Psoriasis Research Review™

Making Education Easy

Issue 30 - 2017

In this issue:

Abbreviations used in this issue:

BMI = body mass index; **CD** = Crohn's disease; **DLQI** = Dermatology Life Quality Index; **IBD** = inflammatory bowel disease; **IGA** = Investigator Global Assessment; **OR** = odds ratio; **PASI** = Psoriasis Area and Severity Index; **PsA** = psoriatic arthritis; **QoL** = Quality of life; TNF = tumour necrosis factor; **UC** = ulcerative colitis.

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Welcome to issue 30 of Psoriasis Research Review.

A multicenter Australian study published in JAMA on the association between paediatric psoriasis and waist-to-height ratio in the absence of obesity suggests a positive association in a group of 200 children attending a tertiary referral center paediatric dermatology clinic and one of two private specialist dermatologists' consultant rooms. This study highlights the potential impact of central adiposity in children with this condition. Another study, from Germany, investigating the German Psoriasis Arthritis Diagnostic (GEPARD) questionnaire developed for the early detection of psoriatic arthritis (PsA), shows the tool to be helpful in screening for such patients. Other studies in this review include the investigation of periodontitis and the risk of psoriasis, stigmatisation in psoriasis, ixekizumab in biologic naive versus experienced patients, and PASI score and quality of life.

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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Association between pediatric psoriasis and waist-to-height ratio in the absence of obesity: A multicenter Australian study

Authors: Lee A et al.

Summary: This multicenter cross-sectional prospective case-control study conducted from February 7, 2014 to July 15, 2015 in Sydney and Gosford, New South Wales, Australia, was undertaken to determine whether children with psoriasis are more likely to have increased waist-to-height ratio, obesity and metabolic syndrome compared to children without psoriasis. Children (110 girls and 98 boys, mean age 8.9 years) attending a tertiary referral center paediatric dermatology clinic and one of two private specialist dermatologists' consultant rooms were included; 135 children had psoriasis and 73 non-inflammatory skin conditions (controls). Compared with controls, a significantly ($p = 0.002$) higher proportion of children with psoriasis were more likely to have increased central adiposity, with a waist-to-height ratio of 0.5 or greater; 29% ($n = 39$) vs 11% ($n = 8$). While no children in the control group had metabolic syndrome, four of 53 children older than 10 years with psoriasis were found to have this condition (8% vs 0%; $p = 0.29$). Among 15 children with moderate-to-severe psoriasis, three had metabolic syndrome, while among 38 with mild psoriasis only one had this condition (20% vs 3%; $p = 0.06$). Children with moderate-to-severe psoriasis exhibited a higher mean waist-to-height ratio than those with mild psoriasis; 0.48 vs 0.46 ($p = 0.04$). There was no significant ($p = 0.91$) difference in overweight and obesity according to BMI between children with psoriasis and controls; 17% vs 16% ($p = 0.91$).

Comment: This is an Australian trial which is published in a very reputable journal. A multicentre cross-sectional prospective case control study from 2014-mid 2015 conducted in Tertiary Referral Paediatric Dermatology Clinics. Two hundred children from 5-16 years of age, of which 135 had psoriasis and 73 had other non-inflammatory skin conditions, who acted as the control group. In this Australian cohort of children with psoriasis there was an elevated waist-to-height ratio. This was found significantly more common in patients with psoriasis than controls. Proportions of participants with metabolic syndrome or BMI-determined obesity were not significantly different between the two groups. Children with moderate-to-severe psoriasis had a higher mean waist-to-height ratio than children with mild psoriasis.

What does this mean to me? It seems that there is from early childhood, a tendency for psoriasis patients to have higher weights than their childhood friends. Certainly this goes on and is reflected strongly in the adult patient group who are a lot larger, suffering metabolic consequences and co-morbidities. Obesity is an ongoing feature that is present in childhood that is associated with the systemic disease of psoriasis. Those with more severe psoriasis had more obvious effects. Why this is so is yet to be discovered.

Reference: JAMA Dermatol. 2016;152(12):1314-19

Abstract

Sensitivity of the GEPARD patient questionnaire to identify psoriatic arthritis in patients with psoriasis in daily practice: The GEPARD-Life Study

Authors: Härle P et al.

