

THE AFIB REPORT

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P Cells and Potassium

By Patrick Chambers MD

Introduction

The late great French cardiologist Philippe Coumel, a giant in the field of arrhythmias who also wrote the foreword for *Lone Atrial Fibrillation: Towards A Cure* by Hans Larsen, was the first to describe vagally mediated atrial fibrillation (VMAF) about 20 years ago. His seminal patient went into AF upon reclining but could terminate the episode upon standing. It is difficult to believe that such a dramatic disease could go unnoticed prior, unless, of course, it didn't exist prior. This suggests that environment plays a significant role in its genesis. To quote from Hans' new book *Lone Atrial Fibrillation: Towards A Cure - Volume 2*, Coumel "developed the concept of the triangle of arrhythmogenesis". "There are always three main ingredients required for the production of a clinical arrhythmia, the arrhythmogenic substrate, the trigger factor and the modulation factors of which the most common is the autonomic nervous system." The role of the ANS in the genesis of AF is obvious to all. Identification of the arrhythmogenic substrate (the tissue in which the arrhythmia starts and propagates) and the trigger factor have been more problematic.

Arrhythmogenic Substrate (P Cells)

Many LAFers are consumed by the search for their AF trigger, some specific item present or absent from their diet. Although this search will undoubtedly improve their general health, for the vast majority frustration will be a constant companion. And this is because of the arrhythmogenic substrate that all LAFers share.

P is for pole cells and they are the pacemaker cells of the heart. These have traditionally been described only in nodal tissue (SA node and AV node). However, in August of 2003 the Cleveland Clinic group was the first to describe P cells in human pulmonary veins (PVs) near their entry into the left atrium. They were found at autopsy in 4/4 AF patients and in 0/6 controls (one without history of tachyarrhythmia and five heart transplant donors). To date they have not been described anywhere else in the heart outside of nodal tissue.

Pacemaker cells are unique in that they slowly depolarize by themselves, hence their greater inherent automaticity. This is due to their unique Na (sodium) and K (potassium) ion channels. They are regulated by the opposing influence of sympathetic (adrenergic) and parasympathetic (vagal) stimulation. Both of these, but especially the vagus, cause shortening of the effective refractory period (ERP). The refractory period is the rest period following a contraction of the heart muscle. Individual heart cells do not respond to stimulation during this period so ectopic

beats or afib cannot be initiated during the ERP. A shortened ERP thus increases the risk of ectopics and afib.

In September of 1998 the Bordeaux group published an electrophysiologic (EP) study of 45 patients with frequent paroxysmal AF. They looked at the location of the triggering atrial ectopic beats and found that 94% were located in the PVs (2-4 cm inside the veins). I'm not sure what per cent of those with paroxysmal AF qualify as lone (LAF), but I would guess that if one accepts any degree of hypertension in the definition of LAF, it would be a clear majority.

In October of 2002 this same group published another EP study of 28 patients with paroxysmal AF (average age about 50) v. 20 age-matched controls. They evaluated the effective refractory period (ERP) of cells in the pulmonary veins and the atrial ERP (AERP) in both groups. First they found that AERP did not differ between the two groups. However, in the AF group the PV ERP was SHORTER than the AERP, whereas in the control group it was LONGER. Furthermore, they found that there was greater dispersion of PV conduction velocity in the AF patients, and that in these same patients AF was more easily induced (by fast pacing) in the PVs (22/90) than in the left atrium (1/81). Consequently, this PV refractoriness and dispersion of conduction properties create a substrate favorable for reentry. It would appear to me that these PVs represent the oft-quoted but elusive "defective substrate" or "arrhythmogenic substrate" of LAF. This is what is responsible for "the loss of physiologic rate adaptation" present in AF, e.g., conditions that should slow down the heart (slower conduction velocity, shortened refractory period) often result in a tachyarrhythmia instead.

