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Everolimus-Based Regimens and CMV Infection Suppression in Kidney Transplantation: Meta-Analysis of Randomized Controlled Trials

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Objectives : Cytomegalovirus (CMV) infection is a major post-transplant complication causing morbidity, graft dysfunction, and indirect immunologic injury. Everolimus (EVR), an mTOR inhibitor, may reduce CMV incidence while allowing calcineurin inhibitor (CNI) minimization because of its antiproliferative and antiviral effects. This meta-analysis compared the efficacy, safety, and infection outcomes of EVR-based and mycophenolate (MPA)-based regimens in kidney transplant recipients.
Methods : A systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Seventeen randomized controlled trials (n = 8,467) comparing EVR + CNI (± corticosteroid) and MPA + CNI were identified through MEDLINE, EMBASE, and the Cochrane Library. The primary endpoints were biopsy-proven acute rejection (BPAR), mortality, renal function (eGFR), and infection outcomes including CMV infection. Pooled risk ratios (RRs) and mean differences (MDs) were calculated using a random-effects model with 95% confidence intervals (CIs). Heterogeneity was evaluated by the I^2 statistic, and publication bias by funnel-plot and Egger's test.
Results : Across studies, EVR-based therapy showed comparable efficacy to MPA-based regimens for BPAR (pooled RR 1.09, 95% CI 0.89–1.34, P = 0.38) and mortality (RR 0.85, 95% CI 0.63–1.16). Mean eGFR at follow-up was similar between groups (MD +0.9 mL/min, 95% CI –2.2 to +4.1). The overall risk of infection was significantly reduced with EVR-based therapy (RR 0.83, 95% CI 0.73–0.93, P < 0.01). When restricted to CMV events, the pooled RR was 0.54 (95% CI 0.36–0.81, P = 0.003), favoring EVR and confirming a consistent antiviral effect across de novo and maintenance cohorts. No significant difference was observed in graft loss or treatment discontinuation.
Conclusions : Everolimus with low-dose CNI provides graft and patient survival outcomes similar to MPA-based therapy, while offering a clear advantage in infection control, especially reducing CMV infection. These findings support EVR-based regimens as an effective alternative for long-term immunosuppression in kidney transplantation.