Summary: The German Psoriasis Arthritis Diagnostic (GEPARD) questionnaire was developed to aid in the early detection of psoriatic arthritis (PsA). This multicentre German study involving 59 dermatology units (university/general hospital/office based) determined the performance of the GEPARD questionnaire in the detection of PsA in psoriasis patients following rheumatology evaluation in daily clinical practice. Referral to a rheumatologist was undertaken for those patients with a sum score of ≥4 positive answers on the GEPARD questionnaire. Of 1512 patients undertaking the questionnaire, approximately 50% were referred. Of those patients, one third were classified as having PsA after rheumatological assessment and a higher percentage of those patients had come from the university/general hospital setting than the doctor's office-based setting (43.7 vs 25.8%).

Comment: As a rule of thumb, of our patients with generalised cutaneous psoriasis, 30% will have PsA at some stage. Of the systemic therapies, methotrexate is the agent of choice for joint disease. Cyclosporine helps symptoms but doesn't stop the ongoing destructive inflammation in joints. Neotigason and phototherapy are unhelpful as treatments for joints in this group. Even in the biologic group there are certain drugs that are better on joints than others. In my practice, I screen my patients by asking for joint symptoms and assessing any involved joints physically. I also spend some time discussing the nature of their joint symptoms as a way of interpreting whether it is osteoarthritis or inflammatory PSA causing their pain. A tool that the patient can fill in that is reproducible and reliable would be very helpful.

This is a group out of Germany who looked at 1512 patients. 50% were referred onto the rheumatology department. This is a huge number of referrals and is not what is reflected in my practice. Of those sent on, one third of the patients were classified as having PsA after the rheumatology assessment. They made the comment that the University Hospital setting had more severe patients than the Doctor's office setting which is understandable in the European system. In Germany, referrals aren't needed and patients present to the dermatologist's office directly. Hospital patients have a more severe spectrum of disease in any case. I understand that this GEPARD questionnaire is helpful, however, it did generate a large number of referrals of which only one in three proved to be positive.

Reference: Dermatology 2016;232(5):597-605
Abstract

Lesions on the back of hands and female gender predispose to stigmatization in patients with psoriasis

Authors: Hawro M et al.

Summary: In a study in 115 patients with psoriasis vulgaris, the links between the involvement of visible and sensitive skin areas and feelings of stigmatisation were assessed using the Feelings of Stigmatization Questionnaire. The presence of psoriatic lesions located on the back of the hands was associated with higher stigmatisation levels ($p = 0.011$), but nail, palm, face or genital area localisation was not, and neither was overall disease severity. Higher stigmatisation levels were observed in patients who claimed not to be able to cover their lesions with clothing ($p = 0.025$), women ($p = 0.001$) and the unemployed ($p = 0.004$). Stigmatisation was the best predictor of poor Dermatology Life Quality Index (DLQI) and World Health Organization Quality of Life-BREF scores.

Comment: Our Medicare system does not acknowledge the stigmata of visible hand lesions on the back of hands. We assess palmar plantar psoriasis. Patients are eligible for a biologic if they have greater than 30% involvement and satisfy the other prescription criteria. The dorsum of the hands doesn't count. I do believe it is time that an application is made to change this. This paper comes from the clinical centre Charite in Berlin and looks at DLQI and other measures of life quality. It makes the obvious scientific link that these visible lesions are highly stigmatising in general, but more so for women. Possibly this is a paper that can be used to sway the authorities that this group also need assistance.

Reference: J Am Acad Dermatol. 2017;Jan 6 [Epub ahead of print]
Abstract

Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial

Authors: Reich K et al.

Summary: The randomised controlled phase III VOYAGE 2 trial in patients with moderate-to-severe psoriasis compared the anti-interleukin-23 monoclonal antibody guselkumab (100 mg at weeks 0 and 4 then every 8 weeks; n = 496) to placebo (placebo at weeks 0, 4 and 12 then guselkumab at weeks 16 and 20; n = 248) and adalimumab (80 mg week 0 then 40 mg week 1, and every 2 weeks through week 23; n = 248). After 16 weeks, 84.1% of guselkumab versus 8.5% of placebo recipients achieved an Investigator Global Assessment (IGA) score of 0 or 1 (cleared or minimal) while PASI 90 scores were 70.0% versus 2.4% (coprimary end points). Guselkumab was also superior ($p < 0.001$) to adalimumab at 16 weeks for IGA 0/1, PASI score improvement ≥75% and PASI 90, and at week 24 for IGA 0/1, PASI 90 and PASI improvement of 100%. Better persistence of response was observed between weeks 28 and 48 in guselkumab maintenance versus withdrawal groups ($p < 0.001$). Among adalimumab nonresponders switched to guselkumab after week 28, 66.1% reached PASI 90 by week 48.