Putting these studies together paroxysmal AFers appear to have a problem with their PVs. It would seem logical to implicate P cells in this process. The increasingly successful reports of catheter ablation via pulmonary vein isolation (PVI) for LAF are certainly consistent with this interpretation. Whether these P cells have been damaged by free radicals or not remains to be determined, although delayed onset of LAF is suggestive of this. Free radical damage to PVs is further supported by the frequent occurrence of AF after surgery. The mechanism involves lipid peroxidation (damage to cell walls caused by ROS or reactive oxygen species, especially peroxynitrite). It is also called ischemic reperfusion injury. Please see pp. 137-138 of Hans' book *Lone Atrial Fibrillation: Towards A Cure* for an eloquent description of how this relates to AF and the PVs. Furthermore, the demonstrated abnormalities in refractory period, conduction velocity, and dispersion in the PVs of LAFers involves many sodium, potassium and calcium channels. This finding is much more consistent with indiscriminate damage to cell membranes due to ROS than that rendered by some specific genetically determined channelopathy. The \$64 question: We all know that LAF is more frequently encountered in endurance athletes (five times more in one study). Is their primary problem an arrhythmogenic substrate created by such action of ROS or is enhanced vagal tone more contributory to their VMAF (or both)? Vitamin C and magnesium have both been shown to be instrumental in preventing damage due to ROS.

Trigger Factor (Low Potassium)

Information on a diurnal rhythm for potassium, if any, is hard to find in the medical literature. I initially assumed that because blood potassium is so intimately associated with aldosterone, any possible diurnal rhythm would follow that of aldosterone (and ACTH/cortisol). But such is not the case.

The diurnal rhythm of aldosterone secretion in healthy individuals parallels that of cortisol and is ACTH dependent. The lowest values are observed from midnight to 4AM. Values peak in the morning around 8AM after which there is a gradual decline throughout the day (assuming a normal sleep-wake cycle).[1]

Furthermore, cortisol and ACTH are not always secreted uniformly throughout the day. Episodic spikes can occur when the body is stressed, e.g., fasting, anxiety, etc. Otherwise, in humans,

urinary potassium excretion peaks in the early morning between 0530 and 0730 with a minimum at night from 2100 to 0530. Therefore, the diurnal rhythm of urinary potassium excretion seems to be controlled by the diurnal rhythm of cortisol and/or aldosterone. Not so for blood potassium.

Plasma potassium follows a diurnal rhythm with a peak at noon and a trough at midnight with an average peak-to-trough difference of 0.62 ± 0.05 mmol/L.[2]

In other words blood potassium is lowest when aldosterone secretion is lowest and blood potassium climbs as blood aldosterone/cortisol are peaking. This seems somewhat contradictory. Is this excreted potassium coming from inside the cells? If aldosterone/cortisol are not driving this drop in blood potassium, what is? A partial answer may be insulin.

As an aside, blood magnesium peaks around 0330 and reaches its lowest point around 1530. Its diurnal variation is greater than that of blood potassium. We all know how critical magnesium is to the maintenance of intracellular potassium.[3]

According to one study, the frequency of hypokalemia (potassium less than or equal to 3.5 mmol/L) is related to the time at which the blood potassium is measured.[4]

Not many blood samples for evaluation of potassium are drawn in the evening, especially around midnight (its diurnal nadir). How many people with lower range blood potassium values on specimens drawn during a daytime visit to the doctor's office are frankly hypokalemic at midnight?

Blood potassium values decrease postprandially because of insulin released in response to an ingested carbohydrate load. Blood potassium after our largest meal of the day (dinner in America) slowly declines due to insulin.

Insulin induced cellular uptake of glucose affects blood potassium in the following manner: Similar to Na, entry of glucose into a cell brings water with it, thereby decreasing the concentration of intracellular potassium. The ATP (requires magnesium) sensitive Na^+/K^+ pump is then stimulated to increase intracellular potassium. Blood potassium consequently drops.

This insulin-induced uptake of glucose (and potassium) occurs primarily in fat, liver and muscle, including cardiac muscle. However, cardiac muscle (v. skeletal muscle) is relatively less dependent on glucose generated ATP and relatively more dependent on oxygen generated ATP. This latter process occurs in the mitochondria and is called cellular respiration. Heart muscle cells have the greatest concentration of mitochondria at about 5,000 per cell. By weight 40% of each heart cell is mitochondria. [This is one reason why CoenzymeQ10 (protects mitochondria from oxidative damage) deficiency associated with statin therapy is causing an epidemic of heart failure.] Also, the cell membrane of the heart is HIGHLY permeable to potassium ions (there are many passive potassium channels). Therefore, it would seem that beneficial glucose and potassium uptake by the heart is relatively less helpful and that the potassium concentration gradient for the heart becomes relatively more problematic (v. skeletal muscle, smooth muscle, liver and fat cells). For spontaneously depolarizing P cells (specialized nerve cells) gradient rules!

