Safety and efficacy of early corticosteroid withdrawal in liver transplant recipients: new-onset diabetes after liver transplantation randomized clinical trial

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Background: Standard practice for immunosuppressive therapy after liver transplantation (LT) is triple therapy, tacrolimus (TAC), mycophenolate mofetil, and corticosteroid triple therapy. Long-term steroid intake significantly increases cardiovascular risk factors with negative effects on patient outcome, especially post-transplantation diabetes associated with morbidity and mortality. In this trial, we examined the efficacy and safety parameters of early steroid withdrawal during the first year after LT.

Methods: In this open-label, multicenter, randomized controlled trial, we randomly assigned LT recipients in a 1:1 ratio to receive either early corticosteroid withdrawal at 2 weeks (group 1) or corticosteroid withdrawal at 3 months (group 2) after LT. The study was performed at four centers across Korea. Only participants between 20 and 70 years of age who were scheduled to receive a single-organ liver transplant from either a living donor or a deceased donor were considered for enrollment. The primary endpoint was the incidence of new-onset diabetes after liver transplantation (NODAT) at 12 months. All analyses were done by intention-to-treat. This trial is registered with ClinicalTrials.gov, number NCT02095418.

Results: Between November 2012 to August 2020, 115 patients were randomly assigned to group 1 (n=60) or group 2 (n=55). The incidence of NODAT in group 1 (32.4%) was increased compared to group 2 (10.0%) in the per-protocol set. Additionally, biopsy-proven acute rejection (BPAR), graft failure, and death were not developed; however, median TAC trough level/dose/weight in group 1 were generally higher than in group 2. Safety parameters such as infection or the incidence of hepatocellular carcinoma recurrence did not differ between the two groups.

Conclusions: Early steroid withdrawal at 2 weeks after LT shows higher NODAT development compared with steroid withdrawal at post-transplant 3 months because of generally high TAC exposure. However, early steroid withdrawal can be achieved without loss of efficacy including BPAR, graft loss, and death.

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