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5.4 Acute Effects of Indapamide Treatment on Haemodynamics and Glycosaminoglycan-Mediated Non-Osmotic Skin Sodium Storage in Healthy Humans

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ABSTRACT

Introduction: The skin may protect against the adverse haemodynamic effects of dietary salt by storing excess sodium in an osmotically inactive form, bound to glycosaminoglycans. However, this novel pathway has not been comprehensively studied in humans.

Methods: 85 healthy volunteers (37 m, 48 f) <50 years of age underwent a one-week run-in to standardise dietary salt intake, before random allocation to either placebo or 2.5 mg indapamide diuretic for eight days. Total body water (TBW), peripheral blood pressure, pulse wave velocity (PWV), stroke volume (SV), cardiac output (CO), and skin biopsies were taken before and after treatment. PWV was measured using SphygmoCor, while SV and CO were measured by inert gas rebreathing. 5 mm skin biopsies were taken from the lower back using sodium-free lignocaine. Biopsies were freeze-dried to establish water content, and sodium content was quantified using inductively coupled plasma – optical emission spectroscopy. Glycsosaminoglycan content was assessed by qPCR. Data were analysed using repeated measures ANOVA.

Results: Following indapamide treatment, skin sodium fell by 10% ($p = 0.004$) with no reduction in skin water content, compared to placebo. There were no significant differences in blood pressure or PWV between groups. TBW, SV, and CO were significantly reduced by indapamide compared to placebo ($p < 0.001$, $p < 0.01$, $p < 0.01$, respectively), whilst systemic vascular resistance increased ($p < 0.001$). Glycosaminoglycan mRNA expression decreased ($p < 0.05$).

Conclusion: This diuretic-induced reduction in skin sodium content and glycomsaminoglycan expression, without commensurate water loss, suggests a release of sodium from osmotically inactive skin stores. This is the first comprehensive evidence of glycosaminoglycan-regulated non-osmotic skin sodium storage in humans, with implications for salt-sensitive hypertension.

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