Furthermore, aerobic training is associated with enhanced insulin sensitivity in skeletal muscle but diminished insulin-stimulated glucose (and potassium) uptake in the heart.[5]

Perhaps such conditioning enhances oxygen exchange so much so that glucose is relegated to an even less significant role as an energy substrate for the heart. Aging further diminishes this insulin sensitivity in the heart. So, especially in the physically fit and the elderly, low blood potassium is more likely to cause arrhythmia.

In one study comparing response to orthostatic challenge between those with high vagal tone and those with low vagal tone “a significant increase in plasma renin activity was found during LBNP (lower body negative pressure) in the HI responders only”. [6]

In other words prolonged standing or the equivalent causes a greater release of aldosterone in those with high vagal tone. During this time, e.g., a round of golf, aldosterone secretion is increased. In VMAFers this is a mixed bag, aldosterone is vagolytic (lengthens ERP) but the potassium loss it induces shortens ERP. While relaxing afterward blood aldosterone drops and its protective effect is lost but not the damage it has done to the potassium gradient. Combine this with a concomitant drop in blood glucose and AF risk is maximized. Much of this was discussed in Session 33 of the Conference Room Proceedings. [7]

Since a one mmole reduction in blood potassium generally translates to a deficit of about 300 mmoles of total body potassium, about 7 grams of potassium must move from the intracellular compartment to the extracellular compartment between its blood concentration trough and its peak. [8]

Part of the intracellular deficit so created is addressed by dietary potassium, but the RDA for potassium is only 3.5 gm in both America and Europe. And this dietary intake is offset by that lost in the urine.

This diurnal nadir of blood potassium certainly correlates well with the preponderance of night time episodes. Indeed the diurnal contribution of the PNS (vagal tone increases during the night, assuming a normal sleep wake cycle) seems to have camouflaged the diurnal contribution of low blood potassium to night time episode.

What to do about it?

Last year Hans brought to my attention an article by Dr Allan Struthers (“What Is the Optimum Serum Potassium Level in Cardiovascular Patients?” - 2004) in which he states that potassium supplementation is pretty useless at least in heart failure patients in the absence of an aldosterone antagonist, e.g., spironolactone or eplerenone. “A serum potassium increase of 0.25 mmol/L elevates serum aldosterone concentrations by 50% or 100%.” Since most of supplemental potassium is absorbed and then distributed in the blood (total blood volume is about 5 liters), just over 1 mmole or about 50 mg of ingested potassium should result in a 50-100% increase in aldosterone.

According to Struthers et al., “Clinicians can be comforted by the fact that hyperkalemia does not typically occur in patients with normal renal status, because large potassium loads are efficiently and rapidly excreted.” [9]

Dr. Michael Lam (www.lammd.com) on p. 246 of his book *How to Stay Young and Live Longer* indicates 15 gm daily potassium as safe in a healthy adult. In a study of eight patients with long QT syndrome the equivalent of 250 mg of spironolactone and 9 gm of supplemental potassium daily (70 kg person) increased blood potassium from 4.0 to 5.2 mmoles/L. Four weeks of this therapy resulted in no serious complications. [10]

So, the combination of an aldosterone antagonist with potassium is certainly effective and does not seem to pose excessive risk. However, although I’m a physician, I’m not your physician and this is not a blank endorsement of the above combination.

Furthermore, these aldosterone antagonists appear to be more effective in increasing blood potassium in the morning and ineffective in the evening. This latter finding is certainly consistent with the diurnal rhythm of aldosterone. It’s hard to block aldosterone, if it’s not being secreted

(evening). Angiotensin converting enzyme inhibitors (ACEIs) decrease urinary potassium excretion and, according to most studies, increase blood potassium.[11]

Although decreased urinary potassium excretion translates to increased blood potassium, changes in blood potassium directly stimulate aldosterone secretion without the renin angiotensin system (RAS). And ACTH, responsible for the diurnal rhythm, also works independently of the RAS.

