ASIDE

ASIDE Gastroenterology

ASIDE GASTROENTEROLOGY

Editorial

Mycophenolate Mofetil Use for Inflammatory Bowel Disease

Ahmed Abomhya[1], Ahmed Elmoursi[2]*

1- Department of Gastroenterology, University of Kentucky, Lexington, KY, USA.
2- Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, Mass; Harvard Medical School, Boston, MA, USA.

ARTICLE INFO

Article history:
Received 18 Mar. 2025
Received in revised form 06 Apr. 2025
Accepted 06 Apr. 2025

Keywords:
Mycophenolate Mofetil
Inflammatory Bowel Disease
Ulcerative Colitis
Crohn's Disease
Immunosuppressive Therapy
Anti-inflammatory Agents
Immunomodulators
Gastrointestinal Inflammation
Mycophenolic Acid

EDITORIAL

Mycophenolate Mofetil (MMF) is a prodrug that gets converted to mycophenolic acid (MPA). MPA inhibits the Akt/mTOR and STAT5 pathways and has a reversible cytostatic effect on T and B lymphocytes [1].

MMF is FDA-approved for immunosuppressive therapy after solid organ transplantation. MMF has been used for multiple inflammatory/autoimmune conditions including psoriasis, dermatomyositis, autoimmune hepatitis, lupus erythematosus, myasthenia gravis, and Takayasu arteritis [2].

In this Editorial, we discuss the recently published systematic review and meta-analysis by Balassiano et al [3]. This systematic review and meta-analysis studied the use of MMF for the treatment of IBD patients. This review included both retrospective studies, case series, and clinical trials that evaluated the use of MMF in patients with IBD. Included patients were intolerant or unresponsive to Azathioprine. MMF was used in the included studies for induction and maintenance of remission, or as a steroid sparing agent/immunomodulator. This study demonstrated MMF's efficacy in both induction and maintenance of remission in IBD patients. MMF was associated with added benefits for patients on steroids as well as those on anti-TNF therapy [3].

MMF has several boxed warnings in the United States, limiting its use outside FDA-approved indications. MMF should be prescribed only by healthcare providers experienced in immunosuppressive therapy and organ transplant management, with access to comprehensive laboratory and medical resources [4].

There is also a significant risk of infections associated with immunosuppression including but not limited to opportunistic infections, which may result in significant morbidity and mortality. MMF use is associated with an increased risk of malignancy including but not limited to lymphoma and skin cancers. There is also a boxed warning suggesting avoiding MMF use in pregnancy if alternative therapies are available as its use is associated with congenital malformation and first-trimester pregnancy loss [5].

*** Corresponding author:** *Ahmed Abomhya, Department of Gastroenterology, University of Kentucky, Lexington, KY 40508, USA. Email Address: mailto: ahmedabdelsatar78@gmail.com*

ISSN (Print): 3066-4004, ISSN (Online): 3066-4012 – See front matter

Citation: Abomhya A, Elmoursi A. Mycophenolate Mofetil Use for Inflammatory Bowel Disease. ASIDE GI. 2025;1(2):1-3. doi:10.71079/ASIDE.GI.04142552

https://doi.org/10.71079/ASIDE.GI.04142552
Journal homepage: https://asidejournals.com/index.php/Gastroenterology

MMF has been associated with endoscopic findings that could be similar to acute colitis, IBD, ischemia, and graft-versus-host disease. Development of such side effects or endoscopic findings can lead to discontinuation of treatment, treatment interruption, or medication non-compliance [6, 7].

In this study, the pooled event rate for adverse events was 26.1% (20.3%-32.8%). The side effect profile is crucial in determining the role of MMF in IBD treatment. The IBD field is evolving around a patient-centered approach when it comes to therapeutic selection. IBDologists extensively discuss potential side effects and explore the patient's risk appetite. In general, more than one in four is considered a relatively high risk.

While side effects could constitute a major challenge for MMF use in IBD patients, their impact on treatment adherence, disease progression, and quality of life must be carefully weighed against MMF's potential benefits. The development of side effects has been associated with specific risk factors that increase the risk of developing side effects which could open the door for drug adjustment and close monitoring that might allow its use. These risk factors include using a non-enteric coated formulation, increased MMF blood levels, concomitant use of other immunosuppressant agents like calcineurin inhibitors, and female sex [8-11].

MMF is relatively inexpensive compared to other IBD therapies. A dose price can be as low as $0.32 for an oral dose and as high as $129.57 for an IV dose. This is cheaper compared to Azathioprine prices [12]. With the evolving widespread use of biosimilars, we are heading to an era with better accessibility to advanced IBD therapies and this will allow gastroenterologists to adopt the recommended top-down approach in therapeutic selection [13].

The ACG guidelines for Crohn's disease recommend combining an immunomodulator with anti-TNF rather than using anti-TNF alone [14]. Hernandez-Camba et al. showed added benefits of anti-TNF when combined with MMF [15]. This suggests potential benefits of MMF as an immunomodulator that could decrease anti-TNF immunogenicity and decrease the risk of secondary non-response.

The study has some significant limitations. The included studies had heterogeneous designs. The study lacked a control group and did not compare MMF to alternatives such as Azathioprine or Mercaptopurine.

The IBD therapies are expanding and it's an evolving field with multiple advancements annually. Selection of therapy in patients with IBD is a multi-step and complex process that involves close consideration of the disease stage, patient population, disease complications, medication history, prognostic factors, presence of extra-intestinal manifestations of IBD, potential side effects of medications, patients' preferences and cost implications [14].

