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Tacrolimus: In Heart Transplant Recipients

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Calcineurin inhibitors have been at the core of immunosuppression for heart transplant recipients. Traditional ciclosporin and later modified microemulsion ciclosporin enabled prolonged cardiac allograft survival and in combination with corticosteroids and either azathioprine or mycophenolate mofetil (MMF) have made cardiac transplantation available to thousands of patients worldwide. Unfortunately, ciclosporin use has been limited by adverse effects including hypertension, gingival hyperplasia, hirsutism and renal insufficiency. In addition, a small number of patients have experienced recurrent allograft rejection despite therapeutic dosing of ciclosporin.

Tacrolimus is a newer calcineurin inhibitor that has been recently approved in the US and the EU for use in heart transplant recipients. It has been used extensively in lung, liver and renal transplantation and although only recently approved, many heart transplant centres have been using tacrolimus for some time as an alternative to ciclosporin for patients with recurrent rejection or adverse effects.

Clinical trials with tacrolimus in heart transplantation have suggested that the overall incidence of significant cellular rejection is either similar or modestly decreased as compared with patients receiving ciclosporin, although there has been no difference in overall survival. In addition, the tolerability profile of tacrolimus may have some advantages over ciclosporin, including decreased incidences of hypertension, dyslipidaemia and haematological abnormalities, and an absence of gingival hyperplasia. Most trials have indicated that renal dysfunction with tacrolimus has been similar to that with ciclosporin; however, some clinicians believe that renal function may deteriorate less with tacrolimus. Tacrolimus may increase the risk of hyperglycaemia, but this finding has not been consistent in the clinical trials.

In heart transplant recipients, tacrolimus is a potent calcineurin inhibitor that provides excellent immunosuppression in combination with azathioprine or MMF and corticosteroids. Its adverse-effect profile is favourable compared with that of ciclosporin. Tacrolimus may be used as a first-line immunosuppressant or as an alternative to ciclosporin for patients with adverse effects or refractory rejection. ▲