

Psoriasis Management in Thailand and U.K. : What are the differences?

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Siriraj Med J 2012;64:60-62

E-journal: <http://www.sirirajmedj.com>

Psoriasis is a chronic inflammatory skin disease which is found worldwide in all populations with prevalence ranging from 0.1% to 11.8%.¹ Genetic predisposition and environmental factors play an important role in the pathogenesis of the disease and most cases present before the age of 40 years. It is characterized by erythematous plaques with silvery scale usually on the scalp, elbows and knees but the whole skin surface may be affected. It can lead to psychosocial stigmatization and significant reduction in quality of life. Patient surveys show that the impairment in quality of life of psoriasis is comparable to that of patients with diabetes mellitus or chronic respiratory disease.² This significant impairment highlights the need for effective management and long term disease control.

Many treatment options for psoriasis are available ranging from topical to systemic. Localized or mild disease can be managed satisfactorily with topical agents including tar, topical corticosteroids, vitamin D analogues, vitamin A analogues, topical calcineurin inhibitors, salicylic acid and combination therapies. On the other hand, phototherapy (UVB or psoralen with UVA) and systemic agents such as methotrexate, ciclosporin, fumaric acid esters, acitretin and biological agents are usually reserved for more widespread or severe disease unresponsive to or unsuitable for topical therapy.

Several treatment guidelines have been developed for psoriasis to help physicians decide when and how to progress along treatment algorithms. Although guidelines in many countries are similar, there are some regional differences in the use of the available therapeutic approaches depending upon local tradition, drug availability and economic status of the country. To illustrate, biological drugs which have been widely used in Western countries such as the U.K., U.S.A. and Germany are used in only a small number of patients in Thailand due to the limitation of the healthcare budget. Moreover, fumaric acid esters, which are used commonly in Germany and also to

a lesser extent in the UK, are not available in Thailand. Therefore, further education and collaboration with well-established centres and academic institutions abroad are important and beneficial for the improvement of patient care and psoriasis practice in Thailand.

The Psoriasis Research Unit at the University of Manchester is regarded as one of the most comprehensive in the world. Professor Christopher Griffiths and Dr Robert Chalmers are world renowned and well recognized specialists in psoriasis at the University of Manchester. Fortunately, Professor Christopher Griffiths kindly gave a great opportunity for the author to study and conduct research in this particular field under his supervision for two years. This is an invaluable experience for the author who will be actively involved in setting up a comprehensive psoriasis clinic at the Department of Dermatology, Siriraj Hospital, Mahidol University. In the present article, the author tries to summarize the differences in management of psoriasis between Thailand and U.K. as follows.

1. Assessment and management of methotrexate hepatotoxicity by using procollagen III aminopeptidase

Methotrexate was the first potent systemic antipsoriatic agent and it has continued to play a central role in the management of psoriasis, despite the advent of newer treatments such as ciclosporin and biological agents. Hepatic fibrosis remains a significant major concern with the long-term use of methotrexate. Unfortunately, hepatic fibrosis is difficult to detect with non-invasive techniques such as standard liver function tests, ultrasound imaging and radionuclide scans. The update guideline from the National Foundation Consensus suggested that when evaluating a patient for methotrexate treatment, risk factors such as alcohol consumption, obesity, hyperlipidemia, diabetes, previous exposure to liver toxins, and hepatitis should be considered.³ In patients without risk factors for hepatotoxicity, the recent data suggest to consider liver biopsy after 3.5 to 4.5 gram total cumulative dosage of methotrexate. If a patient has significant risk factors, the first consideration should be the feasibility of using other systemic agents. If methotrexate is still a favourable agent, baseline liver biopsy should be done at or near the beginning of methotrexate therapy. A repeat of liver biopsy should be planned at a cumulative dose of 1.0-1.5 grams.

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Received 19 December 2011

Revised 13 March 2012

Accepted 13 March 2012

TABLE 1. Procollagen III aminopeptide guidelines (Manchester protocol).

