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An explanation for the “lag phenomenon”

More than 40 years ago, we published our initial studies on the dramatic results that were obtainable using dietary salt restriction to treat hypertension in anuric patients with end-stage renal disease receiving maintenance hemodialysis. I had been schooled in the benefits of salt restriction when I had worked with Sheila Sherlock treating patients with cirrhosis and ascites. I was already familiar with Walter Kempner’s original success with a rice diet in controlling hypertension in patients with chronic renal failure and also the success that Belding Scribner had achieved in Seattle with his original patients. As our results were so dramatic I have always preached the need for salt restriction in patients with chronic kidney disease. We were always impressed that the real benefit occurred *several months after* the patient had reached “dry body weight.”

This benefit was due to a hemodynamic phenomenon which has only recently been explained. The *lag phenomenon*, now recognized by several groups, was associated with a further reduction in blood pressure which was not associated with a further reduction in extracellular water. It was manifested by a reduction in peripheral resistance with a maintenance of cardiac output and an absence of postural hypotension after dialysis.

The possible explanation for this lag phenomenon may be linked to the reduction of non-osmotically active sodium which is potentially bound in the interstitial matrix lining the intimal surfaces of blood vessels containing proteoglycans and glycosaminoglycans. This sodium store leaks out slowly and takes months to become normal if the patient is maintained on 5g of salt intake per day.

Meanwhile, it is associated with activation of the inflammatory cascade, beginning with the hyperosmotic gene HOG1 or mitogen-activated protein kinase 38 (MAPK38). This sequence leads to an inhibition of nitric oxide synthetase and an increase in asymmetric dimethylarginine (ADMA) and at the same time stimulates the formation of TGF β and the inflammatory cascade. Reversal of these pathways occurs with a reduction of the excess sodium stored in non-osmotically active sites by means of a diet restricted in salt to 5g per day or less.

Attempts to achieve this “desalting” by lowering dialysate sodium concentration *without* a low dietary salt intake may lead to severe complications during dialysis. However, a reduction of the sodium content of the dialysate to below 137 mmol/L is recommended *after* the lag phenomenon has been observed, as symptomatic dialysis hypotension rarely occurs.

References:

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Commentary by Todd S. Ing, MD.

Dr. Shaldon, a pioneer in the advocacy of sodium restriction in the treatment of hypertension in ESRD patients, is also among the trail-blazers who championed the concept of the "lag phenomenon." Dr. Shaldon suggests that the "lag phenomenon" is a result of the fall in peripheral resistance and that sodium restriction can provide improvement in blood pressure by means other than that of simple volume depletion.