis hospitalisations, age of onset of psoriasis and clinical outcomes with systemic medications, the association between psoriasis and vitiligo, guselkumab for moderate-to-severe plaque psoriasis, and adherence to systemic psoriasis medications.

We hope you find the latest issue of Psoriasis Research Review stimulating reading and look forward to any feedback.

Kind Regards,

Clinical Associate Professor Kurt Gebauer

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A smartphone application supporting patients with psoriasis improves adherence to topical treatment: a randomized controlled trial

Authors: Svendsen MT et al.

Summary: This RCT evaluated whether a study-specific app improves adherence to treatment and reduces psoriasis symptoms compared with standard treatment. A total of 134 patients (mean age 48 years) with mild-to-moderate psoriasis were treated with once-daily calcipotriol/betamethasone dipropionate cutaneous foam and were randomised to no app (n = 66) or app intervention (n = 68); a total of 122 patients completed the 22-week follow-up period. Adherence, which was defined as medication applied ≥80% of days during the treatment period, was the study's primary outcome measure and was assessed via a chip integrated into the medication dispenser. The app improved short-term adherence to foam treatment, with 65% of app recipients being adherent to treatment compared with only 38% of those not using the app (p = 0.004).

Comment: Australian dermatologists have been slow to adopt the potential value of newer technologies. Equally, such technologies are rarely reported in the medical literature. A small pilot article from the Danes looking at a specific smartphone app to encourage patients to apply their topical therapy. The study ran for 26 weeks, which is not my definition of short term. The conclusion is logical in that electronic reminders via a telephone app improve short-term adherence to therapy and therefore clinical responses. The American Academy is usually the best location to review these newer devices. I look forward to see what new tools will be available in Washington in 2019.

Reference: Br J Dermatol. 2018;179(5):1062-71

Abstract

Sex hormones, erectile dysfunction, and psoriasis; a bad friendship!

Authors: Eltaweel AEAI et al.

Summary: These authors investigated serum sex hormone levels (total testosterone and estradiol) and erectile function (measured via the International Index of Erectile Function version-5) in 50 male psoriasis patients and 30 healthy controls. Compared to controls, psoriasis patients exhibited significantly lower serum levels of total testosterone, higher levels of estradiol, and impaired erectile function. The authors concluded that the detected hormonal disturbance in male psoriasis patients may be a cause of the associated erectile dysfunction.

Comment: An Egyptian article looking at 50 male patients with psoriasis assessing sex hormones. This is another one for the comorbidities list. Male psoriasis patients have a significant reduction in total testosterone, high levels of estradiol and impaired erectile function. Whether this is an obesity-related effect, or a further independent factor arising from psoriasis, is not clear.

Reference: Int J Dermatol. 2018;57(12):1481-84
Abstract

Proposal of a new scoring formula for the Dermatology Life Quality Index in psoriasis

Authors: Rencz F et al.

Summary: Approximately 40% of patients with psoriasis have 'not relevant' responses (NRRs) on the DLQI questionnaire and these responses are scored as the item of the questionnaire having no impact on the patients' lives at all. Consequently, these patients find it more difficult to fulfil the DLQI >10 criterion required to become candidates for systemic treatment including biologics. These authors proposed a new scoring system for the DLQI that corrects for the bias in the NRR option, and tested its construct validity in 242 patients with psoriasis. The findings from two prior cross-sectional surveys were reanalysed (104/242 patients had marked ≥1 NRR). Two methods of calculating the DLQI were undertaken for each patient: (i) according to the original scoring and (ii) by applying a new scoring formula (DLQI-R) that adjusts the total score for the number of NRRs. The PASI and EQ-5D-3L were used to test the construct validity of the DLQI-R. Evaluation revealed mean DLQI and DLQI-R scores of 9.99 and 11.0, respectively, and the DLQI-R enabled eight more patients (3.3%) to achieve the PASI >10 and DLQI >10 threshold for systemic treatment. The DLQI-R correlated slightly better with the PASI than the DLQI correlated with the PASI (*r*s 0.57 vs 0.59, respectively), and the same trend was observed for the EQ-5D-3L index score (*r*s -0.54 vs -0.58, respectively).

Comment: The DLQI is a time-honoured tool that is becoming more frequently utilised in general dermatological practice. A number of my colleagues routinely use this instrument to test patient's progress. It is of course an essential instrument measuring disease impact on patients in clinical trials. Although developed and validated many years ago, there are some questions in the present DLQI that are not directly relevant depending on the skin disease being assessed. This is a Hungarian study, which tinkers with some of these "not relevant" responses. It may seem a lightweight article to some readers at first. However, there are attempts to use the DLQI in the Australian system as an entry criteria for the prescription of biologics. Some years ago Prof. Chris Baker and colleagues from the College published in the Australasian Journal of Dermatology a submission to use the DLQI in assessing clinical impact of psoriasis on patients in assessing patient eligibility for a biologic agent.