Comment: Again data coming from the pharmaceutically sponsored trial VOYAGE 2, looking at a new anti-interleukin-23 monoclonal antibody. The comparator was adalimumab. For me there are two points of interest. Very high PASI response rates, the PASI 90 and IGA results were extremely significant. Additionally those that did not respond to adalimumab and went on to guselkumab had almost comparable clinical results.

Reference: J Am Acad Dermatol. 2016;Dec 29 [Epub ahead of print]
Abstract

Biologic drug survival in Israeli psoriasis patients

Authors: Shalom G et al.

Summary: This Israeli study used data from the Clalit Health Services database to examine drug survival rates (defined as time period of treatment with a certain drug until its cessation) and predictor factors for the use of biologics (adalimumab, infliximab, etanercept, ustekinumab) in 907 patients (1575 biologic treatments) with psoriasis. Ustekinumab had a higher survival rate than TNF inhibitors. Positive predictors for drug survival were biologic treatment naivety and concomitant methotrexate intake; negative predictors were female sex and duration of previous systemic treatments.

Comment: There have been papers presented in this forum arising from America, looking at this question. However, the American market is very different with insurers and co-pay etc. The Israeli system is a more socialist funded system. This paper reviews 907 patients who had 1575 biologic treatments. Ustekinumab had a significantly higher survival rate than the older TNF inhibitors. Not ever having had a biologic therapy previously as well as the use of concomitant methotrexate, were positive predictors for drug survival. The female sex and duration of previous systemic therapies were negative predictors. This paper confirms to me that my request to all my biological patients that they take methotrexate in doses 5-10 mg a week depending on body weight, is a valid manoeuvre as it improves drug survival. Certainly in my experience low-dose methotrexate does not increase side effects.

Reference: J Am Acad Dermatol. 2016;Dec 8 [Epub ahead of print]
Abstract

Psoriasis Research Review™

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.

Inflammatory bowel disease among patients with psoriasis treated with ixekizumab: A presentation of adjudicated data from an integrated database of 7 randomized controlled and uncontrolled trials

Authors: Reich K et al.

Summary: This post-hoc analysis examined the incidence of adjudicated inflammatory bowel disease (IBD) cases among 4209 psoriasis patients receiving ixekizumab (6480 patient-exposure years) from seven randomised controlled and uncontrolled trials. Twelve suspected Crohn's disease (CD) and 17 ulcerative colitis (UC) adverse events were reported during the trials and 19 of these were adjudicated as definite/probable IBD (seven CD [incidence rate 1.1 per 1000 patient-exposure years]; 12 UC [incidence rate 1.9 per 1000 patient-exposure years]). Three occurred during induction (1 CD, 2 UC) and seven during maintenance (four CD, three UC). Among 16 patients with a prior history of IBD, 12 have not had an IBD treatment-emergent adverse event or serious adverse event.

Comment: A large review by the Gods of Biologic therapy sponsored by Lilly, the manufacturers of ixekizumab. There is a question with the anti-IL17 family whether they provoke, aggravate, irritate IBD. This paper looks at seven randomised controlled and uncontrolled databases looking at 4209 patients who took the drug for 6480 years. Therefore, reasonable numbers for this type of study. Looking just at ixekizumab which has recently been released on the Australian market, 12 of 16 patients who had reported IBD did not have an IBD emergent effect. Nineteen adverse events with CD and UC were considered definite or probable. The conclusion was that these cases were uncommon. Until this issue gets worked out, I would avoid the IL17 group in IBD patients. However, the chances of them flaring seems to be low and extremely rare.

Reference: J Am Acad Dermatol. 2016;Dec 24 [Epub ahead of print]
Abstract

Relative versus absolute risk of comorbidities in patients with psoriasis

Authors: Saleem MD et al.

Summary: This systematic review identified comorbidities associated with psoriasis and calculated their relative risks and absolute risks. The relative risks of comorbidities associated with psoriasis were non-melanoma skin cancer (7.5), melanoma (6.12) and lymphoma (3.61) with an attributable risk of 0.64, 0.05 and 0.17 per 1000 person-years, respectively. One of these events could be attributed to psoriasis in 1551, 20,135 and 5823 patients, respectively.

Comment: This is a statistical paper that puts the risks in a different way. I found it interesting in that patients don't understand statistics and any way that helps me explain relative risks in clear language terms is useful. So of the co-morbidities associated with psoriasis, those with the highest relative risk were non-melanoma skin cancer, melanoma and lymphoma. Relative risks being 7.5, 6.12 and 3.61, respectively. One way of reporting this is 0.64 attributable risk for non-melanoma skin cancer, 0.05 for melanoma and 0.17 for lymphoma per 1000 person-years. The other way is we would need to see 1551 patients to find a non-melanoma skin cancer, 20,135 for melanoma and 5823 for lymphoma. These figures my patients can understand a little bit better.

