CASE REPORT

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Improvement in Social Functioning in Kidney Transplant Patients after Conversion from Mycophenolate Mofetil to Enteric-coated Mycophenolate Sodium (*myfortic*®): Three Case Studies

Tariq Shah

National Institute of Transplantation, Los Angeles, California, USA

1. Case Study 1

The patient was a 61-year-old Caucasian woman who had suffered from Wegener's granulomatosis for 4 years, requiring haemodialysis for 3 years. As a result of her condition, she experienced constant tiredness, weakness, depression and lack of motivation, and was unable to work. After receiving a kidney transplant from a 69-year-old female deceased donor, five antigen mismatch, cold ischaemia time of 25 h, she received thymoglobulin induction and maintenance immunosuppression consisting of prednisone 5 mg/day, tacrolimus 1 mg twice a day, and mycophenolate mofetil (MMF) 750 mg three times a day. This dose was chosen as the patient received an extended criteria donor kidney, and it was felt that to maintain good graft function the dose of calcineurin inhibitor should be maintained as low as practicable and the MMF dose should be maximized. Her serum creatinine improved from 406 μmol/l on day 2 posttransplant to 150 μmol/l at one week posttransplant. The patient then started to experience severe abdominal pain, bloating, diarrhoea, nausea and vomiting, within 2 weeks of transplantation, which were present for 3 days before her next hospital visit, although kidney function was unaffected and tacrolimus trough levels were 12.3 ng/ml. As a result of the severity of the symptoms, she felt unable to leave the house and became increasingly depressed; antidepressant therapy was prescribed. In an attempt to ameliorate the severe gastrointestinal symptoms MMF was reduced to a dose of 500 mg three times a day, but the symptoms did not reduce and she was readmitted to hospital. At this point it was decided that, because of the severity of her symptoms, conversion to enteric-coated mycophenolate sodium (EC-MPS; *myfortic*®) would be attempted instead of a further MMF dose reduction or dose splitting. The patient converted from MMF to EC-MPS at a dose of 360 mg three times a day. After conversion, her gastrointestinal symptoms resolved. Serum creatinine levels remain stable at 97 μmol/l.

The patient has now been receiving EC-MPS 360 mg three times a day for 10 months with no recurrence of gastrointestinal complaints. She now feels able to leave the house each day because her diarrhoea has resolved, and she has discontinued antidepressant medication.

2. Case Study 2

The patient is a 52-year-old Asian woman who suffered from type 2 diabetes for 15 years and is now insulin dependent. She also had a history of

seizure disorder for which she received phenytoin. She developed diabetic nephropathy approximately 2 years before transplantation, requiring dialysis for 6 months before transplant. At this stage she was working in an office and was able to undertake some exercise, but tired very easily. She received a kidney transplant from a 56-year-old male deceased donor (six antigen mismatch, cold ischaemia time of 26 h). Induction therapy was basiliximab with maintenance immunosuppression consisting of prednisolone 2 mg/day, cyclosporine microemulsion 200 mg once a day and MMF 1000 mg twice a day. Two years after transplantation, the patient complained of dyspepsia, nausea and bloatedness, with loss of appetite and a continuous feeling of satiety, which caused considerable discomfort. Reducing the MMF dose to 750 mg twice a day for one month only improved her gastrointestinal symptoms minimally; she felt unable to attend any social events and her quality of life was markedly reduced. As a result, she was converted to an equimolar concentration of EC-MPS 540 mg twice a day. After conversion, the symptoms resolved completely and her quality of life has improved greatly. She socialises and travels and has started a new business, reporting that she feels revitalised and has none of her previous anxiety about the gastrointestinal adverse events. The serum creatinine concentration is now stable at approximately 106 μmol/l.

