

Twardowski ZJ. Sodium, hypertension, and an explanation of “lag phenomenon” in hemodialysis patients. *Hemodialysis International* 2008;12(4):412-25

Abstract obtained from Hemodialysis International with permission of Blackwell Publishing, Inc.

Sodium balance is precisely regulated by intake and output. The kidneys are responsible for adjusting sodium excretion to maintain balance at varying intakes. Our distant ancestors were herbivores. Their diet contained little sodium, so they developed powerful mechanisms for conserving sodium and achieving low urinary excretion. About 10,000 years ago, early humans became villagers and discovered that food could be preserved in brine. This led to increased consumption of salt. High salt intake increases extracellular volume (ECV), blood volume, and cardiac output resulting in elevation of blood pressure. High ECV induces release of a digitalis-like immunoreactive substance and other inhibitors of Na(+)-K(+)-ATPase. As a consequence, intracellular sodium and calcium concentrations increase in vascular smooth muscles predisposing them to contraction. Moreover, high ECV increases synthesis and decreases clearance of asymmetrical dimethyl-L-arginine leading to inhibition of nitric oxide (NO) synthase. High concentration of sodium and calcium in vascular smooth muscles, and decreased synthesis of NO lead to an increase in total peripheral resistance. Restoration of normal ECV and blood pressure are attained by increased glomerular filtration and decreased sodium reabsorption. In some individuals, the kidneys have difficulty in excreting sodium, so the equilibrium is achieved at the expense of elevated blood pressure. There is some lag time between reduction of ECV and normalization of blood pressure because the normal levels of Na(+)-K(+)-ATPase inhibitors and asymmetrical dimethyl-L-arginine are restored slowly. In dialysis patients, all mechanisms intended to increase renal sodium removal are futile but they still operate and elevate blood pressure. The sodium balance must be achieved via dialysis and ultrafiltration. Blood pressure is normalized a few weeks after ECV is returned to normal, i.e., when the patient reaches dry body weight. This is called the "lag phenomenon."

Comments by Todd S. Ing, MD

Dr. Twardowski elegantly detailed the complex interplay among sodium intake, fluid overload, hypertension and the “lag phenomenon” in maintenance hemodialysis patients. It is well known that excessive sodium intake in hemodialysis patients with negligible or absent renal function can bring about hypervolemia, hypertension, cardiac dysfunction and a resultant high mortality (1). In addition, excessively fast ultrafiltration during hemodialysis has been demonstrated to lead to transient hypovolemia, hypotension as well as an array of harmful manifestations (2). The great benefits of salt restriction and proper ultrafiltration were also aptly emphasized by Dr.

Twardowski in the present communication. Analysis of USRDS Waves 3 and 4 showed that weight gain between hemodialysis sessions of greater than 4.8% (ie, 3.4 kg in a 70-kg person), a reflection of excessive sodium and water intakes, was accompanied by an increased mortality rate (3). A longer dialysis treatment time and a slower ultrafiltration rate have also been found to be associated with a reduced mortality (4). Strict limitation of daily sodium intake to less than 5 grams of sodium chloride (ie, 2 grams or 85 millimoles of sodium) has been recommended in hemodialysis patients [exceptions being those patients who lose a substantial amount of sodium in their urines and/or via extrarenal routes] by the KDOQI hemodialysis adequacy guidelines (1). Similar sodium restriction approaches have long been championed by Scribner (5), Shaldon (6), Charra (7) and many others.

References:

1. National Kidney Foundation: KDOQI clinical practice guidelines and clinical practice recommendations for hemodialysis adequacy, 2006 updates (Guideline 5. Control of volume and blood pressure). *American Journal of Kidney Diseases* 2006;48, No 1, Suppl 1:S1-90
2. Twardowski ZJ. Treatment time and ultrafiltration rate are more important in dialysis prescription than small molecule clearance. *Blood Purification* 2007;25:90-8
3. Foley RN, Herzog CA, Collins AJ. Blood pressure and long-term mortality in United States hemodialysis patients: USRDS Waves 3 and 4 Study. *Kidney International* 2002;62:1784-90
4. Saran R, Bragg-Gresham JL, Levin NW, et al. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. *Kidney International* 2006;69:1222-8
5. Blumberg A, Nelp WB, Hegstrom RM, Scribner BH. Extracellular volume in patients with chronic renal disease treated for hypertension by sodium restriction. *Lancet* 1967;2(7506):69-73
6. Shaldon S, Ozkahya M, Ok F, Basci A, Dornhout Mees EJ. The long forgotten salt factor. *Kidney International* 2008;76:759-64
7. Charra B, Chazot C. The neglect of sodium restriction in dialysis patients: A short review. *Hemodialysis International* 2003;7:342-7