Serum should be collected for PIIINP measurement prior to starting methotrexate. It should subsequently be measured every 2-3 months during continued treatment.

Indications for considering liver biopsy

- Elevation of pretreatment PIIINP above 8.0 µg/L
- Elevation of PIIINP above the normal range (1.7-4.2 µg/L) in at least three samples over a 12-month period
- Elevation of PIIINP above 8.0 µg/L in two consecutive samples

Indications for considering withdrawal of methotrexate

Elevation of PIIINP above 10.0 µg/L in at least three samples in one 12-month period

The decision whether to perform liver biopsy, withdraw treatment or continue treatment despite raised PIIINP levels must also take into account other factors such as disease severity, patient age and the ease with which alternative therapies may be used in place of methotrexate.

Note: PIIINP is not specific for liver fibrosis. The levels are high in other conditions such as children, adolescents and inflammatory arthritis. PIIINP cannot be relied upon in the first two decades of life.

Liver biopsy is problematic for many reasons such as significant pain, bleeding, mortality, sampling errors and interpretation of the biopsy. Over the past two decades, several groups have evaluated the serum concentration of procollagen III aminopeptide (PIIINP) as a surrogate marker of active hepatic fibrosis in psoriasis patients receiving long-term methotrexate. At Salford Royal Hospital, University of Manchester, Dr. Chalmers and colleagues developed procollagen III aminopeptide (PIIINP) guidelines (Manchester protocol) as follows (Table 1). The study from four centres in the U.K. and Ireland between 1998 and 2000 showed that the patients managed by the Manchester protocol using serial PIIINP measurement and selective liver biopsy were not disadvantaged in comparison with those managed by the 1998 American Academy of Dermatology guidelines.⁴ Moreover, it resulted in significant savings to the healthcare budget. The cost of a liver biopsy was £577.00 while the cost of a single serum PIIINP analysis was £22.50 (in Manchester). Currently, British and European Guidelines recommend using PIIINP testing for monitoring during methotrexate therapy.⁵ Unfortunately, the test for serum PIIINP, which is a non-invasive testing, is not available in Thailand. It might be a huge benefit for Thai psoriasis patients for PIIINP testing to be used in the future.

2. Fumaric acid esters

Fumaric acid esters (fumarates) have been licensed for the treatment of psoriasis in Germany since 1994. They are widely used for treating moderate to severe psoriasis in Germany and are accepted as an effective treatment with few side effects. The commercially available product (Fumaderm®) consists of a mixture of fumaric acid esters and in the U.K. is available only in a limited number of specialist centres. It has been used in Manchester since 1999. It is normally introduced slowly with an initial daily dose of 30 mg once a week for three weeks then twice a week for five weeks. The dosage is increased gradually to obviate mainly subjective side-effects and gastric intolerance up to a maximum dose of 240 mg three times daily.

Patients with severe disease of gastrointestinal tract and/or the kidneys, pregnancy and breast feeding should not take fumarates. It should be used carefully in patients with hematological disease.⁶ Most patients initially experience some flushing of the face and a feeling of warmth. These symptoms are usually harmless and tend to get better

during treatment. Fumarates frequently cause abdominal cramps, diarrhea and indigestion, but these are less likely to occur if the dose is increased gradually. It is best to take fumarates at meal times with plenty of liquid to avoid these side effects. Regular blood tests should be done as fumarates can cause leucocytopenia, lymphocytopenia and eosinophilia. If the leucocyte count drops below 3000/µL and lymphocytes below 500/µL, the dose must be reduced or stopped. An increased eosinophil count is temporary and is usually observed between the fourth and tenth week of treatment.

From the author's point of view, fumarates seem to be a good and reasonable option for Thai psoriasis patients if they are available in Thailand.