Reference: J Am Acad Dermatol. 2016;Dec 13 [Epub ahead of print]
Abstract

Periodontitis and risk of psoriasis: a systematic review and meta-analysis

Authors: Ungprasert P et al.

Summary: This meta-analysis combined data from two cohort studies and three case-control studies to examine the association between periodontitis and the risk of psoriasis. Statistical heterogeneity was insignificant (I^2 18%) and the pooled risk ratio (RR) for psoriasis in patients with periodontitis was 1.55 (95% CI 1.35-1.77). Subgroup analysis indicated a higher risk for developing psoriasis in patients with periodontitis in both the cohort (pooled RR 1.50; 95% CI 1.37-1.64) and case-control (pooled RR 2.33; 95% CI 1.51-3.60) studies.

Comment: A Mayo Clinic paper looking at periodontitis and systemic disease. Patients with periodontitis have a significantly elevated risk of psoriasis. As part of our general systemic work-up we should look in their mouth. If they have terrible teeth and gums, as clinicians we need to arrange that they do something about it. There is a strong risk between oral inflammation and the aggravation of psoriasis. It sort of makes sense on analysis; however, it is something we should look for as we can relatively easily treat and affect an improvement.

Reference: J Eur Acad Dermatol Venereol. 2016;Nov 15 [Epub ahead of print]
Abstract

Treatment outcomes with ixekizumab in patients with moderate-to-severe psoriasis who have or have not received prior biological therapies: an integrated analysis of two Phase III randomized studies

Authors: Gottlieb AB et al.

Summary: This pooled analysis of data from the 12-week induction phase of two phase III studies, aimed to determine the efficacy and safety of ixekizumab 80 mg every 2 (n = 736) or 4 (n = 733) weeks (after 160 mg loading dose) in psoriasis patients with (n = 497) or without (n = 2073) previous biologic exposure. In patients receiving ixekizumab 80 mg every 2 weeks, a PASI 75 score was achieved by 91.5% of biologic-experienced recipients versus 87.7% of biologic-naive recipients. In patients receiving ixekizumab 80 mg every 4 weeks, PASI 75 was achieved by 76.2% of biologic-experienced recipients versus 82.2% of biologic-naive recipients. In control patients receiving etanercept 50 mg twice weekly (n = 740), 34.6% of biologic-experienced versus 50.7% of biologic-naive recipients achieved a PASI 75 score. PASI 90 and PASI 100 response rates were also higher with ixekizumab versus etanercept within subgroups.

Comment: I put this article in as the drug has recently been released in Australia on the PBS. This paper looks at patients who were either biologically naive or had previous biological exposure. The findings in this group were that of the 497 patients who had previous biologic exposure, the final results were very similar to the 2073 who were naive to biologic therapy. I read this as being that this drug would be additionally useful in patients who had failed a previous biologic over some of the others.

Reference: J Eur Acad Dermatol Venereol. 2016;Oct 1 [Epub ahead of print]
Abstract

Clear or almost clear skin improves the quality of life in patients with moderate-to-severe psoriasis: a systematic review and meta-analysis

Authors: Puig L et al.

Summary: This meta-analysis assessed whether greater improvement in PASI scores from PASI 75-89 to PASI 90 was associated with greater Quality of life (QoL) and in particular the association between PASI response and DLQI. The change from baseline in DLQI for PASI 75-89 responders was estimated to be 78% (95% credible intervals [CrI] 75-82) while that for PASI 90 responders was 90% (95% CrI 88-93), suggesting a 12% greater improvement in DLQI in PASI 90 responders. The meta-analysis also indicated a difference in the proportion of patients with a DLQI score of 0/1 between PASI 75-89 and PASI 90 responders of 45% (95% CrI 41.0-50.0) versus 73% (95% CrI 70.0-76.0; Bayesian $p < 0.0001$).

Comment: I participated in a debate at the College Annual Scientific Meeting in Adelaide regarding this topic. I took the negative. This paper points out that I was wrong. Patients do prefer and are happier with a much better clearance rate. Therefore if we are to use a biologic, selecting biologics that are known to give us a higher PASI response rate is the logical and correct thing to do.

Reference: J Eur Acad Dermatol Venereol. 31(2):213-20
Abstract

