Inherited Defect in RBC-K Function and Oxygen Transport: A Novel Paradigm on Body K Physiology, Microvascular Regulation and Renal Tubular Disorders in Essential Hypertension

Purpose: Our description of an inherited defect in RBC-K (K_i) physiology, macrovascular and renal disorders, in 3 generations of hypertensive families, strongly suggests a major hereditary defect in hypertensives (HT). In fact, K_i is critical for capillary blood flow regulation and K-O2 biding by oxyhemoglobin.

Methods: To reassess these pathogenic factors, a random sample (n=500, aged 55±15ys, BP 157±11/89±6 mmHg, 48% males) were selected from a large database (>3,500 HT, 57% men) having Ion Transports, non-invasive aortic pulse waveform (PW), reflected wave (RW) and Inflection (If) time (DynaPulse 200M, Pulse Metric) and Body Composition for total body K, total body water, intra/extracellular spaces (BIA Quantum X, RJL System).

Ion Transport: All HT had low K_i (85.3±6 mmol/l cell vs normal 96.2±4 mmol/l, $p<0.0001$), despite normal (82%) or mild elevated Na_i (7.2±1.3 vs 6.2 ±1.1 mmol/l cell, p=NS) and similar Na excretion (97±22 vs 105±25 mom/l), a defect recorded in 25% of their normal siblings, and 48% of their offspring. Patients with lowest K_i (78.3 ±5 mmol/l cell) had lower urinary K (27±9 mmol/l), TTKG (4.2±0.7 units) and higher 12-hrs overnight polyuria (≥1.3 ml/min) vs those with higher K_i (86.2±6 mmol/l cell, $p<0.002$), urine K (45±9 mmol/l, $p<0.002$), TTKG (7.2±1.3) and 12-h urine volume (<0.85 ml/min, $p<0.001$).

Non-Invasive Aortic PW: All HT had systolic RW (Type II-IV) and rapid If time (≤120 ms), a vascular marker across 3 generations of families. These alterations were associated to severe hypertensive response (BP ≥170/100 mmHg) with lower IF (≤95 ms) after isometric Hand-Grip test (2-3 min) in 40% of controlled HT (≤140/90 mmHg) and 25% of their normal adult siblings. IF was striking correlated with PP (-0.813), LV dP/dT (-0.879), SVC (0.976), SVR (0.791), BAC (-0.535), BAD (0.814), BAR (-0.827).

Bio-Impedance: 67% of HT (n=340) had decreased TBW, ICW and TBK, as compared with normotensive subjects with normal K_i uptake and function, related to nocturnal polyuria and Electrolyte Free H_2O excretion (≥1.35 ml/min) from an impaired tubular function in HT.

Conclusions: These results confirm a major hereditary defect in K_i function in HT and bimodal distribution in their normotensive offspring, explaining the large number of hypertensive population despite life-style modification, dietary advices and treatment.