

The use of mycophenolate mofetil in psoriasis: An educational article and expert opinion

Aamir Al-Mosawi

Advisor doctor and expert trainer, The National Center of Training and Development Iraqi Ministry of Health, Baghdad, Iraq.

***Corresponding Author:** Aamir Al-Mosawi, Advisor doctor and expert trainer, The National Center of Training and Development Iraqi Ministry of Health, Baghdad, Iraq.

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Abstract:

Background: Patients with mild psoriasis are generally treated with topical medications including corticosteroids, coal tar, anthralin (Dithranol), salicylic acid, vitamin D analogues such as calcipotriol, retinoid such as tazarotene, and calcineurin inhibitors such as pimecrolimus. The most commonly used safe systemic non-biological medications include methotrexate which has been used as early as the 1960s, mycophenolate mofetil which has been used as early as the 1970s, and acitretin which has been used as early as the 1980s. Safe systemic biological medications include infliximab which has been used as early as 2001.

Patients and methods: The case of a 51-year-old diabetic and hypertensive male who had moderately severe psoriasis with history of arthritic symptoms is described.

Results: The patient had been treated with several topical medications for years; however, the steroid containing topical therapies have been recently linked with worsening of hyperglycemia. Therefore, topical treatment was replaced with oral methotrexate 5 mg twice weekly. After few weeks of methotrexate treatment, there was slight improvement, and therefore increasing the dose of methotrexate to 7.5 mg twice weekly was suggested by the earlier treating physician, however, the patient was reluctant to increase the dose methotrexate because he has already aware of the possible hepatotoxic effect. When the patient presented to us, he had significant area of his body affected and systemic treatment was considered necessary. The decision was made to add oral mycophenolate with attempt of gradually withdrawing methotrexate. According to the published experiences with the use of mycophenolate monotherapy in psoriasis, a satisfactory response is expected to occur in about 70% or less, and therefore the decision was made add topical calcipotriol 0.005% and give once daily at night.

Conclusion: The current evidence-based expert opinion suggests that the choice of the treatment of methotrexate resistant psoriasis depends to a large extent on the availability of the medication, and the experience of the treating physician with the available medications. Mycophenolate can be used safely with beneficial effect in severe psoriasis and methotrexate psoriasis.

Keywords: psoriasis; expert opinion; mycophenolate

Introduction

Psoriasis is a chronic scaling skin disorder associated with systemic manifestations especially arthritic manifestations, and it may affect about 2% of people throughout the world. The disease was most probably first described by the Roman encyclopedist, Cornelius Celsus Patients (Figure-1) [1].

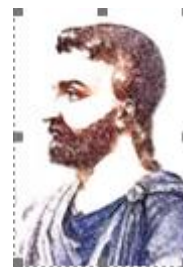


Figure-1: Aulus Cornelius Celsus (25 BC-50 AD), a Roman encyclopedist

Patients with mild disease are generally treated with topical medications including corticosteroids, coal tar, anthralin (Dithranol), salicylic acid, vitamin D analogues such as calcipotriol, retinoid such as tazarotene (AGN 190168), and calcineurin inhibitors such as pimecrolimus [2-6].

The most commonly used safe systemic non-biological medications, include methotrexate which has been used as early as the 1960s, mycophenolate mofetil which has been used as early as the 1970s, and acitretin, oral retinoid which has been used as early as the 1980s. Safe systemic biological medications include infliximab which has been used as early as 2001 [7-12].

Patients and methods

The case of a 51-year-old diabetic and hypertensive male who had moderately severe psoriasis with history of arthritic symptoms is described.

Results

The patient had been treated with several topical medications for years; however, the steroid containing topical therapies have been recently linked with worsening of hyperglycemia. Therefore, the earlier treating physician stopped topical treatment and started oral methotrexate 5 mg twice weekly. After few weeks of methotrexate treatment, there was slight improvement, and therefore the earlier treating physician suggested increasing the dose of methotrexate to 7.5 mg twice weekly, however, the patient was reluctant to increase the dose methotrexate because he has already aware of the possible hepatotoxic effect. The patient has already noticed that stopping methotrexate is associated with some increase in the severity of the disease.

When the patient presented to us, he had significant area of his body affected and systemic treatment was considered necessary.

Leukocyte count and liver function testes showed normal findings.

As there are many therapeutic options, the choice of the treatment depends on the availability of the medication, and the experience of the treating physician with the chosen medication.