Reference: Br J Dermatol. 2018;179(5):1102-08
Abstract

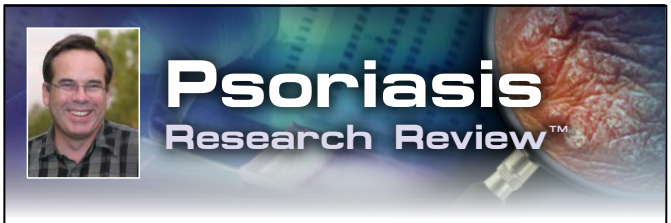
Trends in hospitalization rates for psoriasis flares since the introduction of biologics: a time series in France between 2005 and 2015

Authors: Polivka L et al.

Summary: This French study involving nine hospitals, investigated whether the introduction of biologics for the treatment of patients with moderate-to-severe psoriasis was associated with a reduction in the hospitalisation rate for psoriasis flares between 2005 and 2015. Analysis of 3572 relevant hospital stays revealed that the introduction of biologics was not associated with a decrease in the number of hospitalisations due to a psoriasis flare, but was associated with a non-significant increase in the number of hospitalisations (13 hospitalisations for psoriasis flares per quarter per 10,000 beds). In an analysis of two centres, the introduction of biologics was found to be associated with a significant increase in the rate of hospitalisation of patients receiving topical treatments only (520 hospitalisations per year per 10,000 beds) and those with a first psoriasis flare.

Comment: This is a French article, which looks at a decade of admissions throughout nine French Hospitals. The French have a socialised system, which is very different to ours. In my hometown it is very difficult to ever admit anyone under a dermatologist, as beds are frequently full of medical patients. Among a total of 3572 admissions, these authors found that there was an increase in hospitalisations for psoriasis over the time. In two centres, they looked at the treatment data for these individual patients. The majority of their hospitalisations were for patients receiving topical treatment only. Additionally, patients being admitted for their first psoriasis flare were also over-represented. In France, there has been a higher demand and utilisation of dermatological services for psoriasis over the decade that biologic agents were utilised. The reasons for this uptick in utilisation demand are not clear.

Reference: J Eur Acad Dermatol Venereol. 2018;32(11):1920-29
Abstract



Selection of papers and comments are provided by Clinical Associate Professor Kurt Gebauer MBBS, FACD, FACP

Clinical Associate Professor Kurt Gebauer has been practicing dermatology for 20 years in Australia. Dr. Gebauer has a busy private practice located in Fremantle and can also be found lecturing locally and internationally on different medical topics. As a contributing author on many publications, Dr. Gebauer is a well-known authority on dermatological conditions. Along with his dermatology practice Dr. Gebauer also participates in clinical research studies in order to offer new and innovative treatments for dermatological conditions including acne, atopic dermatitis, psoriasis, actinic keratoses, onychomycosis, and skin cancer.

Effect of age of onset of psoriasis on clinical outcomes with systemic treatment in the Psoriasis Longitudinal Assessment and Registry (PSOLAR)

Authors: Singh S et al.

Summary: The therapeutic response among patients with early-onset psoriasis (EOP; age ≤40 years; n = 5479) and late-onset psoriasis (LOP; age >40 years; n = 2032) receiving adalimumab, etanercept, infliximab, ustekinumab, or methotrexate was investigated in the Psoriasis Longitudinal Assessment and Registry (PSOLAR). Overall, the likelihood of achieving a PGA 0/1 after treatment was higher in the LOP group than in the EOP group (aOR 1.14; 95% CI 1.05-1.25, p = 0.0019); this was also evident in the etanercept-treated (aOR 1.38; 95% CI 1.14-1.66, p = 0.0010) and methotrexate-treated (aOR 1.62; 95% CI 1.16-2.26, p = 0.0049) subgroups. While there was no overall difference observed between the two groups in the likelihood of achieving a percentage body surface area (BSA) involved with psoriasis <1% or <3% between the two groups, achievement of BSA <1% or <3% was more likely in the subgroups treated with etanercept (aOR 1.30 [95% CI 1.06-1.61, p = 0.0123] and aOR 1.34 [95% CI 1.09-1.64, p = 0.0053], respectively) and infliximab (aOR 1.45 [95% CI 1.09-1.93, p = 0.0103] and aOR 1.36 [95% CI 1.03-1.78, p = 0.0290], respectively).

