

Introduction

- Mycophenolic acid (MPA) is an immunosuppressive drug used to prevent rejection after solid organ transplantation and has off-label use in lupus erythematosus. MPA reversibly inhibits inosine monophosphate dehydrogenase (IMPDH), an enzyme important for synthesis and proliferation of T- and B-lymphocytes. MPA is available in two formulations: mycophenolate mofetil (MMF, CellCept), the ester prodrug of MPA, and mycophenolate sodium (EC-MPS, Myfortic), a delayed-release, enteric-coated formulation of active MPA.¹
- This case report documents the transfer of the MPA active moiety into breastmilk from a lactating mother taking MMF.
- The understanding of MPA transfer into breastmilk is greatly limited. Product labeling for MPA includes a boxed warning for increased risk of congenital malformations and is not recommended during pregnancy.² Because transplant recipients must receive immunosuppressive therapy, lactating mothers who require MPA after delivery are advised to discontinue breastfeeding due to unknown infant risk.³

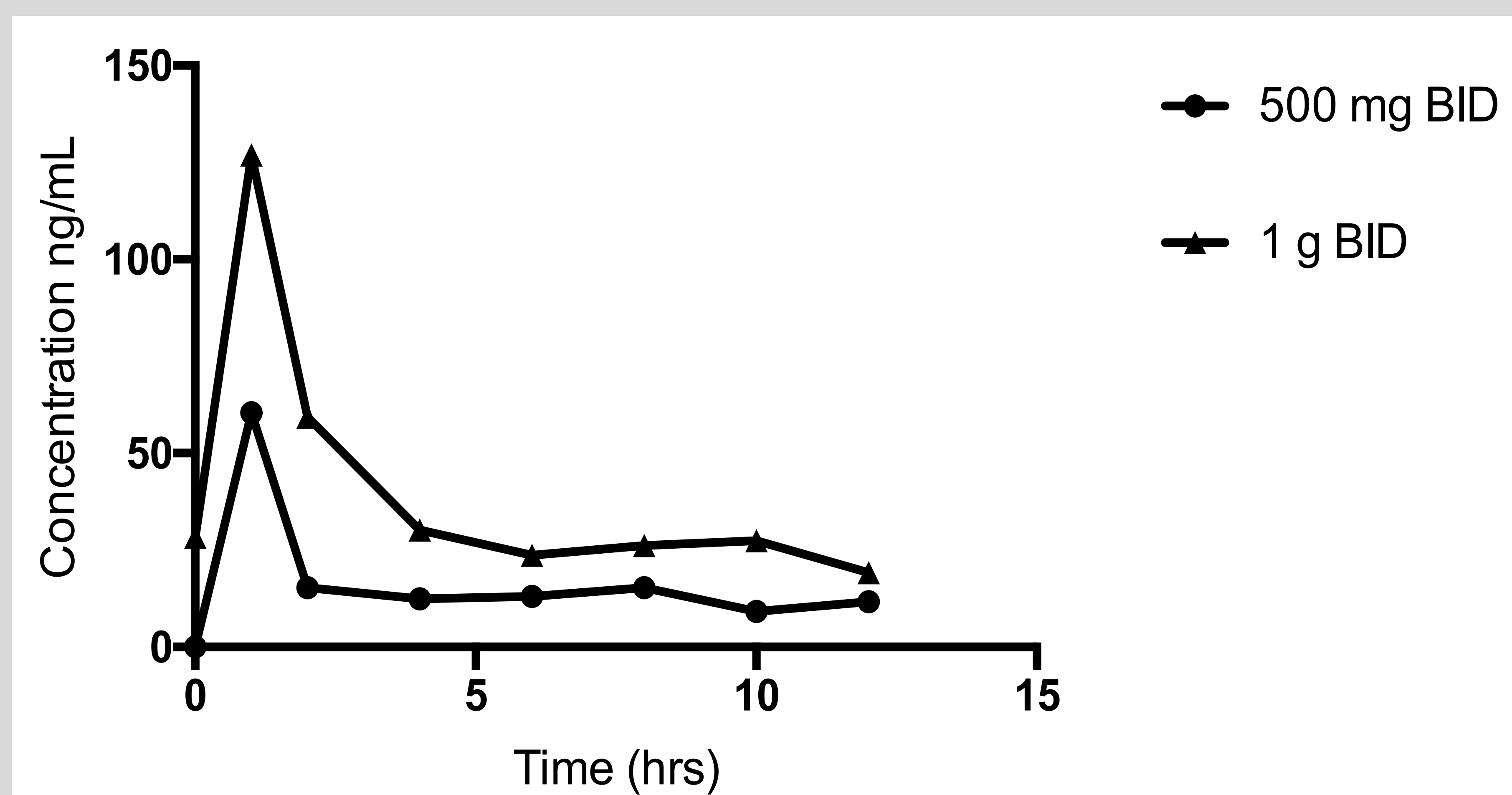
Case Report

Case Report:

