Oral antibiotics lower mycophenolate mofetil drug exposure by interfering with the enterohepatic recirculation: a case series

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Abstract

Mycophenolate mofetil has an important role as immunosuppressive agent in solid organ transplant recipients. Exposure to the active mycophenolic acid (MPA) can be monitored using therapeutic drug monitoring. We present three cases in which MPA exposure severely decreased after oral antibiotic co-administration. By diminishing gut bacteria β-glucuronidase activity, oral antibiotics seem to prevent deglucuronidation of the inactive MPA-7-O-glucuronide metabolite to MPA and thereby prevent its enterohepatic recirculation. This pharmacokinetic interaction could result in rejection, which makes it clinically relevant in solid organ transplant recipients, especially when therapeutic drug monitoring frequency is low. Routine screening for this interaction, preferably supported by clinical decision support systems, is advised.

Dear Mr. Cremers,

Enclosed please find our manuscript "Oral antibiotics lower mycophenolate mofetil drug exposure by interfering with the enterohepatic recirculation: a case series". We consider this manuscript particularly suitable for the *British Journal of Clinical Pharmacology* as we report on three solid organ transplant patients in which mycophenolic acid trough concentrations severely decreased after oral antibiotic co-administration. We believe this effect is due to interference with the enterohepatic recirculation by some antibiotics. To the best of our knowledge, we are the first to report such an effect for oral vancomycin.

We believe it is important to draw the attention of clinicians and researchers to this interaction. The enterohepatic recirculation may account for up to 60% of the mycophenolate acid (MPA) exposure and bacterial infections are common in patients using immunosuppressants such as mycophenolate mofetil (MMF). Interference with the enterohepatic recirculation by antibiotics may thus have a significant impact on MPA exposure and result in potentially ineffective immunosuppression leading to allograft rejection. Therefore, we suggest routine screening for the combination of mycophenolate mofetil and antibiotics interfering with the enterohepatic recirculation, preferably using clinical decision support systems.

This manuscript represents original material, has not been previously published and has not been submitted for publication elsewhere.

I hope you will consider this case report for publication in your journal.

Yours sincerely, also on behalf of all co-authors,

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