As another aside, simultaneous supplementation of magnesium with potassium and an aldosterone antagonist increases cellular uptake of both potassium and magnesium.

It is important to remember that blood potassium levels may vary for reasons other than diurnal variation. Insulin and catecholamines cause transcellular shifts of potassium. The latter also causes urinary potassium wasting. Orthostatic challenge, e.g., prolonged standing or exercise, can also cause urinary potassium wasting via increased RAAS induced aldosterone. This would be more common amongst VMAFers, since they hyper respond with aldosterone during such activities (see above). And, of course, stress does the same for ALAFers (adrenergic lone atrial fibrillation).

On pp. 63-64 of Hans' book it is reported that excessive vagal tone is associated with a flat GTT (glucose tolerance test) curve. In other words VMAFers may have a more prolonged response to insulin. Perhaps the explanation for this lies in hepatic insulin sensitizing substance (HISS). This substance is secreted by the liver under the control of the vagus nerve.[12]

Increased insulin sensitivity would certainly be useful in those whose caloric intake was occasionally insufficient for their daily energy expenditure (endurance athletes). Many LAFers have reported an increase in episodes during weight loss.

So, in VMAF insulin or hypoglycemia (transcellular shifts or urinary potassium wasting respectively) may be the predominant determinant for triggering a daytime episode. In ALAF it might be stress-induced cortisol/aldosterone. All appear to work by increasing the potassium gradient. Emphasis on steady potassium supplementation throughout the day from the moment we arise to bedtime would seem to be a good idea for all LAFers. Decreasing salt intake might also prove beneficial, since it causes urinary potassium wasting. Addition of a potassium sparing diuretic might improve not only this gradient but also magnesium balance as well. In ALAF the contribution of the potassium gradient may be relatively greater than in VMAF, where vagal tone is more critical (see below equation). Obviously under appropriate conditions (a round of golf - see above) aldosterone may aggravate VMAF and insulin can do the same for ALAF.

One brief word on "Waller water". This is an aqueous magnesium preparation divined by our own Erling Waller. He was one of the first to realize that many LAFers may owe their malady to magnesium deficiency, at least in part, since it is inextricably entwined with maintenance of intracellular potassium. He created the recipe (soda water and milk of magnesia), which can be found at www.afibbers.org/Wallerwater.pdf One word of caution concerning supplementing KCl or any powdered organic potassium preparation with magnesium. Potassium inhibits magnesium absorption and you may easily exceed your bowel tolerance for magnesium.

In my opinion the common denominator linking VMAF and ALAF appears to be low potassium, at least in part. P cells, as described above, would be the other link. As the Bordeaux group has shown, those with paroxysmal AF have inexplicably low PV ERP. Both arms of the ANS cause shortening of the ERP, as does low blood potassium. So either arm in combination with low potassium can trigger an episode in the arrhythmogenic heart. ERP x (P cells + Potassium + ANS) => AF Risk

My own personal experience with LAF episodes suggests that vagal tone and low potassium work in concert. My 9AM potassium values are usually 4.5 or less. That would put me well under 4 during the night. The simultaneous appearance of high vagal tone and low potassium would accentuate the shortening of ERP. This would conveniently explain my typical middle of the night episodes.

However, during the late morning or afternoon I've had occasional episodes (less than 10% of the total) that appear to be related to possible dehydration and/or hypoglycemia. Both of these stimulate not only catecholamine but also ACTH and aldosterone release (as does physical or emotional stress). Oftentimes I've had just a pastry for breakfast. Talk about an open invitation to an insulin surge. My HR is usually over 70 with low vagal tone at the time, but the episode is nonetheless triggered by a vagal maneuver. Presumably the insulin and fasting state induce the hypoglycemia. According to one study, ERP is shortest under hypoglycemia (v. hyperglycemia) in the left atrium (v. the right atrium).[13]

Might this be P cell related? A greater potassium gradient would presumably augment this shortening. Another study in rats has shown that insulin-induced hypoglycemia directly stimulates vagal neurons in the brainstem.[14] Perhaps hypoglycemia can induce AF via both vagal stimulation and increased potassium gradient (catecholamine induced).

