MECHNISM AND REGULATION OF NaCl TRANSPORT IN THE RENAL TUBULES

Effect of protamine on ion conductances in upper portion of long-looped nephron

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Summary

To estimate the contribution of paracellular shunt pathway to the cation selective permeability in the upper portion of the descending limb of long-looped nephron (LDLu) of hamsters, we observed effect of protamine on salt diffusion voltage (dV_T) and transmural resistance (R_T). dV_T generated upon reduction of lumen NaCl concentration was decreased from 12.0 ± 1.4 mV to 7.3 ± 1.2 mV when 100 μg/ml protamine was added to the lumen. Although the effect of protamine was persisted after removal of the agent from the lumen, addition of 30 U/ml heparin reversed the dV_T toward the control level. The effect of protamine was dose-dependent in the range from 3 to 1000 μg/ml. Protamine was without effect from the bath. Studies on single salt dilution voltage revealed that 100 and 300 μg/ml protamine inhibited relative Na^+ to Cl^- permeability from 4.03 ± 0.38 to 2.14 ± 0.21 and from 3.75 ± 0.37 to 1.36 ± 0.09, respectively. Protamine markedly decreased the apparent transference number for Na^+ but slightly increased the value for Cl^-. Protamine also inhibited permeabilities for K^+, Rb^+, and Li^+ relative to Cl^-, indicating that the inhibitory effect of protamine was not confined to Na^+ but was generalized to cations. Transmural cable analysis showed that 100 μg/ml protamine increased R_T from 14.0 ± 1.1 Ω cm² to 19.3 ± 1.2 Ω cm², with the effect being reversed by 30 U/ml heparin. Because the effect of protamine on R_T was unaffected by ouabain in the bath, changes in R_T may mainly represent those of the paracellular shunt resistance. Cable analysis with cell puncture in combination with $BaCl_2$ effect further confirmed this view. Protamine at 100 μg/ml increased shunt resistance (R_S) from 34.0 ± 8.3 Ω cm² to 44.0 ± 10.5 Ω cm² without affecting apical (R_A) and basolateral (R_B) membrane resistances. From these observations, we conclude that the use of protamine provides a useful tool to study contribution of the paracellular shunt pathway and that at least about 50 % of total conductance of the LDLu is accounted for by the cation selective paracellular permeability.