Efficacy and safety of mycophenolate mofetil for lichen planopilaris

Bryan K. Cho, MD, PhD,[a] Deborah Sah, MD,[b] Jennifer Chwalek, MD,[c] Ingrid Roseborough, MD,[d] Blanca Ochoa, MD,[e] Charles Chiang, MD,[f] and Vera H. Price, MD[f]
Mountain View, Fremont, Union City, and San Francisco, California; Iowa City, Iowa; and Houston, Texas

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Background: Lichen planopilaris (LPP) is a chronic inflammatory disorder that causes permanent scalp hair loss and significant patient discomfort.

Objectives: We sought to determine the efficacy and safety of mycophenolate mofetil (MMF) for treatment of LPP in patients who had failed prior topical, intralesional, or oral anti-inflammatory medications such as hydroxychloroquine or cyclosporine.

Methods: We conducted a retrospective chart review of 16 adult patients with LPP treated with at least 6 months of MMF in an open-label, single-center study from 2003 to 2007. Subjective and objective end points were quantified using the LPP Activity Index (LPPAI) and scores before and after treatment were assessed using a paired *t* test. Adverse events were monitored.

Results: Patients who completed treatment with MMF had significantly decreased signs and symptoms of active LPP despite having failed multiple prior therapies ($P < .005$). Five of 12 patients were complete responders (LPPAI score decreased>85%), 5 of 12 patients were partial responders (LPPAI score decreased 25%-85%), and two of 12 patients were treatment failures (LPPAI score decreased<25%). Four patients withdrew from the trial because of adverse events.

Limitations: Retrospective analysis and small sample size were limitations.

Conclusions: MMF was effective at reducing the signs and symptoms of active LPP in 83% of patients (10 of 12) who had failed multiple prior treatments after at least 6 months of treatment. (J Am Acad Dermatol 2010;62:393-7.)

Key words: lichen planopilaris; Lichen Planopilaris Activity Index; mycophenolate mofetil.

Lichen planopilaris (LPP) is a rare cicatricial alopecia characterized by chronic lymphocytic inflammation in the upper third of the hair follicle leading to scarring and destruction of the follicle and follicular stem cells.[1] The disease presents as patchy or diffuse scalp hair loss with perifollicular erythema and scaling.[2] Active LPP will have a positive pull test for anagen hairs.[3] The disease is most common in women age 30 to 60 years.

Topical or intralesional corticosteroids and topical immune modulators (pimecrolimus, tacrolimus) are not effective as monotherapy. Most patients require oral immunosuppression.[1] Hydroxychloroquine is used most commonly, but is not always effective.[4,5] For those who fail antimalarials, treatment options are

Abbreviations used:

LPP: lichen planopilaris
LPPAI: Lichen Planopilaris Activity Index
MMF: mycophenolate mofetil

From the Department of Dermatology, Palo Alto Medical Foundation, Mountain View[a]; Urgent Care, Palo Alto Medical Foundation, Fremont[b]; Department of Dermatology, Kaiser Medical Group, Union City[c]; Department of Dermatology, University of Iowa Hospitals and Clinics[d]; Department of Dermatology, Baylor College of Medicine, Houston[e]; and Department of Dermatology, University of California, San Francisco.[f]
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Reprint requests: Vera H. Price, MD, Department of Dermatology, University of California, San Francisco, 1701 Divisadero St, Third Floor, San Francisco, CA 94143. E-mail: pricev@derm.uscf.edu.
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limited. Cyclosporine is helpful but its use is limited by its side effects.[3] Acitretin has been used for lichen planus on glabrous skin, but can cause a telogen effluvium that is poorly tolerated by patients with existing hair loss.[6] Therefore, there is an unmet need for a therapy that arrests LPP in patients who have failed current treatments.