On very rare occasions I've triggered an episode by a short sprint. Here again, the timing of the episodes suggests low blood sugar and underscores the arrhythmogenic risk posed at the extremes of autonomic tone. During heart attacks the humoral catecholamine surge that can occur causes a rapid, transient transcellular shift of potassium, resulting in a short-lived but dramatic fall in blood potassium of approximately 0.5-0.6 mmol/L or more.[15] Although these shifts are evanescent and readily reversible, the transient drop in blood potassium can trigger PACs (and PVCs) and sometimes AF. This, of course, is in addition to the urinary potassium wasting that catecholamines cause.

I've also had episodes that are postprandial, but only in the evening (presumably because there is more reinforcing vagal tone at this time). Initially I thought this was due primarily to the alkaline tide associated with a meal (production of gastric acid by the stomach reflexively causes blood alkalosis) and subsequent urinary potassium loss (low blood potassium both causes and is caused by alkalosis). Then I thought that it was due to the effect of insulin and loss of cardiac intracellular potassium due to the increased concentration gradient. Then I thought I might have a mild problem with gastroesophageal reflux (GERD)/lower esophageal sphincter (LES). GERD is increased in athletes, especially in those that run, which I do (no more marathons, however). However, now I'm inclined to think that evening meals with poor K/glucose and K/Na ratios are the primary problem. I once thought that seafood (lots of salt) at dinner was a trigger. Looking back on such episodes, these meals were often low on the veggies and high on the simple carbs (love my desserts).

Hans went from typical stress related ALAF to typical vagally mediated AF, when he briefly took spironolactone, which has a vagotonic effect (in addition to being a potassium sparing diuretic). So, it seems that LAF can appear anywhere along the spectrum of autonomic tone. And remember, Hans always ran right at the lower limit of normal with his blood potassium. And his aldosterone, a vagolytic, and cortisol were always elevated (both aldosterone and cortisol bind to mineralocorticoid receptors, i.e., cause urinary loss of potassium). Furthermore, although there was never much change in his blood potassium (daytime values of 3.5 - 3.7 mmoles/L), his urinary potassium (and magnesium) excretion continued to escalate, as he approached the next episode. Obviously there was continual leakage of potassium from the intracellular compartment to maintain the constant blood potassium concentration in the face of escalating urinary loss.

Many LAFers have commented on what seems to be a repeating periodicity to their episodes. It seems that the length of my episodes was directly proportional to the time interval before the next episode. On the Bulletin Board (BB) in late 2002 before choosing the inaugural topic for the Conference Room.[16] Hans queried as to why there always seemed to be an abundance of PACs just prior to an episode and none just after termination. He surmised that ANP (atrial natriuretic peptide) might explain this. ANP is secreted during episodes via a mechanism that involves atrial cell stretch. ANP inhibits aldosterone synthesis and renin release thereby conserving blood potassium and helping replete intracellular levels. At some point ERP shortening due to the potassium gradient is sufficiently lengthened and the episode terminates. This point is usually in the AM when vagal tone is low and its associated ERP has also lengthened.

During this natriuresis (sodium in urine) the consequent drop in blood volume and increase in blood K/Na stimulates aldosterone secretion to oppose circulating ANP. Additionally during AF cardiac output drops by about 30% and with it the hydrostatic pressure sensed by the renal baroreceptors (the juxtaglomerular apparatus). This is another reason why aldosterone should be elevated at the end of an episode. I've often noticed on my Polar S810 HR monitor that immediately after termination of an episode my HR albeit NSR is always inappropriately high and my HRV is always inappropriately low for several hours. The vagolytic state caused by elevated aldosterone would easily explain this. It would also explain the complete absence of PACs. The half-life of aldosterone is about 15 minutes. The more aldosterone (vagolytic) present at the end of an episode, i.e., the longer the episode of AF, the longer this post episode PAC free period will last. But it comes with a cost and that is accelerated urinary potassium wasting after the protection of ANP has been removed. Life style and diet might then combine to slowly deplete these intracellular potassium stores until blood potassium level cannot be maintained and some threshold gradient value (for P cells) is breached and another episode is triggered. In this scenario the potassium gradient may be more integral in triggering ALAF episodes and vagal tone may be more integral in triggering VMAF episodes.