3. Case Study 3

The patient is a 54-year-old Hispanic woman who received a living-related kidney transplant in 1981 for end-stage renal disease. The patient subsequently developed nephrosclerosis/chronic allograft nephropathy with deteriorating renal function requiring haemodialysis. She was not working and reported feeling very weak and easily tired most of the time. She received a second transplant in 2003, from a 41-year-old caucasian female deceased donor, six antigen mismatched, cold ischaemia time of 26 h. Induction therapy was thymoglobulin and maintenance immunosuppression was prednisolone 5 mg/day, tacrolimus 1.5 mg/day (as divided into 1.0 and 0.5 mg doses, providing trough levels of 9.3 ng/ml) and MMF 500 mg twice a day. A low dose of MMF was selected because of the presence of mild gastrointestinal symptoms. Her serum creatinine levels at this point were 229 μmol/l. After 18 months, she experienced severe diarrhoea, nausea and vomiting, dyspepsia and mild-to-moderate abdominal pain. She also complained of loss of appetite and spent a considerable amount of time in bed, lacking the energy to work either in or outside the home, and found it impossible to socialise or travel because of frequent diarrhoea. During MMF therapy she lost 5 kg to a final weight of 51 kg (body mass index 22). Reducing the MMF dose (500 mg three times a day to 500 mg twice a day) did not resolve the symptoms. The serum creatinine level at this point was in the range 185–220 μmol/l. As the gastrointestinal symptoms did not resolve by reducing the dose of MMF, she was therefore converted to EC-MPS 360 mg twice a day. After conversion, her gastrointestinal symptoms and nausea resolved completely, her appetite improved, she has maintained her weight and the patient reports significantly improved social functioning. Serum creatinine remains 176 μmol/l.

4. Discussion

In each of these three cases, the potential improvement in well-being and quality of life offered by kidney transplantation was negated by severe gastrointestinal side effects associated with MMF therapy. Quality of life is increasingly recognised by physicians and healthcare policy makers as an important treatment outcome.[1] A recent study has shown that gastrointestinal complaints in renal transplant patients are associated with significantly impaired physical, social and psychological functioning, as measured by validated, standardised patient-reported outcomes instruments.[2] In addition, reducing the MMF dose or discontinuing MMF in patients with gastrointestinal complaints significantly increases the risk of acute rejection and graft loss. [3–7] However, EC-MPS and MMF have been shown to offer equivalent efficacy,[8,9] and conversion to EC-MPS

presents another option for the management of MMF-related gastrointestinal side effects. In the three cases reported here, conversion from MMF to EC-MPS not only resolved the gastrointestinal symptoms, but also resulted in improvements in social functioning, anxiety and depression.

References

1. Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med 1993; 118: 622-9
2. Chan L, Mulgaonkar S, Walker R, et al. Patient-reported gastrointestinal symptom burden and health-related quality of life following conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium. Transplantation 2006; 81: 1290-7
3. Tierce JC, Porterfield-Baxa J, Petrilla AA, et al. Impact of mycophenolate mofetil (MMF)-related gastrointestinal complications and MMF dose alterations on transplant outcomes and healthcare costs in renal transplant recipients. Clin Transplant 2005; 19: 779-84
4. Pelletier RP, Akin B, Henry ML, et al. The impact of mycophenolate mofetil dosing patterns on clinical outcome after renal transplantation. Clin Transplant 2003; 17: 200-5
5. Knoll GA, MacDonald I, Khan A, et al. Mycophenolate mofetil dose reduction and the risk of acute rejection after renal transplantation. J Am Soc Nephrol 2003; 14: 2381-6
6. Hardinger K, Brennan DC, Lowell J, et al. Long-term outcome of gastrointestinal complications in renal transplant patients treated with mycophenolate mofetil. Transplant Int 2004; 17: 609-16
7. Schnitzler MA, Hardinger KL, Burroughs TE, et al. Consequences of immunosuppression minimization following diagnosis of gastrointestinal complications in renal transplant. Am J Transplant 2005; 5(S11): 242
8. Salvadori M, Holzer H, de Mattos AM, et al. Enteric-coated mycophenolate sodium is therapeutically equivalent to mycophenolate mofetil in *de novo* renal transplant patients. Am J Transplant 2004; 4: 231-6
9. Budde K, Curtis J, Knoll G, et al. Enteric-coated mycophenolate sodium can be safely administered in maintenance renal transplant patients: results of a 1-year study. Am J Transplant 2004; 4: 237-43

Correspondence and offprints: *Tariq Shah,* National Institute of Transplantation, 2200 West Third Street, Suite 500, Los Angeles, CA 90057, USA.
Tel: +1 (213) 413 2779; fax: +1 (213) 483 2652;
e-mail: tariq.shah@transplantation.com