In conclusion, this study highlights the potential benefits of MMF as a steroid-sparing agent or as an immunomodulator in conjunction with ant-TNF. It provides evidence for the use of MMF as an alternative for those intolerant or unresponsive to Azathioprine and Methotrexate.

Conflicts of Interest:

None

Ethical Approval:

None

Funding Source:

None

Acknowledgements:

None

Institutional Review Board (IRB) Approval:

None

LLM Statement:

None

Authors Contribution Statement:

All authors have contributed equally to the conception, drafting, review, and final approval of this manuscript. Each author has read and agreed to the final version for publication.

Data Availability Statement:

None

References

1. Allison AC, Eugui EM. Mycophenolate mofetil and its mechanisms of action. Immunopharmacology. 2000: 85 [PMID: 10878285, https://doi.org/10.1016/s0162-3109(00)00188-0]

2. Alakkas Z, Gari AM, Makhdoum S, AlSindi EA. Mycophenolate-induced colitis in a patient with lupus nephritis: a case report and review of the literature. J Med Case Rep. 2024: 229 [PMID: 38689344, https://doi.org/10.1186/s13256-024-04539-7]

3. Balassiano N, Tidwell J, Abdelhalim O, Abusuliman M, Nassar M, Beran A, Cancarevic I, Abosheaishaa H. Mycophenolate Mofetil for the Treatment of Resistant Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. ASIDE Gastroenterology. 2025: 15 https://doi.org/10.71079/aside.Gi.03132515]

4. Kim M, Rostas S, Gabardi S. Mycophenolate fetal toxicity and risk evaluation and mitigation strategies. Am J Transplant. 2013: 1383 [PMID: 23617812, https://doi.org/10.1111/ajt.12238]

5. Pisoni CN, D'Cruz DP. The safety of mycophenolate mofetil in pregnancy. Expert Opin Drug Saf. 2008: 219 [PMID: 18462179, https://doi.org/10.1517/14740338.7.3.219]

6. Calmet FH, Yarur AJ, Pukazhendhi G, Ahmad J, Bhamidimarri KR. Endoscopic and histological features of mycophenolate mofetil colitis in patients after solid organ transplantation. Ann Gastroenterol. 2015: 366 [PMID: 26126799,

7. de Andrade LG, Rodrigues MA, Romeiro FG, Garcia PD, Contti MM, de Carvalho MF. Clinicopathologic features and outcome of mycophenolate-induced colitis in renal transplant recipients. Clin Transplant. 2014: 1244 [PMID: 25142167, https://doi.org/10.1111/ctr.12452]

8. Arns W. Noninfectious gastrointestinal (GI) complications of mycophenolic acid therapy: a consequence of local GI toxicity? Transplant Proc. 2007: 88 [PMID: 17275481, https://doi.org/10.1016/j.transproceed.2006.10.189]

9. Kiang TKL, Ensom MHH. Exposure-Toxicity Relationships of Mycophenolic Acid in Adult Kidney Transplant Patients. Clin Pharmacokinet. 2019: 1533 [PMID: 31332670, https://doi.org/10.1007/s40262-019-00802-z]

10. Langone AJ, Chan L, Bolin P, Cooper M. Enteric-coated mycophenolate sodium versus mycophenolate mofetil in renal transplant recipients experiencing gastrointestinal intolerance: a multicenter, double-blind, randomized study. Transplantation. 2011: 470 [PMID: 21245794, https://doi.org/10.1097/TP.0b013e318205568c]

11. Meaney CJ, Sudchada P, Consiglio JD, Wilding GE, Cooper LM, Venuto RC, Tornatore KM. Influence of Calcineurin Inhibitor and Sex on Mycophenolic Acid Pharmacokinetics and Adverse Effects Post-Renal Transplant. J Clin Pharmacol. 2019: 1351 [PMID: 31062373, https://doi.org/10.1002/jcph.1428]

12. Tse KC, Tang CSO, Lam MF, Yap DYH, Chan TM. Cost Comparison Between Mycophenolate Mofetil and Cyclophosphamide-Azathioprine in the Treatment of Lupus Nephritis. The Journal of Rheumatology. 2009: 76 https://doi.org/10.3899/jrheum.080517]

13. Satsangi J, Nowak J, Kalla R, Colombel JF. Treatment strategies and biomarkers in Crohn's disease: the PROFILE trial. Lancet Gastroenterol Hepatol. 2024: 591 [PMID: 38870964, https://doi.org/10.1016/S2468-1253(24)00082-7]

14. Lichtenstein GR, Loftus EV, Jr., Isaacs KL, Regueiro MD, Gerson LB, Sands BE. Correction: ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018: 1101 [PMID: 29895986, https://doi.org/10.1038/s41395-018-0120-x]

15. Hernandez-Camba A, Arranz L, Vera I, Carpio D, Calafat M, Lucendo AJ, Taxonera C, Marin S, Garcia MJ, Marin GS, Rodriguez ES, Carbajo AY, De Castro ML, Iborra M, Martin-Cardona A, Rodriguez-Lago I, Busquets D, Bertoletti F, Ausin MS, Tardillo C, Malaves JH, Bujanda L, Castano A, Domenech E, Ramos L, Geteccu, Additional member of the Spanish Gg. Real-world use of mycophenolate mofetil in inflammatory bowel disease: Results from the ENEIDA registry. Dig Liver Dis. 2022: 635 [PMID: 34862115, https://doi.org/10.1016/j.dld.2021.10.002]