If one assumes the potassium gradient as vital to triggering an episode, then one can continue further along this line of thinking. Typical night time (vagally mediated) episodes rebalance potassium stores and protect against typical daytime (adrenergic) episodes and vice versa. However, if vagal tone in VMAF is lowered by medication, then daytime episodes should become relatively more frequent. And if potassium loss in ALAF is lowered by medication, then night time episodes should become relatively more frequent. I've experienced the former with disopyramide and Hans has experienced the latter with spironolactone.

LAFers exist all along the spectrum of both autonomic tone and the potassium gradient. Our arrhythmogenic substrate is a given and separates us from "normals". Some LAFers have minimal tone or gradient problems (fortunate) but enough of both to trigger LAF (unfortunate). They are fortunate because either by medication for autonomic tone or lifestyle and diet for potassium gradient they have been able to avoid the beast. Counter-regulating mechanisms (RAS, blood K/Na, ACTH) otherwise make the latter a very difficult proposition. The real question is could this "fortunate" category of LAFers be expanded by addition of medication for better potassium balance? Inbred resistance to combining increased potassium intake with a potassium sparing diuretic makes this a very difficult proposition. Triamterene or amiloride and NOT spironolactone or eplerenone would seem to be the best choices on this count (see below). Neseritide (synthetic BNP) or carperitide (synthetic ANP) might be even better, but are only available by the intravenous route. According to the medical literature ACEIs are vagotonic, but perhaps not all are. For example, enalapril but not captopril significantly inhibits plasma aldosterone concentration and urinary aldosterone excretion. Since aldosterone is vagolytic, perhaps enalapril is vagotonic and captopril is not.[17]

Another interesting question is why proton pump inhibitors (PPI) not only relieve GERD but also appear to relieve AF. Is it only because there is less irritation of the lower esophagus (and less

vagal stimulation)? Or is it also because of an improvement in the potassium gradient? Gastric acid production causes a simultaneous blood alkalosis (alkaline tide). Hypokalemia both causes and is caused by alkalosis. By inhibiting the proton pump (H^+ is no more than a proton) less H^+ is lost in the gastric juice. Less potassium is lost in the urine, because the blood is less alkaline (since the gastric fluid is less acidic).

Jackie Burgess, well known and respected by all of us that frequent the BB and CR, has suggested a balanced snack of protein, complex carbohydrate and healthy fat two hours before bedtime. And, of course, magnesium and potassium are always welcome at anytime. This approach would impede any insulin induced hypokalemia/hypoglycemia and possibly AF as well. She also has reiterated for us an old adage “if you can feel your heart beating at night when lying in bed, you may be low in potassium”. This undoubtedly is due to the mild BP elevating effects of low blood potassium. The heart has to work just a little harder, enough to make you aware of its beating, when all else is quiet.

Due to the insulin induced drop in blood potassium that occurs after a carbohydrate meal, it would seem prudent to always ingest potassium with your carbohydrates. Jackie has also pointed out that KCl can cause gastric irritation, at least if taken on an empty stomach. It can also elevate blood pressure in the salt sensitive. However, potassium in fruit without chloride is less absorbable. According to one source only 40 percent of the potassium in a banana is retained. This is one reason why MDs prescribe potassium as KCl (about 800mg K as KCl per tab of K-Dur). KCl also addresses hypochloremia, which often accompanies hypokalemia. If KCl irritates your stomach, then you should never let a meal go by without potassium supplementation, thereby exploiting its buffering effect in this regard. K-Dur is also a sustained release formulation, most convenient at bedtime to address the midnight diurnal nadir of blood potassium.

I heartily agree with the general recommendation to shift from simple to complex carbohydrates in our diets. I used to think this advice was better directed at those that struggle with their weight. However, given my problems with episodes being triggered when I skip or delay meals, I think thin people can also benefit from it. Eat properly and don't skip meals. Graze rather than gorge. Earlier is better than later.

