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Titel des Beitrags: Effects of progesterone and selective oestrogen receptor modulators on chronic allograft nephropathy in rats.

Abstract: BACKGROUND: We recently demonstrated that oestrogens ameliorate the progression of chronic allograft nephropathy (CAN). In our present study, we investigated the role of progesterone and selective oestrogen receptor modulators (SERMs) in this process. METHODS: Female Fisher (F344) kidneys were orthotopically transplanted into intact or ovariectomized female Lewis recipients. Ovariectomized recipients were divided into four groups and were treated with either progesterone alone or in combination with oestradiol, oestradiol alone or vehicle. Intact recipients were divided into three groups and were treated with SERMs such as tamoxifen and one of its new derivatives, droloxifene or vehicle. Animals were harvested 24 weeks after transplantation for histological and immunohistological studies as well as for molecular analysis. RESULTS: Administration of progesterone resulted in increased urinary protein excretion as well as profound glomerulosclerosis and mononuclear cell infiltration. The combined treatment had similar detrimental effects on the development of CAN. In contrast, oestradiol treatment alone improved graft function, reduced glomerulosclerosis and diminished cellular infiltration. SERMs again impaired allograft function and promoted the development of CAN. Renal allograft damage paralleled intragraft mRNA expression of transforming growth factor-beta1 in all
groups. CONCLUSIONS: Our results suggest that addition of progesterone diminishes the beneficial effects of oestrogens on the development of CAN in rats. Similarly to progesterone, SERMs worsened long-term renal allograft outcome.