Comment: A registry assessment from a number of eminent authors in the psoriasis and dermatological fields. As such it deserves review. The academic question is: If aggressive treatments, particularly biologics but also systemic agents, are instituted early does this affect the long-term prognosis of psoriasis? 7511 patients were analysed, of which 5479 (72.9%) had EOP. Intriguingly, the LOP group had a higher likelihood of achieving a low PGA score after treatment. This was especially so with etanercept and methotrexate treatment. Their data would suggest that patients with LOP respond more readily than those with acute-onset psoriasis. It would be interesting to see if other registry data show the same.

Reference: Am J Clin Dermatol. 2018;19(6):879-86
Abstract

Association between psoriasis and vitiligo: A systematic review and meta-analysis

Authors: Yen H and Chi CC

Summary: This systematic review and random effects meta-analysis investigated the relationship between psoriasis and vitiligo. A total of 10 suitable case-control/cross-sectional studies with a total of 120,866 psoriasis cases and 79,907 vitiligo cases were identified via a search of the MEDLINE and EMBASE electronic databases conducted on 22 January 2018; four of these studies were rated as high risk of bias according to a customised Newcastle-Ottawa Scale. Random effects meta-analysis was used to calculate pooled ORs with 95% CIs and revealed a significantly increased odds for psoriasis in vitiligo patients (summary OR 3.43; 95% CI 1.86-6.33, n = 4 studies) and a significantly elevated odds for vitiligo in psoriasis patients (summary OR 2.29; 95% CI 1.56-3.37, n = 7 studies).

Comment: A systematic review and meta-analysis out of Taiwan. So far dermatologists do not understand why patients develop vitiligo. The mechanism of disease formation has not been clearly established. We do understand a lot more about psoriasis. This review assesses a significant number of citations. A huge number of clinical cases were compared in this study, 120,866 psoriasis patients and 79,907 vitiligo sufferers. The results reported a significant increase of vitiligo incidences in psoriasis patients (summary OR 2.29; 95% CI 1.56-3.37, studies = 7), as well as significantly elevated odds for psoriasis in vitiligo patients (summary OR 3.43; 95% CI 1.86-6.33, studies = 4). Another one for the comorbidities list of psoriasis.

Reference: Am J Clin Dermatol. 2018;Oct 13 [Epub ahead of print]
Abstract

Association of multiple sclerosis with psoriasis: A systematic review and meta-analysis of observational studies

Authors: Liu C-Y et al.

Summary: This Taiwanese systematic review and meta-analysis investigated the association between psoriasis and multiple sclerosis (MS). The analysis included 10 suitable publications reporting a total of 11 studies (5 case-control, 4 cross-sectional and 2 cohort studies) identified via a search of MEDLINE, EMBASE, and CENTRAL databases in July 2018. A total of 18,456 MS patients and 870,149 controls were included in the case-control and cross-sectional studies, while 25,187 MS patients and 227,225 controls were included in the two cohort studies. Three studies were rated with a high risk of bias according to the Newcastle-Ottawa Scale with regard to comparability, non-response rate, and selection of controls. According to a random-effects model meta-analysis, MS was associated with increased odds (OR 1.29; 95% CI 1.14-1.45) and risk (HR 1.92; 95% CI 1.32-2.80) of psoriasis.

Comment: Another Taiwanese article looking at very large numbers of patients (18,456 MS patients and 870,149 in the case-control and cross-section studies). There were two cohort studies involving 25,187 MS and 227,225 controls. With the TNF inhibitors there were significant concerns about the induction of MS. As the newer biologic agents targeting particularly Il-17 and Il-23 come on the market, I have become less concerned about MS in the family tree or even in the past personal history of my patients. It would seem from this meta-analysis that there is a link between psoriasis and MS. This association had increased odds (OR 1.29; 95% CI 1.14-1.45) and risk for psoriasis (HR 1.92; 95% CI 1.32-2.80). It is possible that what we had seen in the TNF-treated group of psoriatic patients is the increased background rate of MS. Certainly the newer agents do not seem to have any increased risk of demyelinating disorders.

Reference: Am J Clin Dermatol. 2018;Oct 25 [Epub ahead of print]
Abstract

Improvement in patient-reported outcomes (Dermatology Life Quality Index and the Psoriasis Symptoms and Signs Diary) with guselkumab in moderate-to-severe plaque psoriasis: Results from the phase III VOYAGE 1 and VOYAGE 2 studies

Authors: Armstrong AW et al.

