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Compared to mycophenolate mofetil, rapamycin induces significant changes on growth factors and growth factor receptors in the early days postkidney transplantation¹

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Abstract

Background. The new immunosuppressive drug Rapamycin (Rapa) is endowed with a mechanism of action that is distinct from that of calcineurin inhibitors. It has been claimed that Rapa does not significantly modulate either the cytokine expression or the transcription of several growth factors in mitogen-activated T cells. Previously, we reported that fine-needle aspiration biopsy (FNAB) sample cultures synthesize a large array of cytokines, and some of them may be powerful predictors of acute rejection in renal transplants. We hypothesized that Rapa may induce significant changes on cytokine production by FNAB sample cultures and on serum cytokine receptors when compared to other immunosuppressive drugs.

Methods. Kidney transplants treated with CsA-Rapa-Pred (Rapa group) were compared with transplants treated with CsA-mycophenolate mofetil-Pred (MMF group). They were studied on day 7 posttransplantation, and they remained rejection free for at least the first 6 months. FNAB samples were cultured and the supernatants were collected at 48 hr of incubation and analyzed by ELISA for interleukin 1 receptor antagonist (IL-1ra), IL-2, IL-6, IL-10, IL-18, monocyte chemotactic protein 1 (MCP-1), soluble tumor necrosis factor I, and transforming growth factor (TGF)- β_1 . The soluble receptors for IL-1, IL-2, IL-6, and tumor necrosis factor α , together with IL-2 and IL-18 were also measured in serum.

Results. Significant differences were observed when comparing Rapa with the MMF group. IL-18 and TGF- β_1 synthesis were up-regulated, whereas IL-6 and MCP-1 were down-regulated in FNAB sample cultures. The Rapa group showed a significant down-regulation of each cytokine receptor and of IL-2 in serum.

Conclusions. Rapa was associated with a decreased synthesis of primarily monocyte-derived cytokines

and enhanced production of TGF- β_1 , which in an appropriate cytokine milieu may promote allograft tolerance. The down-regulation of cytokine receptors and IL-2 may be associated with a depressed immune response towards the kidney allograft.