Development of nafamostat-induced hyperkalemia in rats. －A model of decreased renal excretion by a concomitant administration of amiloride－

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Nafamostat is a serine protease inhibitor and is known to cause hyperkalemia in clinical practice. Its mechanisms have been thought to inhibit sodium channels.The study aimed to develop nafamostat-induced hyperkalemia model to investigate mechanisms of the serine proteases for hyperkalemia. Nine-week-old Wistar-Imamichi male rats were used. Catheters were placed in the femoral vein, bladder, and jugular vein under sevoflurane anesthesia. Urine and blood were collected every 15 min by 8 times. (1) Nafamostat (1.2 mg/kg/h, c.i.) vs 5% Glucose groups. (2) Combination (Nafamostat 0.9, 1.8 or 3.6, c.i. and Amiloride 18.0 μg/kg, i.v. after 54.0 μg/kg/h, c.i.) vs 5% Glucose and Amiloride (18.0, i.v. after 54.0, c.i.) groups. Serum and urinary potassium were measured by the ion electrode method. (1) Changes in serum potassium level and urinary potassium excretion did not increase with nafamostat alone. (2) In the combination group, serum potassium level increased from 30 min to 90 min after administration compared with amiloride alone. Urinary potassium excretion showed a downward trend. A hyperkalemia rat model with decreased renal excretion was developed by nafamostat in combination with amiloride, which mechanism might be appearance of a potential inhibitory action of serine proteases to amiloride-sensitive sodium channels.