

Older immunosuppressive agents: Newer approach in liver transplant recipients

Ashokkumar B. Jain
Temple University, USA

Combined Calcineurin Inhibitors (CI), antiproliferative agents & steroids is now standard immunosuppression post-liver-transplantation. Though acute rejection is uncommon nowadays, it is not eradicated. Renal dysfunction is frequent both pre- and post-transplantation. CIs, known nephrotoxic agents, when included in immunosuppressive cocktails after complicated surgery, with drastic intra-operative hemodynamic changes, only worsen renal impairment.

Oral absorption of Mycophenolate Mofetil (MMF) is <50% in initial weeks after liver transplantation. Intravenous (IV) MMF achieves 100% bioavailability, permitting delayed CI introduction. This combination with standard dose steroids, we have not experienced new onset renal failure. Furthermore, preexisting hepato-renal dysfunction resolved in all cases. A low rate of (<10%) of acute cellular rejection was observed, which were readily reversed with 0.5 to 1.5 gm of methyl prednisolone.

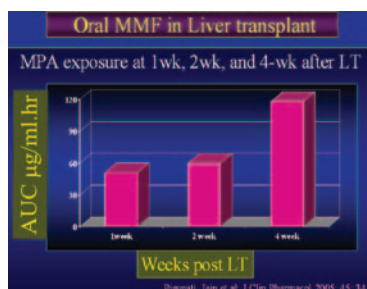


Fig 1. Oral bioavailability of MMF increase from 1-4 wks post transplant.

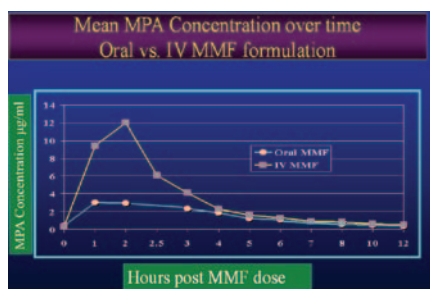


Fig 2. Bioavailability of IV MMF > Oral MMF

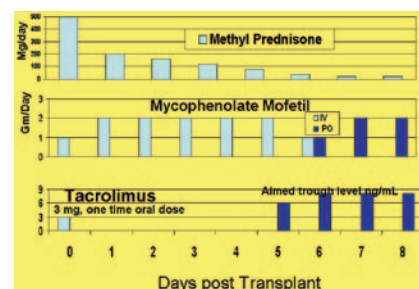


Fig 3. Our approach to post liver transplant immunosuppression.

Fig 3: Steroid: IV Methyl-Prednisone (MP) 500 mg bolus in anhepatic phase, 50 mg q6h (day 1) → 40 mg q6h (day 2) → 30 mg q6h (day 3) → 20 mg q6h (day 4) → 20 mg q12h (day 5) → Prednisone 20 mg po od (day 6 onwards). MMF: 1000 mg IV intra-operatively, then 1000 mg q12h IV from day 1. Tacrolimus: 3 mg po on call to surgery, no tacrolimus in days 1-4. From day 5 oral tacrolimus titrated to achieve trough concentration of about 8 ng/ml.

Biography

Ashokkumar Jain, with 25 years experience in Liver Transplantation, graduated from T.N. Medical College, Bombay, India. Masters in Surgery from Bombay University. Surgical training, UK. At University of Pittsburg, USA, mentored by Thomas Starzl, who performed first successful human liver transplantation. Faculty at Pittsburg for 14 years, then at University of Rochester. Presently Director, Liver Transplantation, Temple University Hospital, Philadelphia, where he restarted liver transplantation after eight years. Performed over 1,500 transplants, authored over 250 articles, constant invitee in conferences worldwide. Member, journal editorial boards and advisory bodies. Made substantial contributions in immunosuppressant pharmacokinetics. Mentored generations of transplant surgeons.

Ashokkumar.Jain@tuhs.temple.edu