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Mycophenolate Sodium Delayed Release

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Mycophenolate mofetil was introduced in 1995 for maintenance immunosuppression in kidney transplantation after its efficacy was established in three large randomised, double-blind studies. Its addition to the current immunosuppressive regimens has resulted in a significant and clinically important improvement in the outcome after kidney transplantation. The proportion of patients receiving mycophenolate mofetil has increased from 11% in 1995 to 77% in 1999 (United Network for Organ Sharing Renal Transplant Registry). However, the use of this agent was associated with a certain number of gastrointestinal adverse effects, which led to dose reductions, discontinuation or withdrawal, thus compromising efficacy and compliance.[1]

Mycophenolate sodium delayed release is an enteric-coated formulation designed to release the active agent (mycophenolic acid) in the small intestine and, therefore, circumvent the problem of gastrointestinal toxicity. Studies have shown that the new formulation of mycophenolic acid is equivalent in efficacy to mycophenolate mofetil in *de novo* and maintenance kidney transplant recipients. With mycophenolate sodium delayed release, the low mycophenolic acid area under the concentration-time curve is confined to the early postoperative phase.[2] Although differences exist in the pharmacokinetic profiles of the two formulations, the adverse events profile is similar. In particular, no relevant improvement in the incidence of gastrointestinal events was revealed; a result, in my opinion, that was foreseeable. The gastrointestinal toxicity of mycophenolic acid is, to a major extent, related to the systemic effect of the drug on enterocytes, which are approximately 50% dependent on the *de novo* pathway of purine synthesis.[1] Therefore, a change of the resorption site and the pharmacokinetics of the new formulation did not influence the systemic adverse events.

Nevertheless, mycophenolate sodium delayed release is a very valuable addition to the armamentarium of immunosuppressive drugs. In my view, maximum therapeutic efficacy for this formulation of mycophenolic acid will only be achieved when the ideal dosage is established. A fixed dose regimen for mycophenolate sodium delayed release should be abandoned. Instead, an individualised, and carefully monitored, regimen that maximises therapeutic efficacy for each patient should be implemented. ▲

References

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