- A 47-year-old mother gave birth at 37 weeks gestation to a 2.3 kg infant.
- The mother has a history of lupus nephritis for which she took the immunosuppressive regimen of mycophenolate mofetil 500 mg twice daily and prednisone 30 mg daily. Her initial MMF dose was later titrated to a dose of 1000 mg twice daily.
- Other medications taken by the mother include daily prenatal vitamins, vitamin D 50,000 units weekly, docusate 150 mg daily, hydroxychloroquine 200 mg daily, aspirin 81 mg daily, labetalol 250 mg twice daily, and enalapril 20 mg daily.

Methods:

- After five days of taking 500 mg twice daily, breastmilk samples were collected at 0, 1, 2, 4, 6, 8, 10, and 12 hours. The same process was repeated for the 1000 mg twice daily dose.
- MPA was quantified using an Agilent 1260 Quadrupole mass spectrometer and a Phenomenex Luna column, 50 x 2 mm, 3 μm. Blank milk and acetonitrile were spiked with MPA and serially diluted for standard curves.
- The relative infant dose (RID) was calculated using an average milk intake of 150 mL/kg/day and is based on a weight-adjusted dose.



Concentration of MPA in breastmilk versus time following an oral dose of 500 mg and an oral dose of 1 gram

Parameter	Dose 1	Dose 2
Dose	500 mg twice daily	1000 mg twice daily
AUC (ng.h/mL)	195.1	464
C _{max} (ng/mL)	60.5	126.9
T _{max} (hr)	1	1
Relative Infant Dose (%)	0.02	0.02

AUC: area under the drug concentration-time curve in milk
 C_{max}: maximum drug concentration during the dosing interval
 Relative Infant Dose (RID): calculated by dividing the infant dose by the maternal dose and multiplying by 100 to express as a percent

Results

- MPA RID = 0.02% of maternal dose for dose 1 (500 mg) and for dose 2 (1000 mg)
- Maximum concentration of 60.5 ng/mL was reached after 1 hour for dose 1
- Maximum concentration of 126.9 ng/mL was reached after 1 hour for dose 2

Discussion

- A relative infant dose of less than 10% is widely considered low risk for the infant and is generally considered the acceptable threshold for breastfeeding.
- With an RID of 0.02%, the results of this case suggest that MPA transfer into breastmilk is minimal.
- The transfer of drugs into human breastmilk greatly depends on the physicochemical properties of the drug, as well as several pharmacokinetic parameters, including maternal plasma concentration, elimination half-life, and plasma protein binding. MPA is bound to plasma albumin at 97%, which could contribute to its minimal transfer into breastmilk.¹
- Following oral administration of MMF, it is immediately hydrolyzed to active MPA. MMF has an oral bioavailability of 94%, which is a parameter that should be considered while taking this drug during breastfeeding.¹ Infants will more easily absorb a drug with higher oral bioavailability.³

Conclusion

- The RID for MPA found in this case report was well below the most conservative theoretical levels of concern for breastfeeding, suggesting that MPA transfer into breastmilk is minimal and potentially unlikely to pose a significant risk to breastfed infants.
- Current practice recommendations support discontinuing MPA during pregnancy due to fetotoxic risk and lactation due to an abundance of caution.³
- While the infant in this case report did not receive breastmilk, these results imply MMF may be a good candidate for further research as a feasible, safe option for treatment in lactating mothers.

References:

- Gold Standard, Inc. Clinical Pharmacology [Internet]. Philadelphia, PA: Elsevier 2021. Mycophenolate.
- CellCept. Package insert. Hoffman-La Roche Inc; 2021.
- Constantinescu S, Pai A, Coscia LA, Davison JM, Moritz MJ, Armenti VT. Breast-feeding after transplantation. *Best Pract Res Clin Obstet Gynaecol.* 2014;28(8):1163-73. doi:10.1016/j.bpobgyn.2014.09.001

