KNOCKOUT OF THE GLUCOCORTICOID RECEPTOR IN THE DISTAL NEPHRON DOES NOT AFFECT DEXAMETHASONE-INDUCED HYPERTENSION

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Glucocorticoids (GCs) are used as a treatment for a variety of conditions and hypertension (HTN) is a well-recognized side effect of their use. The mechanism of GC-induced HTN is incompletely understood and has traditionally been attributed to promiscuous activation of the mineralocorticoid receptor by cortisol. Multiple lines of evidence, however, point to the glucocorticoid receptor (GR) as an important mediator as well. We have developed a mouse model of GC-induced HTN which we shave shown is dependent on GR. To determine the site(s) of GR action relevant to the development of HTN, we studied GC-induced HTN in a mouse with a tissue-specific knockout of GR in the distal nephron. Interestingly, although these knockout mice had similar body weight, nephron number and renal histology compared to littermate controls, their baseline blood pressure was mildly elevated (111.4 ± 1.6 mm Hg vs. 103.8 ± 2.2 mm Hg, p=0.032). Nevertheless, both distal nephron GR knockout mice and control mice had a similar hypertensive response to dexamethasone, both on a normal diet and on a low sodium diet. Urinary excretion of electrolytes, both before and after administration of GC, was also indistinguishable between the two groups. We conclude that GR in the distal nephron is not necessary for the development or maintenance of dexamethasone-induced HTN in our model.