3. Biological Therapies:

Biological therapies or biologics are now an important part of the management of patients with moderate to severe psoriasis. Professor Griffiths has been instrumental in the development of new biologics and has performed much research on these therapies. The U.K. National Institute for Health and Clinical Excellence (NICE) has approved the use of etanercept, infliximab, adalimumab and ustekinumab for psoriasis. Alefacept is unlicensed in the U.K. Due to the fact that these are expensive there are strict eligibility criteria for biologic therapy in patients with psoriasis not only in Thailand, but also in the U.K.

Eligibility criteria for biologic therapy in U.K.⁷

Patients must have severe disease as defined in (a) and fulfill one of the clinical categories in (b).

(a) **Severe disease** defined as chronic plaque psoriasis for at least 6 months, Psoriasis and Severity Index (PASI) ≥10 (or Body Surface Area ≥ 10 if PASI is not applicable) and a Dermatology Life Quality Index (DLQI) >10

In exceptional circumstances: disease affecting high-impact sites with associated significant functional or psychological morbidity such as acral psoriasis.

AND

(b) Fulfill of at least one of the following clinical categories

i. Where phototherapy and standard systemic therapy are contraindicated or cannot be used due to development of, or risk of developing, clinically important treatment related toxicity

- ii. Intolerant to standard systemic therapies
- iii. Unresponsive to standard systemic therapies

Eligibility criteria for biologic therapy in Thailand

1. Has been diagnosed with psoriasis more than 6 months and severe disease

- 1.1 PASI $\geq$ 15 **OR**
- 1.2 Disease affecting high-impact sites such as face, palms and soles and fulfill one of the clinical criteria in 1.2.1 and 1.2.2
 - 1.2.1 severe erythema / infiltration/ desquamation (fulfill at least 2 of 3)
 - 1.2.2 involve more than 30% of the area on face, palms and soles

AND

2. Unresponsive to three of the four standard systemic treatments as follows;

- 2.1 where phototherapy has been performed twice or three times weekly for 20–24 times
- 2.2 where methotrexate has been administered at least 10 mg weekly for 16 weeks
- 2.3 where ciclosporin has been administered at least 3-5mg/kg daily for 16 weeks
- 2.4 where acitretin has been administered at least 0.4 mg/kg daily for 12 weeks

Unresponsive to treatment defined as a lower than 50% response reduction from baseline PASI (PASI 50)

3. Where standard systemic treatment cannot be used due to side-effects such as chronic renal insufficiency, diabetes mellitus, hyperlipidemia and hypertension.

If the patients achieve an adequate response which is defined as a 50% or greater reduction in baseline PASI, they will be allowed to continue the treatment for only a year in Thailand. By contrast, patients in U.K. can continue the biologic treatment beyond 12 weeks if they attain a PASI 75 or PASI 50 and a reduction in DLQI by at least 5 points. Therapy can continue until they lose response to the drug or side-effects necessitate a change. It can be seen that the criteria for biologic treatment in Thailand are more rigorous than in the U.K. due to the healthcare budget. Moreover, the impact on quality of life is not taken into account. Currently, the Dermatological Society of Thailand is undertaking development and improvement of eligibility criteria and guidelines for use of biologic treatment for Thai psoriasis patients.

4.The specialist nurse clinic

The specialist nurse is a key member of the multi-disciplinary team caring for psoriasis patients and deliver-

ing biologic therapy services. The British Dermatological Nursing Group has developed the competencies for nurses involved in the delivery of biologic therapies along the lines of those already developed by the Royal College of Nursing Rheumatology Forum. With additional training, a nurse may take responsibilities for several tasks outlined in the patient pathways including screening, disease assessments, treatment administration, patient education, prescription coordination, patient support, patient monitoring and data collection. This special nurse clinic is crucial for holistic approach to psoriasis patients and should also be established in psoriasis clinics in Thailand.

In summary, the author has tried to overview the significant difference of psoriasis management between Thailand and U.K. From the author's point of view, the ongoing education and collaboration is crucial to develop the best practice for Thai psoriasis patients in the future.

ACKNOWLEDGMENTS

The author is grateful to Professor Kanokvalai Kulthanan, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University.

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