In a past post on the BB I suggested that a portable potassium meter might be a very useful item for a LAfer. Horiba and Hoskin Scientific make good ones, but they are not quite ready for prime time, at least not in humans. I recently purchased an Omron BP monitor (less than \$50 at Costco) and have found that relative evening BP (slightly higher systolic than normal) and/or the presence of PACs when lying on my right side both provide feedback on probable intracellular potassium.[18] Although this is only an indirect approach at best, it may be the difference between PM AF and normal sinus rhythm (NSR).

Being on top of my daily potassium supplementation definitely decreases my evening PACs and BP. This also requires awareness of activities that cause transcellular shifts of potassium and sometimes urinary potassium (and magnesium) wasting as well. Appropriate countermeasures are needed, i.e., more fluid intake, small potassium rich complex carb snacks, e.g., a banana, etc.

My Experience with Spironolactone

I have experimented extensively with potassium and spironolactone. A combination of 3 g/day of potassium and 100 mg/day of spironolactone increased my blood level of potassium to 4.7 mEq/L. Increasing my potassium intake to 6 g/day and my spironolactone to 200 mg/day (blood potassium over 5 mmol/L) increased the frequency and duration of my afib episodes despite also taking 500 mg/day of disopyramide (Norpace). I have now concluded, and Hans' experience supports this, that spironolactone is unlikely to be beneficial for either adrenergic or vagal afibbers for the simple reason that its detrimental vagotonic effect clearly outweighs its positive

effect in regard to potassium conservation. I have therefore terminated my experiment with spironolactone. My next experiment will involve aggressive potassium supplementation starting in the afternoon and escalating until bedtime as well as taking K-Dur (800 mg of elemental potassium in a sustained release formulation) at bedtime. If that produces insufficient improvement I plan on investigating triamterene (Dyrenium) and amiloride (Midamor). *Most, if not all*, ACE inhibitors and angiotensin receptor blockers (ARBs) are decidedly vagotonic so I intend to give them a miss.

Triamterene and amiloride, both potassium-sparing diuretics, work at the level of the distal convoluted tubule in the kidneys, but do not bind to mineralocorticoid receptors. They impair sodium reabsorption in exchange for potassium and hydrogen. Thus, unlike spironolactone and eplerenone, they should not directly increase vagal tone. In fact, they may modestly increase blood potassium and thereby elevate the K/Na ratio. This would increase aldosterone secretion and thereby increase vagolysis. This, in turn, would increase the component of total blood aldosterone due to K/Na compared to the other two sources of aldosterone (RAAS, major and ACTH, minor). This might prove beneficial because increased potassium and decreased sodium intake would have greater impact on aldosterone secretion, in effect providing greater control over aldosterone secretion via diet and/or supplements (especially useful for a VMAFer).

Conclusion

You can't directly control the arrhythmogenic substrate (PVs) except through PVI. You can't effectively control vagal or sympathetic tone except through meds. That leaves low potassium. If you want to get serious about controlling your episodes, then you must get serious about your potassium intake. You must address not only how much you ingest but when you ingest it. Either avoid those situations that assault your blood potassium gradient (stress, hypoglycemia, dehydration, etc) or increase your daily potassium (and magnesium) intake with appropriately time-targeted supplementation. Although food sources are best for most of what we need, for potassium repletion IMHO supplements are superior (fish oils and omega 3s are another such exception). Intake of potassium through diet alone is less convenient, less quantifiable and less absorbable. And then there's the glycemic load problem posed. Presently there is great resistance within mainstream medicine to combining potassium supplementation with a potassium sparing diuretic. Hyperkalemia and life threatening ventricular arrhythmias are of great concern. However, with the pioneering work of Drs. Struthers, MacDonald and others this overemphasized concern may soon take a back seat to a rational combination regimen. In my view it is quite plausible that this LAF epidemic might be reversed, if such an aggressive regimen were pursued by those afflicted. The study that needs to be done is one similar to that referenced above on LQTS (long QT syndrome), but with amiloride or triamterene and on LAF patients instead. But until then please remember my above disclaimer and make sure you have good renal function. My BUN (blood urea nitrogen) and creatinine are well within normal limits, but I still routinely monitor my blood potassium.

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