Mycophenolate mofetil (MMF) is an antimetabolite approved for the treatment and prevention of organ rejection in patients with transplantation. It specifically inhibits activated lymphocytes, and is well tolerated with few effects on other rapidly dividing cells.[7] As lymphocytes likely play a central role in the inflammatory process underlying lichen planus and LPP, the aim of this study is to determine if MMF could safely induce a remission in patients with severe, recalcitrant LPP and prevent further hair loss.

CAPSULE SUMMARY

- Mycophenolate mofetil is significantly effective in decreasing symptoms and signs of active lichen planopilaris in patients who have failed multiple prior treatments.
- Improvement in responders is apparent within 6 months.

METHODS

The medical records and pathology reports of 16 patients with MMF treated at the University of California, San Francisco Hair Center between 2004 and 2007 were reviewed after receiving institutional review board approval. Study participants had biopsy-verified LPP less than 6 months before start of MMF and failed one or more prior systemic treatments (doxycycline, antimalarials, or cyclosporine). Patients excluded were those treated with systemic immunosuppressants less than 30 days before the first dose of MMF, prior hair transplantation, or pregnant/breast-feeding women. From the medical records, demographics, disease duration, scalp biopsy results, laboratories studies, and prior treatments were obtained. Table I shows patient demographics and Table II summarizes prior treatments.

Patients received 0.5 g of MMF orally twice daily for 4 weeks, then 1 g of MMF twice daily for at least 20 weeks although some patients were continued on MMF for up to 1 year. At roughly 12-week intervals, patients taking MMF were assessed using a standardized cicatricial alopecia flow chart[3] that scored subjective (itch, pain, and burning) and objective (scalp erythema, perifollicular erythema, perifollicular scale, anagen pull test, disease spreading) criteria. Laboratory testing (complete blood cell count, liver function tests) was assessed pretreatment, at 4 weeks, and every 12 weeks thereafter.

To quantify pretreatment and posttreatment responses to MMF, several subjective and objective surrogate markers were analyzed using the LPP Activity Index (LPPAI). The index score ranges from 0 (no evidence of clinically active disease) to 10 (most severe). This index has been previously validated to correlate with clinical responses (see Chiang et al this issue*) and allows statistical comparison. The surrogate markers were measured on a scale ranging from absent (0), mild (1), moderate (2), to severe (3). The anagen pull test was scored as negative (0) or positive (1). Assessment of disease spreading was measured on a scale ranging from inactive (0), indeterminate (1), to active spreading (2). LPPAI values were calculated using the following equation:

$$\begin{aligned} LPPAI = {} & (itch + pain + burn)/3 + \\ & (scalp\ erythema + perifollicular \\ & erythema + perifollicular\ scale)/3 + \\ & 2.5(pull\ test) + 1.5(spreading/2) \end{aligned}$$

The pre-MMF and post-MMF LPPAI scores were compared using a paired *t* test to determine if there was a significant improvement. Statistical significance was assumed for P value less than .05. Statistical analysis was performed by the University of California, San Francisco Clinical and Translational Science Institute Epidemiology Department.

To help stratify the clinical effectiveness of MMF treatment, the changes in LPPAI scores were arbitrarily divided into complete responders (>85% LPPAI score improvement), partial responders (25%-85% LPPAI score improvement), or treatment failures (<25% LPPAI score improvement).

RESULTS

Patient demographics

In this study, the overall average age of onset was 51.5 years, with the majority of patients being Caucasian and female (Table I). The onset in male patients occurred at a younger age (46.2 years) than that of female patients (54.7 years). Four patients had lichen planus diagnosed at other sites (25%) similar to the prevalence of non-scalp lichen planus in patients with LPP (28%) reported by Tan et al.[8]

*Chiang C, Sah D, Cho BK, Ochoa BE, Price VH. Hydroxychloroquine and lichen planopilaris: Efficacy and introduction of Lichen Planopilaris Activity Index scoring system. J Am Acad Dermatol 10.1016/j.jaad.2009.08.054.