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Uricosuric action of losartan via the inhibition of urate transporter 1 (URAT 1) in hypertensive patients.

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Abstract

BACKGROUND:

The angiotensin receptor blocker losartan inhibited urate transporter 1 (URAT1) according to in vitro experiments. However, it is still unknown whether the inhibitory effect of losartan on URAT1 contributes to its uricosuric action in humans.

METHODS:

Thirty-two patients with hypertension and nine patients with idiopathic renal hypouricemia (five with and four without hypertension) were enrolled for this study. Hypertensive patients were prescribed oral losartan (50 mg/day, n = 16) or candesartan (8 mg/day, n = 16). Before and after 1-month treatment, the serum concentration of urate (Sur) and creatinine (Scr), and the clearance value of urate (Cur) and creatinine (Ccr) were determined. Clearance studies using the URAT1 inhibitor benzbromarone (100 mg/day) or losartan (50 mg/day) loading test were also performed in these patients.

RESULTS:

Blood pressure (BP) significantly decreased in the patients treated with either losartan or candesartan. Losartan significantly reduced Sur, which was associated with a concomitant increase in the Cur/Ccr ratio, whereas candesartan did not alter these parameters. In hypertensive patients with loss-of-function mutation of URAT1, losartan did not alter either Sur or Cur/Ccr, nor did benzbromarone. The lack of effect of URAT1 inhibitors on renal excretion of urate was independent of the renal function of hypouricemic patients. On the other hand, both losartan and benzbromarone increased Cur/Ccr ratio in hypertensive patients harboring the wild URAT1 gene, regardless of the presence of hypouricemia.

CONCLUSIONS:

These findings suggested that losartan inhibited URAT1 and thereby it lowered Sur levels in hypertensive patients.