Dokumenttyp: journal article

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Titel des Beitrags:
Imatinib attenuates end-organ damage in hypertensive homozygous TGR(mRen2)27 rats.

Abstract:
Imatinib specifically inhibits receptor tyrosine kinase signaling and is clinically used to treat leukemia. Receptor tyrosine kinases not only mediate tumor growth but also initiate adverse signaling in heart failure. We investigated whether imatinib, by inhibiting the platelet-derived growth factor receptor-beta (PDGFRbeta), prevents cardiac and renal damage in TGR(mRen2)27 (Ren2) rats. Eight-week-old male homozygous Ren2 and Sprague Dawley rats were treated either with imatinib (30 mg/kg; STI-571) or placebo for 8 weeks (Ren2 n=12 for each group; Sprague Dawley n=6 for each group). Imatinib did not affect blood pressure or left ventricular (LV) hypertrophy in both groups. Imatinib attenuated the decline in fractional shortening (imatinib versus Ren2 placebo 45+-4.5% versus 32+-3%; n=7-11; P<0.05) and in diastolic function in Ren2 rats (baseline diastolic dP/dt corrected for systolic blood pressure Ren2 imatinib versus Ren2 placebo 38.6+-0.67 versus 35.3+-0.41 [1 . s(-1)]; n=7-11; P<0.05). This was associated with decreased cardiac fibrosis and decreased activation of PDGFRbeta and extracellular signal-regulated kinase 1/2. Renal microvascular hypertrophy and perivascular fibrosis in Ren2 rats were significantly decreased by imatinib. In vitro, imatinib blocked angiotensin II-induced activation of the
PDGFRbeta and significantly decreased fibroblast proliferation and collagen production. In conclusion, imatinib did not affect LV hypertrophy but attenuated the decline in cardiac function and reduced renal microvascular damage associated with reduced activation of the PDGFRbeta. The simultaneous improvement in both heart and kidneys suggests that inhibition of the PDGFRbeta has broad protective effects that may provide novel avenues for a blood pressure-independent protection against end-organ damage.

Zeitschriftentitel / Abkürzung: Hypertension
Jahr: 2006
Band: 47
Heft / Issue: 3
Seiten: 467-74
Sprache: eng
Print-ISSN: 0194-911X
TUM Einrichtung: r Nephrologie

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > II. Medizinische Klinik und Poliklinik (Gastroenterologie) > Fachgebiet Nephrologie (Prof. Heemann) > 2006

entries: