UNDER APPRECIATED ISSUES IN
THE TREATMENT OF CHRONIC
ILLNESS – LOW GRADE, CHRONIC
ACIDOSIS COMBINED WITH
POTASSIUM DEFICIENCY – PART III
– POTASSIUM, METABOLIC
ACIDOSIS, AND HYPERTENSION

INTRODUCTION

In part I and part II of this series I primarily focused
on the work of Anthony Sebastian and Lynda
Frassetto concerning the health implications of low
potassium intake and metabolic acidosis as reported
in the book chapter “An evolutionary perspective
on the acid-base effects of diet” (1). Of the many
fascinating and clinically relevant points made by the
authors, I thought two points were particularly
important given their considerable lack of
appreciation by the public and the alternative and
allopathic medicine communities. First, the
Paleolithic diet is more than just a matter of protein.
In fact, the hunter-gatherer, in addition to having a
fairly high animal protein diet, also had a significant
intake of plant-based foods. This leads to the
second, very much misunderstood and under-
appreciated important point. Because of the high
ingestion of plant-based foods, daily potassium
intake went far beyond what is now generally
regarded as the optimum intake level of
approximately 4.5 g per day. In fact, it appears that
the hunter-gatherer was ingesting over twice
that amount per day, leading to a systemic pH that was
distinctly alkaline.

If we are to accept the Paleolithic diet premise that,
because our genetics, physiology, and metabolism
are virtually the same as the hunter-gatherer, our
diets should closely mimic that of the hunter-
gatherer, then it follows that our potassium intake
and related systemic pH are not just a bit low but
massively too low, which is exactly what Sebastian
et al (1) concluded in their book chapter.

Interestingly, the controversial statements and
claims made in this book chapter were published in
2005. Do the authors maintain the same position 13
years later? To answer this question I would like to
review their latest publication on the subject from
the October 2018 edition of Medical Hypotheses
entitled “Postulating the major environmental
condition resulting in the expression of essential
hypertension and its associated cardiovascular
diseases: Dietary imprudence in daily selection of
foods in respect of their potassium and sodium
content resulting in oxidative stress-induced
dysfunction of the vascular endothelium, vascular
smooth muscle, and perivascular tissues.” (2).

Before beginning my review of this fascinating
paper, though, I would like to make two
introductory points. First, one of the authors is
Loren Cordain, one of the fathers and major
proponents of using the Paleolithic diet as a
guideline for the diets of present day, modern
humans. While much of the publicity surrounding
Cordain has revolved around his high protein,
macronutrient recommendations, by virtue of the
fact that he is an author of paper I am about to
discuss, he is also a proponent of a very high
potassium diet based on current actual and
recommended daily potassium intake levels.

Second, whereas the 2005 book chapter was more
of a general discussion on the benefits of a high
potassium, alkaline diet, this current paper focuses
on an incredibly common chronic illness in
American society, hypertension and related
cardiovascular disorders. Given that so many
Americans suffer from hypertension even with
ingestion of the generally recommended optimal
diet plus hypertensive medication, an important
question needs to be asked, which I believe will be
answered shortly:

Is massively suboptimal potassium intake an
important “X” factor that needs to be
addressed to take treatment of hypertension
to the next level in terms of efficacy?
THE IMPORTANCE OF HIGH POTASSIUM INTAKE IN THE PALEOLITHIC DIET – AN UPDATED PERSPECTIVE

To begin my discussion of the current Sebastian et al (2) paper, I would like to feature an overview comment from the abstract:

“We hypothesize that the major environmental determinant of the expression of essential hypertension in America and other Westernized countries is dietary imprudence in respect to the consumption of daily combinations of foods containing suboptimal amounts of potassium and blood pressure-lowering phytochemicals and supraphysiologically excessive amounts of sodium, and that such dietary imprudence leads to essential hypertension through oxidative stress-induced vascular endothelial and smooth muscle dysfunction. Such dysfunctions restrict nitric oxide bioavailability, impairing endothelial cell-mediated relaxation of the underlying vascular smooth muscle, initiating and maintaining inappropriately increased peripheral and renal vascular resistance.”

The next overview quote from the abstract I would like to feature provides more detail on the specific nature of the diet the authors advocate:

“Because suboptimal intakes of potassium reflect suboptimal intakes of fruits and vegetables, associated contributors to oxidative stress include suboptimal intakes of magnesium, nitrate, polyphenols, carotenoids, and other phytochemical antioxidants for which fruits and vegetables contain abundant amounts. Currently Americans consume potassium-to-sodium in molar ratios of less than or close to 1.0 and the Institute of Medicine (IOM) recommends a molar ratio of 1.2. Ancestral diets to which we are physiologically adapted range from molar ratios of 5.0 to 10.0 or higher.”

Before continuing, please note again from the above quotes that a metabolic factor rarely discussed in relation to hypertension and potassium was highlighted – oxidative stress. This potassium/oxidative stress connection will be discussed in more detail shortly.

The first quote from the general text of the Sebastian et al (2) I would like to discuss is the following:

“For the 21st century, the expert panel on nutrition of the Institute of Medicine (IOM) has specified an ‘Adequate Intake (AI)” for potassium, namely that adults consume at least 120 mmol (4700 mg) of potassium per day, except for those with diseases that render them potassium intolerant. Americans have largely ignored that guideline or do not know about it.”

The authors then refer to a table that indicates the average daily potassium consumption for Americans from 2005 to 2010. As suggested by the above quote, the amount on this table is shockingly low – 2668 mg per day. The authors then go on to point out that values for 2013 to 2014 are similar. Before continuing, I would like to share two thoughts on this data. First, please note again that the IOM indicates that 4700 mg per day is only “adequate.” What is the optimal amount? As I have been suggesting and will continue to point out as this review continues, based on Paleolithic data, the optimal amount is at least twice as much. My second thought, admittedly, is a bit cynical but, as they say, “If the shoe fits…” Based my discussions, readings, and experiences, I would suggest the American public is not the only group in this country that have ignored or are not aware of the recommendations by the IOM concerning daily potassium intake. In fact, I would also suggest that the vast majority of the medical community and far too many in the alternative medicine community have ignored or are not aware of IOM guidelines.

The next quote I would like to feature from the latest Sebastian et al paper (2) discusses potassium deficiency in relation to different age groups:

“Elderly persons may be more potassium deficient than younger persons as total body potassium declines with age.”

Why might this be? One major reason relates to a subject I have discussed previously in many newsletters and lectures – loss of muscle mass – sarcopenia. As I have pointed out, the major storage depot in the body for potassium is skeletal muscle. In turn, because older individuals are more likely to experience loss of muscle mass, it would naturally follow that they are going to have lower total body potassium and, therefore, have an even greater need for emphasis on dietary potassium intake.
Sebastian et al (2) then address the adequate versus optimal issue to which I alluded above:

“While 120 mmol of potassium consumption per day would certainly improve body potassium content by comparison with what Americans currently consume on average, no evidence indicates that 120 mmol of potassium per day provides the amount necessary for optimal physiological health. Estimates of adequate potassium intakes from an evolutionary perspective would suggest that 120 mmol per day still falls far short of optimal. The lineage of our species, Homo sapiens, subsisted as hunters-gatherers for at least 5 million years, during which time they adapted to dietary intakes of potassium in the range of 200-400 mmol per day on average. Because Homo sapiens evolved only in the last 1-2% of that 5 million year lineage, we can conclude that too little time has elapsed for the requirement for adapted potassium consumption to have changed, given that conserved core metabolic processes depend on potassium.”

(1 mmol of potassium equals 40 mg)

Of course, popular thought among both health care professionals and the American public is that the amount of dietary potassium ingested by the hunter-gatherer would undoubtedly place an unacceptable strain on kidney function. Sebastian et al (2) address this concern with a quote from the paper

“Achieving the benefits of a high-potassium, paleolithic diet, without the toxicity by Palmer et al (3):

““The normal kidney has the capacity to maintain K+ homeostasis in the setting of a high dietary intake. As an example, serum K+ levels are maintained in the normal range even when dietary K+ intake is increased to approximately 15 g/d (586 mmol/d) for 20 days.””

The healthy kidney can tolerate 15,000 mg of dietary potassium per day? Truly a highly controversial claim based on current nutritional standards in this country. Therefore, I will explore the Palmer et al (3) paper in more detail shortly.

The potassium-hypertension connection

Next, Sebastian et al (2) discuss the research on the connection between potassium intake and hypertension. The first quote I would like you to consider is the following:

“Intervention studies in which investigators have increased potassium intake demonstrate significant reductions in blood pressure and in the incidence of those cardiovascular diseases for which hypertension predicts an increased risk.”

Furthermore:

“Conversely, patients with low dietary intakes of potassium have a greater risk of hypertension, and increased sensitivity to blood pressure increases with sodium loads.”

Concerning the relationship between potassium and sodium, the authors next make a fascinating observation that increased potassium intake has an increasingly positive impact on optimizing blood pressure as sodium intake increases:

“Plasma potassium concentration is sensitive to reduction in potassium intake and more so as potassium intake approaches the minimum average intake for Americans. The effects are exaggerated with higher sodium intakes.”

What is the reason for this exaggerated effect as sodium intake increases? Sebastian et al (2) point out the following:

“The exaggerated anti-hypertensinogenic effect of potassium at high dietary sodium intakes reflects in part the effect of potassium to suppress sodium-induced endothelial production of transforming growth factor beta (TGF-β), a growth factor that causes morphological changes that promote hypertension (arterial stiffness, hypertrophy of vascular smooth muscle, increased local production of extracellular matrix proteins).”

The potassium – intracellular acidity connection

Next, Sebastian et al (2) explore the relationship between potassium and acid/alkaline dynamics. Their first statement in this section of the paper is the following:
“As we will discuss subsequently, increased intracellular acidity can contribute to dysfunction of the vascular endothelial cell and the underlying vascular smooth muscle. Physiologists have known for decades that cellular deficiency of potassium increases cellular acidity, in particular when caused by a reduction in dietary potassium.”

In addition, as you might expect from the previous discussion on the potassium-sodium connection:

“Salt loading also increases intracellular acidity.”

Unfortunately, as noted above, many Americans are not only consuming diets that are low in potassium but high in sodium. What is the impact?

“...in the circumstance in which a person consumes suboptimal amounts of dietary potassium and supraphysiological amounts of dietary sodium, we would find intracellular acidity at greater than optimal for physiological health.”

How much sodium is too much?

We all know that the average American ingests too much sodium. What are the guidelines and actual intake levels? The authors state:

“The IOM recommends that adults consume no more than 100 mmol of sodium per day. Yet Americans consume between 120 and 190 mmol of sodium per day or more. Therefore, Americans consume more sodium than the IOM considers the upper tolerable limit for healthy eating.”

What is the optimal sodium intake from an evolutionary perspective? Consider the following:

“The IOM has set the tolerable upper limit for sodium consumption at too high a value. Estimates of ancestral human consumption of sodium per day amount to less than 50 mmol per day.”

Potassium and oxidative stress

The next section of the Sebastian et al (2) paper explores the connection between potassium and oxidative stress that was mentioned above. The first quote I would like to feature introduces the subject of oxidative stress in general and its specific relationship with cardiovascular disease:

“Oxidative stress occurs when the rate and the amount of reactive oxygen species (ROS)/reactive nitrogen species (RNS) exceeds the rate of which the antioxidant mechanisms can maintain redox balance. Oxidative stress-induced vascular endothelial dysfunction is associated with inflammation.”

Concerning the relationship between cardiovascular disease and oxidative stress, the authors feature a quote from the paper “Endothelial dysfunction: a comprehensive appraisal” by Esper et al (4):

“Cardiovascular risk factors cause oxidative stress that alters the endothelial cells’ capacity and leads to the so called endothelial ‘dysfunction’ reducing its capacity to maintain homeostasis and leads to the development of pathological inflammatory processes and vascular disease.”

Sebastian et al (2) next discuss the relationship between oxidative stress and nitric oxide production. The quote below noted by the authors comes from the paper “Oxidative stress and endothelial dysfunction in hypertension” by Schulz et al (5):

“A major mechanism for the impact of oxidative stress on vascular tone is the decrease in nitric oxide (NO) bioavailability and/or signaling, leading to endothelial dysfunction, and ROS may also promote vascular cell proliferation and migration, inflammation and apoptosis, as well as extracellular matrix alterations.”

Where does potassium fit into this relationship between oxidative stress, endothelial dysfunction, nitric oxide, and hypertension? The authors state:

“One of the contributors to the development of oxidative stress with dietary imprudence of potassium and sodium is an increase in the production of asymmetric dimethylarginine (ADMA), an inhibitor of nitric oxide synthase and as a consequence a reduction in nitric oxide bioavailability. A high dietary potassium intake decreases ADMA levels, increasing nitric oxide bioavailability, and reducing blood pressure in salt sensitive subjects.”
Furthermore:

“Potassium depletion induced by reducing dietary potassium increases superoxide production and sensitizes arteries to vasoconstriction.”

Sodium and oxidative stress

Where does sodium come into play in this oxidative stress/cardiovascular disease connection? Sebastian et al (2) answer this question with the following:

“A high sodium diet results in oxidative stress-induced vascular endothelial dysfunction and consequent reduced nitric oxide bioavailability and impaired vasodilation. High sodium diets increase oxidative stress and reduce nitric oxide bioavailability by decreasing the activity of nitric oxide synthase. High sodium intakes increase the production of reactive oxygen species which play an important role in inducing vascular endothelial dysfunction and reducing endothelial mediated vasodilation.”

In addition:

“Earlier studies had shown that plasma sodium concentration stiffens vascular endothelium and reduces nitric oxide release. The reduction in endothelial nitric oxide synthase activity associated with high sodium diets is mediated by the small increase in plasma sodium concentration that occurs with the high salt intake.”

Finally, concerning the relationship between sodium and vascular inflammation, the authors note the following:

“High salt diets can also induce inflammatory changes in the vascular endothelial wall and contribute to vascular endothelial dysfunction.”

The relationship between acidity and oxidative stress

So far, acid/alkaline balance and oxidative stress have been discussed as fairly separate entities. Do they have, in fact, a more intimate relationship? As noted by Sebastian et al (2), they certainly do, via a mechanism you may not suspect involving iron:

“Intracellular acidosis can release iron bound to protein, which then can lead to production of very destructive hydroxyl radicals. Because the activity of enzymes peaks at their optimal pH, increased intracellular acidity might reduce the activity of antioxidant enzymes, in particular because they evolved in the more alkaline environment of a high potassium-to-sodium ratio.”

The importance of bicarbonate

As most of you know, I have been a long advocate of potassium bicarbonate. What is the role of bicarbonate in the paradigm I have been describing? The authors state:

“Because the current American diet contains suboptimal amounts of potassium it also contains suboptimal amounts of bicarbonate precursors, organic anions combustible to bicarbonate, that charge-balance the potassium cation.”

Why is this important?

“[This] contributes to the subphysiological intracellular pH (increased acidity) which might affect the activity of antioxidant enzymes, reducing their effectiveness.”

Was the hunter-gatherer diet, in addition to being high in protein and potassium, also high in bicarbonate?

“Compared to the hunter-gatherer diet of our pre-agricultural ancestors to which we genetically physiologically adapted, the American diet has a subnormal ratio of bicarbonate-to-chloride.”

From a supplemental standpoint, the above information would lead us to wonder whether the most predominant supplemental form of potassium, potassium chloride, is, in fact, optimal in terms of optimizing health. The following quote answers this question:

“…Tanaka et al. investigated the effects of potassium chloride and potassium bicarbonate on blood pressure, frequency of stroke and severity of the renal lesions in the stroke prone spontaneously hypertensive rats, finding that potassium chloride induced significantly greater increases in blood pressure than did potassium bicarbonate.”
Some final, big picture thoughts from Sebastian et al

With all of the above in mind, Sebastian et al (2) conclude that vascular dysfunction and elevated blood pressure is almost inevitable in American society, which most of us have seen first-hand with family, friends, and virtually all patient populations:

“Because the average American consumes foods containing suboptimal amounts of potassium and physiologically excessive amounts of sodium under their usual conditions of daily living, such individuals will already have some degree of oxidative stress. That would imply also that such individuals have some degree of vascular endothelial dysfunction and blood pressures that are already higher than optimal.”

Furthermore, in what would be a radical departure from current standard nutritional dogma in this country, the authors firmly suggest that blood pressure irregularities are not so much an issue of too much sodium but too little potassium:

“Given that oxidative stress-induced vascular endothelial dysfunction already exists with potassium intakes of ~60 mmol (2400 mg) per day, and that blood pressures in the so-called normotensive individuals might already be abnormally high to a moderate degree, long-term high salt loads might not increase blood pressures further.”

SOME FINAL, BIG PICTURE THOUGHTS ON THE LAST SEBASTIAN ET AL PAPER

Does the American public in general and many, if not most, of our patients in particular, ingest far too much sodium, mainly from processed foods? We all know, and the published literature and general mass media has made it very clear that this is true. However, is the answer to the problem as simple as making the usual proscriptions about reducing sodium intake? The conflicted research on the impact of low sodium diets on blood pressure also makes it very clear that the issue is more than just an issue of dietary sodium. What is the missing “X” factor that has made this situation so complicated? As suggested by Sebastian et al (2) it is actually something quite simple – potassium. What makes the subject of potassium so complicated in terms of gaining more widespread acceptance for the need for greatly increased dietary intake and supplementation? Based on the large body of research presented by Sebastian et al (2) in the two papers I have reviewed, there is a gross misunderstanding about how much potassium we need per day to maintain optimal health and a gross misunderstanding about the health risks of such doses.

However, even though there is substantial research evidence that many if not most Americans would benefit from a significantly higher potassium intake than what is usual, does it follow that high doses of potassium, particularly in the range of 10,000 mg per day or higher that were discussed by Sebastian et al in their two papers (1, 2) are without risk for some individuals? Of course, the answer is no. Therefore, how can we determine those patients who might benefit from daily potassium intake of as much as 10,000 mg per day or more and those who should adhere to the RDI of approximately 4500 mg per day or even lower? This question was addressed by the Palmer and Clegg paper mentioned above, “Achieving the benefits of a high-potassium, Paleoolithic diet, without the toxicity” (3).

The key premise of their paper is that the risks of high potassium intake revolve solely around kidney function. Therefore, with healthy kidney function, high potassium intakes are well tolerated and, as suggested by Sebastian et al (1, 2), can provide substantial benefits to health. Please note again the comment by Palmer and Clegg (3) that was featured above:

“One prevailing hypothesis is that our current diet represents a mismatch between what our body has the capability to metabolize and what we are actually consuming. The normal kidney has the capacity to maintain K+ homeostasis in the setting of high dietary intake. As an example, serum K+ levels are maintained in the normal range even when dietary K+ intake is increased to approximately 15 g/d for 20 days. This ability to maintain a normal serum K+ concentration when challenged with large intake over a prolonged period of time suggests humans are able to consume and excrete high K+ loads.”
With the above in mind, the authors conclude:

“The great facility and prodigious capacity of the healthy (normal) kidney to excrete K+ suggests and substantiates metabolic benefits associated with the consumption of a high K+ diet.”

Who should avoid a high potassium diet? Palmer and Klegg (3) suggest individuals prone to hyperkalemia. These patients are most likely to be those with kidney disease or those using certain medications:

“The risk of hyperkalemia is particularly high in patients with chronic kidney disease and in the setting of drugs that interfere with K+ homeostasis, such as renin-angiotensin-aldosterone system (RAAS) blockers.”

Other drugs that might pose a risk with high potassium diets, according to the authors, are ACE inhibitors.

Interestingly, while the Palmer and Clegg (3) paper is both compelling and fascinating, it does not answer one very clinically important question. Just because a patient with healthy kidneys and taking no medications that affect potassium metabolism can tolerate 10,000 mg of dietary potassium per day or more, does it mean that these patients need this amount of dietary potassium to attain optimal health? Assuming that patients are ingesting a reasonable amount of sodium and are engaging in other health optimizing behaviors, it is my guess that the answer is no. Why? Given that the average individual in the US is currently ingesting dietary potassium at a rate of approximately ½ of the RDI of ~4500 mg per day, it makes sense to me that it is very likely that patients will respond well to increasing intake to the RDI. If the response is less than what is desired, check serum potassium and, if it is not above 5.0 mEq/L, increase dietary/supplemental intake incrementally while continuing to monitor patient response and serum potassium levels. By increasing dietary/supplemental potassium intake levels in this fashion, both safety and chances of efficacy can be optimized.

However, one last note of caution. Please recall from the information discussed above that the preferred form of ingested potassium is an alkaline form, i.e., potassium bicarbonate, which is found in fruits and vegetables and can be provided as a supplement. In contrast, the most common form of potassium supplementation is an acidifying form not found in food, potassium chloride. Therefore, based on the research discussed by Sebastian et al (1, 2), when attempting to increase potassium intake to the significant amounts mentioned by using supplementation, only alkalizing forms of potassium supplementation are recommended. Potassium chloride is expressly contraindicated.

In part IV of this series, I will continue my exploration of the large body of research on the clinical importance of optimal acid/alkaline balance and the role of potassium in attaining and maintaining this balance.

REFERENCES