Summary: Pooled phase III VOYAGE 1 and VOYAGE 2 data were evaluated through week 24 to compare improvements in DLQI and Psoriasis Symptoms and Signs Diary (PSSD) scores and skin clearance between patients receiving guselkumab (100 mg) and those receiving placebo or adalimumab (40 mg); at week 16, patients receiving placebo switched to guselkumab. Improvements from baseline DLQI were significantly greater with guselkumab than with placebo (weeks 8 and 16) or with adalimumab (week 24; p < 0.001). At week 24, the proportion of patients achieving a DLQI 0/1 ("no impact") was higher in guselkumab recipients than in adalimumab recipients (58.9 vs 40.2%; p < 0.001), and more patients achieved a ≥4-point reduction in DLQI minimal clinically important difference at this time point (p < 0.001). Individual DLQI domain changes were significantly greater for guselkumab recipients than for adalimumab recipients, and among patients with individual baseline domain scores of 3 or 6 (severest impact), more guselkumab recipients than adalimumab recipients achieved a score of 0 across all domains at week 24. Furthermore, at week 24, DLQI 0/1 scores were associated with a PSSD symptom or signs score of 0 (no impact) and greater improvement of IGA and PASI.

Comment: Guselkumab will be on the Australian market very shortly. Hence Australian dermatologists need to know about it. This paper has an Australian author, Prof. Peter Foley. I put this paper in to remind readers that the newer agents that we will be using are far superior in clinical improvements to those from a decade ago. Certainly because of the newness of these agents we don't have the extensive safety profile that makes ustekinumab and adalimumab so reassuring.

Reference: Am J Clin Dermatol. 2018;Nov 12 [Epub ahead of print]
Abstract

Drug utilization patterns and adherence in patients on systemic medications for the treatment of psoriasis: A retrospective, comparative cohort study

Authors: Dommasch ED et al.

Summary: This retrospective, comparative cohort study using a large US health insurance claims database including psoriasis patients (n = 22,742) who were new users of acitretin, adalimumab, etanercept, methotrexate, or ustekinumab, examined drug utilisation patterns and adherence to treatment (measured by proportion of days covered dichotomised as adherent [≥0.80] or non-adherent [<0.80]). Compared to treatment with methotrexate, adherence to adalimumab (OR 2.24; 95% CI 2.05-2.45), etanercept (OR 1.77; 95% CI 1.63-1.92) and ustekinumab (OR 2.54; 95% CI 2.24-2.87) was greater, and adherence to acitretin was lower (OR 0.57; 95% CI 0.50-0.63).

Comment: A retrospective comparative cohort study using a US Health Insurance claims database investigating 22,742 patients who were new users of systemic psoriasis medications. Adherence to adalimumab, etanercept and ustekinumab was greater than with methotrexate. This makes sense clinically as the PASI response rate of these drugs is superior to methotrexate. The inconvenience and side effects associated with methotrexate would make it less popular for patients over biologics. Acitretin was found to have lower adherence than methotrexate, which again would make clinical sense. Certainly in my patients acitretin works far less effectively with far more patient complaints than methotrexate.

Reference: J Am Acad Dermatol. 2018;79(6):1061-68
Abstract

Narrowband ultraviolet B treatment for psoriasis is highly economical and causes significant savings in cost for topical treatments

Authors: Boswell K et al.

Summary: These Scottish authors performed data linkage of comprehensive treatment records and prescribing data for all narrowband-UVB treatment episodes spanning 6 years in a population of 420,000 in order to define the actual costs of narrowband-UVB incurred by the service provider, as well as treatment-associated cost savings. It was estimated that the U.K. National Institute for Health and Care Excellence spent an average of £1882 per narrowband-UVB treatment course, compared with an average of £257 per narrowband-UVB treatment course estimated for the National Health Service Tayside (across four independent treatment sites). The cost of topical treatments for the National Health Service Tayside averaged £128 per patient in the 12 months prior to narrowband-UVB, which accounted for 42% of the overall drug costs incurred by these patients. In the 12-month period following narrowband-UVB treatment, this cost was reduced by 40% to £53 per patient, while psoriasis-unrelated drug prescription remained unchanged (these findings suggest disease-specific effects of narrowband-UVB).

Comment: A Scottish study from the English centre of photobiology excellence. It starts with the premise that narrowband-UVB treatment for psoriasis is considered expensive. The English NHS system of course has a very different funding model than ours. Their national health service spent an average £257 per treatment course on UVB. In Australia, Item No. 14050, which is for phototherapy attracts a rebate of $44.85 per visit suggesting that a course of phototherapy in Australia will be more expensive. I have included this article as a reminder that older therapies do have their merit and value in the right patient and certainly comparing the cost of biologics to phototherapy, it is a bargain.

Reference: Br J Dermatol. 2018;179(5):1148-56
Abstract

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