Because of our extensive experience with mycophenolate in the treatment of a variety of conditions including refractory urticaria, nephrotic syndrome, and systemic lupus erythematosus, the decision was made to add oral mycophenolate 2000 mg five days a week (Not given during the days when methotrexate is taken) with attempt of gradually withdrawing methotrexate.

According to the published experiences with the use of mycophenolate monotherapy in psoriasis, a satisfactory response is expected to occur in about 70% or less, and therefore the decision was made add topical calcipotriol 0.005% and give once daily at night.

Discussion

Mycophenolic acid was first isolated by Bartolomeo Gosio (Figure-2) from *Penicillium brevicompactum* in 1896. However, his discovery was forgotten. However, it was rediscovered by Alsberg and O.M. Black from the United States in 1912. Mycophenolate mofetil (Cellcept), a derivative of mycophenolic acid was introduced by Anthony Allison a geneticist from South African and his wife Elsie M Eugui during the early 1970s, and has become an immunosuppressive agent [13].



Figure-2: Bartolomeo Gosio (17 March 17, 1863-April 13, 1944), an Italian medical scientist

Everett Linn Jones from the United States (Figure-3) and his research groups were the first to report the use of mycophenolate mofetil in the treatment of psoriasis during the 1970s. They reported the treatment of 29 patients with psoriasis treated with oral mycophenolate mofetil for at least three months. The daily dose of mycophenolate mofetil was increased from 1.6 to 4.8 g depending on occurrence of adverse effects. One patient experienced total clearing of the skin lesions, and 14 patients experienced almost total clearing of the skin lesions, definite improvement was observed in 13 patients, and slight or doubtful improvement was observed in one patient. However, discontinuing treatment was associated with relapses that were observed at a median time of one month (Range: 3-8 weeks). Side effects included nausea, anorexia, and soft or frequent bowel motions or diarrhea. One patient experienced reversible, dose-related leukopenia [9, 10].



Figure-3: Everett Linn Jones from the United States

In 1977, Lynch and Roenigk reported a placebo-controlled study which included 38 patients with psoriasis treated with mycophenolate. The study showed mycophenolic acid was effective in treating psoriasis (P less than .01) [14].

In 1978, Spatz and colleagues reported a study which included 28 patients with psoriasis. The study showed that about 75% of patients treated with mycophenolate experience good to excellent improvement, and toxicity was low. Spatz and colleagues emphasized that mycophenolate can be very useful in treating patients with severe psoriasis [15].

In 1979, Gomez and colleagues reported a placebo-controlled study which included 21 patients with psoriasis. 10 of 11 patients treated with mycophenolate experienced more than 25% reduction in severity while only 2 of 10 patients treated with placebo experience such improvement.

The placebo group experienced a slight increase in severity, while patients treated with mycophenolate experienced about 50% decrease in severity. When the placebo group was treated with mycophenolate, experienced a 60% reduction in severity

Adverse effects included nausea, anorexia, vomiting, and diarrhea. One patient experienced an uncomplicated herpes zoster infection. Mild reduction in hemoglobin level was observed in some patients [16].

In 2001, Geilen and colleagues reported a study which included 11 patients with severe stable plaque-type psoriasis. They were treated with oral mycophenolate 2000 mg in 2 divided doses daily for 3 weeks and then 1000 mg in 2 divided doses daily for 3 weeks. Within 3 weeks of mycophenolate treatment, 7 of 11 patients experienced significant reduction in severity. Gastrointestinal and hematological toxicity didn't occur in any of the treated 11 patients.

Geilen and colleagues suggested that 2000 mg daily dose of mycophenolate is safe, and can be effective and in the treatment of patients with severe psoriasis [17].

In 2003, Youwen Zhou from Canada and his research group reported the treatment of 18 patients with moderate to severe psoriasis treated with mycophenolate mofetil alone in a dose of 2000-3000 mg daily for three months. 77% of the 18 patients experienced marked improvement. Five

patients complained of mild nausea. One patient developed peri-orbital edema, one patient's experienced pruritus, and one patient developed transient leukopenia [18].

In 2006, Herrera et al reported a study which showed that mycophenolate mofetil can treatment improves blood pressure in hypertensive patients with psoriasis [19].

Conclusion

The current evidence-based expert opinion suggests that the choice of the treatment of methotrexate resistant psoriasis depends to a large extent on the availability of the medication, and the experience of the treating physician with the available medications. Mycophenolate can be used safely with beneficial effect in severe psoriasis and methotrexate psoriasis.

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