Pharmacological activity of calcimimetic NPS R-568 administered intravenously in rats: dose dependency

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Abstract:
Calcimimetics administered orally cause “pharmacological parathyroidectomy” confirmed by a decrease in parathyroid hormone secretion (PTH) and in plasma Ca²⁺ concentration. Parathyroids are also the source of parathyroid hypertensive factor (PHF). The aim of this study was to determine the dose-dependent effect of an intravenously (iv) applied calcimimetic, NPS R-568, on plasma Ca²⁺ concentration, urinary phosphate excretion and mean arterial blood pressure (MAP) in rats. Clearance experiments were performed on male Wistar rats anesthetized with thiopental and infused iv with saline supplemented with ³H inulin for glomerular filtration rate (GFR) determination. NPS R-568 was administered iv as a bolus at the doses: 0.5, 1.0, 2.5 and 5.0 mg/kg. Control group of rats received vehicle only. MAP was monitored continuously in the carotid artery. Urine was collected from cannulated urinary bladder. NPS R-568 applied iv dose-dependently decreased plasma Ca²⁺ and fractional phosphate excretion (FEₚ). In the control group, no significant changes in plasma Ca²⁺ and FEₚ were observed. The most efficient hypotensive effect vs. control group was induced by the NPS R-568 of a dose of 1.0 mg/kg. Our results indicate that the dose of 1 mg/kg of the calcimimetic NPS R-568 administered iv is sufficient to induce the decrease in plasma Ca²⁺ and urinary phosphate excretion accompanied with hypotensive effect in Wistar rats.

Key words:
calcimimetics, pharmacological parathyroidectomy, parathormone, blood pressure, parathyroid hypertensive factor