Differential expression of type 1 angiotensin II receptor mRNA and aldosterone responsiveness to angiotensin in aldosterone-producing adenoma.

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摘要

Abstract

Aldosterone secretion in most patients with aldosterone-producing adenomas (APAs) is typically unresponsive to angiotensin II stimulation (AII-unresponsive, AII-U). In some patients, however, plasma aldosterone increases in response to AII stimulation (AII-responsive, AII-R). This differential aldosterone responsiveness could be related to the levels of type 1 AII receptors (AT1R) in the APA. To test this hypothesis, plasma aldosterone levels in response to upright posture and/or sequential high- and low-salt diets were measured by radioimmunoassay in nine patients with APAs. AT1R mRNA levels in the adenomas were quantified by competitive reverse transcription-polymerase chain reaction and correlated to the cellular composition of the adenoma. Two patients were categorised as AII-R by an increase of plasma aldosterone greater than 50% over the baseline. The remaining seven patients who had blunted plasma aldosterone responses were classified as AII-U. Histologically, the AII-R APAs consisted predominantly of zona glomerulosa (ZG)-like cells (> 90%), while the AII-U APAs contained zona fasciculata (ZF)-like cells ranging from 28 to 72%. There was an inverse relationship between the levels of AT1R mRNA in the APA and the percentageof ZF-like cells in the adenoma ($n = 9$, $r = 0.73$, $P < 0.05$). In situ hybridisation findings demonstrated that AT1R mRNA was more uniform and intensive in ZG-like cells than in ZF-like cells. These results suggest that heterogenous aldosterone responsiveness to angiotensin in APAs is histologically dependent and related to the differential expression of AT1R mRNA in the adenoma