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Donor dopamine pretreatment influences leukocyte infiltration and cytokine expression in the Brown Norway to Lewis renal transplantation model

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In a retrospective case-control study we have previously shown that donor catecholamine treatment lowers the incidence of acute rejection and improves renal transplantation outcome in men. In the present study we used the Brown-Norway (BN) to Lewis model as a model for acute rejection and tested the hypothesis that dopamine (DA) treatment of BN donors significantly reduces the inflammatory response after renal transplantation.

In this study, BN and Lewis rats (Isograft-controls) were treated for 24 hours with DA (5µg/kg/min) or NaCl (0.9%) respectively. After 24 hours of cold storage in UW solution, renal allografts were orthotopically transplanted into Lewis recipients. All recipients received immunosuppression (cyclosporine A 2.5 mg/kg/day) until they were sacrificed. Allografts were harvested 1, 3, 5 and 10 days after transplantation and analyzed by light microscopy, immunohistochemistry (CD3, MHC class II, ED1, P-selectin and ICAM-1) and by RNase protection assay for cytokine mRNA.

Ten days after transplantation Banff tubulitis scores were significantly lower in DA- than in NaCl treated allografts. No significant differences were found in Banff interstitial infiltration scores. The numbers of MHC class II + and CD3 + cells were significantly decreased in DA treated animals, as assessed by immunohistochemistry. No differences were found in the number of ED1 +, P-Selectin +, ICAM-1 + cells. The expression of Lta -, TNFα -, IL-1β - and IL-2 mRNA was significantly reduced in DA treated animals.

In conclusion, our data indicate that donor DA treatment significantly inhibits tubulitis in renal allografts subjected to prolonged cold preservation. A reduced number of infiltrating MHC class II + and CD3+ cells together with decreased cytokine expression could diminish renal scarring, reduce allograft immunogenicity and hence improve transplantation outcome. Although the underlying mechanisms remain to be fully elucidated, these animal experiments seem to confirm our clinical findings: donor pretreatment with catecholamine inhibits the occurrence of acute rejection episodes in a MHC-mismatched combination.