Effects of High NaCl and High KCl Diet on Hepatic Na^+- and K^+- Receptor Sensitivity and Expression of NKCC1 in Rats

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Summary

We have demonstrated that Na^+ and K^+ receptors exist in the hepatoportal region plays an important role in regulating body fluid homeostasis. These receptors sense Na^+ and K^+ concentration via the bumetanide-sensitive Na^+-K^+-$2Cl^-$ cotransporter (NKCC1) and transduce to electrical activity of the hepatic nerve, and project to the nucleus solitary tract, area postrema, paraventricular hypothalamic nucleus, and supraoptic nucleus. Then reflexively control renal excretory and intestinal absorptive functions. It has been reported that high or low Na^+ and high or low K^+ diet affected the expression of Na^+ and K^+ transporter in the intestine and kidney. These changes in expression might contribute to regulating body fluid homeostasis by altering amounts of absorption and excretion. Accordingly, there is a possibility that alternation of oral intake of Na^+ or K^+ alters NKCC1 expression in the liver. To test this hypothesis, we investigated the effects of high NaCl and high KCl diet on sensitivity of the hepatic Na^+ and K^+ receptor and the expression of NKCC1 in the liver of Sprague-Dawley rat. The rats were randomly assigned to the 3 experimental groups and put on normal diet (Na^+ 0.3 %, K^+ 0.8 %), high NaCl diet (Na^+ 3 %, K^+ 0.8 %), and high KCl diet (Na^+ 0.3 %, K^+ 8 %) for 4 weeks (from 7-weeks old to 11-weeks old). While measuring hepatic afferent nerve activity, hypertonic NaCl solutions (0.375 M, 0.75 M, and 1.5 M) and isotonic KCl + NaCl solutions (25 mM KCl + 125 mM NaCl, 50 mM KCl + 100 mM NaCl, and 100 mM KCl + 50 mM NaCl) were injected as bolus doses of 0.1, 0.2, 0.5, and 1.0 ml/kg via the portal venous catheter. In response to injections, hepatic afferent nerve activity increased in a Na^+ or K^+ concentration dependent manner. Under intakes of high NaCl or high KCl diet for 4 weeks, the responses of hepatic afferent nerve activity were significantly attenuated compared to those on normal diet. RT-PCR and Western blot were used to measure the NKCC1 mRNA and protein expression, respectively. In both high NaCl and high KCl diet groups, the level of NKCC1 mRNA expression was significantly lower than normal diet (1.13 ± 0.15 in normal diet, 0.67 ± 0.40 in high NaCl diet and 0.64 ± 0.11 in high KCl). Furthermore, the expression of NKCC1 protein was also significantly depressed by high NaCl diet and KCl diet (2075 ± 202 in normal diet, 1016 ± 113 in high NaCl diet and 866 ± 209 in high KCl). These results suggest that intakes of high NaCl or high KCl diet decrease the expression of NKCC1 in the liver and it may cause the attenuation of hepatic Na^+- and K^+-receptor sensitivity.