Effects of molidustat, a HIF-PHD inhibitor, on sodium dynamics and distribution in hypertensive subtotally nephrectomized rats

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Aim: Prolyl-hydroxylase domain protein inhibitor (HIF-PHD inhibitor) is developed for the treatment of renal anemia. Patients treated with the HIF-PHD inhibitor often have complications such as renal dysfunction and high blood pressure. Renal damage often disrupts water and electrolytes regulation, and could retain salt, which further disrupts the homeostasis. In this study, we investigated the effect of a HIF-PHD inhibitor, molidustat, on salt excretion and distribution in the rats with subtotal nephrectomy-induced nephron loss.

Methods: Male Wistar rats were performed with 5/6 nephrectomy. After confirming the blood pressure elevation (>150 mmHg), the rats were divided into four groups and given either vehicle, molidustat (2.5 and 5 mg/kg/day, p. o.) or erythropoietin (100 IU/kg, twice a week, s.c.) for 1 week.

Results: Molidustat treatment was initiated after 4 weeks of 5/6 nephrectomy. After one week of treatment, molidustat did not improve blood cell volume or blood pressure. Molidustat had no effect on urinary sodium excretion or concentration after the acute oral salt loading (1 g/kg). Furthermore, tissue accumulation levels of sodium, potassium, and water in the skin, carcass and bones were not affected by molidustat.

Conclusion: Molidustat affected neither excretion nor accumulation of salt in the rats model of nephron loss.